Wolters Kluwer

Clinical features and diagnosis of acute bacterial meningitis in adults

AUTHOR: Rodrigo Hasbun, MD, MPH, FIDSA
SECTION EDITOR: Allan R Tunkel, MD, PhD, MACP
DEPUTY EDITOR: Jennifer Mitty, MD, MPH

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Jan 2024.**
This topic last updated: **Oct 11, 2022.**

INTRODUCTION

Meningitis is an inflammatory disease of the leptomeninges, the tissues surrounding the brain and spinal cord, and is characterized by an abnormal number of white blood cells (WBCs) in the cerebrospinal fluid (CSF) in the majority of patients [1]. The meninges consist of three parts: the pia, arachnoid, and dura maters (figure 1). Bacterial meningitis reflects infection of the arachnoid mater and the CSF in both the subarachnoid space and the cerebral ventricles.

The clinical and laboratory features of acute bacterial meningitis in adults will be reviewed here. The pathogenesis, epidemiology, treatment, prognosis, and prevention of acute bacterial meningitis in adults and issues related to acute bacterial meningitis in children and to chronic, recurrent, and aseptic meningitis are discussed separately. (See "Pathogenesis and pathophysiology of bacterial meningitis" and "Epidemiology of community-acquired bacterial meningitis in adults" and "Initial therapy and prognosis of community-acquired bacterial meningitis in adults" and "Treatment of bacterial meningitis caused by specific pathogens in adults" and "Bacterial meningitis in children older than one month: Clinical features and diagnosis" and "Bacterial meningitis in children older than one month: Treatment and prognosis" and "Approach to the patient with chronic meningitis" and "Approach to the adult with recurrent infections", section on 'Meningitis' and "Aseptic meningitis in adults".)

EPIDEMIOLOGY

Bacterial meningitis can be community acquired or health care associated.

- The major causes of community-acquired bacterial meningitis in adults in developed countries are *Streptococcus pneumoniae*, *Neisseria meningitidis*, and, primarily in patients over 50 years of age or those who have deficiencies in cell-mediated immunity, *Listeria monocytogenes* (table 1).

- The major causes of health care-associated ventriculitis and meningitis are different (usually staphylococci and aerobic gram-negative bacilli) and occur more commonly after neurosurgical procedures (eg, post-craniotomy, ventriculoperitoneal shunts, lumbar shunts, external ventricular drains or following head trauma such as basilar skull fracture with or without clinical evidence of leak of cerebrospinal fluid) [2].

A more detailed discussion of the epidemiology of and risk factors for bacterial meningitis is presented elsewhere. (See "Epidemiology of community-acquired bacterial meningitis in adults".)

CLINICAL FEATURES

Patients with bacterial meningitis are usually quite ill and often present soon after symptom onset. In the largest prospective study of 1412 episodes of bacterial meningitis, for example, approximately half of the patients presented less than 24 hours after onset of illness [3].

Determinants of the pace of bacterial meningitis are related to both host and microbial virulence factors. Any form of bacterial meningitis that is untreated or treated very late in its course is almost uniformly fatal. (See "Initial therapy and prognosis of community-acquired bacterial meningitis in adults", section on 'Avoidance of delay'.)

Presenting manifestations — The classic triad of acute bacterial meningitis, which occurs in 41 percent of patients, consists of fever, nuchal rigidity, and a change in mental status, usually of sudden onset [3,4]. Older patients (age >60 years) more commonly present with the triad than younger patients (58 versus 36 percent) [5].

The most common clinical features include a severe headache (84 percent), fever greater than 38°C (74 percent), stiff neck (74 percent), a Glasgow Coma scale <14 (71 percent), and nausea (62 percent) [3,4,6]. In a 2004 prospective study of 696 cases of community-acquired bacterial meningitis, almost all patients (95 percent) presented with at least two of four symptoms (ie,

headache, fever, stiff neck, and altered mental status) [4]. The absence of all of these findings essentially excludes the presence of bacterial meningitis [7].

In addition to the classic findings, less common manifestations are seizures (23 percent), aphasia or hemi- or monoparesis (22 percent), coma (13 percent), cranial nerve palsy (9 percent), rash (8 percent), and papilledema (4 percent) [3,4,8,9]. Concomitant infections may include sinusitis or otitis (34 percent), pneumonia (9 percent), and endocarditis (1 percent) [3].

Some findings may be suggestive of a particular bacterial etiology:

- In an observational study of 696 patients with community-acquired bacterial meningitis, cerebral infarction occurred in 25 percent of episodes and in 36 percent of patients with pneumococcal meningitis [10]. Delayed cerebral infarctions have been described in 1 to 4 percent of patients with bacterial meningitis with a possible association with adjunctive dexamethasone [11].

- Patients with *Listeria* meningitis have an increased tendency to have seizures and focal neurologic deficits early in the course of infection. In addition, some patients may present with rhombencephalitis affecting the brainstem and cerebellum, manifested as ataxia, cranial nerve palsies, and/or nystagmus. In a review of 367 episodes of central nervous system infections caused by *L. monocytogenes* [12], the most common findings were fever (92 percent) and altered sensorium (65 percent). A more detailed discussion of clinical manifestations of central nervous system (CNS) listeriosis are discussed elsewhere [13]. (See "Clinical manifestations and diagnosis of Listeria monocytogenes infection".)

- Certain bacteria, particularly *N. meningitidis*, can cause characteristic skin manifestations, such as petechiae and palpable purpura. In two large series of patients with community-acquired bacterial meningitis, rash was present in 11 and 26 percent; among those with rash, 75 and 92 percent were associated with meningococcal meningitis [4,8]. In another study of 258 adults with meningococcal meningitis [14], rash was present in 64 percent and characterized as petechial in 91 percent of patients. However, others have observed a rash in ≤26 percent of cases of meningococcal meningitis and, if present, the rash was more likely to be scanty or more atypical appearing than the rash seen in patients with meningococcal septicemia [15]. A petechial rash is not specific for meningococcal infection, and some patients with meningococcal meningitis have a maculopapular rash [8]. (See "Clinical manifestations of meningococcal infection".)

- Arthritis occurs in some patients with bacterial meningitis. In a case series of 696 episodes of community-acquired bacterial meningitis, arthritis was diagnosed in 48 (7 percent) of the episodes, with *N. meningitidis* the etiologic agent in two-thirds of these joint infections

[16]. Joint fluid aspiration was performed in 23 patients and was positive by culture in 6 (26 percent). Recognition of the concurrent arthritis is important since prolonged antibiotic therapy is necessary. (See "Septic arthritis in adults".)

Examination for meningeal irritation — Although patients may not complain specifically of a stiff neck, it is important to assess for meningeal irritation. Passive or active flexion of the neck will usually result in an inability to touch the chin to the chest. Difficulty in lateral motion of the neck is a less reliable finding.

Tests to illustrate meningismus (such as Kernig and Brudzinski signs) were originally developed and tested in patients with severe, late-stage untreated bacterial and tuberculous meningitis in the preantibiotic era (table 2).

- The classic Brudzinski sign refers to spontaneous flexion of the hips during attempted passive flexion of the neck.
- The Kernig sign refers to the inability or reluctance to allow full extension of the knee when the hip is flexed 90 degrees. The Kernig test is usually performed in the supine position, but it can be tested in the seated patient.

Nuchal rigidity and the Kernig and Brudzinski signs were described over a century ago. These tests may be less sensitive in modern day community-acquired bacterial meningitis. As an example, in a large, well-designed prospective study of 297 patients with suspected meningitis, the sensitivity was extremely low (5 percent for each sign and 30 percent for nuchal rigidity); the specificity was 95 percent for each sign and 68 percent for nuchal rigidity [17].

Jolt accentuation of headache may be a more sensitive maneuver for the diagnosis of meningitis. A positive test consists of accentuation of headache by horizontal rotation of the head at a frequency of two to three times per second.

The diagnostic value of this maneuver has been evaluated in several studies with mixed results [18-20]. Although one study showed a sensitivity of jolt accentuation for the diagnosis of meningitis of 97 percent, other studies have revealed lower sensitivity and specificity highlighting the limited predictive value of the test in the diagnosis of meningitis.

LABORATORY EVALUATION

Blood tests — Initial blood tests should include a complete blood count with differential and platelet count and two aerobic blood cultures of appropriate volume (ideally, prior to the initiation of antimicrobial therapy). Serum electrolytes and glucose, blood urea nitrogen, and

creatinine concentrations are helpful in determining the cerebrospinal fluid- (CSF) to-blood glucose ratio. It is important to draw the serum glucose within one hour of obtaining the lumbar puncture to have a reliable ratio [21]. In addition, coagulation studies may be indicated, especially if petechiae or purpuric lesions are noted [22].

- The white blood cell (WBC) count is usually elevated, with a shift toward immature forms; however, severe infection can be associated with leukopenia. The platelet count may also be reduced. Leukopenia and thrombocytopenia have correlated with a poor outcome in patients with bacterial meningitis [23,24].

- Coagulation studies may be consistent with disseminated intravascular coagulation.

- Serum chemistry results are usually commensurate with the severity of the overall process and may reveal an anion gap metabolic acidosis or hyponatremia; in one series, hyponatremia was present in 30 percent of patients but was usually mild and did not require specific treatment [25].

- Blood cultures are often positive and can be useful in the event that CSF cannot be obtained before the administration of antimicrobials. Approximately 50 to 90 percent of patients with bacterial meningitis have positive blood cultures [3,4,6]; lower yields have been reported in some studies in patients with meningococcal infection [26]. Cultures obtained after antimicrobial therapy are much less likely to be positive, particularly for meningococcus [26-28]. In health care-associated ventriculitis and meningitis, previous antibiotic therapy can significantly reduce the sensitivity of the CSF Gram stain and culture [28]. Tests of serum and urine for bacterial antigens, as well as cultures of mucosal surfaces for the causative pathogen, are not generally helpful.

Cerebrospinal fluid examination — Every patient with suspected meningitis should have CSF obtained unless lumbar puncture (LP) is contraindicated. Examination of the CSF is crucial for establishing the diagnosis of bacterial meningitis, identifying the causative organism, and performing in vitro susceptibility testing [29].

Precautions — Although there are no absolute contraindications to performing the procedure, caution should be used in patients with (see "Lumbar puncture: Technique, contraindications, and complications in adults", section on 'Contraindications and precautions for high-risk patients'):

- Possible raised intracranial pressure with risk for cerebral herniation due to obstructive hydrocephalus, cerebral edema, or space-occupying lesion
- Thrombocytopenia or other bleeding diathesis, including ongoing anticoagulant therapy

- Suspected spinal epidural abscess

Indications for CT scan before LP — An important early decision relates to whether a head computed tomography (CT) should be performed prior to LP to exclude a mass lesion or increased intracranial pressure. These abnormalities might rarely lead to cerebral herniation during removal of large amounts of CSF, and cerebral herniation could have devastating consequences.

A head CT should be performed **before** LP in adults with suspected bacterial meningitis who have one or more of the following risk factors (algorithm 1) [30-32]:

- Immunocompromised state (eg, HIV infection, immunosuppressive therapy, solid organ or hematopoietic cell transplantation)
- History of central nervous system (CNS) disease (mass lesion, stroke, or focal infection)
- New onset seizure (within one week of presentation)
- Papilledema
- Abnormal level of consciousness
- Focal neurologic deficit

Patients without these indications should not undergo a CT scan as it is of no clinical benefit and delays therapy [33] In one report, adherence to the Infections Diseases Society of America (IDSA) guidelines in adults with bacterial meningitis identified all patients with major intracranial abnormalities [34].

The bacterial meningitis guidelines in Sweden were revised in 2009 to remove impaired mental status as a contraindication to LP without prior CT scan, and the effect of this change was evaluated in a retrospective study using the Swedish quality registry [35]. After the change to the guidelines was implemented, adequate treatment was started 1.2 hours earlier, and more patients were treated within 2 hours of presentation; in addition, mortality was lower (7 versus 12 percent), and the risk of sequelae at follow-up was decreased (38 versus 49 percent) following the change to the guidelines and in comparison with other society guidelines [36]. However, this finding may be because, in clinical practice, patients who have a CT before LP are sicker [33] or often not started on antibiotics before neuroimaging, despite recommendations to the contrary. (See 'If LP is delayed or deferred' below.)

It has been suggested that a normal CT scan does not always mean that performance of an LP is safe and that certain clinical signs of impending herniation (ie, deteriorating level of consciousness, particularly a Glasgow Coma scale <11; brainstem signs including pupillary changes, posturing, or irregular respirations; or a very recent seizure) may be predictive of patients in whom an LP should be delayed irrespective of CT findings (table 3) [37]. (See

"Lumbar puncture: Technique, contraindications, and complications in adults", section on 'Cerebral herniation'.)

If LP is delayed or deferred — It is essential that antimicrobial therapy not be delayed if there is a contraindication to or inability to perform an LP, or if the LP is delayed by the need for cranial imaging. In any of these situations, blood cultures should be obtained and empiric antibiotics administered as soon as is possible (before the imaging study in patients who require imaging). (See "Initial therapy and prognosis of community-acquired bacterial meningitis in adults", section on 'Empiric regimens'.)

In addition, dexamethasone (0.15 mg/kg intravenously every 6 hours) should be given shortly before or at the same time as the antimicrobial agents if the preponderance of clinical and laboratory evidence suggests bacterial meningitis with a plan to stop therapy, if indicated, when the evaluation is complete. Adjunctive dexamethasone should not be given to patients who have already received antimicrobial therapy because it is unlikely to improve patient outcome even though the European and United Kingdom guidelines recommend administering dexamethasone up to 4 and 12 hours after receipt of antimicrobial therapy, respectively [38]. Indications for adjunctive dexamethasone are discussed in greater detail separately. (See "Dexamethasone to prevent neurologic complications of bacterial meningitis in adults" and "Initial therapy and prognosis of community-acquired bacterial meningitis in adults", section on 'Avoidance of delay'.)

Prior administration of antimicrobials tends to have minimal effects on the chemistry and cytology findings [28,39] but can reduce the yield of Gram stain and culture [26-28]. However, a pathogen can still be cultured from the CSF in most patients up to several hours after the administration of antimicrobial agents [27,28], with the possible exception of the meningococcus. This issue was addressed in a review of 128 children with bacterial meningitis in whom LP was first performed after initiation of therapy and serial LPs were obtained [27]. Among patients with meningococcal infection, CSF culture was negative in 3 of 9 samples obtained within one hour. In contrast, 4 to 10 hours were required before CSF cultures were sterile in patients with pneumococcal meningitis.

Opening pressure — The opening pressure with the patient lying in the lateral decubitus position should be measured and documented. The opening pressure is typically elevated in patients with bacterial meningitis. In the series of 301 adults cited above, the mean opening pressure was approximately 350 mm H_2O (normal up to 200 mm H_2O) [3]. However, there is a wide range of values as illustrated in a report of 296 episodes of community-acquired bacterial meningitis: 39 percent had values ≥300 mm H_2O, while 9 percent had values below 140 mm H_2O [8].

Cerebrospinal fluid analysis

Overview — CSF should be sent for:

- Cell count and differential
- Glucose concentration
- Protein concentration
- Gram stain and bacterial culture
- Other appropriate tests (eg, rapid tests, polymerase chain reaction [PCR]), depending upon the level of concern for other etiologies of meningitis or meningoencephalitis

Characteristic findings in bacterial meningitis include a CSF glucose concentration <40 mg/dL (<2.22 mmol/L), a CSF to serum glucose ratio of ≤0.4, a protein concentration >200 mg/dL (>2000 mg/L), and a WBC count above 1000/microL, with a percentage of neutrophils usually greater than 80 percent [3,32,40]. The spectrum of CSF values in bacterial meningitis is so wide, however, that the absence of one or more of the typical findings is of little value [4,8]. For example, in a prospective study of 1412 adults with bacterial meningitis, a CSF WBC >1000/microL was seen in only 66 percent of patients [3]. Why some patients have milder CSF abnormalities cannot usually be identified. Potential causes include early presentation, recent prior antimicrobial therapy, and neutropenia. (See "Cerebrospinal fluid: Physiology and utility of an examination in disease states", section on 'CSF in CNS infection'.)

An observational study found that bacterial meningitis was highly probable (≥99 percent certainty) when any one of the following parameters was present: a CSF glucose concentration below 34 mg/dL (1.9 mmol/L), a protein concentration above 220 mg/dL (2200 mg/L), a WBC count above 2000/microL, or a neutrophil count more than 1180/microL [41]. However, clinicians must recognize that many exceptions exist and that empiric antimicrobial therapy is warranted when bacterial meningitis is suspected clinically even if the CSF abnormalities are not diagnostic.

A false-positive elevation of the CSF WBC count can be found after traumatic LP or in patients with intracerebral or subarachnoid hemorrhage in which both red blood cells (RBCs) and WBCs are introduced into the subarachnoid space. If a traumatic LP is suspected and the peripheral WBC count is not abnormally low or high, a good rule of thumb for estimating the adjusted WBC count is to subtract one WBC for every 500 to 1000 RBCs measured in the CSF. This "corrected" CSF WBC has better diagnostic accuracy in differentiating culture-positive bacterial meningitis than patients with intracerebral hemorrhage alone [42]. The formula in the following calculator can also be used to determine the adjusted WBC count in the presence of CSF RBCs (calculator 1) [42,43].

Determination of the CSF lactate concentration has been suggested as a useful test to differentiate bacterial from viral meningitis. Two meta-analyses that included 25 studies (1692 patients) and 31 studies (1885 patients) concluded that the diagnostic accuracy of CSF lactate was superior to that of CSF WBC count, glucose, and protein concentration in differentiating bacterial from aseptic meningitis [44,45], although sensitivity was lower in patients who received antimicrobial treatment prior to LP [44], and CSF lactate may be elevated in patients with other CNS diseases. A CSF lactate may help differentiate health care-associated ventriculitis from chemical meningitis in patients with recent neurosurgical procedures, but it is only performed in approximately 50 percent of the patients [46].

Gram stain — A Gram stain should be obtained whenever there is suspicion of bacterial meningitis. It has the advantage of suggesting the bacterial etiology one day or more before culture results are available [26]. The following findings may be seen:

- Gram-positive diplococci suggest pneumococcal infection (picture 1).
- Gram-negative diplococci suggest meningococcal infection (picture 2).
- Small pleomorphic gram-negative coccobacilli suggest *Haemophilus influenzae* infection (picture 3).
- Gram-positive rods and coccobacilli suggest listerial infection (picture 4).

The reported sensitivity of Gram stain for bacterial meningitis has varied from 50 to 90 percent; however, the specificity approaches 100 percent [4,11,47]. In the report of 696 patients with community-acquired bacterial meningitis, CSF Gram stain had a sensitivity of 80 percent and a specificity of 97 percent [4]. In a trial of 301 adults with bacterial meningitis, for example, the Gram stain was positive in 74 percent and the CSF culture was positive in 78 percent [3].

The Gram stain is positive in 10 to 15 percent of patients who have bacterial meningitis but negative CSF cultures [8]. As noted above, the yield of both Gram stain and culture may be reduced by prior antibiotic therapy [26-28].

Rapid tests — Several rapid diagnostic tests have been developed to aid in the diagnosis of bacterial meningitis. Latex agglutination tests detect the antigens of the common meningeal pathogens in the CSF, although these tests are no longer routinely recommended because results do not appear to modify the decision to administer antimicrobial therapy and false-positive results have been reported [32]. An immunochromatographic test for detection of *S. pneumoniae* in CSF was found to be 100 percent sensitive and specific for the diagnosis of pyogenic pneumococcal meningitis [48]; the overall sensitivity is 95 to 100 percent [49]. More studies are needed, however, before this test can be routinely recommended.

Polymerase chain reaction — Nucleic acid amplification tests, such as the polymerase chain reaction (PCR), have been evaluated in patients with bacterial meningitis and have shown high sensitivity and specificity [50,51]. A rapid multiplex PCR that tests for the most common viruses, bacteria, and fungi is now widely available and has been shown to be useful, especially in those with a negative-CSF Gram stain or culture, or in those who have received prior antimicrobial therapy. Use of PCR for the two most common meningeal pathogens (*S. pneumoniae* and *N. meningitidis*) is routinely recommended in the United Kingdom guidelines for patients presenting with meningitis [52]. Studies evaluating the multiplex PCR assay for detection of *N. meningitidis*, *S. pneumoniae*, and *H. influenzae* type b have shown sensitivities and specificities of 100 percent [50,51]. Problems with false-positive results have been reported with PCR but false negatives are very uncommon [53].

Molecular diagnosis of bacterial meningitis is discussed in greater detail separately. (See "Molecular diagnosis of central nervous system infections", section on 'Meningitis'.)

DIAGNOSIS

Acute bacterial meningitis should be promptly suspected in adults who present with fever, headache, stiff neck, and/or altered mental status. Late diagnosis is associated with a delay in antibiotic therapy, a lower use of empiric adjunctive steroids, and a higher mortality [54].

Isolation of a bacterial pathogen from the cerebrospinal fluid (CSF; by culture or other diagnostic techniques) confirms the diagnosis of bacterial meningitis. Isolation of bacteria from blood cultures in a patient with CSF pleocytosis also confirms the diagnosis, even if the CSF culture remains negative.

It may be difficult to definitively establish the diagnosis of bacterial meningitis in those patients who have received antibiotics prior to lumbar puncture which decreases the yield of culture and Gram stain. This is especially problematic in health care-associated meningitis where concomitant antibiotics are often present. The approach to patients with negative cultures where bacterial meningitis is still suspected is discussed in detail elsewhere. (See "Initial therapy and prognosis of community-acquired bacterial meningitis in adults", section on 'Negative CSF culture'.)

DIFFERENTIAL DIAGNOSIS

The clinical and laboratory findings of bacterial meningitis overlap with those of meningitis caused by viruses, mycobacteria, fungi, or protozoa. Differentiation of these disorders from

bacterial meningitis requires careful examination of cerebrospinal fluid (CSF) parameters (table 4) and neuroimaging (when indicated), as well as consideration of any epidemiologic factors that would raise the possibility of specific bacterial or nonbacterial central nervous system infections.

For patients with abnormal CSF findings, the differential diagnosis includes the following:

- Viral meningitis – Aseptic (usually viral) meningitis is a less severe disease that is often monitored in the outpatient setting without antimicrobial therapy, whereas bacterial meningitis is a life-threatening illness that requires hospital admission. Similar to bacterial meningitis, viral meningitis presents acutely with classic signs and symptoms of meningitis. Unlike bacterial meningitis, the CSF normally has a lymphocytic pleocytosis, normal glucose, moderate elevation of protein, and negative-CSF Gram stain and culture. Definitive diagnosis of viral meningitis is generally made by CSF polymerase chain reaction (PCR), although serologies are typically used for the diagnosis of meningitis due to arboviruses (eg, West Nile virus). (See "Aseptic meningitis in adults" and "Clinical manifestations and diagnosis of West Nile virus infection", section on 'Diagnosis'.)

- TB meningitis – Patients with tuberculous (TB) meningitis may have classic signs and symptoms of meningitis at presentation, however, it is generally a subacute process. CSF exam typically reveals a lymphocyte predominant pleocytosis with elevated protein and decreased glucose. Certain scoring systems (eg, the Lancet consensus scoring system and the Thwaites system) have been developed to help differentiate bacterial from TB meningitis [55]; these are based primarily on clinical and CSF findings. A definitive diagnosis of TB meningitis is made by identification of mycobacterium from the CSF either by culture or PCR. (See "Central nervous system tuberculosis: An overview".)

- Fungal meningitis – Several fungal species may cause meningitis including *Candida*, *Cryptococcus*, *Histoplasma*, *Blastomyces*, and *Coccidioides*. Although fungal meningitis may present with classic symptoms of meningitis, it often is a subacute process in patients with epidemiologic risk factors for fungal disease (eg, immunocompromise, HIV). (See "Candida infections of the central nervous system" and "Epidemiology, clinical manifestations, and diagnosis of Cryptococcus neoformans meningoencephalitis in patients with HIV" and "Clinical manifestations and diagnosis of Cryptococcus neoformans meningoencephalitis in patients without HIV" and "Coccidioidal meningitis" and "Diagnosis and treatment of disseminated histoplasmosis in patients without HIV" and "Approach to the patient with chronic meningitis".)

- Generalized seizures without meningitis – Generalized seizures may also induce a mild transient CSF pleocytosis, although this has not been well studied [56-58]. However, CSF pleocytosis should not be ascribed to seizure activity alone unless the fluid is clear and colorless, the opening pressure and CSF glucose are normal, the CSF Gram stain is negative, and the patient has no clinical evidence of bacterial meningitis.

When the Gram stain is negative, studies in both adults and children have concluded that, in the setting of an elevated CSF white blood cell (WBC) count, no single CSF biochemical variable can reliably exclude bacterial meningitis [41,47,59]. (See "Cerebrospinal fluid: Physiology and utility of an examination in disease states", section on 'CSF in CNS infection' and "Aseptic meningitis in adults".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Bacterial meningitis in adults".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or email these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Bacterial meningitis (The Basics)")

SUMMARY AND RECOMMENDATIONS

- **Etiologic agents** – The major causes of community-acquired bacterial meningitis in adults in developed countries are *Streptococcus pneumoniae*, *Neisseria meningitidis*, and, primarily in patients over age 50 years or those who have deficiencies in cell-mediated immunity, *Listeria monocytogenes*. The major causes of health care-associated bacterial meningitis are staphylococci and aerobic gram-negative bacilli. (See 'Epidemiology' above.)

- **Clinical features** – Patients with bacterial meningitis are usually quite ill and often present soon after symptom onset. (See 'Clinical features' above.)

  The classic triad of acute bacterial meningitis consists of fever, nuchal rigidity, and a change in mental status, usually of sudden onset. However, an appreciable number of patients do not have all three features. (See 'Presenting manifestations' above.)

- **Evaluation** – Acute bacterial meningitis should be suspected in adults who present with fever and signs of meningeal inflammation. The initial evaluation includes:

  - **Blood tests** – Initial blood tests should include a complete blood count with differential and platelet count and two aerobic blood cultures of appropriate volume (ideally, prior to the initiation of antimicrobial therapy). Serum electrolytes and glucose, blood urea nitrogen, and creatinine concentrations are helpful in determining the cerebrospinal fluid- (CSF) to-blood glucose ratio. Coagulation studies may be indicated, especially if petechiae or purpuric lesions are noted. Blood cultures are often positive and can be useful in the event that CSF cannot be obtained before the administration of antimicrobials. Approximately 50 to 90 percent of patients with bacterial meningitis have positive blood cultures. (See 'Blood tests' above.)

  - **Lumbar puncture** – Every patient with suspected meningitis should have CSF obtained unless a lumbar puncture (LP) is contraindicated. A CT scan is sometimes performed before LP to exclude a mass lesion or increased intracranial pressure, which rarely leads to cerebral herniation during subsequent CSF removal. However, a screening CT scan is not necessary in the majority of patients. (See 'Cerebrospinal fluid examination' above.)

  - **Indications for CT scan prior to LP** – A CT scan of the head before LP should be performed in adult patients with suspected bacterial meningitis who have one or more of the following risk factors (see 'Indications for CT scan before LP' above):

    - Immunocompromised state (eg, HIV infection, immunosuppressive therapy, solid organ or hematopoietic stem cell transplantation)

- History of central nervous system (CNS) disease (mass lesion, stroke, or focal infection)
- New onset seizure (within one week of presentation)
- Papilledema
- Abnormal level of consciousness
- Focal neurologic deficit

- **If LP is delayed or deferred** – If LP is delayed or deferred, blood cultures should be obtained and antimicrobial therapy should be administered empirically before the imaging study, followed as soon as possible by the LP. In addition, dexamethasone (0.15 mg/kg intravenously every six hours) should be given shortly before or at the same time as the antimicrobial agents if the preponderance of clinical and laboratory evidence suggests bacterial meningitis with a plan to stop therapy, if indicated, when the evaluation is complete. Adjunctive dexamethasone should not be given to patients who have already received antimicrobial therapy because it is unlikely to improve patient outcome. (See 'If LP is delayed or deferred' above.)

- **Diagnosis** – Isolation of a bacterial pathogen from the CSF (by culture or other diagnostic techniques) confirms the diagnosis of bacterial meningitis. Isolation of bacteria from blood cultures in a patient with CSF pleocytosis also confirms the diagnosis, even if the CSF culture remains negative. (See 'Diagnosis' above.)

  The usual CSF findings in patients with bacterial meningitis are a white blood cell (WBC) count of 1000 to 5000/microL (range of <100 to >10,000) with a percentage of neutrophils usually greater than 80 percent, protein of 100 to 500 mg/dL (1000 to 5000 mg/L), and glucose <40 mg/dL (2.22 mm/L; with a CSF:serum glucose ratio of ≤0.4). Despite these typical CSF findings, the spectrum of CSF values in bacterial meningitis is wide, and the absence of one of more of the typical findings does not rule out the diagnosis (table 4).

- **Differential diagnosis** – The clinical and laboratory findings of bacterial meningitis overlap with those of meningitis caused by viruses, mycobacteria, fungi, or protozoa. Differentiation of these disorders from bacterial meningitis requires careful examination of CSF parameters (table 4), neuroimaging (when indicated), as well as consideration of any epidemiologic factors that would raise the possibility of specific bacterial or nonbacterial CNS infections. (See 'Differential diagnosis' above.)

REFERENCES

1. Erdem H, Ozturk-Engin D, Cag Y, et al. Central nervous system infections in the absence of cerebrospinal fluid pleocytosis. Int J Infect Dis 2017; 65:107.
2. Tunkel AR, Hasbun R, Bhimraj A, et al. 2017 Infectious Diseases Society of America's Clinical Practice Guidelines for Healthcare-Associated Ventriculitis and Meningitis. Clin Infect Dis 2017.
3. Bijlsma MW, Brouwer MC, Kasanmoentalib ES, et al. Community-acquired bacterial meningitis in adults in the Netherlands, 2006-14: a prospective cohort study. Lancet Infect Dis 2016; 16:339.
4. van de Beek D, de Gans J, Spanjaard L, et al. Clinical features and prognostic factors in adults with bacterial meningitis. N Engl J Med 2004; 351:1849.
5. Weisfelt M, van de Beek D, Spanjaard L, et al. Community-acquired bacterial meningitis in older people. J Am Geriatr Soc 2006; 54:1500.
6. Aronin SI, Peduzzi P, Quagliarello VJ. Community-acquired bacterial meningitis: risk stratification for adverse clinical outcome and effect of antibiotic timing. Ann Intern Med 1998; 129:862.
7. Attia J, Hatala R, Cook DJ, Wong JG. The rational clinical examination. Does this adult patient have acute meningitis? JAMA 1999; 282:175.
8. Durand ML, Calderwood SB, Weber DJ, et al. Acute bacterial meningitis in adults. A review of 493 episodes. N Engl J Med 1993; 328:21.
9. Zoons E, Weisfelt M, de Gans J, et al. Seizures in adults with bacterial meningitis. Neurology 2008; 70:2109.
10. Schut ES, Lucas MJ, Brouwer MC, et al. Cerebral infarction in adults with bacterial meningitis. Neurocrit Care 2012; 16:421.
11. Gallegos C, Tobolowsky F, Nigo M, Hasbun R. Delayed Cerebral Injury in Adults With Bacterial Meningitis: A Novel Complication of Adjunctive Steroids? Crit Care Med 2018; 46:e811.
12. Mylonakis E, Hohmann EL, Calderwood SB. Central nervous system infection with Listeria monocytogenes. 33 years' experience at a general hospital and review of 776 episodes from the literature. Medicine (Baltimore) 1998; 77:313.
13. Charlier C, Perrodeau É, Leclercq A, et al. Clinical features and prognostic factors of listeriosis: the MONALISA national prospective cohort study. Lancet Infect Dis 2017; 17:510.

14. Heckenberg SG, de Gans J, Brouwer MC, et al. Clinical features, outcome, and meningococcal genotype in 258 adults with meningococcal meningitis: a prospective cohort study. Medicine (Baltimore) 2008; 87:185.
15. Pace D, Pollard AJ. Meningococcal disease: clinical presentation and sequelae. Vaccine 2012; 30 Suppl 2:B3.
16. Weisfelt M, van de Beek D, Spanjaard L, de Gans J. Arthritis in adults with community-acquired bacterial meningitis: a prospective cohort study. BMC Infect Dis 2006; 6:64.
17. Thomas KE, Hasbun R, Jekel J, Quagliarello VJ. The diagnostic accuracy of Kernig's sign, Brudzinski's sign, and nuchal rigidity in adults with suspected meningitis. Clin Infect Dis 2002; 35:46.
18. Uchihara T, Tsukagoshi H. Jolt accentuation of headache: the most sensitive sign of CSF pleocytosis. Headache 1991; 31:167.
19. Nakao JH, Jafri FN, Shah K, Newman DH. Jolt accentuation of headache and other clinical signs: poor predictors of meningitis in adults. Am J Emerg Med 2014; 32:24.
20. Tamune H, Takeya H, Suzuki W, et al. Absence of jolt accentuation of headache cannot accurately rule out meningitis in adults. Am J Emerg Med 2013; 31:1601.
21. Shrikanth V, Salazar L, Khoury N, et al. Hypoglycorrhachia in adults with community-acquired meningitis: etiologies and prognostic significance. Int J Infect Dis 2015; 39:39.
22. Thomas AE, Baird SF, Anderson J. Purpuric and petechial rashes in adults and children: initial assessment. BMJ 2016; 352:i1285.
23. Kaplan SL. Clinical presentations, diagnosis, and prognostic factors of bacterial meningitis. Infect Dis Clin North Am 1999; 13:579.
24. Kornelisse RF, Westerbeek CM, Spoor AB, et al. Pneumococcal meningitis in children: prognostic indicators and outcome. Clin Infect Dis 1995; 21:1390.
25. Brouwer MC, van de Beek D, Heckenberg SG, et al. Hyponatraemia in adults with community-acquired bacterial meningitis. QJM 2007; 100:37.
26. Geiseler PJ, Nelson KE, Levin S, et al. Community-acquired purulent meningitis: a review of 1,316 cases during the antibiotic era, 1954-1976. Rev Infect Dis 1980; 2:725.
27. Kanegaye JT, Soliemanzadeh P, Bradley JS. Lumbar puncture in pediatric bacterial meningitis: defining the time interval for recovery of cerebrospinal fluid pathogens after parenteral antibiotic pretreatment. Pediatrics 2001; 108:1169.
28. Rogers T, Sok K, Erickson T, et al. Impact of Antibiotic Therapy in the Microbiological Yield of Healthcare-Associated Ventriculitis and Meningitis. Open Forum Infect Dis 2019; 6:ofz050.

29. Brouwer MC, Thwaites GE, Tunkel AR, van de Beek D. Dilemmas in the diagnosis of acute community-acquired bacterial meningitis. Lancet 2012; 380:1684.
30. Hasbun R, Abrahams J, Jekel J, Quagliarello VJ. Computed tomography of the head before lumbar puncture in adults with suspected meningitis. N Engl J Med 2001; 345:1727.
31. Gopal AK, Whitehouse JD, Simel DL, Corey GR. Cranial computed tomography before lumbar puncture: a prospective clinical evaluation. Arch Intern Med 1999; 159:2681.
32. Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis 2004; 39:1267.
33. Salazar L, Hasbun R. Cranial Imaging Before Lumbar Puncture in Adults With Community-Acquired Meningitis: Clinical Utility and Adherence to the Infectious Diseases Society of America Guidelines. Clin Infect Dis 2017; 64:1657.
34. Park N, Nigo M, Hasbun R. Comparison of Four International Guidelines on the Utility of Cranial Imaging Before Lumbar Puncture in Adults with Bacterial Meningitis. Clin Neuroradiol 2022; 32:857.
35. Glimåker M, Johansson B, Grindborg Ö, et al. Adult bacterial meningitis: earlier treatment and improved outcome following guideline revision promoting prompt lumbar puncture. Clin Infect Dis 2015; 60:1162.
36. Glimåker M, Sjölin J, Åkesson S, Naucler P. Lumbar Puncture Performed Promptly or After Neuroimaging in Acute Bacterial Meningitis in Adults: A Prospective National Cohort Study Evaluating Different Guidelines. Clin Infect Dis 2018; 66:321.
37. Joffe AR. Lumbar puncture and brain herniation in acute bacterial meningitis: a review. J Intensive Care Med 2007; 22:194.
38. van de Beek D, Cabellos C, Dzupova O, et al. ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. Clin Microbiol Infect 2016; 22 Suppl 3:S37.
39. Blazer S, Berant M, Alon U. Bacterial meningitis. Effect of antibiotic treatment on cerebrospinal fluid. Am J Clin Pathol 1983; 80:386.
40. van de Beek D, Brouwer M, Hasbun R, et al. Community-acquired bacterial meningitis. Nat Rev Dis Primers 2016; 2:16074.
41. Spanos A, Harrell FE Jr, Durack DT. Differential diagnosis of acute meningitis. An analysis of the predictive value of initial observations. JAMA 1989; 262:2700.
42. Montes K, Jenkinson H, Habib OB, et al. Corrected white blood cell count, cell index, and validation of a clinical model for the diagnosis of health care-associated ventriculitis and meningitis in adults with intracranial hemorrhage. Clin Neurol Neurosurg 2019; 178:36.

43. Hasbun R, Tunkel AR. Approach to the patient with central nervous system infection. In: Principles and Practice of Infectious Diseases, 9th ed, Bennett JE, Dolin R, Blaser MJ (Eds), Elsevier Saunders, Philadelphia 2020. p.1176.
44. Sakushima K, Hayashino Y, Kawaguchi T, et al. Diagnostic accuracy of cerebrospinal fluid lactate for differentiating bacterial meningitis from aseptic meningitis: a meta-analysis. J Infect 2011; 62:255.
45. Huy NT, Thao NT, Diep DT, et al. Cerebrospinal fluid lactate concentration to distinguish bacterial from aseptic meningitis: a systemic review and meta-analysis. Crit Care 2010; 14:R240.
46. Srihawan C, Castelblanco RL, Salazar L, et al. Clinical Characteristics and Predictors of Adverse Outcome in Adult and Pediatric Patients With Healthcare-Associated Ventriculitis and Meningitis. Open Forum Infect Dis 2016; 3:ofw077.
47. Fitch MT, van de Beek D. Emergency diagnosis and treatment of adult meningitis. Lancet Infect Dis 2007; 7:191.
48. Saha SK, Darmstadt GL, Yamanaka N, et al. Rapid diagnosis of pneumococcal meningitis: implications for treatment and measuring disease burden. Pediatr Infect Dis J 2005; 24:1093.
49. Werno AM, Murdoch DR. Medical microbiology: laboratory diagnosis of invasive pneumococcal disease. Clin Infect Dis 2008; 46:926.
50. Tzanakaki G, Tsopanomichalou M, Kesanopoulos K, et al. Simultaneous single-tube PCR assay for the detection of Neisseria meningitidis, Haemophilus influenzae type b and Streptococcus pneumoniae. Clin Microbiol Infect 2005; 11:386.
51. Leber AL, Everhart K, Balada-Llasat JM, et al. Multicenter Evaluation of BioFire FilmArray Meningitis/Encephalitis Panel for Detection of Bacteria, Viruses, and Yeast in Cerebrospinal Fluid Specimens. J Clin Microbiol 2016; 54:2251.
52. McGill F, Heyderman RS, Michael BD, et al. The UK joint specialist societies guideline on the diagnosis and management of acute meningitis and meningococcal sepsis in immunocompetent adults. J Infect 2016; 72:405.
53. González-Donapetry P, García-Rodríguez J, Cendejas-Bueno E. A case of a FilmArray® ME false negative in meningococcal meningitis. J Infect 2019; 79:277.
54. Bodilsen J, Brandt CT, Sharew A, et al. Early versus late diagnosis in community-acquired bacterial meningitis: a retrospective cohort study. Clin Microbiol Infect 2018; 24:166.
55. Sulaiman T, Medi S, Erdem H, et al. The diagnostic utility of the "Thwaites' system" and "lancet consensus scoring system" in tuberculous vs. non-tuberculous subacute and

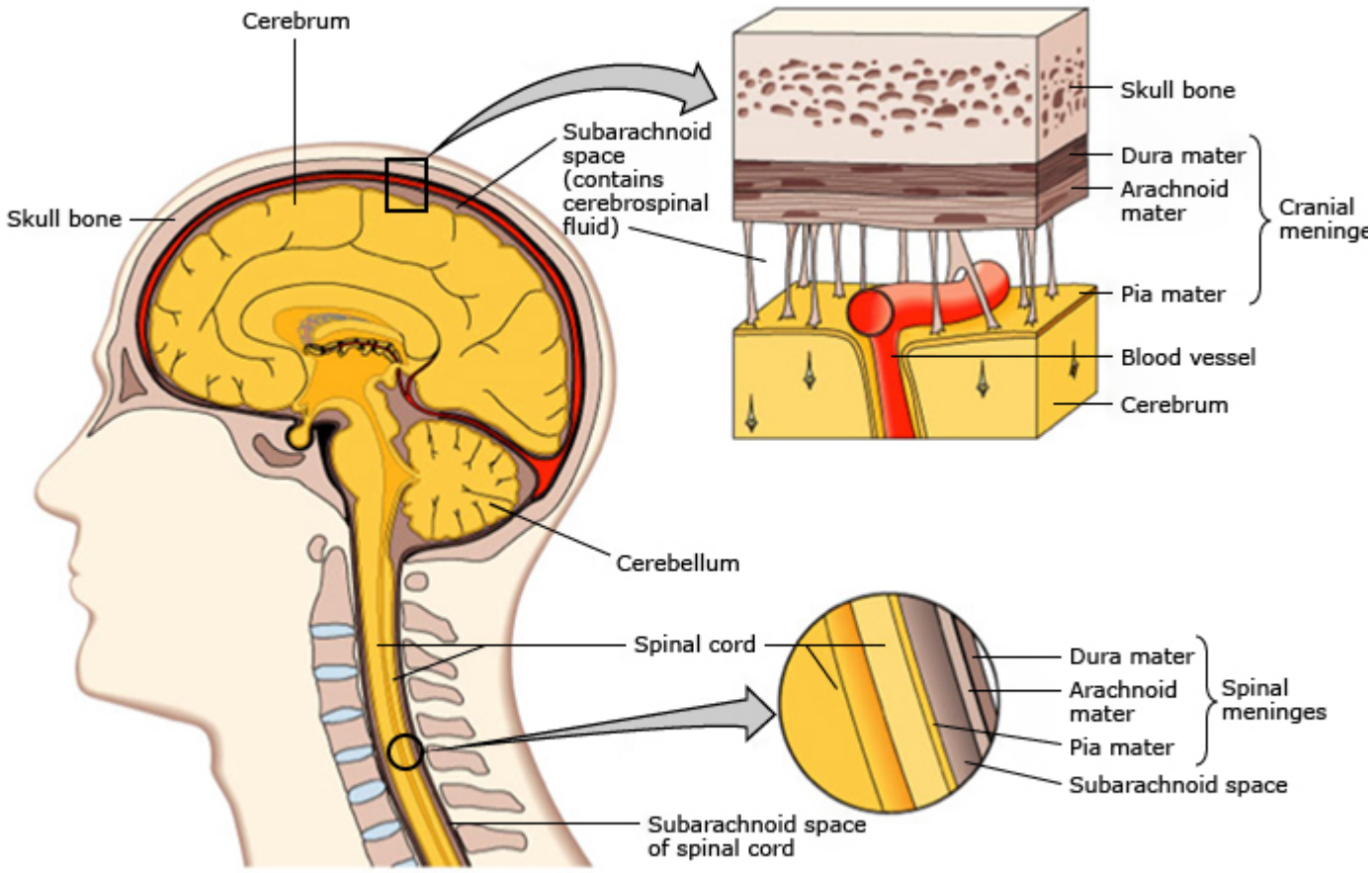
chronic meningitis: multicenter analysis of 395 adult patients. BMC Infect Dis 2020; 20:788.

56. Schmidley JW, Simon RP. Postictal pleocytosis. Ann Neurol 1981; 9:81.
57. Edwards R, Schmidley JW, Simon RP. How often does a CSF pleocytosis follow generalized convulsions? Ann Neurol 1983; 13:460.
58. Tumani H, Jobs C, Brettschneider J, et al. Effect of epileptic seizures on the cerebrospinal fluid--A systematic retrospective analysis. Epilepsy Res 2015; 114:23.
59. Negrini B, Kelleher KJ, Wald ER. Cerebrospinal fluid findings in aseptic versus bacterial meningitis. Pediatrics 2000; 105:316.

Topic 1287 Version 36.0

GRAPHICS

Meningeal layers of the brain and spinal cord



Graphic 126644 Version 1.0

Characteristic features of common causes of bacterial meningitis

Organism	Site of entry	Age range	Predisposing conditions
Neisseria meningitidis	Nasopharynx	All ages	Usually none, rarely complement deficiency
Streptococcus pneumoniae	Nasopharynx, direct extension across skull fracture, or from contiguous or distant foci of infection	All ages	All conditions that predispose to pneumococcal bacteremia, fracture of cribriform plate, cochlear implants, cerebrospinal fluid otorrhea from basila skull fracture, defects of the ear ossicle (Mondini defect)
Listeria monocytogenes	Gastrointestinal tract, placenta	Older adults and neonates	Defects in cell-mediated immunity (eg, glucocorticoids, transplantation [especially renal transplantation]), pregnancy, liver disease, alcoholism, malignancy
Coagulase-negative staphylococci	Foreign body	All ages	Surgery and foreign body, especially ventricular drains; dermal sinus
Staphylococcus aureus	Bacteremia, foreign body, skin	All ages	Endocarditis; surgery and foreign body, especially ventricular drains; cellulitis; dermal sinus; decubitus ulcer
Gram-negative bacilli	Various	Older adults and neonates	Advanced medical illness, neurosurgery, ventricular drains, disseminated strongyloidiasis
Haemophilus influenzae	Nasopharynx, contiguous spread from local infection	Adults; infants and children if not vaccinated	Diminished humoral immunity

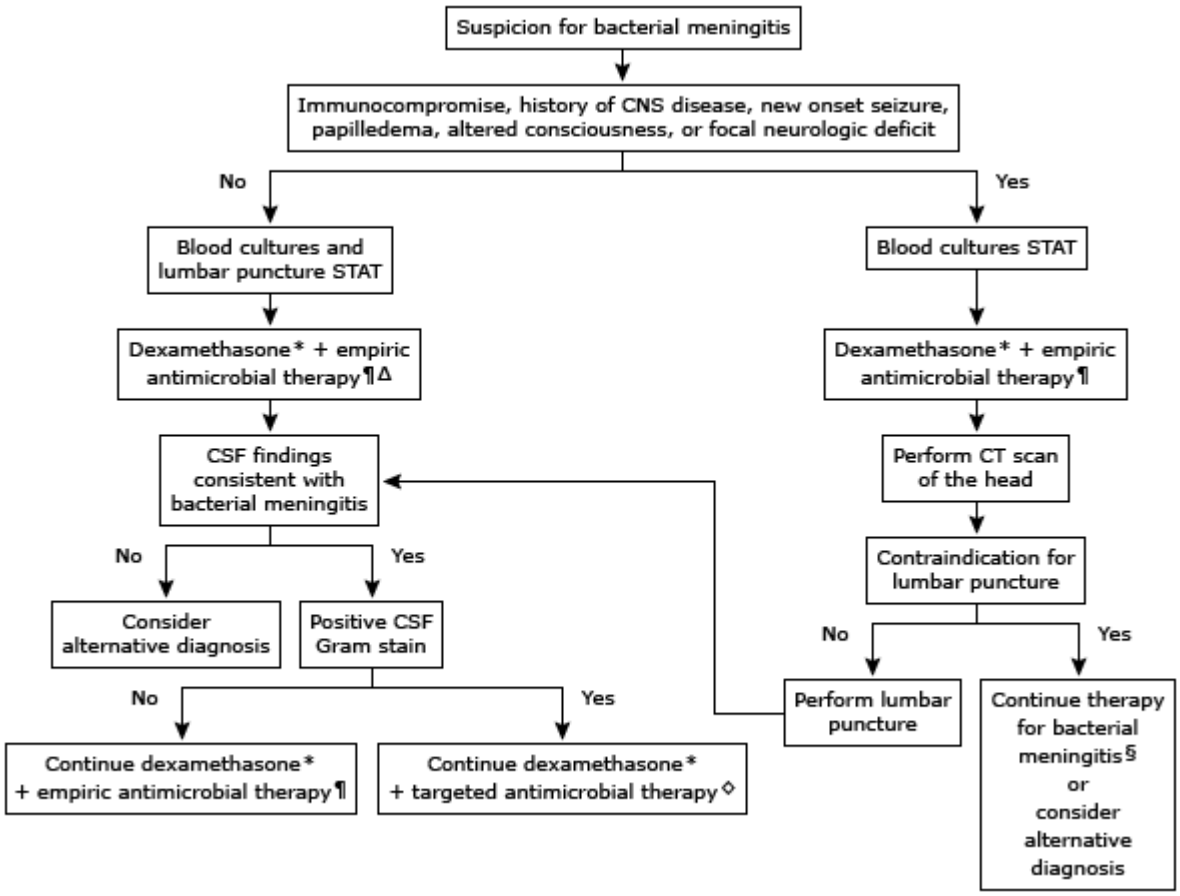
Graphic 73706 Version 9.0

Signs of meningeal irritation

Signs of meningeal irritation	Maneuver	Positive test
Kernig sign	Place patient supine with hip flexed at 90 degrees. Attempt to extend the leg at the knee.	The test is positive when there is resistance to extension at the knee to >135 degrees or pain in the lower back or posterior thigh
Brudzinski sign	Place patient in the supine position and passively flex the head toward the chest.	The test is positive when there is flexion of the knees and hips of the patient.
Jolt accentuation of headache	Patient rotates his/her head horizontally two to three times per second.	The test is positive if the patient reports exacerbation of his/her headache with this maneuver.

Graphic 82677 Version 4.0

Management algorithm for adults with suspected bacterial meningitis



"STAT" indicates that the intervention should be done emergently.

CNS: central nervous system; CSF: cerebrospinal fluid; CT: computed tomography.

* Refer to UpToDate topic review on dexamethasone to prevent neurologic complications of bacterial meningitis in adults for specific recommendations.

¶ Refer to UpToDate table on recommendations for empiric antimicrobial therapy for purulent meningitis based on patient age and specific predisposing condition.

Δ Administer dexamethasone and antibiotic therapy immediately after CSF is obtained.

◇ Refer to UpToDate table on recommendations for antimicrobial therapy in adults with presumptive pathogen identification by positive Gram stain.

§ If the diagnosis of bacterial meningitis is likely.

Graphic 50114 Version 5.0

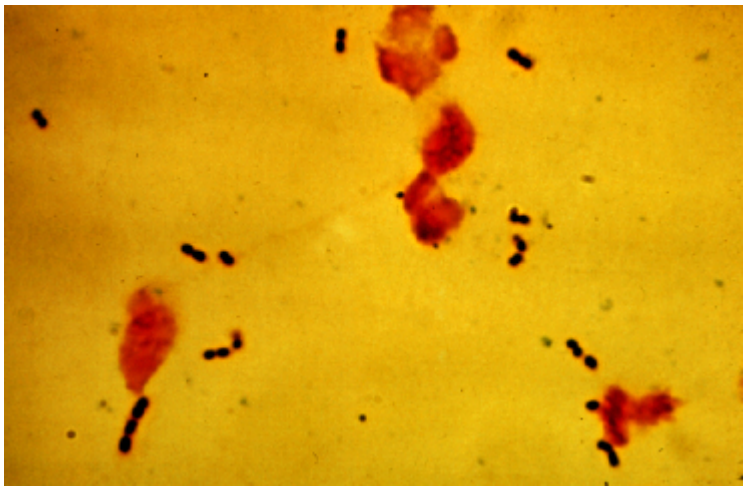
Glasgow Coma Scale (GCS)

	Score
Eye opening	
Spontaneous	4
Response to verbal command	3
Response to pain	2
No eye opening	1
Best verbal response	
Oriented	5
Confused	4
Inappropriate words	3
Incomprehensible sounds	2
No verbal response	1
Best motor response	
Obeys commands	6
Localizing response to pain	5
Withdrawal response to pain	4
Flexion to pain	3
Extension to pain	2
No motor response	1
Total	

The GCS is scored between 3 and 15, 3 being the worst and 15 the best. It is composed of three parameters: best eye response (E), best verbal response (V), and best motor response (M). The components of the GCS should be recorded individually; for example, E2V3M4 results in a GCS score of 9. A score of 13 or higher correlates with mild brain injury, a score of 9 to 12 correlates with moderate injury, and a score of 8 or less represents severe brain injury.

Graphic 81854 Version 9.0

Streptococcus pneumoniae in cerebrospinal fluid

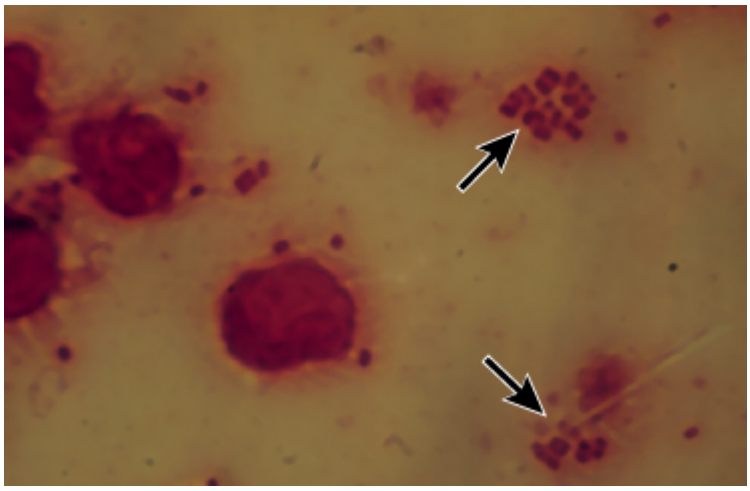


Gram stain of cerebrospinal fluid (x1000) shows inflammatory cells and gram-positive diplococci. *Streptococcus pneumoniae* grew from this specimen.

Courtesy of Harriet Provine.

Graphic 72926 Version 6.0

Neisseria meningitidis in cerebrospinal fluid

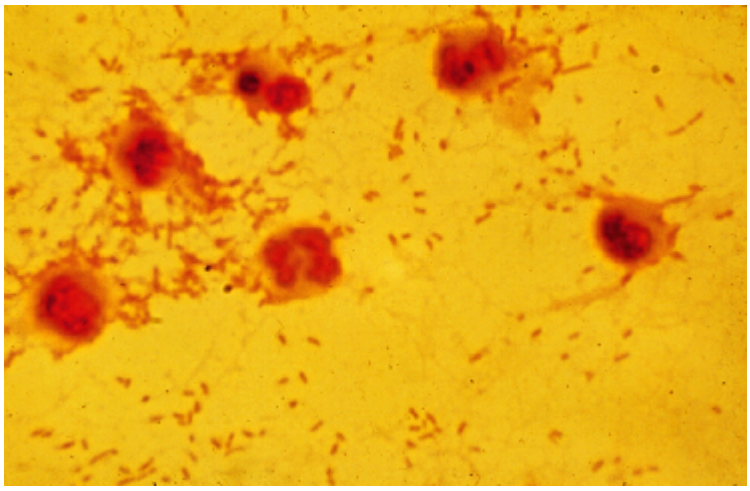


Gram stain of cerebrospinal fluid (×1000) shows inflammatory cells and kidney-shaped, gram-negative diplococci (arrows). *Neisseria meningitidis* grew from this specimen.

Courtesy of Harriet Provine.

Graphic 61788 Version 5.0

Haemophilus influenzae in cerebrospinal fluid

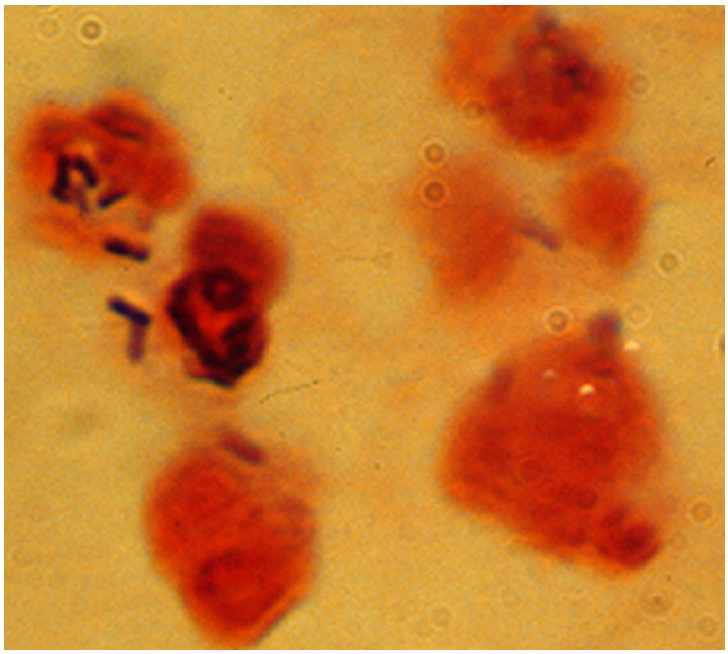


Gram stain of cerebrospinal fluid (x1000) shows inflammatory cells and small, pleomorphic, gram-negative coccobacilli. *Haemophilus influenzae* grew from this specimen.

Courtesy of Harriet Provine.

Graphic 52680 Version 5.0

Listeria monocytogenes in cerebrospinal fluid



Gram stain of cerebrospinal fluid (x1000) shows inflammatory cells and small, gram-positive rods and coccobacilli. Culture of this specimen revealed moderate-sized beta-hemolytic colonies composed of small, motile gram-positive rods, confirmed to be *Listeria monocytogenes*.

Courtesy of Harriet Provine.

Graphic 79633 Version 6.0

Typical cerebrospinal fluid findings in central nervous system infections*

	Glucose (mg/dL)		Protein (mg/dL)		Total white blood cell (cells/microL)		
	<10¶	10 to 40Δ	100 to 500◇	50 to 300§	>1000	100 to 1000	
More common	Bacterial meningitis	Bacterial meningitis	Bacterial meningitis	Viral meningitis Nervous system Lyme disease (neuroborreliosis) Encephalitis Neurosyphilis TB meningitis¥	Bacterial meningitis	Bacterial or viral meningitis TB meningitis	Ea ba me Vir me Ne TB me
Less common	TB meningitis Fungal meningitis	Neurosyphilis Some viral infections (such as mumps and LCMV)		Early bacterial meningitis	Some cases of mumps and LCMV	Encephalitis	En

TB: tuberculosis; LCMV: lymphocytic choriomeningitis virus.

* It is important to note that the spectrum of cerebrospinal fluid values in bacterial meningitis is so wide that the absence of one or more of these findings is of little value. Refer to the UpToDate topic reviews on bacterial meningitis for additional details.

¶ <0.6 mmol/L.

Δ 0.6 to 2.2 mmol/L.

◇ 1 to 5 g/L.

§ 0.5 to 3 g/L.

¥ Cerebrospinal fluid protein concentrations may be higher in some patients with tuberculous meningitis; concentrations >500 mg/dL are an indication of blood-brain barrier disruption or increased intracerebral production of immunoglobulins, and extremely high concentrations, in the range of 2 to 6 g/dL, may be found in association with subarachnoid block.

Graphic 76324 Version 11.0