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Adult Acute Bacterial Meningitis In The United States: 2009 Update

Paramedics bring in a 68-year-old man with a complaint of weakness and an altered level of consciousness. The patient's wife called 9-1-1 because he had been sleepy all day, and when she attempted to wake him, he moaned and seemed to have difficulty speaking. She reports that he has been ill and lying in bed for the last 3 days and has complained of a headache. She indicates that he reported no fever but adds that she did not take his temperature. On examination, his blood pressure is 108/46 mm Hg, his heart rate is 126 bpm, and he has a rectal temperature of 39.4°C (103°F). His mental status is significantly altered, with a Glasgow Coma Scale score of 8 (E2, V2, M4). His neck feels stiff, but the remainder of the examination is unremarkable. The patient does not have a rash. You suspect acute bacterial meningitis but wonder which antibiotics you should choose given the current state of multidrug-resistant bacteria and whether the patient should also be treated for a viral infection. You are concerned that his prognosis is poor and consider additional therapies that may improve his outcome.

Later in the shift, a colleague signs out a patient to you: a previously healthy 24-year-old man who presented with a fever, severe headache, runny nose, and cough that have persisted for 5 days. Viral meningitis was suspected, and a lumbar puncture was performed. The sign-out recommends that the patient be sent home if the results of the CSF analysis are negative. The CSF results arrive and show a WBC count of 150 cells/mL with 95% lymphs, a glucose level of 50 mg/dL, and a protein value of 90 mg/dL. The CSF Gram stain is negative for organisms. The patient does not appear toxic; however, knowing the morbidity associated with bacterial meningitis,

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CME Objectives

Upon completion of this article, the reader should be able to:

1. Identify the clinical features of community-acquired bacterial meningitis in adults.
2. Review the indications for a cranial computed tomography scan prior to an lumbar puncture.
3. Initiate empiric treatment based on patient age and medical history.
4. Discuss the advantages of corticosteroid use in acute bacterial meningitis.

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you wonder if you should admit him for treatment with parenteral antibiotics pending culture results.

Acute bacterial meningitis (ABM) is an uncommon but potentially fatal neurologic emergency that requires prompt recognition, diagnostic evaluation, and initiation of parenteral antibiotics. Management principles are well defined, and treatment is generally considered time sensitive. The overall mortality rate is between 10% and 30%, and up to one-third of survivors experience long-term neurologic sequelae. The diagnosis becomes challenging when patients present with nonspecific clinical features and seem to improve with supportive therapy while in the Emergency Department (ED). Lawsuits charging that medically negligent practices contributed to adverse patient outcomes from bacterial meningitis are among the most common claims filed against emergency medicine clinicians.

Meningitis results from inflammation of the pia-arachnoid meninges as well as cerebrospinal fluid (CSF).[1,2] Thus, patients with meningitis often present with signs of meningeal irritation, such as nuchal or spinal rigidity. Encephalitis refers to inflammation of the brain parenchyma and is typically characterized by cognitive deficits. The clinical distinction between meningitis and encephalitis is frequently blurred as patients often present with signs and symptoms of both conditions. These patients can best be described as having meningoencephalitis, the pathologic condition that results when inflammation spreads from the CSF and meninges to the adjacent brain parenchyma.

Inflammation of the central nervous system can be acute, subacute, or chronic in duration and community or nosocomial in origin. Although meningeal inflammation may be due to medications, neoplastic or autoimmune processes, or nonbacterial microbes (eg, viruses, fungi, or parasites), bacterial infection remains the most studied cause. This issue of *Emergency Medicine Practice* reviews the ED approach to and treatment of community-acquired ABM in adults.

Critical Appraisal Of The Literature

Using the subject heading meningitis, the MEDLINE® (1950 to September 2008), CINAHL®, and LILACS databases were searched. Major search terms included combinations of the following: *meningitis, epidemiology, diagnosis, clinical presentation, prognosis, lumbar puncture, practice guideline, antibiotics, steroids, dexamethasone,* and *emergency.* The search was initially limited to observational trials, case series, and randomized trials that were performed in adult patients and that had an available English abstract. The search was extended to pediatric patients when limited or no data existed on adults. The Cochrane Database of Systematic Reviews, Best Evidence Topics, and Emergency Medical Abstract databases were also reviewed. The strategy yielded approximately 200 articles that form the basis of this review. In addition, the evidence-based practice guidelines for the management of bacterial meningitis published in 2004 by the Infectious Diseases Society of America (IDSA)[3] and the 2003 update to the 1999 consensus guidelines for the management of ABM in immunocompetent adults (provided by the British Infection Society) were reviewed.[4,5]

The existing literature on ABM is limited in several ways. First, much of the research on the pathophysiology of meningitis has been based on experimental rabbit and rat models. Second, much of our current understanding about the clinical features, diagnosis, and prognosis of ABM has been extracted from chart reviews. These reviews rarely report methodology and are heavily dependent on the availability and accuracy of the medical records. Furthermore, because reviewers cannot adequately control for confounding variables, the retrospective data cannot be used to establish cause-effect relationships; only potential associations between variables can be pointed out. Third, a good number of trials involving bacterial etiology and therapy have been conducted in the international setting. In general, the results of these studies cannot be extrapolated to practice within the United States. The external validity of all studies must be assessed before a new treatment strategy can be adopted. Thus, we have limited this review to data generated in the United States and in countries that share our practice patterns with respect to vaccination, bacterial epidemiology, and management of bacterial meningitis.

Epidemiology, Etiology, And Pathophysiology

Risk factors for meningitis are listed in **Table 1**. The most commonly isolated bacteria in adult cases of ABM within the United States are *Streptococcus pneumoniae, Neisseria meningitidis,* and *Listeria monocytogenes.*[6] A 2002-2003 population-based surveillance study involving 781 cases of meningitis collected by the Centers for Disease Control and Prevention (CDC) noted that these three agents were responsible for nearly 4 out of every 5 episodes of community-acquired bacterial meningitis infections in adults.[7] The current bacteriologic landscape is expected to change with the administration of effective vaccines against *S pneumoniae* and *N meningitidis* as well as improvements in food processing designed to control for *L monocytogenes.* New multi-drug resistant bacteria will also have an impact on the efficacy of available antibiotics.[8] (For additional information, **see the Controversies/Cutting Edge section on page 17.**)

Meningitis typically develops after encapsulated bacteria that have colonized the nasal or oral pharynx penetrate the intravascular space and enter the subarachnoid space through vulnerable sites within the blood-brain barrier.[9,10] Once the pathogens enter

the central nervous system (CNS), they replicate rapidly, consuming glucose and liberating protein within the CSF. The ensuing inflammatory reaction occurs in response to the liberation of bacterial cell wall and cell membrane components (eg, lipopolysaccharide, peptidoglycan, lipoteichoic acid) as well as the induction of proinflammatory cytokines.[11-14] These events culminate in injury to the vascular endothelium, resulting in increased permeability of the blood-brain barrier, meningeal inflammation, and cerebral vasculitis. The accompanying cerebral edema and increase in intracranial pressure (ICP) contribute to CNS hypoperfusion and neuronal cell death.[10]

Invasion of the CNS secondary to bacteremia in a remote focus (eg, endocarditis, pneumonia) and direct inoculation of bacteria into the CNS as a result of neurosurgical procedures or head trauma provide alternate routes of penetration.

Differential Diagnosis

The 4 cardinal signs and symptoms of meningitis are headache, fever, neck stiffness, and altered mental status. Although the differential diagnoses of patients presenting with all 4 features are limited, the list of possibilities for patients presenting with only 1 or 2 is quite extensive. A review of 156 patients with meningitis who presented to a single hospital in Taiwan revealed that the initial ED diagnosis was correct in only 58% of the cases. The 3 most common alternative diagnoses were nonmeningeal infection, metabolic encephalopathy, and nonspecific conditions.[15]

In this section, we will focus on distinguishing community-acquired bacterial meningitis from encephalitis, aseptic meningitis, and intracranial abscess.

Encephalitis

Encephalitis refers to inflammation of the brain parenchyma, which may coexist with inflammation of the meninges (ie, meningoencephalitis) or spinal cord (ie, encephalomyelitis). Herpes simplex virus (HSV) is the most common cause of sporadic viral encephalitis, but a host of other viral and nonviral etiologies have been described.[16]

There is significant overlap between the presentations of ABM and acute viral encephalitis. Whereas both conditions can present with fever and headache, symptoms and signs of meningeal irritation (eg, neck stiffness, nuchal rigidity) are characteristically absent with encephalitis. Although the clinical course of encephalitis is typically insidious, in distinction to acute bacterial meningitis, rapidly progressive forms have been described.[16] Encephalitis should be considered in the differential diagnosis in patients with new psychiatric symptoms and cognitive deficits and in patients with focal or diffuse neurologic changes. The mental status changes associated with encephalitis include agitation, aphasia, amnestic syndrome, confusion, lethargy, stupor, and even coma. With HSV infection as well as other CNS processes, nonconvulsive seizures manifesting as taste and smell hallucinations, speech disorders, and strange behavior have been reported.[17,18]

The findings on CSF analysis of patients with encephalitis may be close to normal or similar to those seen in patients with viral meningitis (ie, an increased CSF WBC count, usually < 250 cells/mL, a normal or mildly elevated CSF protein value, and a normal or mildly reduced glucose level).[19] (**See Table 2, page 4.**) Excessive red blood cell (RBC) counts in an atraumatic spinal tap are suggestive of HSV encephalitis, but can also present in other viral and nonviral encephalitides.[20] A review of 16 cases of HSV encephalitis revealed an average CSF RBC count of 2518 cells/mL (range, 0-27,566 cells/mL).[21] Results on noncontrast computed tomography (CT) scan are typically normal, although HSV encephalitis may show diffuse or classically frontal and temporal edema.[22]

Acyclovir 10 mg/kg IV every 8 hours should be initiated in all patients with suspected encephalitis or meningoencephalitis and in patients with confirmed HSV encephalitis.[23,24] Failure to administer acyclovir in the ED is associated with substantial delays in administration once the patient reaches the inpatient ward.[25] Other empiric antimicrobial agents, including appropriate therapies for presumed bacterial meningitis, should be concomitantly initiated on the basis of specific epidemiologic and clinical risk factors. In practice, the recommendation based on the best available evidence is to give acyclovir to patients with suspected meningoencephalitis when they have compatible CSF findings and a negative CSF Gram stain.

The use of corticosteroids for HSV encephalitis was associated with favorable outcomes in a small retrospective study involving 45 patients.[26] Updated recommendations regarding the use of corticosteroids in this setting await publication of the German trial of acyclovir and corticosteroids in HSV encephalitis (GACHE) trial.[27] To date, the use of

Table 1. Risk Factors For Meningitis

- Age greater than 50 years
- Upper respiratory tract infection
- Otitis media
- Sinusitis
- Mastoiditis
- Head trauma
- Recent neurosurgery
- Compromised immune system (eg, resulting from human immunodeficiency virus [HIV], diabetes mellitus, asplenia, alcoholism, cirrhosis/liver disease, malnutrition, malignancy, cirrhosis/liver disease, malnutrition, malignancy, and immunosuppressive drug therapy)
- Crowded living conditions

steroids in patients with suspected bacterial or viral meningoencephalitis has not been associated with any significant harm.

Aseptic Meningitis

Aseptic meningitis is characterized by clinical and laboratory evidence of meningeal inflammation with negative routine bacterial cultures. The presentation is often similar to that of ABM; however, these patients generally have a benign course that resolves without specific therapy. Aseptic meningitis is most commonly a result of viral infection, but it can also be due to a fungal, parasitic, or atypical bacterial infection. Other causes include medications, reactions to vaccines, and specific systematic diseases with meningeal or parameningeal involvement. (**See Table 3.**)

The enteroviruses are the most common viral cause of aseptic meningitis in adults. Adults can be exposed through direct contact with the respiratory secretions of an infected person or while changing the diaper of an infected infant.[28] Patients present with abrupt onset of headache, fever, nausea, vomiting, photophobia, nuchal rigidity, and occasionally a rash. CSF analysis usually shows a lymphocyte predominance of < 250 cells/mL, a normal glucose level, and a mildly elevated protein value < 150 mg/dL. (**See Table 2.**) This pattern is also seen in meningeal infection due to *L monocytogenes* and *Mycobacterium tuberculosis*.[29,30] The pediatric literature suggests that a polymerase chain reaction (PCR) test on the CSF demonstrating enterovirus infection confirms the diagnosis, decreases the cost of unnecessary antibiotics, and can result in shorter hospital stays.[31]

Intracranial Abscess

A cerebral abscess is a focal infection that begins as a localized area of inflammation and develops into a collection of pus surrounded by a well-vascularized capsule. The infection can spread from a contiguous focus (eg, mastoiditis, sinusitis, odontogenic infection), or it can result from hematogenous seeding.[32]

The presenting signs and symptoms of a brain abscess are often nonspecific and vary according to the location and severity of the primary infection, the virulence of the bacterium, the size and location(s) of the cerebral abscess, and the patient's ability to mount an adequate immune response. Headache is the most common presenting symptom and is described as gradual in onset, constant and progressive in nature, and moderate to severe in intensity. Sudden worsening of the headache accompanied by new meningismus may signify rupture of the abscess into the intraventricular space, a life-threatening complication.[33,34] Fever is present in only half of patients and may be low-grade in a significant number.[35] Focal neurologic deficits are variably present depending on the size and location of the brain abscess and may mimic a stroke-like syndrome.

Successful management of intracranial abscess involves the administration of parenteral antibiotics and neurosurgical consultation. The combination of a third-generation cephalosporin (cefotaxime 50 mg/kg IV every 4 hours, with a maximum dose of 2 gm; or ceftriaxone 50 mg/kg IV every 12 hours, with a maximum dose of 2 gm), metronidazole (15 mg/kg IV every 12 hours), and vancomycin (15 mg/kg IV every 6 hours with a maximum dose of 500 mg) can be used in most patients who are presumed to have a contiguous source of infection (eg, an ear, sinus, or dental infection). Although some experimental evidence suggests that corticosteroids (dexamethasone 10 mg IV followed by 4 mg every 6 hours) reduce edema surrounding brain abscesses,[36,37] no quality trials in humans have demonstrated clinical benefits from corticosteroid therapy. Emergent neurosurgical drainage should be considered in patients with signs

Table 2. Cerebrospinal Fluid Findings In Central Nervous System Infections[3]

Infection	White Blood Cell Count (cells/mL)	Glucose Level	Protein Level
Bacterial Meningitis	Elevated (100-5000) Polymorphonuclear leukocytes predominate*	Decreased	Elevated
Viral Meningitis	Elevated (10-500) Lymphocytes predominate	Normal	Elevated
Fungal Meningitis	Normal to elevated (0-500) Lymphocytes predominate	Normal to decreased	Elevated
Tuberculous Meningitis	Normal to elevated (0-1000) Lymphocytes predominate	Decreased	Elevated
Brain Abscess	Normal to elevated (0-500) Mixed differential	Normal	Elevated

Note: In 10% of cases, lymphocytes predominate - see the **Lumbar Puncture** section on page 8 for details.

of increased ICP; otherwise, patients may be observed for clinical response to parenteral antibiotics.[37]

Prehospital Care

Prehospital management priorities in patients with suspected meningitis include the recognition of the potentially life-threatening disease and patient stabilization. Prehospital care providers should assess the patient's vital signs and mental status during transport. If the patient appears to have altered mental status prior to transfer, paramedics should not only administer supplementary oxygen and obtain a rapid blood glucose check, but they should also calculate an initial Glasgow Coma Scale (GCS) score for reference upon arrival at the ED. Even if a formal GCS score is not obtained, the prehospital provider should indicate if the patient is alert, responsive only to verbal stimuli, responsive only to painful stimuli, or unarousable. While en route, 2 large-bore IVs should be started with normal saline infused based on patient's volume and perfusion status. This is especially important if the patient appears dehydrated or displays clinical signs or symptoms of hypovolemia. Depending on county-based pain control protocols, the patient may be given a reasonable dose of pain medication to alleviate discomfort. Currently, no US protocols exist for administration of antibiotics in an ambulance in cases of suspected bacterial meningitis.

Paramedics should be aware of the potential for transfer of infection, and standard personal protective equipment such as facial masks should be worn by everyone in close contact with the patient. Chemoprophylaxis is recommended for those who have intubated (and had other mucous membrane contact with) patients with suspected as well as confirmed meningococcal meningitis.

Table 3. Causes Of Aseptic Meningitis

Viruses – Enteroviruses, herpes simplex virus types 1 and 2, lymphocytic choriomeningitis virus, varicella-zoster virus, cytomegalovirus, Epstein-Barr virus, human herpesvirus 6, 7, and 8, human immunodeficiency virus, poliovirus, coxsackie virus A
Fungi – *Cryptococcus neoformans, Blastomyces dermatidis*
Parasites – *Toxoplasma gondii*
Bacteria – Partially treated meningitis, *Mycobacterium tuberculosis, Borrelia burgdorferi, Treponema pallidum, Brucella*
Medications – Nonsteroidal anti-inflammatory drugs, amoxicillin, trimethoprim-sulfamethaxozole, isoniazid, intravenous immunoglobulin, azathioprine, allopurinol
Systemic Diseases – mucocutaneous lymph node syndrome, sarcoidosis, systemic lupus erythematosus, Wegener granulomatosis, multiple sclerosis, Guillain-Barré syndrome, leukemia, lymphoma

Emergency Department Evaluation

The onset of ABM is often quite rapid, with symptoms quickly developing and progressing over the first 24 hours in nearly 50% of patients.[39] In the case of meningococcal disease, symptoms can develop over a few hours.

A constellation of features from the patient's medical history and physical examination at presentation may lead the ED clinician to quickly suspect ABM. Several retrospective studies, including a systematic review of research conducted between 1966 and 1997[38] and a recent large prospective cohort involving nearly 700 cases[39] have attempted to clarify the utility of physical examination signs and historical symptoms associated with this diagnosis. Although these studies may help clinicians understand the value of specific findings, they are of limited usefulness in the ED since the results were not derived from undifferentiated ED populations. Additionally, as previously mentioned, medical record reviews rarely describe methodology and are heavily dependent on the availability and accuracy of the documents.

The classic triad of ABM symptoms are fever, neck stiffness, and altered mental status. In a prospective study of 696 episodes of community-acquired bacterial meningitis, this combination was present in 44% of cases;[39] a meta-analysis of 3 trials involving 426 cases of ABM demonstrated similar results (pooled sensitivity, 46%; 95% confidence interval (CI), 22%-69%).[38] Headache is often added as a cardinal symptom for ABM. At least 2 of the 4 cardinal features of ABM (ie, the classic triad plus headache) are present in 95% of cases and at least 1 of the 4 is present in 99% of patients with bacterial meningitis.[39] Unfortunately the features of headache and fever are seen much more frequently in non-meningeal conditions. A review of 156 patients with confirmed ABM showed that patients who lacked these typical symptoms were more likely to receive a diagnosis of non-CNS infection or metabolic encephalopathy in the ED.[15] This finding illustrates the difficulty faced by emergency clinicians, as many cases of bacterial meningitis lack the typical collection of findings that would help to discriminate this infrequent life-threatening diagnosis from more frequent and benign conditions.

Headache And Nausea

The headache typically described by patients with ABM is generalized and severe and unlike "normal" headaches. A pooled analysis of 7 studies involving 303 episodes of confirmed meningitis found headache was present in 50% (95% CI, 32%-68%) of these cases. The same analysis indicates that nausea was present in less than one-third of the patients.[38] A contemporary prospective study of more than

600 patients with culture-proven bacterial meningitis found headache to be a presenting complaint in nearly 90% of cases and nausea to be present in nearly three-fourths.[39]

Jolt accentuation, or amplification of a headache with rapid horizontal head rotation at a rate of 2 to 3 rotations per second, has been shown in 1 small prospective study of 54 patients to have a sensitivity of 97% and a specificity of 60% for the detection of ≥ 5 WBC/mL in the CSF.[40] Despite the fact that these findings have not been replicated and that only 1 patient in this study group met the criteria for bacterial meningitis, several authors have suggested that the absence of jolt accentuation can be used to exclude the diagnosis of bacterial meningitis.[38,41]

Fever

Fever is the most sensitive classic sign of meningitis. A review of 279 adult patients with community-acquired meningitis at one institution indicated that 95% had a temperature ≥ 37.8ºC (100ºF) at presentation. Another 4% developed a fever within 24 hours of observation.[38] Fever has a pooled sensitivity of 85% (95% CI, 78%-91%) for the diagnosis of meningitis.[38] However, because fever is common to many disorders, its specificity in patients with suspected meningitis is less than 50%.[40] In a study by van de Beek et al,[39] about 77% (522/678) of adult patients with bacterial meningitis were febrile (≥ 38ºC [100.4ºF]) at presentation, with an average temperature of 38.8ºC ± 1.2ºC (101.8ºF ± 2.1°F). Hypothermia may also be seen with bacterial meningitis, and like hyperthermia, is a cardinal sign of the systemic inflammatory response syndrome.

Altered Mental Status

Subtle changes in a patient's mental status may be apparent to family and friends but not to an unacquainted clinician. Thus, when ABM is suspected, the emergency clinician should ask any available contacts about the patient's mental state. A pooled analysis of 10 studies involving 811 patients with meningitis found that 67% (95% CI, 52%-82%) had some degree of altered mental status on presentation.[38] Similar results were seen in studies by Pizon et al[42] and van de Beek et al.[39] One study of 493 cases of ABM showed that about half of all adult patients were confused or lethargic upon arrival at the hospital, another 25% were responsive only to pain, and about 5% were unresponsive to all stimuli.[43] The finding of altered mental status in the setting of ABM is thought to result from elevated intracranial pressure secondary to meningeal inflammation and cerebral edema.[38] Alternatively the finding of altered mental status may indicate the patient has a component of encephalitis (ie, meningoencephalitis).

Neck Stiffness/Nuchal Rigidity

Neck stiffness was a presenting symptom in 569 of 685 cases of bacterial meningitis (83%) in a study by van de Beek et al.[39] When bacterial meningitis is suspected, the patient's neck should be examined for rigidity, using gentle forward flexion while the patient is supine during the physical examination. Difficulty in lateral movement of the neck is a less reliable finding. A pooled analysis of 10 studies involving 733 episodes of meningitis revealed a sensitivity of 70% (95% CI, 58%-82%) for neck stiffness on physical examination.[38] In a subsequent prospective observational trial of 297 adult patients with suspected meningitis, Thomas et al[44] found that nuchal rigidity had a sensitivity of 30% and a specificity of 68% for the detection of ≥ 6 WBC/mL in the CSF. The sensitivity (and negative predictive value) improved to 100% for the detection of ≥ 1000 WBC/mL in the CSF, although only 4 patients met this threshold.[44]

Kernig And Brudzinski Signs

The Kernig sign (pain in the back and legs with extension of the knee when the hip is flexed) and the Brudzinski sign (passive flexion of the neck resulting in flexion of the hips) are commonly recommended during the physical examination of a patient with suspected meningitis. Thomas et al[44] assessed the performance of these signs. Each sign had a sensitivity of 5% and a specificity of 95% for the detection of ≥ 6 WBC/mL in the CSF. Whereas the sensitivity of the Brudzinski sign improved to 25% for the detection of ≥ 1000 WBC/mL in the CSF, the sensitivity of the Kernig sign dropped to 0%. These signs do not appear to be useful in the ED.

Other Signs/Symptoms

- Patients with severe meningeal irritation may spontaneously assume the tripod position with the knees and hips flexed, the back arched at a lordotic angle, the neck extended, and the arms brought back to support the thorax.
- Focal neurologic deficits are seen in up to one-third of patients with ABM on presentation, with a significant number experiencing palsy or dysfunction of cranial nerves III, VI, VII, and VIII.[39] Focal cerebral abnormalities including hemiparesis, monoparesis, and aphasia are seen when ischemia and infarction secondary to cerebral infectious thrombophlebitis complicate meningitis. Hemiparesis was present in 7% (49/682) of cases, and seizures were noted in 5% (32/666) of cases presenting with community-acquired bacterial meningitis in one ED.[39]
- Patients with bacterial meningitis can present with a variety of skin conditions. In a pooled analysis of 3 studies involving 446 cases of meningitis, rash was present in 22% (95% CI, 1%-43%).[38] In the study by van de Beek et al,[39]

rash was observed in 176 of 683 patients with meningitis (26%). *N meningitidis* was the organism most commonly associated with rash (92% of all patients with a rash). A petechial rash was seen most often (89% of all rashes) and was associated with both meningococcal and nonmeningococcal infections.[39] Purpuric rashes can also occur with *N meningitidis* infections.

- The coexistence of bacterial meningitis and arthritis has been noted in several studies. van de Beek et al found that 48 of 696 adult patients with community-acquired bacterial meningitis (7%) had coexisting arthritis.[39] In patients with meningitis due to *N meningitides*, 12% (32/257) had arthritis. Early-onset arthritis and monoarticular arthritis were more common in patients with pneumococcal meningitis than in patients with meningococcal meningitis.[45]

Diagnostic Studies

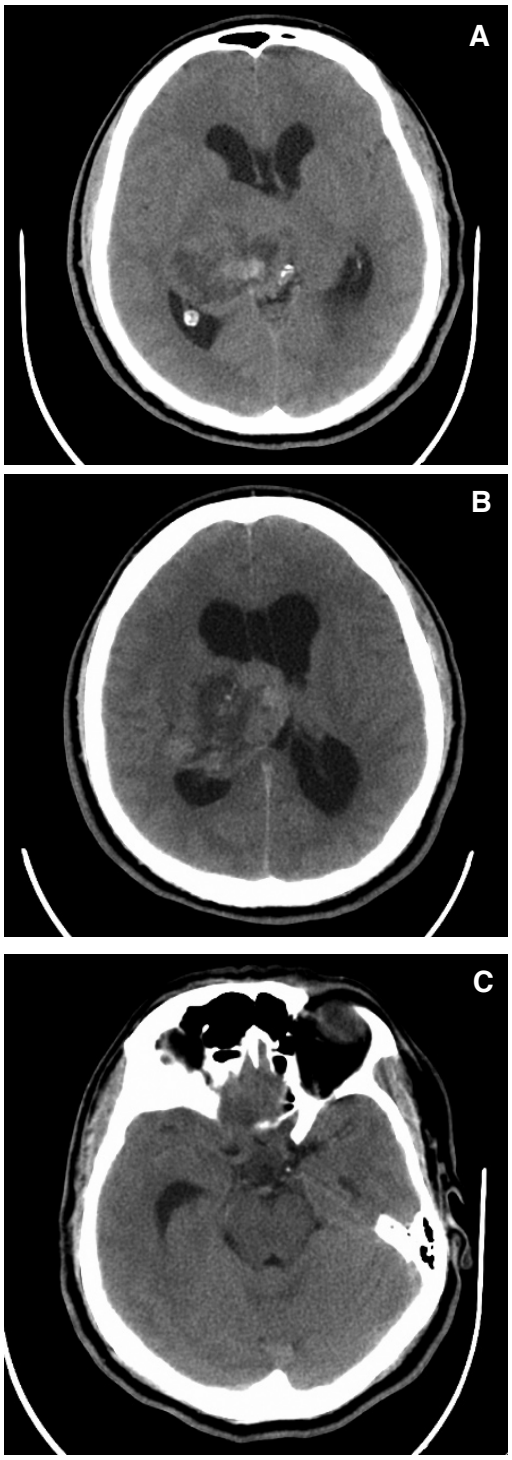
Computed Tomography

Some clinicians routinely order a computed tomography (CT) scan of the head before performing a lumbar puncture (LP) in order to identify occult intracranial abnormalities and thus avoid the risk of brain herniation resulting from removal of CSF. This approach, however, should not delay initiation of parenteral antibiotics in any patient with significant clinical suspicion of meningitis.

Several findings on CT scan are generally accepted as contraindications to LP: (1) a lateral shift of midline structures, indicating unequal supratentorial ICP; (2) loss of the suprachiasmatic and basilar (circummesencephalic) cisterns, indicating the supratentorial pressure may be greater than the infratentorial pressure, the lateral ventricles may be small, or in the setting of obstructive hydrocephalus, they may be large; (3) obliteration or shift of the fourth ventricle, indicating increased posterior fossa pressure; and (4) obliteration of the superior cerebellar and quadrigeminal plate cisterns with sparing of the ambient cisterns, indicating upward cerebellar transtentorial herniation.[46] **(See Figure 1.)**

The usefulness of the initial clinical presentation in predicting which patients can safely undergo LP without CT screening was evaluated in 2 prospective studies. Gopal et al studied 113 adult patients in the ED who needed an LP.[47] They found that 12.4% of the patients showed a lesion on CT and 2.7% showed a contraindication to LP on CT (according to the previously mentioned criteria). Predictors of a lesion on CT included altered mental status (likelihood ratio [LR], 2.2; 95% CI, 1.5-3.2), focal neurologic deficit on examination (LR, 4.3; 95% CI, 1.9-10.0), and papilledema (LR, 11.1; 95% CI, 1.1-115.0). Overall clinical impression had the highest predictive value in distinguishing patients with CT-defined

Figure 1. Evidence Of Mass Effect On CT Of The Brain



These three images demonstrate evidence of increased intracranial pressure, a contraindication to emergency department lumbar puncture. Image A and B show evidence of midline shift due to a left-sided irregular periventricular mass with a central necrotic area that contains an area of hemorrhage. The mass appears to cause obstructive hydrocephalus at the level of the aqueduct (image C). This is an example of potentially impending transtentorial herniation.

Images are courtesy of Amandeep Singh, MD and Highland General Hospital, Oakland, CA.

contraindications to LP (LR, 18.8; 95% CI, 4.8-43.0).[47]

Hasbun et al studied 301 patients who presented with suspected meningitis and derived a rule to assist clinicians in determining if a CT scan of the head is necessary before a lumbar puncture. According to the authors, the following characteristics predicted the low-risk group for whom a CT scan could be omitted prior to an LP:[48]

- Age less than 60 years
- No history of immunocompromised state (eg, HIV or AIDS, use of immunosuppressive therapy, transplant recipient)
- No history of a CNS disease (eg, mass lesion, stroke, focal infection)
- No seizure upon presentation or within 1 week before presentation
- No abnormal results on neurologic examination

If any of these factors were present, there was a 38% chance of an abnormal CT finding versus 3% if none were present. Overall, only 5% of patients in the series had a contraindication to LP based on CT interpretation.[48] Neither the Gopal et al[47] study nor the Hasburn et al[48] study has been prospectively validated.

The IDSA guidelines recommend a CT scan prior to LP for adults with suspected meningitis who are immunocompromised, have a history of a CNS disease, present with a new-onset-seizure (or experience a new-onset seizure within 1 week of presentation), have a finding of papilledema on physical examination, or have an abnormal result on neurologic examination or abnormal mental status.[3]

A limitation of CT is that normal results do not preclude the possibility of brainstem herniation after LP in patients with bacterial meningitis.[49,50] A systematic review of 4 case reports and 3 small case series revealed 19 documented cases of patients who had normal CT scan results and likely experienced brainstem herniation after LP.[51] Unfortunately, no prospective clinical features can predict which patients with normal results on CT scan will go on to experience herniation after LP.

Lumbar Puncture

Confirmation of meningitis requires CSF obtained through an LP. Because prior treatment with antibiotics significantly reduces the likelihood that a Gram stain and culture will be positive, CSF should be obtained as quickly as possible in patients who likely have the disorder. Contemporary data indicates that CSF sterilization can occur as soon as 2 to 4 hours after parenteral antibiotic administration;[52] however, a short interval between antibiotic therapy and LP does not significantly alter the WBC count or the protein and glucose levels in the CSF.[53-55]

The opening pressure in adults with bacterial meningitis ranges from 20 to 50 cm H_2O. In a study of 696 episodes of bacterial meningitis, the average opening pressure was 37 ± 13 cm H_2O.[39] Up to 20% of patients will have normal opening pressures, and another 20% to 40% will have an extremely elevated opening pressures (> 40 cm H_2O).[39,43] Opening pressure should be obtained with the patient in the lateral recumbent position; however, many clinicians prefer that the patient adopt a flexed sitting position for LP. One small study found a mean difference of 10 cm H_2O in opening pressure between patients in the lying and sitting positions. The authors used a linear regression analysis to produce a useful conversion formula: lateral recumbent opening pressure = 0.7 * flexed sitting opening pressure – 0.8 cm H_2O.[56] However, this formula has not been validated.

The laboratory analysis of CSF should include a WBC count with differential cell count, glucose and protein levels, a Gram stain, and most importantly, a culture. In untreated bacterial meningitis, the CSF WBC count is typically elevated, usually in the range of 1000 to 5000 cells/mL, although these values can range from < 100 cells/mm^3 to > 10,000 cells/mL. (**See Table 2, page 4.**) Normal or marginally elevated CSF WBC counts occur in up to 20% of patients.[39,42,43] A CSF WBC count > 500 cells/mL increases the likelihood of bacterial meningitis (LR, 15; 95% CI, 10-22), whereas a count < 500 cells/mL lowers the likelihood (LR, 0.3; 95% CI, 0.2-0.4).[57] A neutrophil predominance of 80% to 95% is common, but about 10% of patients with ABM present with a lymphocyte predominance (ie, greater than 50% lymphocytes) in the CSF.[42,43,58,59]

The CSF glucose concentration is < 40 mg/dL in approximately 50% to 60% of patients with ABM, and the CSF protein concentration is > 45 mg/dL in more than 90% of patients.[42,43] A systematic review of high-quality trials revealed that a CSF to blood glucose ratio of ≤ 0.4 demonstrated a strong association with the diagnosis of bacterial meningitis (LR, 18; 95% CI, 12-27), whereas a normal CSF to blood glucose ratio made this diagnosis less likely (LR, 0.31; 95% CI, 0.21-0.45).[60]

Physicians who practice in or travel to resource-depleted environments can use a urinary reagent strip and bedside glucometer to rapidly detect leukocytes, proteins, and glucose level within the CSF. In a small study of 41 patients, no significant difference was found between the CSF glucose readings obtained with the bedside glucometer and those obtained with formal laboratory methods. This same study found no difference between protein values obtained with the urinary reagent strip and those obtained through laboratory methods.[62] Another study of 494 patients found that the leukocyte esterase test conducted with the urinary reagent strip had a sensitivity of 22% and a specificity of nearly 100% for the detection of 5 or more WBCs per high-powered field within the CSF.[63]

A Gram stain is a rapid and inexpensive test used to guide therapy, with a sensitivity of 50% to 90% and a specificity of up to 97% in identifying the causative bacterial organism in an illness.[39,42,43,60,61] The likelihood of Gram stain visualization of the offending bacterium directly correlates with the bacterial concentration in the CSF, the specific bacterial pathogen responsible for the infection, prior antibiotic administration, and operator technique.[3]

Complete Blood Cell Count, Chemistry Panel, Lactate Level, And Blood Cultures

Several indices of infection are elevated in ABM, including serum WBC count, erythrocyte sedimentation rate, and C-reactive protein (CRP) level.[39] A normal or low WBC count can be seen in patients with immunocompromised systems and in geriatric patients. The platelet count may be elevated as an acute phase reactant. However, the presence of thrombocytopenia is a poor prognostic indicator in both bacterial meningitis and sepsis.[39,64-66]

Serum electrolyte, bicarbonate, and glucose levels as well as renal function should be evaluated in patients with suspected meningitis. Vomiting may lead to electrolyte abnormalities and evidence of volume contraction and dehydration on laboratory testing. Hyponatremia (serum sodium level < 135 mmol/L) was seen in approximately 30% (208/685) of patients with bacterial meningitis, with a serum sodium level < 130 mmol/L occurring in 6% (38/685).[67] The serum bicarbonate level may reflect evidence of metabolic alkalosis in patients with excessive vomiting or metabolic acidosis in patients with signs of poor perfusion. Renal function tests are useful indicators of renal perfusion and assist in determining the optimal dosing and timing of medications.

Serum lactate has been used as a surrogate marker for tissue perfusion and can be used to predict mortality in patients with infection. Shapiro et al studied a heterogeneous group of 1278 hospitalized patients with a significant infection and reported that mortality correlated with initial serum lactate level.[68] An initial lactate level of 0 to 2.4 mmol/L was associated with a 1.5% mortality rate at 3 days and a 5% mortality rate at 28 days. An initial lactate level of 2.5 to 3.9 mmol/L was associated with a 4.5% mortality rate at 3 days and a 9% mortality rate at 28 days. An initial lactate level of ≥ 4 mmol/L was associated with a 22% mortality rate at 3 days and a 28% mortality rate at 28 days.[68] The concept of lactate clearance (ie, [initial lactate – 6-hour lactate]/initial lactate) has important prognostic implications. Nguyen et al noted that the in-hospital mortality rate was twice as high in patients who metabolized less than 10% of their total initial lactate value in the first 6 hours compared with patients who metabolized 10% or more of their total initial lactate value (in-hospital mortality, 68% vs 33%, respectively; P < .001).[69]

Blood cultures should be obtained before antibiotic therapy is initiated in patients with suspected

Table 4. Infectious Diseases Society of America-United States Public Health Service System For Ranking Recommendations In Clinical Guidelines

Grade	Explanation
A	Good evidence to support a recommendation for use; should always be offered
B	Moderate evidence to support a recommendation for use; should generally be offered
C	Poor evidence to support a recommendation; optional
D	Moderate evidence to support a recommendation against use; should generally not be offered
E	Good evidence to support a recommendation against use; should never be offered
Quality Of Evidence	**Explanation**
I	Evidence from 1 or more properly randomized controlled trials
II	Evidence from 1 or more well-designed clinical trials without randomization, from cohort or case-control analytical studies (preferably from more than 1 center), or from multiple time-series; or dramatic results from uncontrolled experiments
III	Opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

(Adapted from Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis. 2004;39(9):1267-1284.)

Table 5. Infectious Diseases Society Of America Ranking Of Newer Tests For Diagnosing Bacterial Meningitis

Test	Rank
Polymerase Chain Reaction	B-II if negative CSF Gram stain
Latex Agglutination	D-II; C-II recommendation if negative Gram stain
Litmus Lysate	D-II
Microarray	No IDSA recommendation
Serum C-Reactive Protein	B-II if negative CSF Gram stain
Serum Procalcitonin	C-II
Cerebrospinal Fluid Lactate	D-III
Cerebrospinal Fluid Cortisol	No IDSA recommendation

(Adapted from Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis. 2004;39(9):1267-1284.)

meningitis. Positive blood cultures are obtained in approximately two-thirds of patients with bacterial meningitis.[39]

Newer Tests

Several newer tests have shown promise in distinguishing bacterial meningitis from nonbacterial meningitis. These tests include PCR, latex agglutination tests, litmus lysate assays, and microarrays, as well as analysis of serum CRP and serum procalcitonin. CSF analysis of lactate and cortisol levels are also being studied. **Tables 4 and 5** list the IDSA levels of evidence and recommendations for these tests.

Polymerase chain reaction assays can be used to amplify bacterial DNA from the CSF of infected patients. Recent studies suggest sensitivities and specificities of greater than 90% for this indication.[70-72] An added benefit of PCR assays is their ability to simultaneously amplify viral nucleic acids, which aids in distinguishing viral meningitis from bacterial meningitis. The latest generation of PCR assays promise rapid (< 2 hour) and accurate identification of microbial DNA or RNA.[73-75] They may eventually replace CSF culture as the criterion standard for the diagnosis of bacterial meningitis, especially in patients who have been treated with antibiotics before CSF is obtained for analysis.[76]

Latex agglutination tests routinely used for rapid (< 15 minutes) detection of specific bacterial pathogens have shown good sensitivity for the detection of antigens of common meningeal pathogens;[77] however, the test results rarely affect clinical therapy or hospital course.[78,79] The limulus lysate assay, in which a positive test result suggests the presence of gram-negative bacteria, is also of limited value in the ED evaluation of suspected meningitis.[3]

Microarrays, also known as biochips, are the newest technology for rapid detection of bacterial genetic material. DNA probes can be synthesized using various bacterial sequences and then attached to a chip, which binds genetic material from the CSF sample.[80] A benefit of micorarray technology is that simultaneous analysis of a large number of relevant bacterial genes can be tested. In a study of 50 patients, the microarray method provided a more accurate and rapid diagnosis than traditional culture methods.[81]

Cerebrospinal fluid lactate measurement has been used to distinguish bacterial meningitis from other nonbacterial conditions. A retrospective study of 78 adult patients with meningitis showed that patients with bacterial meningitis had a median CSF lactate level of 13.6 mmol/L (range, 3.5-24.5 mmol/L) compared with a median CSF lactate level of 2.7 mmol/L (range, 1.4-4.2 mmol/L) in patients with viral meningitis ($P < .05$).[82] A meta-analysis of 3 trials that involved a CSF lactate cutoff of ≥ 3.5 mmol/L found that patients meeting this criterion had a high probability of bacterial meningitis (LR, 21; 95% CI, 14-32). An equally important finding was that a CSF lactate level < 3.5 mmol/L was associated with reduced probability of bacterial meningitis (LR, 0.12; 95% CI, 0.07-0.23).[60]

Measurement of intrathecal endogenous cortisol levels has been suggested as a method of distinguishing bacterial meningitis from aseptic meningitis. A case-control study involving 47 patients with bacterial meningitis and a combination of 50 controls (37 patients with aseptic meningitis and 13 healthy participants) evaluated the role of CSF cortisol for this purpose. The median value for CSF cortisol was 133 mmol/L (interquartile range (IQR), 59-278 mmol/L) for patients with bacterial meningitis, compared with median values of 17 mmol/L (IQR, 13-28 mmol/L) in patients with aseptic meningitis and 10 mmol/L (IQR, 8-12 mmol/L) in healthy participants ($P < .001$). The authors of this study propose using a CSF cortisol cutoff value of 46 mmol/L for differentiating septic from aseptic meningitis.[83]

Both serum CRP and serum procalcitonin have been evaluated as a means of distinguishing bacterial from nonbacterial meningitis during diagnosis.[84-88] In a prospective multicenter trial involving 151 consecutive adult patients with CSF findings compatible with meningitis, the median serum CRP level was 162 mg/L (range, 39-275 mg/L) in patients with bacterial meningitis, compared with 13 mg/L (range, 9-17 mg/L) in patients with nonbacterial meningitis ($P < .05$). Additionally, the median serum procalcitonin level was 3.75 ng/mL (range, 0.10-6.16 ng/mL) in patients with bacterial meningitis, compared with 0.07 ng/mL (range, 0-0.08 ng/mL) in patients with nonbacterial meningitis ($P < .05$).[89] In this study, serum CRP had a sensitivity of 78% and a specificity of 74% in the diagnosis of bacterial meningitis. Serum procalcitonin yielded better results, with a sensitivity of 87% and a specificity of 100% in this population.[89] It is important to note that many studies reporting the sensitivity and specificity of these agents include only patients with confirmed meningitis or with a high clinical suspicion for meningitis. The operating characteristics of these 2 tests are sure to be diminished if they are haphazardously applied to a lower risk population. The true clinical utility of these tests may lie in distinguishing bacterial from nonbacterial meningitis in patients with CSF pleocytosis and a negative Gram stain.

Treatment

The most important principles in the treatment of community-acquired bacterial meningitis are the rapid initiation of effective antimicrobial agents and supplementary anti-inflammatory therapy.

Antibiotics

Initial empiric antimicrobial therapy should be

based primarily on the patient's age and specific predisposing conditions. (**See Table 6.**) *S pneumoniae* (pneumococcus) and *N meningitidis* (meningococcus) are the most common pathogens seen in community-acquired bacterial meningitis in adults. An effective treatment regimen combines ceftriaxone 50 mg/kg every 12 hours (maximum dose, 2 gm) and vancomycin 15 mg/kg every 6 hours (maximum dose, 500 mg). Immunocompromised patients and patients over the age of 50 are susceptible to infection with *L monocytogenes*. In these patients, ampicillin 50 mg/kg IV every 6 hours (maximum dose, 3 gm) should be added to the combination of ceftriaxone and vancomycin.[3] Meningitis due to *Staphylococcus aureus*, coagulase-negative staphylococci (eg, *Staphylococcus epidermidis*), and aerobic gram-negative bacilli (eg, *Pseudomonas aeruginosa*) can be seen in patients with recent penetrating head injury or recent neurosurgical manipulation and in patients with CSF shunts. These patients can be treated with vancomycin 15 mg/kg every 6 hours (maximum dose, 500 mg) plus either cefepime 50 mg/kg every 8 hours (maximum dose, 2 gm), ceftazidime 50 mg/kg every 8 hours (maximum dose, 2 gm), or meropenem 40 mg/kg every 8 hours (maximum dose, 2 gm).[3]

Several trials have evaluated the impact of adequate antimicrobial therapy versus inadequate antimicrobial therapy in patients admitted for sepsis.[90-95] The results of these trials have consistently shown an association between patients who receive adequate antimicrobial therapy and reduced mortality. Although CNS infections have not been formally evaluated for this outcome, the results of these sepsis trials indicate that initial antimicrobial therapy should be used for a broad spectrum of conditions. *(For more information on Sepsis, subscribers can view the May 2008 Emergency Medicine Practice issue,"Sepsis: Evaluating The Evidence," at no charge at www.ebmedicine.net/topics.)*

Timing of Antibiotics

A causal relationship between the timing of antimicrobial administration and clinical outcome in patients with ABM has not been established. It is unlikely that a prospective, randomized, blinded trial will ever be completed, as deliberately delaying the administration of antibiotics in patients with meningitis cannot be justified. The available data are limited to retrospective case series and prospective observational trials that can only suggest an association between these variables.[96-101]

In the 1990s, 2 separate systematic reviews critically examined the relationship between antibiotic administration and neurological outcome. These reviews concluded that there is insufficient evidence to link the duration of symptoms with the final neurologic outcome. The authors of these analyses suggested that trials must delineate the duration of patients' symptoms from the duration of meningitis and that antibiotic delays during the nonspecific illness phase of meningitis are unlikely to result in increased morbidity.[102,103] The lack of high-quality data establishing this causal relationship is reflected in the following statement by the authors of the 2004 IDSA Practice Guidelines for the Management of Bacterial Meningitis: "On the basis of the available evidence, we think that there are inadequate data to delineate specific guidelines on the interval between the initial physician encounter and the administration of the first dose of antimicrobial therapy."[3]

It is clear that a significant delay in the initiation of antibiotics occurs in patients who undergo a CT scan or LP.[96,104,105] Despite the lack of data linking the timing of antibiotics to neurological outcome, antibiotics should not be delayed for this reason in patients with suspected ABM.[3] Furthermore, antibiotics should be administered as soon as possible in patients with meningitis who present in septic shock.[98] Kumar et al found in both a retrospective review of 2731 patients[106] and a prospective animal model[107] that the duration of hypotension before effective antibiotic administration was associated with overall mortality. Despite the previously mentioned limitations of a retrospective study design, these findings prompted the authors of the 2008 Surviving Sepsis Campaign to recommend that broad-spectrum antibiotics be administered within 1 hour of recognition of a severe infection.[108]

Table 6. Recommendations For Empiric Antimicrobial Therapy For Bacterial Meningitis

Predisposing Factor	Common Bacterial Pathogen	Antimicrobial Therapy
Age 16-50 years	*Neisseria meningitidis, Streptococcus pneumoniae, Haemophilus influenzae* (nonimmunized patients)	Vancomycin plus a third-generation cephalosporin
Age > 50 years	*Streptococcus pneumoniae, Neisseria meningitidis, Listeria monocytogenes*, aerobic gram-negative bacilli	Vancomycin plus a third-generation cephalosporin and ampicillin
Immunocompromised System	*Listeria monocytogenes*, aerobic gram-negative bacilli, *Streptococcus pneumoniae, Neisseria meningitidis*	Vancomycin plus a third-generation cephalosporin and ampicillin
Neurosurgery, Head Trauma, Cerebrospinal Trauma	Staphylococci, aerobic gram-negative bacilli, *Streptococcus pneumoniae*	Vancomycin plus either a third-generation cephalosporin with anti-pseudomonal coverage or meropenem

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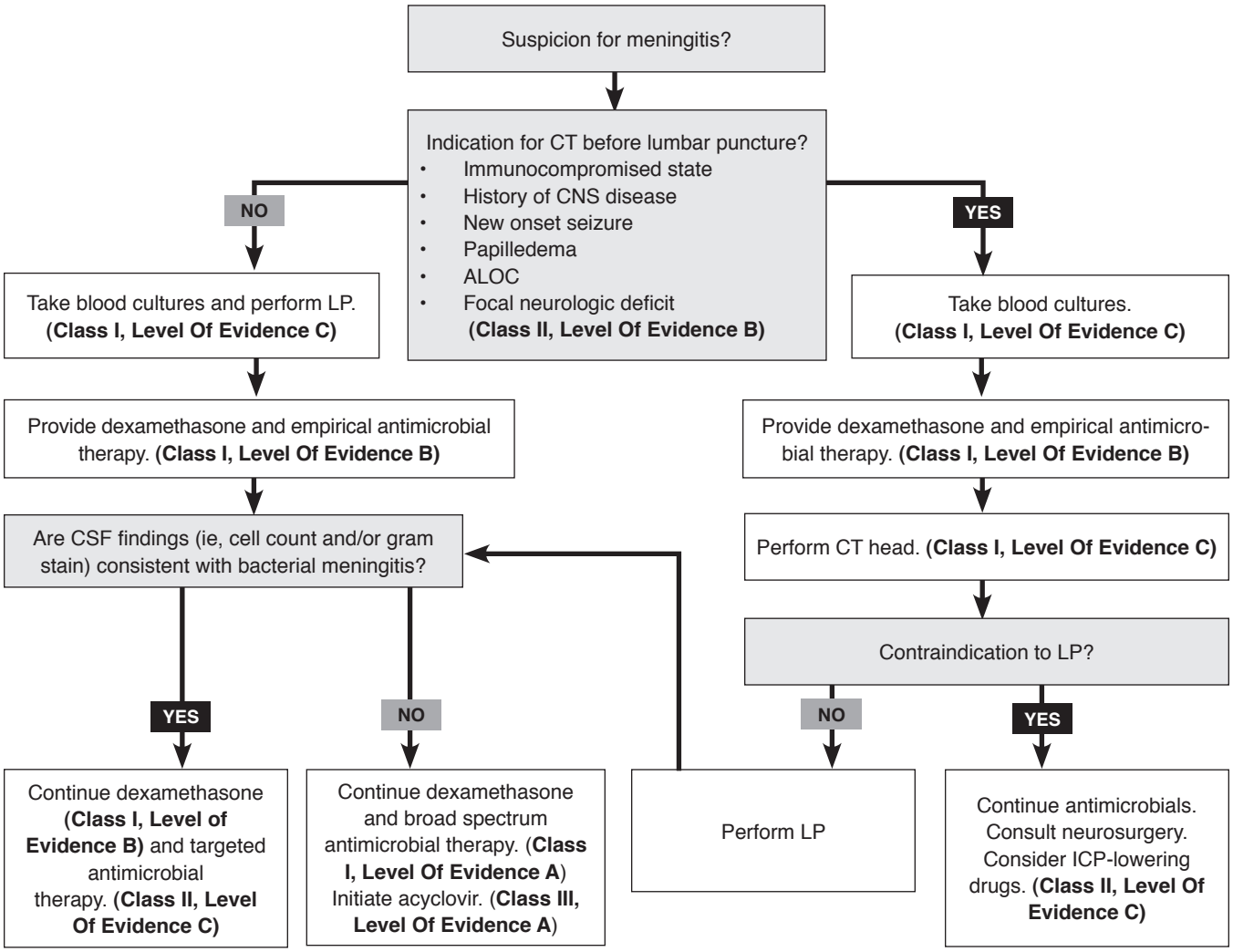

Abbreviations: LP, lumbar puncture; CSF, cerebrospinal fluid; CNS, central nervous system; ALOC, altered level of consciousness; CT, computed tomography.

Adapted from Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis. 2004;39:1267-1284.

See Table 4 on page 9 for class of evidence definitions.

Steroids

Corticosteroids are thought to improve the outcome in patients with bacterial meningitis by suppressing the inflammatory response that occurs with bacterial cell lysis. Therefore, steroids must be given prior to or concurrent with the first dose of parenteral antibiotics. Supplementary anti-inflammatory therapy with high-dose dexamethasone has been the subject of several recent high-quality trials. Two randomized, double-blind, placebo-controlled clinical trials demonstrated a consistent clinical benefit with the use of dexamethasone in adults with bacterial meningitis. A trial by de Gans et al[109] involving 301 adult patients with bacterial meningitis in the Netherlands found that the use of dexamethasone was associated with a significant reduction in mortality at 8 weeks compared with placebo treatment (relative risk [RR] of death, 0.48; 95% CI, 0.24-0.96). Subgroup analysis of this study revealed the benefit was most profound in patients with a GCS score greater than 12 and in patients infected with *S pneumoniae*. A study involving 300 adult patients with confirmed bacterial meningitis in Vietnam demonstrated similar results with respect to reduction in mortality at 1 month (RR death, 0.43; 95% CI, 0.20-0.94).[110] There were no significant differences between the rate of adverse events in the dexamethasone and placebo groups within these 2 trials. The rate of dexamethasone discontinuation was 2.5% in the Dutch trial and 0.7% in the Vietnamese trial. In contrast, no mortality benefit was seen with the use of corticosteroids in a randomized, double-blind, placebo-controlled clinical trial involving 465 adults in sub-Saharan Africa.[111]

It is unclear why there was such a striking difference between the results seen in the trials from the Netherlands and Vietnam and the trial from sub-Saharan Africa. Two theories have emerged to explain this difference.[112] First, the baseline mortality rate in the sub-Saharan African trial was 53%, far greater than the baseline rate of 14% to 15% in the Netherlands and Vietnam trials. This difference may reflect a sicker group of patients in the African trials (ie, patients with advanced disease may be less likely to improve with additional therapy such as dexamethasone, contributing to the high mortality rate). Second, 90% of the patients in the African trial were HIV positive, compared with < 1% of patients in the Vietnamese trial. The presence of HIV may attenuate the body's own immunologic response to the presence of bacterial lysis with the administration of antibiotics. It is thought that corticosteroids may not be effective when the host has a limited immune response.

Data on 18 trials and 2750 patients published through July 2006 in the Cochrane Database were reviewed and revealed that the use of corticosteroids in ABM was associated with a significant reduction in mortality (RR, 0.57; 95% CI, 0.40-0.99) as well as a reduction in short-term adverse neurologic outcomes (RR, 0.42; 95% CI, 0.22-0.87) in adults. The reduction in mortality rate was most pronounced in patients with *S pneumoniae* meningitis (RR, 0.59; 95% CI, 0.45-0.77). An overall trend toward benefit was seen with *N meningitidis* (RR, 0.71; 95% CI, 0.31-1.62); however, the trend was not statistically significant.[113]

Vancomycin And Dexamethasone

With the increasing resistance of *S pneumoniae* to penicillins and cephalosporins, vancomycin has become the antibiotic of choice to treat multidrug-resistant *S pneumoniae* (MDRSP) as well as methicillin-resistant *S aureus.* However, vancomycin has limited ability to cross the blood-brain barrier, and concern has been raised that the use of dexamethasone may decrease meningeal inflammation and thus further reduce vancomycin's penetration into the CSF. A recent small observational study of 14 patients with bacterial meningitis who were treated with vancomycin 15 mg/kg load followed by 60 mg/kg per day along with dexamethasone 10 mg IV every 6 hours for 4 days and cefotaxime 200 mg/kg per day IV demonstrated adequate vancomycin penetration into the CSF.[114] In all patients treated with this regimen, CSF vancomycin levels were significantly above the minimum inhibitory concentration and positively correlated with serum levels. The authors of this study concluded that dexamethasone may be used without fear of impeding vancomycin penetration in the CSF in patients with meningitis.

Fluid Administration

Management of fluids and electrolyte balance is an important aspect of supportive therapy for meningitis. Both overresuscitation and underresuscitation with IV fluids have been associated with adverse outcomes. A combined analysis of 3 randomized controlled trials demonstrated no overall mortality difference between the use of maintenance fluid administration and restricted fluid administration in patients with acute bacterial meningitis (RR, 0.82; 95% CI, 0.53-1.27). Additionally, no difference was seen in the patient care outcomes of severe neurologic sequelae (RR, 0.67; 95% CI, 0.41-1.08) or mild to moderate neurologic sequelae (RR, 1.24; 95% CI, 0.58-2.65).[115] Compared with the use of restricted fluid, the use of maintenance fluid was associated with improved outcome in individual neurologic analysis of spasticity (RR, 0.50; 95% CI, 0.27 to 0.93), seizures at 72 hours (RR, 0.59; 95% CI, 0.42 to 0.83), seizures at 14 days (RR, 0.19; 95% CI, 0.04 to 0.88), and chronic neurologic sequelae at 3 months' follow-up (RR, 0.42; 95% CI, 0.20 to 0.89).[115]

Early Goal-Directed Therapy

Patients presenting to the ED with meningitis and signs of septic shock (ie, persistent hypotension despite 20-40 cc/kg IV bolus of normal saline or serum

lactate levels > 4 mmol/L) should receive initial resuscitative measures according to the protocol put forth by Rivers et al.[116] By targeting central venous pressure to 8 to 12 mm Hg, mean arterial pressure to > 65 mm Hg, and central venous oxygen saturation to > 70%, these authors were able to significantly reduce 28-day mortality in patients with severe sepsis (RR death, 0.58; 95% CI, 0.39-0.87).[116]

Recombinant Human Activated Protein C

No randomized controlled clinical trials have evaluated the use of recombinant human activated protein C (rhAPC) in patients with meningitis, and significant controversy surrounds the use of rhAPC in patients with severe sepsis.[117-125] An industry-sponsored retrospective analysis of placebo-controlled, open-label compassionate-use trials found an 18% mortality rate in 106 adult patients and an 8% mortality rate in 48 pediatric patients diagnosed with meningitis who were concomitantly treated with rhAPC. Although overall rates of serious bleeding were low, 6% of the adult patients with meningitis experienced an intracerebral hemorrhage within 28 days of the administration of rhAPC.[126] Consequently, the use of rhAPC should be avoided in patients with meningitis.

Intensive Insulin Therapy

Tight glucose control in adults with ABM has not been formally evaluated. Although results from an initial report of intensive insulin therapy in critically ill patients were promising,[127] subsequent large-scale clinical trials failed to show a significant mortality benefit with this therapy.[128-130] An initial glucose lev-

Ten Risk Management Pitfalls For Meningitis (Continued on page 15)

1. **"Bacterial meningitis was at the top of my list, but I wanted to wait for the CT scan and LP results before I initiated antibiotics."**
   Waiting for a CT scan to be completed and then interpreted, followed by an LP and an additional wait for the laboratory results, can cause significant delays of up to several hours. In a sick patient with altered mental status, focal neurologic deficits, or hypotension, time to antibiotics may be of critical importance. Parenteral antibiotics and steroids should be administered before CT scanning or the LP is complete (with blood cultures ideally obtained beforehand).

2. **"I knew the patient had AIDS and was posturing. I thought I should perform the LP as quickly as possible to evaluate for infectious meningitis."**
   Although an LP has critical value in the diagnosis of meningitis, do not overlook the fact that this patient may have a contraindication to LP (ie, evidence of increased ICP) or an alternative diagnosis (eg, brain abscess, toxoplasmosis) that would be picked up by cranial CT scan. There are established recommendations for performing a CT scan prior to an LP in patients with compromised immune systems.

3. **"I can't believe that older man had bacterial meningitis. Although he did have a headache and was mildly confused, he did not have fever or neck stiffness."**
   Elderly patients may not present with the typical signs and symptoms of meningitis. Although fever commonly occurs, a temperature in the reference range or hypothermia is also possible. A study of 84 afebrile elderly patients with altered mental status found that 15 of these patients (18%) had abnormal LP results (95% CI, 10%-26%). A final diagnosis of meningitis was made for 10 of the 15 patients (bacterial meningitis, 2 patients; aseptic meningitis, 6 patients; lymphomatous meningitis, 2 patients).[172]

4. **"There is no way she could have bacterial meningitis. Her symptoms have persisted for 5 days. If she has had untreated bacterial meningitis for that long, she'd be dead."**
   In a large review of adult patients with ABM, only 50% of the patients reported a symptom duration of less than 24 hours.[39] Many patients will describe flulike symptoms for several days preceding the onset of worsening headache and neck pain. Unfortunately, there is currently no reliable way to distinguish a viral syndrome from early meningitis other than doing an LP with CSF analysis. Although some lawyers and medical experts may argue that a WBC count should be obtained in these patients, no guidelines recommend use of this test in adults to determine if they will benefit from an LP.

5. **"I got the antibiotics on as quickly as possible. I left the decision to give corticosteroids to the admitting doctor."**
   Corticosteroids are thought to work by suppressing the inflammatory response that occurs with antibiotic-induced bacterial cell lysis. Their use in immunocompetent adults with ABM is associated with a favorable survival benefit and neurologic outcome. Corticosteroids are ideally

el > 150 mg/dL is seen in about 40% of nondiabetic patients with ABM, but this finding has not been correlated with subsequent mortality.[131] In patients with ABM, the risk of hypoglycemia may outweigh the benefits of intensive insulin therapy.

Anticonvulsant Therapy

Seizures occur in 17% of adult patients with bacterial meningitis during hospital evaluation and are associated with a poor prognosis.[132] Seizures are associated with severe CNS inflammation (as reflected in high CSF protein level), severe systemic inflammation (as reflected in a high erythrocyte sedimentation rate), CSF WBC count < 1000 cells/ml, focal neurological abnormalities, focal lesions on cranial CT scan, altered immune status, and infection with *S pneumoniae*.[132] It is generally recommended that seizures in these patients be treated with anticonvulsant drugs; however, no prospective clinical trials have examined the efficacy of this intervention or the long-term prognosis of treated patients compared with untreated patients.

Increased Intracranial Pressure

Patients with bacterial meningitis typically have an increased opening pressure on LP, with an extremely elevated opening pressure > 40 cm H_2O seen in 20% to 40% of patients.[39,43] The standard treatment of increased ICP has included use of mannitol, mild hyperventilation, and neurosurgical intervention. A study of 15 patients with a GCS score ≤ 8 and ICP > 20 mm Hg showed that a protocol to reduce ICP to < 20 mm Hg in patients with bacterial meningitis was well tolerated and safe.[133] An experimental model of

Ten Risk Management Pitfalls For Meningitis (Continued from page 14)

given immediately before the first dose of antibiotics in the ED.

6. **"I can't believe that patient was admitted for bacterial meningitis. He did not have nuchal rigidity, and I thought I had excluded this diagnosis with negative Kernig and Brudzinski test results."**
   The absence of nuchal rigidity or other specific signs of meningeal irritation does not exclude the possibility of ABM. Although the specificity of Kernig and Brudinski signs is high, the sensitivity of these signs is extremely low. Similarly, the sensitivity of nuchal rigidity is only 30% for the detection of ≥ 6 WBC/mL in the CSF.

7. **"I thought for sure that patient had ABM. He had a fever, headache, and an altered mental status. The tap was atraumatic, but his CSF showed an RBC count of 2500 cells/mL and a WBC count of 200 cells/mL. His glucose and protein levels were normal. I gave him antibiotics and steroids, but I was surprised when his CSF Gram stain came back negative."**
   Don't be surprised. The presentation of encephalitis can greatly overlap with that of meningitis. For patients with a negative Gram stain and a CSF analysis that is consistent with viral meningitis, think about the possibility of HSV or encephalitis. Our approach in the ED is to give empiric acyclovir to these patients.

8. **"Did you just admit that patient for meningococcal meningitis? I saw his wife a few days ago and admitted her for the same thing."**
   If only you had contacted the patient's family and told them to come to the ED for chemoprophylaxis with ciprofloxin or rifampin after you made the initial diagnosis! Remember that household contacts, intimate nonhousehold contacts, and health care workers who have direct mucosal contact with the patient's secretions (eg, during endotracheal intubation, respiratory suctioning) are at risk of developing meningococcal disease after exposure to a patient with meningococcal meningitis.

9. **"That older man I admitted had gram-positive rods in his CSF. I wonder what he will grow out."**
   Don't forget that immunocompromised patients and patients older than 50 years are susceptible to infection with *L monocytogenes*. In these patients, empiric antibiotic coverage should include ampicillin 50 mg/kg IV every 6 hours (maximum dose, 3 gm) as well as ceftriaxone and vancomycin.

10. **"My colleague just went to trial over a missed case of bacterial meningitis. She told me that the plaintiff's expert witness testified that antibiotics should be given to everybody remotely suspected of having meningitis."**
    Although antibiotics are generally considered benign, there are far-reaching consequences to their indiscriminate use in every patient who may have a serious infection. Severe morbidity—and even death—can result from allergic reactions and antibiotic-associated colitis. Haphazard antibiotic administration is also blamed for the increased prevalence of multidrug-resistant bacteria in the United States.

Escherichia coli meningitis recently demonstrated that hypertonic saline was effective for the treatment of increased ICP.[134] A subsequent review of the medical records of 68 patients with transtentorial herniation due to various intracerebral conditions (1 patient with meningitis) revealed that patients treated with 23.4% hypertonic saline in addition to standard medical and surgical treatments for increased ICP had a rapid reduction in ICP. Among patients with an ICP monitor, pressure decreased from 23 ± 16 mm Hg (mean +/- standard deviation) at the time of transtentorial herniation to 14 ± 10 mm Hg at 1 hour after treatment (P = .002). Although transtentorial herniation was successfully reversed in 75% (57/76) of patients, only one-third of them survived to hospital discharge. More than three-fourths of the survivors experienced severe neurologic disability.[135]

Special Circumstances

Immunocompromised Patients

Increased rates of atypical meningeal infections are seen in patients with severe malnutrition, AIDS, and hematologic malignancy and in those receiving immunosuppressive medications (eg, chemotherapy, corticosteroids, disease-modifying antirheumatic drugs, immunosuppressive medications after transplant). Atypical pathogens that should be considered in these patients include *Cryptococcus neoformans, M tuberculosis*, and *L monocytogenes*.

C neoformans is the most common cause of meningitis in patients with AIDS and a CD4 count of less than 100/mL; however, it can also be seen in patients with other immunocompromising conditions and rarely in healthy, mostly geriatric, patients. Tuberculous (TB) meningitis is seen in patients who have been exposed to TB through airborne contact with an infected person or through travel to a region with endemic TB. AIDS is a common cofactor in patients with TB meningitis. *L monocytogenes* is typically seen in patients older than 50 years and those with immunocompromised systems or chronic alcoholism. A review of 30 patients with meningitis due to *L monocytogenes* revealed that two-thirds were immunocompromised patients, with the remainder being patients older than 50 years.[136]

In immunocompromised patients, ABM often presents with typical signs and symptoms. For example, patients with crytococcal meningitis usually present with the subacute onset of fever and progressively worsening headache, typically without neck stiffness or meningeal signs on examination. Other presenting symptoms may include new seizures, bizarre behavior, confusion, progressive dementia, and unexplained fever. In contrast, in patients infected with atypical organisms, the disorder can present with more understated findings.[136]

Cranial CT is recommended prior to LP in patients with a compromised immune system to evaluate for signs of increased ICP and to exclude focal intracerebral infections (eg, with *Toxoplasmosis gondii*).[3] The opening pressure should be recorded and the CSF sent for routine analysis as well as acid-fast bacillus (AFB) stain, TB culture, cryptococcal antigen titer, and India ink stain. The diagnosis of *Cryptococcus* meningitis is initially suspected with an elevated opening pressure (seen in 76% of patients) and is confirmed through a positive India ink stain (observed in 85% of patients) or positive cryptococcal antigen testing (observed in > 99% of patients).[137,138] The combination of certain historical and laboratory findings can increase suspicion for TB meningitis.[139] Although a bacterial culture is the diagnostic standard, the identification of bacteria in the CSF using an AFB stain is presumptive evidence for the diagnosis of TB meningitis. At least 5 to 10 mL of CSF fluid should be obtained and examined for 30 minutes under the microscope to improve diagnostic yield of the AFB stain.[140] Several serodiagnostic and biochemical tests are available for the diagnosis of TB.[141]

Inpatient treatment recommendations are based on the isolated pathogen. The use of concomitant corticosteroid therapy has been assessed in 2 clinical situations involving immunocompromised patients:[111,142,143] patients with HIV and bacterial meningitis in sub-Saharan Africa and patients with *M tuberculosis* meningitis in Vietnam. Whereas no benefit from corticosteroid therapy was found in adult patients with HIV and bacterial meningitis in sub-Saharan Africa,[111] a significant mortality benefit was found in adult patients with TB meningitis treated with corticosteroids.[142,143] The mechanism responsible for this benefit in patients with TB meningitis is unclear.[144] Results from a study of dexamethasone therapy for the treatment of cryptococcal meningitis are forthcoming.[145]

Postneurosurgical And Head Trauma Patients

The diagnosis of ABM should be considered when fever, neck stiffness, altered mental status, and/or headache is observed in patients with recent neurosurgical manipulation including CSF shunt insertion or revision. A retrospective review of 78 cases of CSF shunt-associated infections in adults found that nearly two-thirds of the infections occurred within the first month following shunt surgery. The clinical presentation was often subacute (median time to presentation, 5 days; range 0-21 days) and nonspecific, with fever absent in 22% of patients and symptoms such as neck stiffness, altered mental status, and headache each occurring in less than 50% of patients.[146] Local signs and symptoms are seen around the surgical site in nearly 50% of postsurgical infections. Skin and soft-tissue organisms such

as coagulase-negative *Staphylococcus* species and *S aureus* are the most common bacteria identified. Polymicrobial infections are occasionally seen, as is infection due to aerobic gram-negative bacilli (eg, *P aeruginosa*). Postneurosurgical patients and those with a CSF shunt and suspected meningitis can be treated with vancomycin 15 mg/kg every 6 hours (maximum dose, 500 mg) plus either cefepime 50 mg/kg every 8 hours (maximum dose, 2 gm), ceftazidime 50 mg/kg every 8 hours (maximum dose, 2 gm), or meropenem 40 mg/kg every 8 hours (maximum dose, 2 gm). No data support or refute the use of dexamethasone in this patient population. Specific indications for intraventricular administration of antimicrobial therapy and CSF shunt removal or reimplantation are available.[3]

Basilar skull fracture, particularly when accompanied by pneumocephalus or a CSF leak, is thought to be associated with an increased risk of bacterial meningitis. An 8-year review of patients with head trauma who developed meningitis showed that more than three-fourths (21/27) of these patients had an underlying basilar skull fracture and nearly half had a CSF leak.[147] The role of prophylactic antibiotics in the treatment of patients with a basilar skull fracture was recently evaluated in a well-done meta-analysis of 4 randomized controlled trials involving 208 patients. The authors of this review found no difference in the rates of meningitis or all-cause mortality between patients who received prophylactic antibiotics and those who did not.[148] These results are consistent with findings from an earlier systematic review of nonrandomized trials.[149] Unfortunately, these results may be subject to a β error; a larger well-done randomized, double-blind clinical trial of adequate statistical power may (or may not) produce results divergent with the results of this meta-analysis. A forthcoming study on prophylactic antibiotics in patients with basilar skull fracture accompanied by pneumocephalus (current enrollment, 200 patients) should provide additional insight into this condition.[150]

Controversies/Cutting Edge

Impact Of Vaccines

The full impact of childhood vaccination on adult meningitis has not been experienced because of several changes in the nature of the bacteria responsible for bacterial meningitis, as previously noted.

The heptavalent *S pneumoniae* vaccine, introduced in 2000, has had a substantial affect on the rate of invasive pneumococcal disease in infants and children.[151-156] A moderate decline in the incidence of pneumococcal infections among adults and elderly persons has been a serendipitous benefit of vaccine administration; this decline is attributed to decreased transmission of the organism from children to their parents and grandparents. A 2003 study by the CDC noted that following the inaugural year of routine pneumococcal vaccination, the overall rate of invasive pneumococcal disease fell by 32% in adults aged 20 to 39 years, by 8% in adults aged 40 to 64 years, and by 18% in adults older than 65 years.[156] The largest declines in pneumococcal infection have occurred in vaccine serotypes. The administration of the quadrivalent meningococcal vaccine is also expected to considerably decrease rates of infection due to *N meningitidis*. Although contemporary postlicensure data are lacking for the meningococcal vaccine, its routine administration in teenagers and young adults is projected to decrease the overall incidence of invasive disease (ie, isolation of bacteria from a normally sterile site) due to *N meningitidis* by 70% to 90%.[157,158]

The term serotype replacement has been used to describe the increased incidence of non–vaccine-related bacterial serotypes after the administration of a new vaccine. Concern has been raised about serotype replacement with the pneumococcal vaccine as a result of the emergence of multi-drug resistant streptococcus pneumoniae (MDRSP); a similar concern exists with the meningococcal vaccine, as a result of the lack of protection against *N meningitidis* serotype B. In several multicenter surveillance trials, the rate of MDRSP increased yearly from 1994 to 2000, accounting for up to 45% of all *S pneumoniae* infections by the end of 2000.[153,154,156,159,160] With the introduction of the heptavalent pneumococcal vaccine, the overall rate of invasive disease due to MDRSP has declined by 27% to 67%.[153,154,156]

Role Of Glycerol

Glycerol, a naturally occurring trivalent alcohol, is an essential component of the human cell membrane that has been used as a hyperosmolar agent and osmotic diuretic to reduce elevated ICP.[161] There are no clinical trials that have evaluated the use of glycerol in adults; however, a recent well-done randomized double-blind trial of glycerol in Latin American children with bacterial meningitis found significant morbidity and mortality benefits with the use of this agent compared to placebo. Although one-third of these children had *Haemophilus influenzae* type b (Hib) meningitis, the subgroup of children with non–Hib meningitis who were treated with glycerol showed benefits in the combined outcomes of severe neurologic sequelae and death compared with children with non–Hib meningitis who received placebo (OR, 0.46; 95% CI, 0.23-0.91; $P < .025$).[162] These results suggest that using an agent to reduce ICP in all patients with ABM may lead to improved clinical outcomes. If additional high-quality randomized double-blind trials confirm these results, the initial treatment of ABM may one day include an agent to reduce ICP. The use of glycerol in adults is also the subject of an ongoing trial in sub-Saharan Africa.[163]

Clinical Rule For Predicting Low Risk Of Meningitis

Nigrovic et al[164] developed and validated a clinical prediction rule known as the Bacterial Meningitis Score that can be used to distinguish bacterial meningitis from aseptic meningitis in the pediatric population. Predictors of bacterial meningitis include a positive CSF Gram stain, a CSF absolute neutrophil count ≥ 1000 cells/mL, a CSF protein value ≥ 80 mg/dL, a peripheral absolute neutrophil count ≥ 10,000 cells/mL, and seizure at or before presentation. Pediatric patients with none of these features were at low risk for bacterial meningitis (negative predictive value, 100%; 95% CI, 97%-100%).[164] Retrospective application of this score to a multicenter cohort of 3295 children with pleocytosis (CSF WBC count ≥ 10 cells/µL) demonstrated a negative predictive value of 99.9% (95% CI, 99.6%-100%), with misidentification in only 2 children younger than 2 months.[165] The use of the Bacterial Meningitis Score may put to rest the debate on whether CSF fluid analysis can accurately distinguish bacterial meningitis from aseptic meningitis.[89,166,167] Whether this rule can be successfully applied to adults remains to be seen.

Disposition

There is substantial overlap between the clinical presentation of bacterial meningitis, which is a life-threatening illness requiring rapid diagnosis, treatment, and hospital admission, and aseptic meningitis, which can often be monitored in an outpatient setting without antibiotic therapy. When a patient's presentation is ambiguous, the emergency clinician should take into account the underlying risk factors for bacterial meningitis, the results of the physical examination, and the findings on CSF analysis. Patients with CSF profiles consistent with bacterial meningitis require hospital admission for administration of parenteral antibiotics and further monitoring.[3] The disposition of well-appearing patients with CSF leukocytosis and findings consistent with viral meningitis is more variable. Management options include hospital admission and treatment with parenteral antibiotics or discharge with 24- to 48-hour follow-up if the patient is reliable.

Prognosis

Multiple models have been developed to predict outcomes in patients with ABM. Many of these studies are limited in their application to adults because of their retrospective design, the inclusion of pediatric patients, the small sample sizes, and their mathematical complexity. A recent prospective study involving nearly 1000 cases of adult meningitis derived and validated a complicated bedside risk score for unfavorable outcome in adults with bacterial meningitis. Independent risk factors for poor neurologic outcome includes advanced patient age, heart rate > 120 bpm on presentation, lower initial GCS score, cranial nerve palsy on presentation, CSF WBC count < 1000 cells/mL, and infection with *S pneumoniae*.[168] The usefulness of this scale in the ED has not been evaluated.

Sequelae

Systemic complications, deterioration of consciousness, and focal neurologic abnormalities may all be seen with bacterial meningitis. The most common systemic complication is cardiorespiratory failure

Time-Saving And Cost-Effective Strategies

- Don't delay the LP. It is easy to give a dose of antibiotics and then see other patients before finding time to do this procedure; however, a significant time delay between antibiotic administration and CSF analysis may lead to lower CSF yields for the Gram stain and culture results. Some authors have reported CSF clearing of bacteria within 15 minutes of parenteral antibiotic administration.
- In resource-poor environments, use a urinary reagent strip and glucometer to obtain preliminary results from a CSF sample. Both of these modalities provide accurate information about the content of the CSF. Nevertheless, neither should replace laboratory results when these are readily available.
- Use a face mask and shield when performing an LP. The use of a face mask is thought to prevent oropharyngeal and nasopharyngeal microbe transmission from doctor to patient that may result in a false-positive CSF Gram stain or culture results. Additionally, sterile gloves and strict sterile cleaning techniques should be employed.
- Obtain an adequate amount of CSF. A minimum of 4 to 8 mL of CSF should be obtained during the LP. In addition to routine CSF analysis (ie, WBC cell count, glucose and protein concentrations, Gram stain, and blood cultures), additional samples may be used for PCR assays or special cultures.
- Measure the opening CSF pressure. Not only is the opening pressure an early clue to the presence of meningitis, but it may also be used to justify placement of a neurosurgical device to monitor ICP.

with or without the need for mechanical ventilation, which occurs in nearly 30% of adult patients. Another significant systemic complication is disseminated intravascular coagulation, which is seen in nearly 10% of patients. Hearing loss and seizures are seen in 14% to 23% of adults.[169] The presence of seizures portends an unfavorable prognosis.[132] In meningitis, focal cerebral abnormalities (hemiparesis, monoparesis, or aphasia) are most commonly a result of cerebrovascular infarction and/or seizures. Cerebrovascular complications occur in 15% to 20% of adults with bacterial meningitis.[169]

Two-thirds of patients with bacterial meningitis leave the hospital with mild or no disability as measured by the Glasgow Outcome Scale. One of 10 patients has moderate disability, and 3% have severe disability. Long-term cognitive impairments are seen in 10% of cases.[169] In a prospective study, cognitive impairment was detected in 27% of patients who had a good recovery from pneumococcal meningitis.[170]

Community-acquired bacterial meningitis due to *S pneumoniae* has a case fatality rate of 19% to 37%. Up to 30% of survivors develop long-term neurologic sequelae including hearing loss and focal neurologic deficits.[169] Meningitis due to *N meningitides* has a case fatality rate of 3% to 13%, with 3% to 7% of survivors experiencing long-term neurologic sequelae.[169]

It is important to note that these data likely overestimate the morbidity and mortality of ABM in the United States because the majority are derived from studies completed before dexamethasone was routinely administered.

Chemoprophylaxis

Exposure to patients with meningococcal meningitis can pose dangers to others. Household or close contacts, intimate nonhousehold contacts, and healthcare workers who have direct contact with patients' mucosal secretions (eg, during endotracheal intubation, respiratory suctioning) are at risk of developing meningococcal disease after exposure. Additionally, schoolmates and coworkers who have had prolonged contact with the patient in the previous 7 days should receive prophylaxis. A meta-analysis of 3 studies involving 3804 household contacts of patients with meningococcal meningitis found that the risk of meningococcal disease can be reduced by an estimated 89% if the contacts take antibiotics known to eradicate meningococcal carriage.[171] Single-dose chemoprophylaxis agents for meningococcal meningitis include ciprofloxin 500 mg by mouth and ceftriaxone 250 mg intramuscularly. Alternatively, rifampin 10 mg/kg taken orally every 12 hours for a total of 4 doses (maximum dose, 600 mg) can be used.

Chemoprophylaxis is not given for contact with pneumococcal meningitis. Rifampin prophylaxis is recommended for household contacts of patients with Hib meningitis if they are younger than 4 years.

Summary

Acute bacterial meningitis is an uncommon but deadly diagnosis that should not be missed in the ED. Although the clinical presentation can be subtle, most patients with this disease are ill appearing. The cardinal features of headache, fever, neck stiffness, and altered mental status should each prompt consideration of this diagnosis. A noncontrast head CT scan, if indicated, and an LP should be expedited. Empiric antibiotic coverage with adjunctive corticosteroid therapy should be instituted once the diagnosis is considered likely and before the CT scan or LP is performed if the patient's mental status is altered or if he or she is ill appearing. The combination of prompt recognition, diagnostic evaluation, and initiation of parenteral antibiotics with adjunctive corticosteroid therapy is pivotal for treatment success and optimal patient outcome.

Case Conclusion

You return to your 68-year-old male patient and immediately intubate him because of his depressed level of consciousness. You obtain 2 sets of blood cultures, a complete blood count with differential cell count, a standard metabolic panel, and a lactate level. Your plan is to order a CT scan of his head and perform an LP, but recognizing the delays inherent in these tests, you immediately write an order for parenteral ceftriaxone to cover the most common pathogens associated with ABM. Considering the patient's age, you add ampicillin to cover the potential pathogen L monocytogenes and vancomycin to cover multidrug-resistant S pneumoniae. Before the antibiotics are infused, you administer dexamethasone to improve overall outcome. The patient's CSF results are consistent with ABM, and he is sent to the ICU.

You struggle with the decision to send home the well-appearing male patient signed out to you with CSF pending. Once his CSF profile returns, you see it is consistent with viral meningitis and that the Gram stain is negative. You go back to the patient to assess how he feels and find him happy and smiling. He tells his wife that he feels "100% better" after analgesia, antiemetics, and some fluid hydration. Still concerned, you talk to the patient about hospital admission, but he declines, stating that he feels well enough to go home and will follow up with his primary care provider in 24 hours. Although you feel somewhat uneasy with this disposition, you closely document your reassessment with the patient and send him home. A few days later, when you call the patient at home to tell him that his CSF culture is negative for bacteria, you find him doing well.

At the end of your shift, you call Employee Health and inquire about meningitis prophylaxis for yourself,

as you intubated the first patient who had a CSF profile consistent with bacterial meningitis. After your single dose of ciprofloxin, you reflect upon the day and realize the importance of being vigilant for this deadly infectious disease.

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Evidence-based medicine requires a critical appraisal of the literature based upon study methodology and number of subjects. Not all references are equally robust. The findings of a large, prospective, randomized, and blinded trial should carry more weight than a case report.

To help the reader judge the strength of each reference, pertinent information about the study, such as the type of study and the number of patients in the study, will be included in bold type following the reference, where available. In addition, the most informative references cited in this paper, as determined by the authors, will be noted by an asterisk (*) next to the number of the reference.

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CME Questions

1. Which of the following best represents the overall mortality rate of bacterial meningitis?
a. 10%
b. 10% to 30%
c. 50% to 70%
d. > 70%

2. What is the approximate sensitivity of the classic triad of ABM (fever, neck stiffness, and altered mental status)?
a. < 10%
b. 10% to 30%
c. 30% to 50%
d. > 50%

3. By what mechanism are corticosteroids thought to improve patient outcome in bacterial meningitis?
a. Decrease in pain due to inflammation of the meninges
b. Improved penetration of antibiotics into the CSF
c. Prevention of increased ICP
d. Suppression of inflammatory response due to bacterial cell lysis
e. None of the above

4. Although CSF sterilization is known to occur as soon as 2 to 4 hours after administration of parenteral antibiotics, a short interval between antibiotic therapy and an LP does not significantly change the CSF WBC count or protein and glucose values.
a. True
b. False

5. Which statement is true regarding CSF glucose and protein levels in about 90% of patients with bacterial meningitis and a normal serum glucose level?
a. Their CSF glucose level is low, and their CSF protein level is high.
b. Their CSF glucose level is high, and their CSF protein level is low.
c. Their CSF glucose level is low, and their CSF protein level is low.
d. Their CSF glucose level is high, and their CSF protein level is high.

6. What is the most common cause of delay to antibiotics in the treatment of meningitis?
a. Awaiting admission orders
b. Awaiting delivery of antibiotics from the pharmacy
c. Awaiting results of serum blood tests
d. Delaying consideration of meningitis as a diagnosis
e. Waiting for a CT scan to be completed

7. Which statement best describes the role of fluid administration in the management of suspected meningitis?
a. Hypertonic saline is contraindicated in cases of herniation.
b. Maintenance fluids are associated with improved outcomes in some neurologic paramenters.
c. Fluid restriction is recommended to decrease CNS edema.
d. Fluid restriction is essential in lowering the cerebral perfusion pressure.

8. Which empiric antibiotic regimen should be given to a 75-year-old male patient with suspected meningitis?
a. Ampicillin
b. Cefepime and meropenem
c. Ceftriaxone and vancomycin
d. Ceftriaxone, vancomycin, and ampicillin
e. Vancomycin and meropenem

9. Which of these signs/symptoms is the least sensitive indicator of meningitis?

a. Fever
b. Headache
c. Jolt accentuation
d. Kernig sign
e. Neck stiffness

10. About 10% of patients with ABM present with a lymphocyte predominance (> 50%) in their CSF.

a. True
b. False

11. Which finding correlates with poor neurologic outcome in ABM?

a. Cranial nerve palsy on examination
b. Neck stiffness on examination
c. Normal CT scan results
d. Normal serum glucose level
e. Rash

12. In cases of meningococcal meningitis, who should receive prophylaxis?

a. The nurse who triaged the patient
b. The resident who intubated the patient
c. The spouse who cared for the patient at home for 2 days prior to arrival in the ED
d. B and C
e. All of the above

Physician CME Information

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Needs Assessment: The need for this educational activity was determined by a survey of medical staff, including the editorial board of this publication; review of morbidity and mortality data from the CDC, AHA, NCHS, and ACEP; and evaluation of prior activities for emergency physicians.

Target Audience: This enduring material is designed for emergency medicine physicians, physician assistants, nurse practitioners, and residents.

Goals & Objectives: Upon completion of this article, you should be able to: (1) demonstrate medical decision-making based on the strongest clinical evidence; (2) cost-effectively diagnose and treat the most critical ED presentations; and (3) describe the most common medicolegal pitfalls for each topic covered.

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Now you can diagnose and treat your pediatric patients with life-threatening hemorrhage, airway compromise, or brain injuries with absolute confidence.

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Initial Evaluation And Resuscitation Of The Injured Child

Special Report

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CME Objectives

Upon completion of this article, you should be able to:

1. Recognize life-threatening hemorrhage, airway compromise, and brain injuries.
2. Describe the management of life-threatening hemorrhage, airway compromise, and brain injuries.

Date of original release: August 1, 2009
Date of most recent review: April 30, 2009
Termination date: August 1, 2012
Medium: Print and online
Method of participation: Print and online answer form and evaluation

Prior to beginning this activity, see "Physician CME Information" on the back page.

Traumatic injury is the leading cause of morbidity and mortality in children in the United States, resulting in more death and disability than all other childhood diseases combined.[1] Early and effective recognition and resuscitation of life-threatening hemorrhage, airway compromise, and brain injuries may significantly reduce this morbidity and mortality.[2,3] However, despite initiatives to address this issue, children continue to die as a result of trauma,[4] and the medical personnel who care for them continue to search for the optimal system and best protocols for managing these injuries.

Treating young trauma patients can be more challenging than treating adult patients. A young child's inability to communicate and to describe his or her symptoms and history or to explain the events leading to an injury can complicate the initial evaluation. Psychological differences (eg, extreme fear) can also cause the child to cry and be uncooperative during the examination. In addition, the child's initial vital signs may be difficult to interpret until it is clear that any tachypnea and tachycardia are not the result of significant underlying injury. Finally, a child's higher body surface area to mass ratio increases the likelihood of sub-

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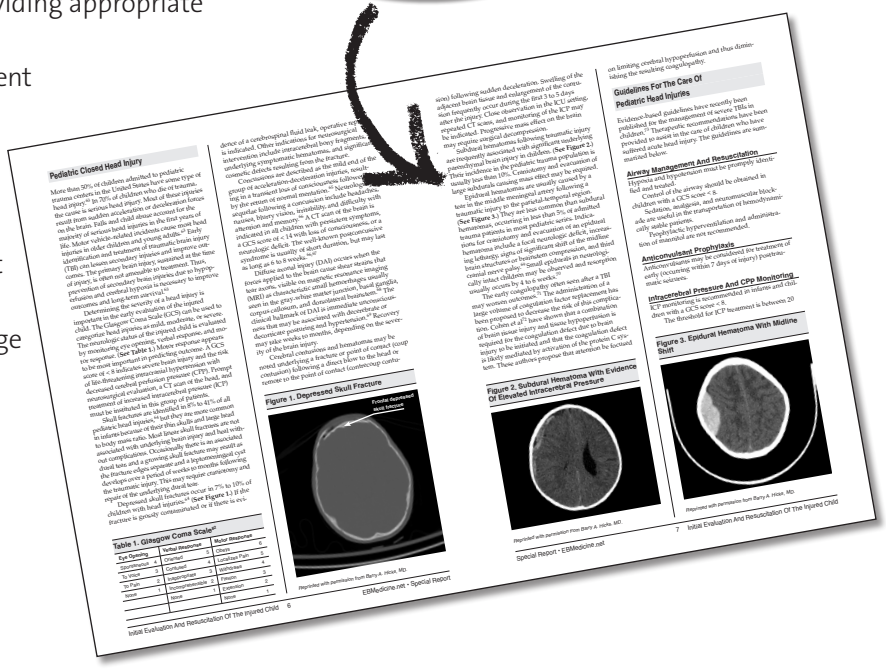

Pediatric Closed Head Injury

Figure 1. Depressed Skull Fracture

Figure 2. Subdural Hematoma With Evidence Of Elevated Intracerebral Pressure

Guidelines For The Care Of Pediatric Head Injuries

Airway Management And Resuscitation

Anticonvulsant Prophylaxis

Intracerebral Pressure And CPP Monitoring

Figure 3. Epidural Hematoma With Midline Shift

Table 1. Glasgow Coma Scale[27]

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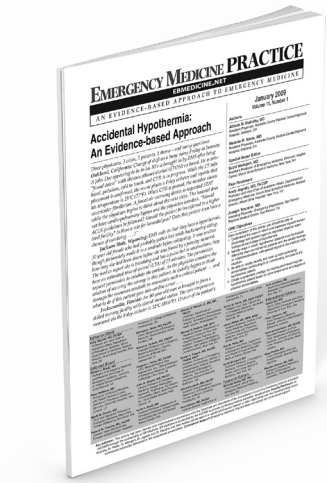

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EVIDENCE-BASED PRACTICE RECOMMENDATIONS

Adult Acute Bacterial Meningitis In The United States: 2009 Update

Sadoun T, Singh A. September 2009; Volume 11, Number 9

This issue of Emergency Medicine Practice reviews the ED approach to and treatment of community-acquired ABM in adults. For a more detailed discussion of this topic, including figures and tables, clinical pathways, and other considerations not noted here, please see the complete issue at www.ebmedicine.net/topics.

Key Points	Comments
Consider acute bacterial meningitis (ABM) in the differential.	The initial presentation of ABM can resemble that of an acute viral illness. Indeed, an Internet search of *meningitis* and *sent home* yields numerous cases of both children and adults who presented with nonspecific illnesses and were subsequently discharged from the ED.
The classic triad of fever, neck stiffness, and altered mental status is present in 44% of patients with ABM.[39]	Headache appears to be much more common on presentation. One report found that nearly 90% of adults with community-acquired meningitis complained of headache.[39] The presence or absence of Kernig and Brudizinski signs is of little diagnostic value.[44]
Do not delay antibiotic administration pending the results of a cranial computed tomography (CT) scan or lumbar puncture (LP) analysis in patients strongly suspected of having bacterial meningitis.	The initial choice of antibiotics in immunocompetent adults typically includes ceftriaxone and vancomycin.[3]
Administer corticosteroids to immunocompetent adults with ABM prior to or concurrent with the first dose of antibiotics.[113]	Giving a single dose of dexamethasone to patients who turn out to have a nonmeningitis diagnosis will not likely cause significant morbidity.
Administer fluids to patients with bacterial meningitis. Both overresusciation and underresusciation with IV fluids have been associated with adverse outcomes.[115]	A combined analysis of 3 randomized controlled trials demonstrated no overall mortality difference between the use of maintenance fluid administration and restricted fluid administration.[115] Additionally, no difference was seen in the patient care outcomes of severe neurologic sequelae or mild to moderate neurologic sequelae. Compared with the use of restricted fluid, the use of maintenance fluid was associated with improved outcome in individual neurologic analysis of spasticity, seizures at 72 hours, seizures at 14 days, and chronic neurologic sequelae at 3 months' follow-up.
Avoid recombinant human activated protein C (rhAPC) in patients with meningitis.[126]	An industry-sponsored retrospective analysis of placebo-controlled, open-label compassionate-use trials found an 18% mortality rate in 106 adult patients and an 8% mortality rate in 48 pediatric patients diagnosed with meningitis who were concomitantly treated with rhAPC.[126] Although overall rates of serious bleeding were low, 6% of the adult patients with meningitis experienced an intracerebral hemorrhage within 28 days of the administration of rhAPC.
Do not overlook contraindications to LP,[46] and consider that alternative diagnoses (eg, brain abscess, toxoplasmosis) will be picked up by cranial CT scan.	Findings on CT scan generally accepted as contraindications to LP include: (1) a lateral shift of midline structures; (2) loss of the suprachiasmatic and basilar (circummesencephalic) cisterns; (3) obliteration or shift of the fourth ventricle; and (4) obliteration of the superior cerebellar and quadrigeminal plate cisterns with sparing of the ambient cisterns.[46]

** See reverse side for reference citations.*

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