PRACTICE GUIDELINES FOR THE MANAGEMENT OF BACTERIAL MENINGITIS.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Each recommendation includes a ranking for the strength and the quality of evidence supporting it, as well as performance indicators. Definitions of the levels of evidence (I-III) and grades of recommendation (A-E) are repeated at the end of the "Major Recommendations" field.

Initial Management Approach

The initial treatment approach to the patient with suspected acute bacterial meningitis depends on early recognition of the meningitis syndrome, rapid diagnostic evaluation, and emergent antimicrobial and adjunctive therapy. The management algorithm for infants and children is shown in figure 1 in the original guideline document, and that for adults is shown in figure 2 of the original guideline document. Once there is suspicion of acute bacterial meningitis, blood samples must be obtained for culture and a lumbar puncture performed immediately to determine whether the cerebrospinal fluid (CSF) formula is consistent with the clinical diagnosis. In some patients, the clinician may not emergently perform the diagnostic lumbar puncture (e.g., secondary to the inability to obtain CSF), even when the diagnosis of bacterial meningitis is considered to be likely, or the clinician may be concerned that the clinical presentation is consistent with a central nervous system (CNS) mass lesion or another cause of increased intracranial pressure and will thus order a computed tomography (CT) scan of the head prior to lumbar puncture. In those patients in whom lumbar puncture is delayed or a CT scan is performed, however, there may be a significant interval between establishing the diagnosis of bacterial meningitis and initiating appropriate therapy. In these patients, blood samples must be obtained for culture and appropriate antimicrobial and adjunctive therapy given prior to lumbar puncture or before the patient is sent for CT. Delay in the initiation of therapy introduces the potential for increased morbidity and mortality, if the patient does indeed have acute bacterial meningitis. The choice of empirical antimicrobial therapy in this situation should be governed by the patient's age and by various conditions that may have predisposed the patient to meningitis. Although the yield of CSF cultures and CSF Gram stain may be diminished by antimicrobial therapy given prior to lumbar puncture, pretreatment blood cultures and CSF findings (i.e., elevated white blood cell [WBC] count, diminished glucose concentration, and elevated protein concentration) will likely provide evidence for or against the diagnosis of bacterial meningitis (see "What Specific CSF Diagnostic Tests Should Be Used to Determine the Bacterial Etiology of Meningitis?" below). Once CSF analysis is performed, for patients with a positive CSF Gram stain result, targeted antimicrobial therapy can be initiated in adults with bacterial meningitis. In children >1 month of age with bacterial meningitis, however, empirical antimicrobial therapy with vancomycin combined with either cefotaxime or ceftriaxone can be provided pending culture results;

this recommendation is based on the concern that interpretation of the CSF Gram stain depends on the expertise of the person reading the slide; some experts would also use this strategy in adults with bacterial meningitis. However, a positive CSF Gram stain result may modify this approach by the addition of another agent (e.g., ampicillin for the presence of gram-positive bacilli) to these 2 standard drugs. If the Gram stain result is negative, empirical antimicrobial therapy is given, with choices of agents based on the patient age and certain predisposing conditions.

Which Patients with Suspected Bacterial Meningitis Should Undergo CT of the Head prior to Lumbar Puncture?

Recommended Criteria for Adult Patients with Suspected Bacterial Meningitis Who Should Undergo CT Prior to Lumbar Puncture (B-II)

Criterion	Comment
Immunocompromised state	Human immunodeficiency virus (HIV) infection or acquired immunodeficiency syndrome (AIDS), receiving immunosuppressive therapy, or after transplantation
History of CNS disease	Mass lesion, stroke, or focal infection
New onset seizure	Within 1 week of presentation; some authorities would not perform a lumbar puncture on patients with prolonged seizures or would delay lumbar puncture for 30 minutes in patients with short, convulsive seizures
Papilledema	Presence of venous pulsations suggests absence of increased intracranial pressure
Abnormal level of consciousness	...
Focal neurologic deficit	Including dilated nonreactive pupil, abnormalities of ocular motility, abnormal visual fields, gaze palsy, arm or leg drift

What Specific CSF Diagnostic Tests Should Be Used to Determine the Bacterial Etiology of Meningitis?

Several rapid diagnostic tests should be considered to determine the bacterial etiology of meningitis.

Gram Stain

The Practice Guideline Committee recommends that all patients being evaluated for suspected meningitis undergo a Gram stain examination of CSF **(A-III)**.

Latex Agglutination

Given that bacterial antigen testing does not appear to modify the decision to administer antimicrobial therapy and that false-positive results have been reported, the Practice Guideline Committee does not recommend routine use of this modality for the rapid determination of the bacterial etiology of meningitis **(D-II)**, although some would recommend it for patients with a negative CSF Gram stain result **(C-II)**. Latex agglutination may be most useful for the patient who has been pretreated with antimicrobial therapy and whose Gram stain and CSF culture results are negative **(B-III)**.

Limulus Lysate Assay

The Practice Guideline Committee does not recommend routine use of the *Limulus* lysate assay for patients with meningitis **(D-II)**.

Polymerase Chain Reaction (PCR)

Broad-based PCR may be useful for excluding the diagnosis of bacterial meningitis, with the potential for influencing decisions to initiate or discontinue antimicrobial therapy. Although PCR techniques appear to be promising for the etiologic diagnosis of bacterial meningitis, further refinements of the available techniques may lead to their use in patients with bacterial meningitis for whom the CSF Gram stain result is negative **(B-II)**.

What Laboratory Testing May Be Helpful in Distinguishing Bacterial from Viral Meningitis?

Determination of Lactate Concentration

Measurement of CSF lactate concentration is not recommended for patients with suspected community-acquired bacterial meningitis **(D-III)**

However, measurement of CSF lactate concentrations was found to be superior to use of the ratio of CSF to blood glucose for the diagnosis of bacterial meningitis in postoperative neurosurgical patients, in which a CSF concentration of 4.0 mmol/ L was used as a cutoff value for the diagnosis. The sensitivity was 88%, the specificity was 98%, the positive predictive value was 96%, and the negative predictive value was 94%. CSF lactate concentrations may be valuable in this subgroup of patients, in whom the usual CSF findings--elevated white blood cell (WBC) counts (total and differential), positive Gram stain results, diminished glucose concentrations, and elevated protein concentrations--are neither sensitive nor specific to reliably distinguish bacterial from a nonbacterial meningeal syndrome. Therefore, in the postoperative neurosurgical patient, initiation of empirical antimicrobial therapy should be considered if CSF lactate concentrations are $\geq$ 4.0 mmol/L, pending results of additional studies **(B-II)**.

Determination of C-reactive Protein (CRP) Concentration

Measurement of serum CRP concentration may be helpful in patients with CSF findings consistent with meningitis, but for whom the Gram stain result is negative and the physician is considering withholding antimicrobial therapy, on the basis of the data showing that a normal CRP has a high negative predictive value in the diagnosis of bacterial meningitis **(B-II)**.

Determination of Procalcitonin Concentration

At present, because measurement of serum procalcitonin concentrations is not readily available in clinical laboratories, recommendations on its use cannot be made at this time **(C-II)**.

Polymerase Chain Reaction

In patients who present with acute meningitis, an important diagnostic consideration is whether the patient has enteroviral meningitis. Rapid detection of enteroviruses by PCR has emerged as a valuable technique that may be helpful in establishing the diagnosis of enteroviral meningitis. Enteroviral reverse transcription (RT)-PCR has been tested in clinical settings by numerous investigators and has been found to be more sensitive than viral culture for the detection of enterovirus, with a sensitivity and specificity of 86-100% and 92-100%, respectively. In addition, the time to identification of the enterovirus using RT-PCR is significantly reduced (from hours to a day), compared with cell culture, which may lead to shortened patient hospitalization, decreased use of antimicrobial therapy for treatment of presumed bacterial meningitis, and reduced need for ancillary diagnostic tests **(B-II)**.

How Quickly Should Antimicrobial Therapy Be Administered to Patients with Suspected Bacterial Meningitis?

On the basis of the available evidence, the Practice Guideline Committee thinks 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 **(C-III)**. That being said, bacterial meningitis is a neurologic emergency, and appropriate therapy (see "What Specific Antimicrobial Agents Should Be Used in Patients with Suspected or Proven Bacterial Meningitis?" below) should be initiated as soon as possible after the diagnosis is considered to be likely.

What Specific Antimicrobial Agents Should Be Used in Patients with Suspected or Proven Bacterial Meningitis?

Once the diagnosis of bacterial meningitis is established by CSF analysis, antimicrobial therapy should be initiated. Targeted antimicrobial therapy is based on presumptive pathogen identification by CSF Gram stain (see "Recommendations for Antimicrobial Therapy in Adult Patients with Presumptive Pathogen Identification by Positive Gram Stain" below), although (as stated above) the combination of vancomycin plus either ceftriaxone or cefotaxime is used for infants and children--and recommended by some experts for adults--with suspected bacterial meningitis. Empirical antimicrobial therapy is initiated either when the lumbar puncture is delayed (e.g., in those patients sent for

CT of the head [see "Which Patients with Suspected Bacterial Meningitis Should Undergo CT of the Head prior to Lumbar Puncture?" above]) or for patients with purulent meningitis and a negative CSF Gram stain result (see below). The choice of specific antimicrobial agents for targeted or empirical therapy is based on the current knowledge of antimicrobial susceptibility patterns of these pathogens. For initial therapy, the assumption should be that antimicrobial resistance is likely. Evidence-based recommendations for specific agents and dosages are reviewed below in "Recommendations for Specific Antimicrobial Therapy in Bacterial Meningitis Based on Isolated Pathogen and Susceptibility Testing" and in "Recommended Dosages of Antimicrobial Therapy in Patients with Bacterial Meningitis" (Table 6 in the original guideline document).

Recommendations for Antimicrobial Therapy in Adult Patients with Presumptive Pathogen Identification by Positive Gram Stain

Microorganism	Recommended therapy	Alternative therapies
Streptococcus pneumoniae	Vancomycin plus a third-generation cephalosporin[a,b]	Meropenem **(C-III)**, fluoroquinolone[c] **(B-II)**
Neisseria meningitidis	Third-generation cephalosporin[a]	Penicillin G, ampicillin, chloramphenicol, fluoroquinolone, aztreonam
Listeria monocytogenes	Ampicillin[d] or penicillin G[d]	Trimethoprim-sulfamethoxazole, meropenem **(B-III)**
Streptococcus agalactiae	Ampicillin[d] or penicillin G[d]	Third-generation cephalosporin[a] **(B-III)**
Haemophilus influenzae	Third-generation cephalosporin[a] **(A-I)**	Chloramphenicol, cefepime **(A-I)**, meropenem **(A-I)**, fluoroquinolone
Escherichia coli	Third-generation cephalosporin[a] **(A-II)**	Cefepime, meropenem, aztreonam, fluoroquinolone, trimethoprim-sulfamethoxazole

NOTE. All recommendations are **A-III**, unless otherwise indicated. In children, ampicillin is added to the standard therapeutic regimen of cefotaxime or ceftriaxone plus vancomycin when *L. monocytogenes* is considered and to an aminoglycoside if a gram-negative enteric pathogen is of concern.

[a] Ceftriaxone or cefotaxime
[b] Some experts would add rifampin if dexamethasone is also given **(B-III)**.
[c] Gatifloxacin or moxifloxacin
[d] Addition of an aminoglycoside should be considered.

Recommendations for Empirical Antimicrobial Therapy for Purulent Meningitis Based on Patient Age and Specific Predisposing Condition (A-III)

Predisposing factor	Common bacterial pathogens	Antimicrobial therapy
Age		
<1 month	*Streptococcus agalactiae, Escherichia coli, Listeria monocytogenes, Klebsiella* species	Ampicillin plus cefotaxime or ampicillin plus an aminoglycoside
1-23 months	*Streptococcus pneumoniae, Neisseria meningitidis, S. agalactiae, Haemophilus influenzae, E. coli*	Vancomycin plus a third-generation cephalosporin[a,b]
2-50 years	*N. meningitidis, S. pneumoniae*	Vancomycin plus a third-generation cephalosporin[a,b]
>50 years	*S. pneumoniae, N. meningitidis, L. monocytogenes, aerobic gram-negative bacilli*	Vancomycin plus ampicillin plus a third-generation cephalosporin[a,b]
Head trauma		
Basilar skull fracture	*S. pneumoniae, H. influenzae*, group A beta-hemolytic streptococci	Vancomycin plus a third-generation cephalosporin[a]
Penetrating trauma	*Staphylococcus aureus*, coagulase-negative staphylococci (especially *Staphylococcus epidermidis*), aerobic gram-negative bacilli (including *Pseudomonas aeruginosa*)	Vancomycin plus cefepime, vancomycin plus ceftazidime, or vancomycin plus meropenem
Postneurosurgery	Aerobic gram-negative bacilli (including *P. aeruginosa*), *S. aureus*, coagulase-negative staphylococci (*especially S. epidermidis*)	Vancomycin plus cefepime, vancomycin plus ceftazidime, or vancomycin plus meropenem
CSF shunt	Coagulase-negative staphylococci (especially *S. epidermidis*), *S. aureus*, aerobic gram-negative bacilli (including	Vancomycin plus cefepime,[c] vancomycin plus

Predisposing factor	Common bacterial pathogens	Antimicrobial therapy
	P. aeruginosa), *Propionibacterium acnes*	ceftazidime,[c] or vancomycin plus meropenem[c]

[a] Ceftriaxone or cefotaxime
[b] Some experts would add rifampin if dexamethasone is also given.
[c] In infants and children, vancomycin alone is reasonable unless Gram stains reveal the presence of gram-negative bacilli.

Recommendations for Specific Antimicrobial Therapy in Bacterial Meningitis Based on Isolated Pathogen and Susceptibility Testing

Microorganism, susceptibility	Standard therapy	Alternative therapies
Streptococcus pneumoniae		
Penicillin minimum inhibitory concentration (MIC)		
<0.1 micrograms/mL	Penicillin G or ampicillin	Third-generation cephalosporin,[a] chloramphenicol
0.1-1.0 micrograms/mL[b]	Third-generation cephalosporin[a]	Cefepime **(B-II)**, meropenem **(B-II)**
≥2.0 micrograms/mL	Vancomycin plus a third-generation cephalosporin[a,c]	Fluoroquinolone[d] **(B-II)**
Cefotaxime or ceftriaxone MIC ≥1.0 micrograms/mL	Vancomycin plus a third-generation cephalosporin[a,c]	Fluoroquinolone[d] **(B-II)**
Neisseria meningitidis		
Penicillin MIC		
<0.1 micrograms/mL	Penicillin G or ampicillin	Third-generation cephalosporin,[a] chloramphenicol

Microorganism, susceptibility	Standard therapy	Alternative therapies
0.1-1.0 micrograms/mL	Third-generation cephalosporin[a]	Chloramphenicol, fluoroquinolone, meropenem
Listeria monocytogenes	Ampicillin or penicillin G[e]	Trimethoprim-sulfamethoxazole, meropenem **(B-III)**
Streptococcus agalactiae	Ampicillin or penicillin G[e]	Third-generation cephalosporin[a] **(B-III)**
Escherichia coli and other Enterobacteriaceae[g]	Third-generation cephalosporin **(A-II)**	Aztreonam, fluoroquinolone, meropenem, trimethoprim-sulfamethoxazole, ampicillin
Pseudomonas aeruginosa[g]	Cefepime[e] or ceftazidime[e] **(A-II)**	Aztreonam,[e] ciprofloxacin,[e] meropenem[e]
Haemophilus influenzae		
beta-Lactamase negative	Ampicillin	Third-generation cephalosporin[a], cefepime, chloramphenicol, fluoroquinolone
beta-Lactamase positive	Third-generation cephalosporin **(A-I)**	Cefepime **(A-I),** chloramphenicol, fluoroquinolone
Staphylococcus aureus		
Methicillin susceptible	Nafcillin or oxacillin	Vancomycin, meropenem **(B-III)**
Methicillin resistant	Vancomycin[f]	Trimethoprim-sulfamethoxazole, linezolid **(B-III)**
Staphylococcus epidermidis	Vancomycin[f]	Linezolid **(B-III)**
Enterococcus species		
Ampicillin susceptible	Ampicillin plus gentamicin	...
Ampicillin resistant	Vancomycin plus	...

Microorganism, susceptibility	Standard therapy	Alternative therapies
	gentamicin	
Ampicillin and vancomycin resistant	Linezolid **(B-III)**	...

NOTE. All recommendations are **A-III**, unless otherwise indicated.

[a] Ceftriaxone or cefotaxime
[b] Ceftriaxone/cefotaxime-susceptible isolates
[c] Consider addition of rifampin if the MIC of ceftriaxone is >2 micrograms/mL.
[d] Gatifloxacin or moxifloxacin
[e] Addition of an aminoglycoside should be considered.
[f] Consider addition of rifampin.
[g] Choice of a specific antimicrobial agent must be guided by in vitro susceptibility test results.

Please see Table 6 in the original guideline document for recommended dosages of antimicrobial therapy in patients with bacterial meningitis.

What Is the Role of Adjunctive Dexamethasone Therapy in Patients with Bacterial Meningitis?

Neonates

At present, there are insufficient data to make a recommendation on the use of adjunctive dexamethasone in neonates with bacterial meningitis **(C-I)**

Infants and Children

Despite some variability in result of published trials, the Practice Guideline Committee believes the available evidence supports the use of adjunctive dexamethasone in infants and children with *H. influenzae* type b meningitis **(A-I)**. Dexamethasone should be initiated 10-20 min prior to, or at least concomitant with, the first antimicrobial dose, at 0.15 mg/kg every 6 h for 2-4 days. Adjunctive dexamethasone should not be given to infants and children who have already received antimicrobial therapy, because administration of dexamethasone in this circumstance is unlikely to improve patient outcome **(A-I)**. In infants and children with pneumococcal meningitis, there is controversy concerning the use of adjunctive dexamethasone therapy **(C-II)**. The 2003 statement by the Committee on Infectious Diseases of the American Academy of Pediatrics on the use of steroids for pneumococcal meningitis is as follows: "For infants and children 6 weeks of age and older, adjunctive therapy with dexamethasone may be considered after weighing the potential benefits and possible risks. Experts vary in recommending the use of corticosteroids in pneumococcal meningitis; data are not sufficient to demonstrate clear benefit in children." Furthermore, the incidence of

pneumococcal meningitis in children has decreased dramatically since the recommendation for use of the 7-valent pneumococcal conjugate vaccine, and it is unlikely that the efficacy of adjunctive dexamethasone will be determined definitively in further randomized trials conducted in the United States.

Adults

On the basis of the available evidence on the use of adjunctive dexamethasone in adults, the Practice Guideline Committee recommends use of dexamethasone (0.15 mg/kg every 6 h for 2-4 days with the first dose administered 10-20 min before, or at least concomitant with, the first dose of antimicrobial therapy) in adults with suspected or proven pneumococcal meningitis **(A-I)**. Some experts would only administer adjunctive dexamethasone if the patient had moderate-to-severe disease (Glasgow Coma Scale score $\leq$11). However, the Practice Guideline Committee thinks that adjunctive dexamethasone should be initiated in all adult patients with suspected or proven pneumococcal meningitis, because assessment of the score may delay initiation of appropriate therapy. Dexamethasone should only be continued if the CSF Gram stain reveals gram-positive diplococci, or if blood or CSF cultures are positive for *S. pneumoniae*. Adjunctive dexamethasone should not be given to adult patients who have already received antimicrobial therapy, because administration of dexamethasone in this circumstance is unlikely to improve patient outcome **(A-I)**. The data are inadequate to recommend adjunctive dexamethasone to adults with meningitis caused by other bacterial pathogens, although some authorities would initiate dexamethasone in all adults, because the etiology of meningitis is not always ascertained at initial evaluation **(B-III)**.

Pneumococcal Meningitis

The Practice Guideline Committee recommends that adjunctive dexamethasone be administered to all adult patients with pneumococcal meningitis, even if the isolate is subsequently found to be highly resistant to penicillin and cephalosporins **(B-III)**. Careful observation and follow-up are critical to determine whether dexamethasone is associated with adverse clinical outcome. For data on outcome in patients with meningitis caused by resistant pneumococcal isolates, case reports and small case series may help ascertain whether dexamethasone is harmful to these patients. Furthermore, in patients with suspected pneumococcal meningitis who receive adjunctive dexamethasone, addition of rifampin to the empirical combination of vancomycin plus a third-generation cephalosporin may be reasonable pending culture results and in vitro susceptibility testing **(B-III)**.

Once the Bacterial Etiology of Meningitis Is Established, What Specific Antimicrobial Agents Should Be Used for Treatment?

Cephalosporins

In clinical trials, the third-generation cephalosporins have been found to be superior to chloramphenicol and cefuroxime (a second generation cephalosporin) and are recommended for the treatment of childhood bacterial meningitis **(A-I)**. In patients with

pneumococcal and meningococcal meningitis, the third-generation cephalosporins are recommended in patients with meningitis caused by strains that are not susceptible to penicillin (MIC, ≥0.1 micrograms/mL) **(A-III)**.

The third-generation cephalosporins are also quite effective in meningitis caused by aerobic gram-negative bacilli (e.g., *Escherichia coli* or *Klebsiella* species); cure rates of 78-94% have been reported, compared with mortality rates of 40-90% for previous regimens that usually included an aminoglycoside, with or without chloramphenicol **(A-II)**. However, given the increasing frequency of antimicrobial resistance among gram-negative bacilli, especially in the hospital setting, in vitro susceptibility testing of isolates is critical to guide antimicrobial therapy. One agent, ceftazidime, has also shown efficacy in several studies of patients with *Pseudomonas* meningitis **(A-II)**. A fourth-generation cephalosporin, cefepime, has been shown to be safe and therapeutically equivalent to cefotaxime in the treatment of bacterial meningitis in infants and children. Cefepime also has greater in vitro activity than the third-generation cephalosporins against *Enterobacter* species and *Pseudomonas aeruginosa* and has been used successfully in some patients with meningitis caused by these bacteria, making it a useful agent in the treatment of patients with bacterial meningitis **(A-II).**

Vancomycin

Vancomycin is not recommended in the treatment of bacterial meningitis caused by isolates that are susceptible to other agents (i.e., penicillins and cephalosporins) **(E-II)**. Even in patients with meningitis caused by highly penicillin- and cephalosporin-resistant strains, vancomycin should be combined with a third generation cephalosporin **(A-III)** and should not be used as a single agent. When used for the treatment of bacterial meningitis, vancomycin should be administered to maintain serum vancomycin trough concentrations of approximately 15-20 micrograms/mL **(B-III)**. Intrathecal administration of vancomycin may be considered in patients who are not responding to parenteral administration **(B-III)**.

Rifampin

Rifampin should only be added if the organism is shown to be susceptible and there is a delay in the expected clinical or bacteriologic response **(A-III)**. Rifampin should also be combined with vancomycin in patients with CSF shunt infections caused by staphylococci, especially in cases in which the shunt cannot be removed **(A-III)**.

Carbapenems

Imipenem has been successfully used in 2 patients with pneumococcal meningitis caused by penicillin- and cephalosporin-resistant strains and in 1 patient with *Acinetobacter* meningitis, although the potential for seizure activity (which was 33% in one study of children with bacterial meningitis) argues against its use in most patients with bacterial meningitis **(D-II)**. Meropenem, which has a broad range of in vitro activity and less seizure proclivity than imipenem, has been studied in both children and adults with bacterial meningitis. In these studies, meropenem has been shown to have clinical and microbiologic outcomes similar to those of cefotaxime or ceftriaxone and can be recommended as an alternative to these agents for treatment of bacterial meningitis **(A-I)**. Meropenem has also been used successfully in isolated patients with

pneumococcal meningitis caused by highly penicillin- and cephalosporin-resistant strains. However, in a recent study of 20 cefotaxime-resistant *S. pneumoniae* isolates, 4 were intermediate and 13 were resistant to meropenem, suggesting that meropenem may not be a useful alternative agent for treatment of pneumococcal isolates that are highly resistant to penicillin and cephalosporins **(D-II)**. However, meropenem may be useful in patients with meningitis caused by gram-negative isolates that are resistant to standard therapy. Meningitis caused by gram-negative bacilli that produce extended-spectrum beta-lactamases or those that may hyperproduce beta-lactamases (i.e., *Enterobacter* species, *Citrobacter* species, or *Serratia marcescens*) may best be treated with a regimen that contains meropenem **(A-III)**.

Fluoroquinolones

The fluoroquinolones (especially ciprofloxacin) have been used successfully in some patients with meningitis due to gram-negative organisms. However, on the basis of limited published literature, these agents should only be utilized for meningitis caused by multidrug-resistant gram-negative bacilli, or when patients have not responded to or cannot receive standard antimicrobial therapy **(A-III)**. The newer fluoroquinolones (e.g., trovafloxacin, gatifloxacin, and moxifloxacin) have enhanced in vitro activity against *S. pneumoniae* and have been studied in experimental animal models of pneumococcal meningitis. Trovafloxacin was compared with ceftriaxone, with or without vancomycin, in a multicenter, randomized trial in children with bacterial meningitis (27% of cases caused by *S. pneumoniae*). The overall efficacy in both treatment groups was comparable in terms of CSF sterilization and clinical success at the end of treatment. Although trovafloxacin is no longer utilized because of concerns of liver toxicity, these data suggest the potential usefulness of the new fluoroquinolones in patients with bacterial meningitis. Pending results of ongoing trials, these agents (i.e., gatifloxacin and moxifloxacin) should only be used as alternative agents in patients with bacterial meningitis **(B-II)**. Because these agents have not been studied in newborns and children with bacterial meningitis, they should only be considered in these patients who are not responding to standard therapy.

In Patients Who Develop Bacterial Meningitis after Placement of CSF Shunt, Is It Necessary to Administer Antimicrobial Therapy by the Intraventricular Route?

The principles of antimicrobial therapy for CSF shunt infections are generally the same as those for the treatment of acute bacterial meningitis. However, direct instillation of antimicrobial agents into the ventricles through either an external ventriculostomy or shunt reservoir is occasionally necessary in patients who have shunt infections that are difficult to eradicate or who cannot undergo the surgical components of therapy **(A-III)**. No antimicrobial agent has approved by the US Food and Drug Administration for intraventricular use, and the specific indications are not well-defined. Antimicrobial dosages have been used empirically (see table below entitled "Recommended Dosages of Antimicrobial Agents Administered by the Intraventricular Route"), with dosage adjustments and dosing intervals based on the ability of the agent to achieve adequate CSF concentrations. After administration of the first intraventricular dose, additional doses can be determined by calculation of the "inhibitory quotient." Prior to administration of the next intraventricular dose, a sample of CSF is withdrawn to obtain

the trough CSF concentration. The inhibitory quotient is then determined by taking the trough CSF concentration divided by the MIC of the agent for the isolated bacterial pathogen; it should exceed 10-20 for consistent CSF sterilization. Although not standardized, this approach is reasonable to ensure that adequate CSF concentrations of specific antimicrobial agents are attained **(B-III)**.

In Patients with CSF Shunts Who Develop Bacterial Meningitis Directly from the Shunt (and Not from Hematogenous Dissemination of Encapsulated Microorganisms), Does the Shunt Need to Be Removed for Optimal Therapy, and When Can a New Shunt Be Implanted?

Removal of all components of the infected shunt and some component of external drainage, in combination with appropriate antimicrobial therapy, appears to be the most effective treatment for CSF shunt infections; the ventriculitis of the shunt infection appears to clear more rapidly with the drainage catheter, and the presence of the catheter allows continued treatment of the hydrocephalus until the infection has cleared **(A-II)**.

The timing of shunt reimplantation is dependent upon the isolated microorganism, the extent of infection as defined by culture of samples obtained after externalization, and, occasionally, on CSF findings **(B-II)**. In patients with infections caused by coagulase-negative staphylococci and normal CSF findings, the presence of negative CSF culture results after externalization generally confirms that removal of the hardware affected a cure, and the patient can be reshunted on the third day after removal. If CSF abnormalities are present and a coagulase-negative staphylococcus is isolated, 7 days of antimicrobial therapy are recommended prior to reshunting as long as additional CSF culture results are negative and the ventricular protein concentration is appropriate (<200 mg/dL); if additional culture results are positive, antimicrobial therapy is continued until CSF culture results remain negative for 10 consecutive days before a new CSF shunt is placed. For shunt infections caused by *S. aureus*, 10 days of negative culture results are recommended prior to reshunting and for gram-negative bacilli, a 10-14 day course of antimicrobial therapy should be used, although longer durations may be needed depending on the clinical response. Some experts also suggest that consideration be given to a 3-day period off antimicrobial therapy to verify clearing of the infection prior to shunt reimplantation; although this approach is optional, it may not be necessary for all patients **(C-III)**.

What Are the Indications for Repeated Lumbar Puncture in Patients with Bacterial Meningitis?

In patients with bacterial meningitis who have responded appropriately to antimicrobial therapy, repeated CSF analysis to document CSF sterilization and improvement of CSF parameters is not routinely indicated. Repeated CSF analysis should be performed, however, for any patient who has not responded clinically after 48 h of appropriate antimicrobial therapy **(A-III)**. This is especially true for the patient with pneumococcal meningitis caused by penicillin-or cephalosporin-resistant strains, especially for those who have also received adjunctive dexamethasone therapy. The neonate with meningitis

due to gram-negative bacilli should undergo repeated lumbar punctures to document CSF sterilization, because the duration of antimicrobial therapy is determined, in part, by the result **(A-III)**. In patients with CSF shunt infections, the presence of a drainage catheter after shunt removal allows for monitoring of CSF parameters to ensure that the infection is responding to appropriate antimicrobial therapy and drainage.

What Is the Duration of Antimicrobial Therapy, Based on the Isolated Pathogen?

The duration of antimicrobial therapy in the patient with bacterial meningitis has often been based more on tradition than on evidence-based data. Recommendations are shown below. However, it must be emphasized that these guidelines are not standardized and that the duration of therapy may need to be individualized on the basis of the patient's clinical response. Pending further data, intravenous antimicrobial therapy is recommended for the duration of treatment to ensure that adequate CSF concentrations of specific antimicrobial agents are attained.

Duration of Antimicrobial Therapy for Bacterial Meningitis Based on Isolated Pathogen (A-III)

Microorganism	Duration of therapy, days
Neisseria meningitidis	7
Haemophilus influenzae	7
Streptococcus pneumoniae	10-14
Streptococcus agalactiae	14-21
Aerobic gram-negative bacilli[a]	21
Listeria monocytogenes	≥21

[a] Duration in the neonate is 2 weeks beyond the first sterile CSF culture or ≥3 weeks, whichever is longer.

What Specific Criteria Should Be Used for Outpatient Antimicrobial Therapy in the Patient with Bacterial Meningitis?

Criteria for Outpatient Antimicrobial Therapy in Patients with Bacterial Meningitis (A-III)

Inpatient antimicrobial therapy for ≥6 days
Absence of fever for at least 24-48 h prior to initiation of outpatient therapy

No significant neurologic dysfunction, focal findings, or seizure activity
Clinical stability or improving condition
Ability to take fluids by mouth
Access to home health nursing for antimicrobial administration
Reliable intravenous line and infusion device (if needed)
Daily availability of a physician
Established plan for physician visits, nurse visits, laboratory monitoring, and emergencies
Patient and/or family compliance with the program
Safe environment with access to a telephone, utilities, food, and refrigerator

Definitions

Quality of Evidence

I. Evidence from at least one properly randomized, controlled trial
II. Evidence from at least one well-designed clinical trial without randomization, from cohort or case-control analytic studies (preferably from more than one center), from multiple time-series, or from dramatic results from uncontrolled experiments
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

Strength of Recommendation

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

CLINICAL ALGORITHM(S)

Clinical algorithms are provided for management of infants and children with suspected bacterial meningitis and for adults with suspected bacterial meningitis

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

- Tunkel AR, Hartman BJ, Kaplan SL, Kaufman BA, Roos KL, Scheld WM, Whitley RJ. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis 2004 Nov 1;39(9):1267-84. [120 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

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GUIDELINE DEVELOPER(S)

Infectious Diseases Society of America - Medical Specialty Society

SOURCE(S) OF FUNDING

Infectious Diseases Society of America (IDSA)

GUIDELINE COMMITTEE

IDSA Practice Guidelines Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Allan R. Tunkel, Drexel University College of Medicine, Philadelphia, Pennsylvania; Barry J. Hartman, Weill Cornell Medical Center, New York, New York; Sheldon L. Kaplan, Baylor College of Medicine, Houston, Texas; Bruce A. Kaufman, Medical College of Wisconsin, Milwaukee; Karen L. Roos, Indiana University School of Medicine, Indianapolis; W. Michael Scheld, University of Virginia School of Medicine, Charlottesville; Richard J. Whitley, University of Alabama at Birmingham

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Potential conflict of interest. A.R.T. has served as a consultant for Centocor. S.L.K. has received grant support from Pfizer, Aventis-Pasteur, and Roche Laboratories and has served as a consultant for Aventis-Pasteur and Wyeth. W.M.S. has served on the speaker's bureaus for Bayer, Pfizer, GlaxoSmithKline, and Bristol-Myers Squibb and has served on the Pfizer Advisory Board.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Infectious Disease Society of America (IDSA)

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Kish MA. Guide to development of practice guidelines. Clin Infect Dis 2001 Mar 15;32(6):851-4.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on November 26, 2004.