Infectious Disease

Central Nervous System Infections

Meningitis

Viral Meningitis

Causes

Viral meningitis is the most common cause of "aseptic" meningitis, in which cerebrospinal fluid (CSF) bacterial cultures are negative. Most patients have typical meningitis symptoms, such as fever, nuchal rigidity, headache, and photophobia.

A substantial proportion of viral meningitis is caused by enteroviruses, which commonly occur in the summer and fall in temperate climates when these organisms circulate in the environment. Enteroviral meningitis can also occur in winter and spring months; seasonal enteroviral infections are typically caused by coxsackievirus, echovirus, or other nonpolio enteroviruses.

Herpes simplex virus (HSV) can also cause meningitis. These meningitis syndromes can be related to primary infections, with central nervous system (CNS) involvement as a secondary consequence, or reactivation of latent infection presenting as aseptic meningitis. Most patients with HSV meningitis associated with primary infection will have genital lesions. HSV type 2 (HSV-2) is more commonly associated with meningitis, whereas HSV type 1 (HSV-1) is associated with encephalitis. An association exists between Mollaret meningitis, a benign recurring form of lymphocytic meningitis, and HSV-2; at least 84% of patients have evidence of HSV-2 in CSF.

Primary HIV infection can present with an aseptic meningitis syndrome, which may occur in isolation from the other symptoms. Meningitis due to acute HIV infection is typically self-limited and may be clinically indistinguishable from other viral meningitis syndromes.

Mumps virus can cause meningitis, with typical symptoms of fever, headache, and neck stiffness. Since the advent of universal childhood vaccination for measles, mumps, and rubella, the incidence of mumps-related meningitis has dramatically decreased. Meningitis from mumps virus can occur at any point during the course of clinical mumps infection. Parotitis or orchitis may be present.

Infections with arboviruses, such as West Nile virus or St. Louis encephalitis virus, can cause meningitis, although these infections more typically produce encephalitis. Cytomegalovirus, Epstein-Barr virus, adenovirus, and varicella virus infections can also cause meningitis.

Diagnosis

Symptoms of viral meningitis include fever, headache, neck stiffness, photophobia, and change in mental status and may be indistinguishable from symptoms of bacterial meningitis. Characteristics of the CSF profile are outlined in **Table 1**. Additional physical examination findings (rash and pharyngitis in acute HIV infection; parotitis or orchitis in mumps-related meningitis) can support the presumptive diagnosis. Polymerase chain reaction (PCR) and other molecular tests are available for diagnosis of numerous viral causes. CSF PCR studies may be used for diagnosing HSV and enterovirus meningitis; antibody detection in CSF is preferred for West Nile virus meningitis. Viral cultures of CSF are not clinically useful because of poor sensitivity and long turn-around times. Serologic testing may be an adjunctive diagnostic tool in meningitis caused by mumps.

TABLE 1. Typical CSF Findings in Patients with Viral and Bacterial Meningitis

CSF Parameter	Viral Meningitis[a]	Bacterial Meningitis
Opening pressure	≤250 mm H_2O	200-500[b] mm H_2O
Leukocyte count	50-1000/μL (50-1000 × 10^6/L)	1000-5000/μL (1000-5000 × 10^6/L)[c]
Leukocyte predominance	Lymphocytes[d]	Neutrophils
Glucose	>45 mg/dL (2.5 mmol/L)	<40 mg/dL (2.2 mmol/L)[e]
Protein	<200 mg/dL (2000 mg/L)	100-500 mg/dL (1000-5000 mg/L)
Gram stain	Negative	Positive in 60%-90%[f,g]
Culture	Negative	Positive in 70%-85%[g]

CSF = cerebrospinal fluid.

[a]Primarily nonpolio enteroviruses (echoviruses and coxsackieviruses).

[b]Values exceeding 600 mm H_2O suggest the presence of cerebral edema, intracranial suppurative foci, or communicating hydrocephalus.

[c]Range may be <100/μL (100 × 10^6/L) to >10,000/μL (10,000 × 10^6/L).

[d]May have neutrophil predominance early in infection, but lymphocyte predominance occurs after the first 6 to 48 hours.

[e]The CSF-to-plasma glucose ratio is ≤0.40 in most patients.

[f]The likelihood of a positive Gram stain correlates with number of bacteria in the CSF.

[g]The yield of positive results is significantly reduced by previous administration of antimicrobial therapy.

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Meningitis can also result from medications; autoimmune diseases; malignancy; and other nonviral infectious causes, including spirochetes, fungi, or mycobacteria. Serology may be helpful to diagnose aseptic meningitis caused by syphilis, *Borrelia burgdorferi* (Lyme disease), or certain fungal organisms.

Treatment

Anti-infective treatments are not available for viral meningitis with the exception of underlying herpes viruses. The primary focus of management in viral meningitis is to distinguish it from other causes of infectious meningitis, particularly bacterial meningitis. Symptomatic and supportive management for viral meningitis and rigorous evaluation to exclude bacterial meningitis are the cornerstones of management. Empiric antimicrobial agents may be initiated until full CSF profiles and cultures are finalized and bacterial meningitis can be excluded. Antibiotics can be started and continued as empiric treatment for 48 to 72 hours, after which most routine CSF cultures will show preliminary results. The increasing availability of enteroviral PCR testing can shorten the time required to exclude bacterial infection. Repeat lumbar puncture can be performed after the initial 2 to 3 days if lack of clinical response is a concern or if documenting the evolution of the CSF profile to that more characteristic of viral meningitis is desired.

KEY POINTS

- Viral meningitis is most commonly caused by enteroviruses, herpes simplex virus type 2, and arboviruses.
- Clinical signs and symptoms aiding in the diagnosis of viral meningitis include parotitis or orchitis with mumps virus, rash in enterovirus and HIV, pharyngitis with acute HIV, and genital lesions with herpes simplex virus.

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- Viral meningitis is managed supportively, with empiric antimicrobials given only until cerebrospinal fluid cultures exclude bacterial meningitis.

Bacterial Meningitis

Causes

Bacterial meningitis usually results from bacteremic dissemination of meningeal pathogens that colonize the nasopharynx or from another distant focus of infection but may also occur from contiguous spread of infection to the CSF (sinusitis or otitis media), direct inoculation (traumatic injury or neurosurgical procedure), or prosthetic device infection (CSF shunts or drains, intracranial pressure monitors).

Individual host factors, such as colonization of the nasopharynx with potential meningeal pathogens, complement deficiency, anatomic or functional asplenia, glucocorticoid use, diabetes, hypogammaglobulinemia, and altered cell-mediated immunity, can also contribute to increased susceptibility to acute bacterial meningitis. Exposure to other persons with bacterial meningitis (for certain pathogens, such as *Neisseria meningitidis*) or travel to regions of the world where certain organisms are more prevalent and endemic (such as sub-Saharan Africa, where endemic meningococcal disease is present) will also increase the risk for bacterial meningitis.

The two most common organisms causing bacterial meningitis are *Streptococcus pneumoniae* and *N. meningitidis*, which together are responsible for more than 80% of infections (**Table 2**).

Diagnosis

Bacterial meningitis is classically described as producing fever, nuchal rigidity, and altered mental status. However, all three symptoms may not be present in many patients with confirmed disease. Other clinical manifestations that suggest bacterial meningitis include photophobia, headache (often a very severe headache distinctly different from what the patient may typically experience), and dermatologic manifestations (rash, petechiae, purpura) or neurologic abnormalities

TABLE 2. Causes of Bacterial Meningitis

Infecting Organism	Cases (%)	Comments
Streptococcus pneumoniae	>70	Many cases caused by serotypes not covered by pneumococcal vaccination; functionally and anatomically asplenic patients at greater risk
Neisseria meningitidis	12	Can be transmitted through droplet exposure; functionally and anatomically asplenic patients at greater risk
Group B streptococci	7	Persons with diabetes, alcoholism, malignancy, liver disease at risk
Staphylococcus aureus	<5	Primary infection is associated with neurosurgery or CNS prosthetic device; secondary infection arises from bacteremia
Haemophilus influenzae	6	Decreased prevalence in the pediatric age group since type B conjugate vaccine; functionally and anatomically asplenic patients at greater risk
Listeria monocytogenes	<5	Immunosuppressed and decreased cell-mediated immunity (because of medications or medical conditions) as well as age (very old and very young) are risk factors
Gram-negative bacteria	<5	Nosocomial settings; complication of neurosurgery

CNS = central nervous system.

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(focal neurologic or cranial nerve deficits, seizures). Physical examination maneuvers, such as testing for Brudzinski and Kernig signs, lack adequate sensitivity and specificity, although the presence of one or both of these findings is consistent with bacterial meningitis.

Before proceeding with lumbar puncture, it should be determined whether CT of the head should be performed. CT of the head before lumbar puncture is indicated if signs or symptoms of increased intracranial pressure or a CNS mass lesion, such as papilledema, focal neurologic deficits, or altered mental status, are present; it is also indicated in patients who are immunocompromised or have a history of CNS disease (mass lesion, stroke, focal infection). In the absence of these findings, lumbar puncture can be undertaken without CNS imaging. Elevated CSF opening pressure is common. Characteristic CSF profiles in bacterial meningitis are outlined in Table 1. CSF Gram stain and cultures, when obtained before antimicrobial therapy initiation, are usually diagnostic for the infecting organism. Rapid CSF tests, such as latex agglutination and molecular testing with PCR, can be supplemental diagnostic tools, although the diagnostic utility of latex agglutination testing is limited by a lack of specificity. Elevated CSF lactate levels suggest bacterial meningitis, but this is not a specific finding. Blood cultures, if obtained before antimicrobial therapy, are often positive and may be an adjunctive diagnostic tool in isolating the bacterial causative pathogen if CSF cannot be obtained before antibiotic administration.

Management

Suspected bacterial meningitis demands prompt therapy; because of the risk for substantial morbidity and mortality with delayed treatment, empiric therapy is often initiated before CSF results are available (**Figure 1**). When a presumptive diagnosis of bacterial meningitis has been made, empiric

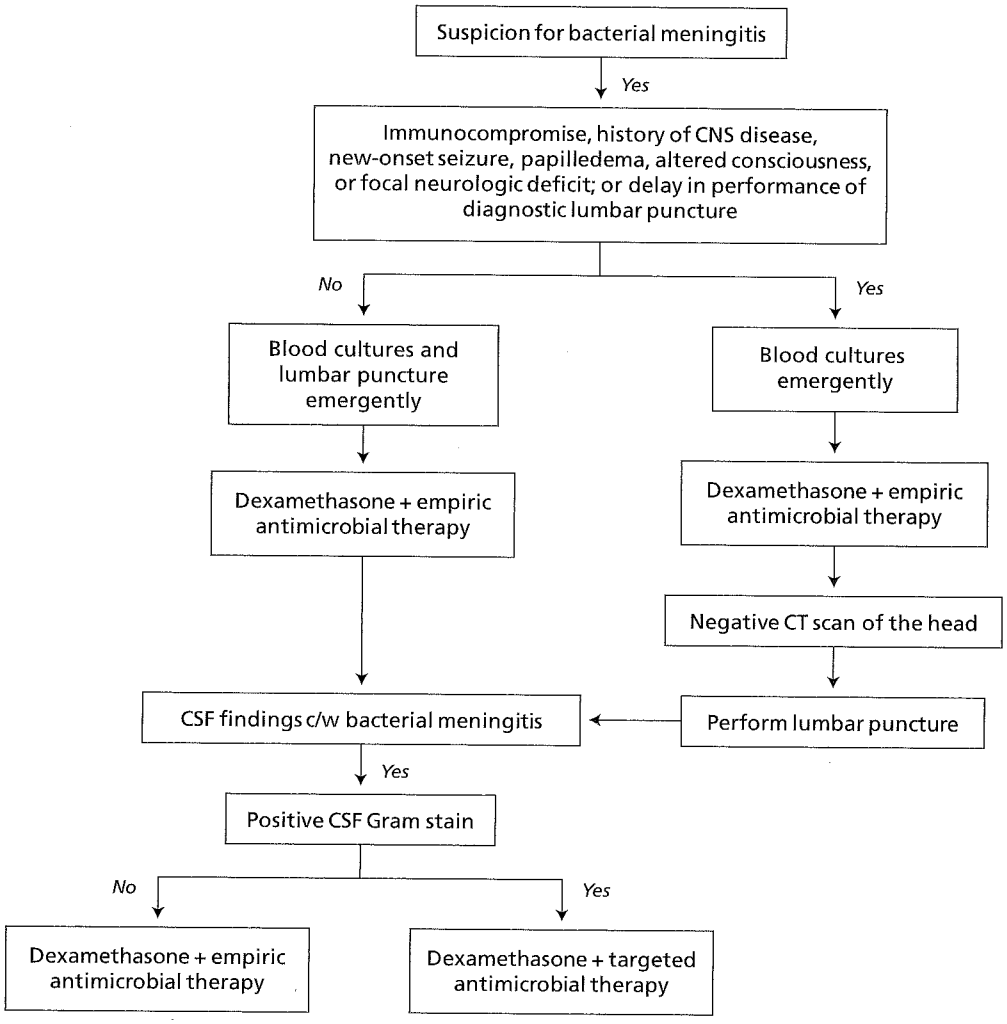

FIGURE 1. Management algorithm for adults suspected of having bacterial meningitis.

CNS = central nervous system; c/w = consistent with; CSF = cerebrospinal fluid.

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antimicrobials directed toward the most likely causes are initiated, as outlined in **Table 3**. Because of the potential neurologic complications of bacterial meningitis, particularly pneumococcal meningitis (seizures, hearing loss, cranial nerve deficits, paresis), adjunctive dexamethasone is recommended; it should be given approximately 15 minutes before administration of antimicrobial agents and should be continued for a full course (0.15 mg/kg every 6 hours for 4 days) in patients with suspected or confirmed pneumococcal meningitis. Although benefit has been shown with dexamethasone in developed countries, the drug has not been proven beneficial in resource-poor settings. When CSF cultures have been finalized, antimicrobial therapy can be altered on the basis of the specific cause and confirmed susceptibilities. Therapy duration varies depending on the causative agent and clinical response; duration may be 7 days (*N. meningitidis*, *Haemophilus influenzae*), 10 to 14 days (*S. pneumoniae*), or up to 21 days (staphylococcal, gram-negative, or *Listeria* meningitis).

KEY POINTS

- The most common organisms causing bacterial meningitis are *Streptococcus pneumoniae*, *Neisseria meningitidis*, group B streptococcus, *Haemophilus influenzae*, and *Listeria monocytogenes*.
- Empiric antimicrobial therapy should be initiated immediately in suspected bacterial meningitis, with more specific targeted therapy implemented after culture results are obtained.
- Dexamethasone is recommended as adjunctive therapy in all cases of bacterial meningitis in developed countries.

TABLE 3. Antibiotic Management of Bacterial Meningitis

Clinical Characteristics	Empiric Antibiotic Regimen
Immunocompetent host age <50 y with community-acquired bacterial meningitis	IV ceftriaxone *or* cefotaxime plus IV vancomycin
Patient age >50 y or those with altered cell-mediated immunity	IV ampicillin (*Listeria* coverage) plus IV ceftriaxone *or* cefotaxime plus IV vancomycin
Allergies to β-lactams	IV moxifloxacin instead of cephalosporin
	IV trimethoprim-sulfamethoxazole instead of ampicillin
Hospital-acquired bacterial meningitis	IV vancomycin plus either IV ceftazidime, cefepime, or meropenem
Neurosurgical procedures	IV vancomycin plus either IV ceftazidime, cefepime, or meropenem

IV = intravenous.

Focal Central Nervous System Infections

Brain Abscess

A brain abscess is a focal infection of the brain parenchyma that arises from hematogenous dissemination or, more commonly, direct spread of infection from contiguous anatomic structures. Multifocal brain abscesses more commonly arise from hematogenous routes of infection, whereas solitary brain abscesses most often result from extension of contiguous infections into the brain. Brain abscesses caused by contiguous infections may be a complication of otitis media, sinusitis, or odontogenic infections. Brain abscesses can also present as complications from foreign bodies that become lodged in the brain parenchyma or arise postoperatively from neurosurgical procedures. No source of infection is determined in approximately 20% to 40% of brain abscesses.

Many brain abscesses are polymicrobial, and a substantial proportion of cases involve anaerobic organisms. The microbiology and clinical characteristics of brain abscesses are outlined in **Table 4**.

Clinical presentation of brain abscess includes headache, which can be severe and unresponsive to analgesia; fever is not always present. Neck stiffness is typically present only with occipital lobe involvement. Mental status changes and vomiting indicate later-stage progression of the brain abscess and are poor prognostic signs. Physical examination may show focal neurologic signs and cranial nerve deficits. CNS imaging is the cornerstone of diagnosis; lumbar puncture is contraindicated because of the potential for increased intracranial pressure and risk for herniation. Although MRI is more sensitive than CT, contrast-enhanced CT can often be performed more rapidly. Stereotactic CT-guided aspiration can be performed to obtain microbiologic samples, but this invasive diagnostic method is often impractical before a clinical decision is made to treat a suspected brain abscess.

If brain abscess is suspected, empiric antimicrobial therapy should be started. Empiric regimens are based on predisposing conditions and suspected causative agents (see Table 4). Abscesses larger than 2.5 cm should be surgically excised or drained stereotactically. If abscesses are not drained, follow-up CNS imaging should occur within several days to assess for worsening cerebral edema. CNS imaging should be repeated urgently if any mental status or neurologic changes are noted.

Antimicrobial therapy duration is typically 4 to 8 weeks. Therapy duration should be guided by follow-up clinical evaluation and repeat neuroimaging, ideally by using the same modality as the original imaging study. Expert opinion recommends administration of glucocorticoids when substantial cerebral edema is present. A substantial portion of patients with brain abscess can have residual neurologic sequelae, particularly seizures.

TABLE 4. Predisposing Conditions, Causative Agents, and Empiric Antimicrobial Therapy in Patients with Bacterial Brain Abscess

Predisposing Condition	Usual Causative Agents	Empiric Antimicrobial Therapy
Otitis media or mastoiditis	Streptococci (aerobic or anaerobic), *Bacteroides* species, *Prevotella* species, Enterobacteriaceae	Metronidazole plus a third-generation cephalosporin[a]
Sinusitis	Streptococci, *Bacteroides* species, Enterobacteriaceae, *Staphylococcus aureus*, *Haemophilus* species	Metronidazole plus a third-generation cephalosporin[a,b]
Dental sepsis	Mixed *Fusobacterium, Prevotella,* and *Bacteroides* species; streptococci	Penicillin plus metronidazole
Penetrating trauma or after neurosurgery	*S. aureus*, streptococci, Enterobacteriaceae, *Clostridium* species	Vancomycin plus a third-generation cephalosporin[a,c]
Lung abscess, empyema, bronchiectasis	*Fusobacterium, Actinomyces, Bacteroides,* and *Prevotella* species; streptococci; *Nocardia* species	Penicillin plus metronidazole plus a sulfonamide[d]
Endocarditis	*S. aureus*, streptococci	Vancomycin plus gentamicin
Hematogenous spread from pelvic, intra-abdominal, or gynecologic infections	Enteric gram-negative bacteria, anaerobic bacteria	Metronidazole plus a third-generation cephalosporin[a,b,c]
Immunocompromised patients HIV-infected patients	*Listeria* species, fungal organisms (*Cryptococcus neoformans*), or parasitic or protozoal organisms (*Toxoplasma gondii*); *Aspergillus*, *Coccidioides*, and *Nocardia* species	Metronidazole plus a third-generation cephalosporin[a,b,c,d,e]; antifungal or antiparasitic agent

[a]Cefotaxime or ceftriaxone; the fourth-generation cephalosporin cefepime may also be used.

[b]Add vancomycin if infection caused by methicillin-resistant *Staphylococcus aureus* is suspected. Vancomycin can then be transitioned to antistaphylococcal β-lactam (oxacillin-nafcillin)-penicillin if methicillin-sensitive *Staphylococcus aureus* is confirmed.

[c]Use ceftazidime or cefepime if infection caused by *Pseudomonas aeruginosa* is suspected. Meropenem can also be used for antipseudomonal coverage.

[d]Use trimethoprim-sulfamethoxazole if infection caused by *Nocardia* species is suspected.

[e]Use ampicillin if infection caused by *Listeria* species is suspected.

NOTE: If predisposing condition is unknown, empiric treatment should include vancomycin plus metronidazole and third-generation cephalosporin.

KEY POINT

- Empiric antimicrobial therapy should be initiated immediately if brain abscess is suspected, and successful treatment usually combines antimicrobial therapy with surgical drainage.

Spinal Epidural Abscess

Spinal epidural abscesses (SEAs) usually result from contiguous spread from infected vertebrae or intervertebral body disc spaces or hematogenous dissemination from a distant site. Risk factors include prolonged epidural catheter placement, paraspinal glucocorticoid or analgesic injections, diabetes mellitus, HIV infection, trauma, injection drug use, tattooing, alcoholism, and acupuncture. Most SEAs are caused by *Staphylococcus aureus.* Other, less frequent, causative organisms include gram-negative bacilli, *Streptococcus* species, anaerobic organisms, and, rarely, fungi or other unusual pathogens.

SEA can be challenging to diagnose because symptoms can be mild or nonspecific and fever may not always be present. A high index of suspicion, particularly in patients with atypical or persistent back pain, will facilitate more prompt diagnosis. Symptoms may progress from back pain to accompanying neurologic symptoms, such as bowel or bladder dysfunction, lower-extremity weakness, paresthesias, and, in the last stages, paralysis. MRI of the spine with contrast is the preferred imaging modality for diagnosis. If MRI cannot be done, CT of the spine with contrast may be an acceptable alternative. Microbiologic sampling with CT-guided needle aspiration can be attempted, and blood cultures should be obtained. At least two blood culture sets should be drawn in patients suspected of having SEA because the causative agent can be confirmed from these cultures more than 60% of the time. Empiric antibiotics can be started if the suspicion for SEA is high.

SEA is treated with a combination of antimicrobial therapy and surgical drainage. Medical therapy alone is often successful if no neurologic deficits are present at the time of diagnosis or if substantial complications from surgery are likely because of comorbid conditions. Serial clinical evaluations and follow-up MRI of the spine (at approximately 4-6 weeks into therapy or with any sign of clinical deterioration) are necessary adjuncts to management without surgery. Empiric parenteral antimicrobial therapy should include coverage for *S. aureus*, *Streptococcus* species, and gram-negative bacilli and may be narrowed on the basis of culture results, if available. Therapy typically lasts between 6 and 8 weeks (or until resolution of abscess on follow-up MRI) but may require

CONT. modification depending on clinical and radiologic recovery. Antibiotic therapy is parenteral to ensure adequate penetration into the CNS.

KEY POINTS

- Spinal epidural abscesses often arise from infected vertebral discs or intervertebral body disc spaces; risk factors include prolonged epidural catheter placement, glucocorticoid or analgesic injections, diabetes mellitus, HIV infection, trauma, injection drug use, tattooing, alcoholism, and acupuncture.
- Microbiologic sampling with CT-guided needle aspiration of the spinal epidural abscess can be attempted, and two sets of blood cultures should be obtained.

Cranial Subdural Empyema

Subdural empyema is a focal infection or abscess that occurs between the dura mater and the arachnoid mater. This condition is a medical emergency warranting immediate neurosurgical intervention. Sinusitis, otitis media, or mastoiditis can be the inciting infection, with subdural empyema arising as a complication. Patients with subdural empyema initially have fevers and altered cognition, with deteriorating mental status as the infection progresses. Microbiologic testing of these infections reflects the source, with most subdural empyemas caused by *S. pneumoniae*, *H. influenzae*, aerobic and anaerobic *Streptococcus* species, *Staphylococcus* species (coagulase-positive and coagulase-negative), gram-negative bacilli, and anaerobic organisms (*Bacteroides* species). Diagnosis is based on clinical presentation, which often includes fever; headache; nausea and vomiting; mental status changes; and a history of preceding sinusitis, otitis, meningitis, mastoiditis, or recent neurosurgical procedures or sinus surgeries. The diagnosis is confirmed by MRI with gadolinium; CT with contrast is an alternative. Lumbar puncture is contraindicated when increased intracranial pressure is evident. Prompt and immediate neurosurgical intervention to drain the infected collection of purulent material is necessary. Empiric antimicrobial therapy consists of intravenous vancomycin, ceftriaxone (or another cephalosporin that penetrates the CSF well), and metronidazole. Therapy duration is guided by clinical and radiologic improvement. Surgical intervention directed toward the primary source of infection may be a necessary adjunct to successful treatment.

KEY POINT

- Cranial subdural empyema, usually arising as a complication of sinusitis, otitis media, or mastoiditis, is a medical emergency warranting immediate evaluation and neurosurgical intervention.

Encephalitis

Encephalitis is a life-threatening condition. Select viral pathogens causing encephalitis are shown in **Table 5**. Encephalitis often exists as an overlap syndrome with meningitis or inflammation of the spinal cord (encephalomyelitis). Clinically, encephalitis is defined as alteration in mental status lasting 24 hours or more that is associated with two or more of the following: fever, focal neurologic deficit, seizure, CSF pleocytosis, and abnormal findings on electroencephalography or

TABLE 5. Selected Viral Causes of Acute Encephalitis

Organism	Epidemiology and Transmission	Clinical Features	Laboratory Diagnosis	Treatment
Herpes simplex virus type 1	Reactivation of latent virus	Fever, altered mental status, temporal lobe seizures	Herpes simplex virus type 1 PCR on CSF[a]	Acyclovir (IV)
Varicella zoster virus	Can occur at time of acute infection or reactivation, increased risk in HIV	Cutaneous lesions variably present	Varicella zoster virus PCR on CSF, CSF antibodies (if vasculitis suspected)	Acyclovir (IV)
Enterovirus	Typically late summer-fall	Fever, altered mental status, variable rash or oral lesions	Enterovirus PCR on CSF	Supportive care
West Nile virus	Mosquito-borne (summer/fall)	Fevers, altered mentation with or without muscle weakness (including acute asymmetric flaccid paralysis); seizures rare	West Nile virus IgM antibody on CSF	Supportive care
Rabies virus	Bite from infected animal (most commonly bat)	Paresthesia at site of inoculation, hydrophobia, progressive obtundation	Nape of neck skin biopsy for immunohistochemistry Rabies PCR of saliva or CSF (testing coordinated with local health department)	Supportive care; prophylaxis of close contacts

CSF = cerebrospinal fluid; IV = intravenous; PCR = polymerase chain reaction.

[a]Herpes simplex virus PCR result can be negative at the time of initial presentation; must repeat test on a second CSF sample in 3-7 days if clinical suspicion remains high.

CONT. neuroimaging. A specific cause is found in less than 50% of patients despite intensive investigation; even when a pathogen is identified, no antimicrobial therapy is available for many viral causes, and care is supportive. Nevertheless, an attempt to define the cause is indicated because establishing a diagnosis allows directed treatment, discontinuation of ineffective therapies, and determination of prognosis.

Initial management requires attention to potential comorbidities, particularly in patients with a decreased level of consciousness. All patients should undergo neuroimaging to exclude a mass lesion or cerebral edema as a contraindication to lumbar puncture. If the delay in obtaining CSF is significant (>30 minutes), empiric antimicrobial agents should be administered. Patients with evidence of cerebral edema are usually best managed in an intensive care setting with close neurologic monitoring and consideration of ventriculostomy for patients whose condition deteriorates with medical management. Electroencephalography should be considered in all patients with depressed consciousness, even without seizure activity, because nonconvulsive status epilepticus may be present in the absence of myoclonic movements.

Herpes Simplex Encephalitis

Infection with HSV-1 is the most common cause of endemic encephalitis in the United States. Most infections result from reactivation of latent virus. Herpes simplex encephalitis (HSE) is characterized by unilateral or bilateral localized infection of the temporal lobes, but the clinical presentation is nonspecific. Cerebrospinal fluid testing typically shows lymphocytic pleocytosis and, when necrosis is extensive, abundant erythrocytes. The presence of temporal lobe abnormalities on imaging is highly suggestive of HSE, with MRI (**Figure 2**) being more sensitive than CT. Periodic lateralizing epileptiform discharges on electroencephalography suggest HSE but may not be present.

Atypical presentations of HSE may occur, and laboratory testing for HSV-1 infection is recommended for all patients with encephalitis regardless of the presence of temporal lobe lesions. HSV PCR of the CSF allows rapid diagnosis of HSE, with sensitivity greater than 95% and specificity approaching 100%; however, very early in the course of infection, the result of this test may be negative. For cases with a high suspicion based on imaging consistent with HSE, testing should be performed on a subsequent CSF sample. PCR findings remain positive for up to 1 week following initiation of acyclovir treatment. The sensitivity of viral culture of CSF for HSV is less than 5%; as a result this test is discouraged. Serologic testing has limited utility because most adults have detectable HSV-1 antibody related to previous infection.

Delay in acyclovir therapy is a negative prognostic factor, and empiric therapy should be initiated for all patients suspected of having encephalitis. Acyclovir must be administered parenterally to achieve therapeutic levels in brain parenchyma. Empiric treatment can be discontinued when an alternative cause of encephalitis is discovered or, in patients with a relatively low suspicion of HSE, when the HSV PCR has negative results. When HSE is confirmed, high-dose intravenous acyclovir should be continued for 14 to 21 days.

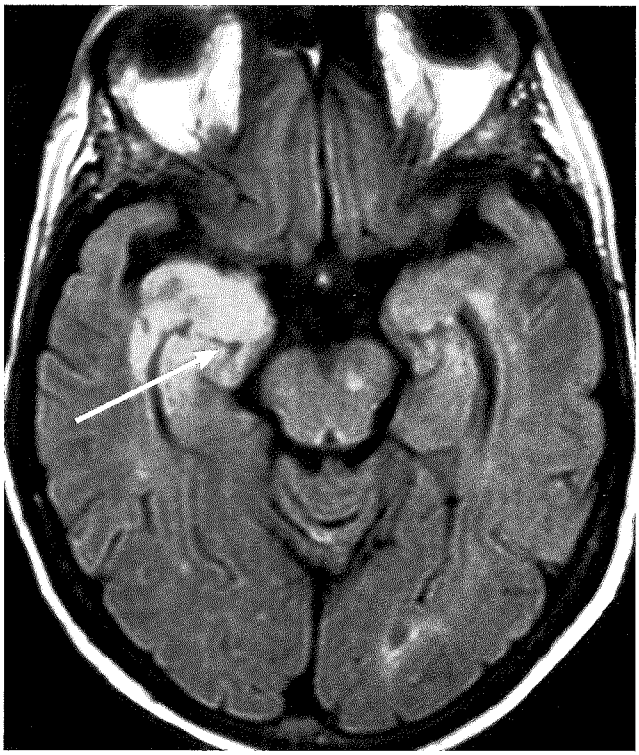

FIGURE 2. Brain MRI exhibiting right temporal lobe enhancement (*arrow*) in a patient with herpes simplex encephalitis.

KEY POINTS

- Herpes simplex encephalitis is characterized by unilateral or bilateral localized infection of the temporal lobes; cerebrospinal fluid testing typically shows lymphocytic pleocytosis and, when necrosis is extensive, abundant erythrocytes; and MRI may show temporal lobe abnormalities.
- Herpes simplex virus polymerase chain reaction testing on the cerebrospinal fluid is highly sensitive and specific for herpes simplex encephalitis.
- Empiric intravenous acyclovir therapy should be initiated for all patients suspected of having encephalitis.

Varicella-Zoster Virus Encephalitis

Varicella-zoster virus (VZV) encephalitis may occur at the time of acute varicella infection or with viral reactivation. VZV encephalitis is more common in patients with HIV/AIDS or defects in cellular immunity but also may occur in otherwise healthy persons.

Besides the characteristic skin findings, few specific features suggest VZV encephalitis. The time between the onset of zoster and the development of CNS symptoms may be prolonged, and in some cases encephalitis may predate onset of

CONT. skin lesions. Even the presence of zoster in a patient with encephalitis is not sufficient proof of CNS infection because cutaneous reactivation may result from the physiologic stress of another infection. Most diagnostically challenging is the condition "herpes sine zoster," in which central nervous system infection occurs in the absence of skin lesions. VZV may also infect cerebral arteries, presenting as an ischemic stroke rather than encephalitis.

Confirmation of VZV encephalitis requires identification of viral infection of the CNS. Findings on VZV PCR of CSF are typically positive in cases of encephalitis associated with acute varicella or zoster. When vasculitis predominates, or when symptoms are more insidious, intrathecal VZV antibodies also should be measured because VZV PCR results can be negative in these cases. Although data on treatment are limited, parenteral acyclovir is recommended in cases of VZV encephalitis or vasculopathy.

KEY POINTS

- Varicella-zoster virus encephalitis is more common in patients with HIV/AIDS or defects in cellular immunity.
- Varicella-zoster virus polymerase chain reaction testing of cerebrospinal fluid should be performed to identify viral infection of the central nervous system.
- Parenteral acyclovir is recommended for varicella-zoster virus encephalitis or vasculopathy.

Neuroinvasive West Nile Virus

West Nile virus (WNV), first detected in the United States in 1999, has emerged as a national public health problem, with infections reported throughout the continental United States. Mosquitoes serve as the primary vector, and most human infections occur during the summer and early fall. Transmission through blood transfusion and organ transplantation has been reported but is much less frequent since the advent of universal screening of donor blood products. Most infected persons remain asymptomatic, with approximately 20% developing West Nile fever. The most severe clinical presentation, West Nile neuroinvasive disease (WNND), occurs in less than 1% of cases. These patients may present with meningitis, encephalitis, or myelitis, either singly or as overlap syndromes. WNND is significantly more common among adults age 50 years or older and in solid organ and bone marrow transplant recipients. HIV infection does not appear to be a significant risk factor for WNND.

Limb weakness, which may be symmetric or involve a single extremity, is a characteristic feature of WNND. Severe disease may manifest as acute asymmetric flaccid paralysis and may progress to cause respiratory failure, akin to that seen with poliomyelitis. Other clinical findings of WNND are rarely helpful in suggesting the diagnosis. Fever is almost universally present. A nonspecific viral exanthema may be found in less than 50% of patients. MRI may show focal lesions of the thalami, basal ganglia, and spinal cord in some patients.

CSF serology is the preferred test to confirm WNND. Most acutely infected patients have detectable IgM antibody to WNV in the first week of symptoms, although titers may remain detectable for more than 1 year. Detection of IgG antibody may confirm previous infection but is less sensitive for diagnosis of acute illness. Serologic cross-reactivity between WNV and other flaviviruses is significant, and caution should be used in interpreting a positive WNV IgG result in a patient with natural infection or vaccination against St. Louis encephalitis virus, Japanese encephalitis virus, yellow fever virus, or dengue virus. For these reasons, testing of CSF is preferred, and the presence of intrathecal WNV IgM antibody is considered diagnostic of acute infection. Results of WNV PCR of serum or CSF are infrequently positive except in immunocompromised patients, who may exhibit delayed viral clearance. Viral culture is insensitive and is not recommended.

No antiviral therapy is effective for WNV infection, and treatment is limited to supportive care. Patients with substantial muscle weakness should be monitored in an intensive care setting for impending respiratory failure.

KEY POINTS

- West Nile neuroinvasive disease occurs in less than 1% of infections with West Nile virus and presents with meningitis, encephalitis, or myelitis, either singly or as overlap syndromes.
- Cerebrospinal fluid serology is the preferred diagnostic test for West Nile neuroinvasive disease, with most patients having detectable IgM antibody to West Nile virus in the first week of symptoms.

Autoimmune Encephalitis

A newly described autoimmune condition termed anti-*N*-methyl-D-aspartate receptor (anti-NMDAR) antibody encephalitis has emerged as an increasingly common cause of encephalitis. Anti-NMDAR encephalitis is associated with ovarian teratomas in greater than 50% of patients with the disease because of production of an antibody to a tumor protein that cross-reacts with neuronal tissue. In patients without evidence of teratoma, an inciting antigenic stimulus is rarely identified. The diagnosis is suggested by the presence of choreoathetosis, psychiatric symptoms, seizures, and autonomic instability and is confirmed by detection of anti-NMDAR antibody in serum. Treatment includes removal of the teratoma to eradicate the immune stimulus and immunosuppression with glucocorticoids or intravenous immune globulin.

KEY POINTS

- Anti-*N*-methyl-D-aspartate receptor (anti-NMDAR) antibody encephalitis presents with choreoathetosis, psychiatric symptoms, seizures, and autonomic instability; is associated with ovarian teratomas in greater than 50% of patients with the disease; and is confirmed by detection of anti-NMDAR antibody in serum.
- Treatment of anti-NMDAR encephalitis includes removal of the teratoma and immunosuppression with glucocorticoids or intravenous immune globulin.

Prion Diseases of the Central Nervous System

Introduction

Prion diseases (also known as transmissible spongiform encephalopathies) are a group of rare, closely related, fatal, neurodegenerative conditions that occur in humans and other mammals. They are caused by an accumulation of aggregated forms of the prion protein in the central nervous system. Human prion diseases include sporadic, infectiously transmitted, and genetic disorders. Sporadic disease accounts for most cases. Known infectious acquisition is very rare in humans and accounts for less than 1% of cases in most populations.

The infectiously transmitted forms of prion disease are kuru, variant Creutzfeldt-Jakob disease (CJD), and iatrogenic CJD. Prion disease has been transmitted to humans through dietary practices and iatrogenic exposure. Kuru was the first prion disease recognized to be transmissible and was linked to cannibalism among tribes in New Guinea.

Creutzfeldt-Jakob Disease

CJD is the most common form of prion disease in humans, with most cases being sporadic. Iatrogenic transmission of CJD is possible and has resulted mainly from receipt of growth hormone prepared from cadaveric pituitaries and contaminated cadaveric dura mater allografts. Contaminated surgical instruments have also been documented to transmit CJD in rare instances. Sporadic CJD does not appear to be transmissible by blood. Although the age range of affected persons is wide, onset usually occurs in the seventh decade of life. The most prominent neurologic sign is disordered cognition. Typically, patients also have motor signs, such as ataxia or spasticity, vague sensory problems, or changes in visual perception. Myoclonus is common. Progressive neurologic decline resulting in death occurs rapidly, typically within 6 to 12 months.

Variant Creutzfeldt-Jakob Disease

Variant CJD is a novel infectious human prion disease caused by the bovine spongiform encephalopathy agent. Most infections have occurred after consumption of infected beef, although transmission by blood and blood products from donors with variant CJD has been reported. Compared with sporadic CJD, variant CJD has a younger age at onset, psychiatric and sensory signs earlier in the disease process, and development of dementia and motor signs more than 6 months after disease onset; however, it typically resembles sporadic CJD, with the most common neurologic sign being impaired cognition. Motor signs, such as ataxia, spasticity, and myoclonus, are prominent.

Prion disease should be considered in the differential diagnosis of any patient who presents with rapidly progressive dementia. Elevated cerebrospinal fluid levels of the 14-3-3 protein are relatively specific for CJD. Definitive diagnosis is made by brain biopsy. No effective treatment exists.

KEY POINTS

- Creutzfeldt-Jakob disease is the most common form of prion disease in humans, with most cases being sporadic.
- Iatrogenic transmission of Creutzfeldt-Jakob disease (CJD) has resulted mainly from receipt of growth hormone prepared from cadaveric pituitaries and contaminated cadaveric dura mater allografts, whereas variant CJD infection has occurred after consumption of infected beef as well as reports of transmission by blood and blood products from donors with variant CJD.

Skin and Soft Tissue Infections

Introduction

Skin and soft tissue infections (SSTIs) usually occur when skin microbes penetrate underlying layers of the epidermis. Predisposing conditions include skin trauma, onychomycosis, tinea pedis, vascular insufficiency, lymphatic compromise, obesity, diabetes mellitus, and immune suppression. The most common organisms causing SSTIs are β-hemolytic streptococci, particularly group A β-hemolytic streptococci (GABHS), and *Staphylococcus aureus*. See **Table 6** for cellulitis risk factors and the associated causative microorganisms.

Erysipelas is a superficial infection of the epidermis that usually involves the lower extremities or face. It is typically caused by GABHS. Involved skin is erythematous (with well-demarcated borders), glistening, indurated, painful, and warm. Fever and malaise are often present. Desquamation may develop, but necrosis of the skin does not.

Cellulitis is a diffuse, spreading skin infection that involves the dermis and subcutaneous tissues. Clinical features include warmth, redness, swelling, and tenderness in addition to fever and malaise; regional lymphadenopathy also may be present. Unlike erysipelas, cellulitis is characterized by poorly defined erythema. Cellulitis is categorized as purulent or nonpurulent. Cellulitis associated with purulent drainage or exudate is typically caused by methicillin-resistant *S. aureus* (MRSA). Nonpurulent cellulitis is usually caused by β-hemolytic streptococci.

Skin infection is usually diagnosed clinically. Radiography may be helpful when the diagnosis is uncertain, when necrotizing fasciitis is suspected, or when an associated abscess is a concern. A causative agent is established in few patients. Cultures obtained directly from a purulent skin lesion may be helpful. Blood cultures are positive in less than 5% of patients. It also is estimated that the clinical diagnosis of lower-extremity cellulitis is inaccurate in up to one third of patients. Mimics include stasis dermatitis, contact dermatitis,

TABLE 6. Cellulitis Pathogens and Associated Risk Factors and Clinical Signs

Pathogen	Risk Factor	Comment
Aeromonas hydrophila	Contact with or participation in recreational sports in fresh water lakes, streams, or rivers (including brackish water)	Cellulitis is nonspecific in clinical appearance; minor trauma to skin usually leads to inoculation of organism
	Contact with medicinal leeches	
Vibrio vulnificus, other *Vibrio* species	Contact with salt water or brackish water or contact with drippings from raw seafood	May cause cellulitis through direct inoculation into skin or may be ingested, leading to bacteremia with secondary skin infection
		Hallmark is hemorrhagic bullae in area of cellulitis
Erysipelothrix rhusiopathiae	Contact with saltwater marine life (also associated with freshwater fish); contact with infected animals such as swine and poultry	Cellulitis usually involves the hand or fingers in those handling fish, shellfish, or, occasionally, poultry or meat contaminated with bacterium
		Causes erysipeloid disease
Pasteurella multocida	Contact primarily with cats	Cellulitis occurs as a result of cat scratch or bite
Capnocytophaga canimorsus	Contact primarily with dogs	Cellulitis and sepsis particularly in patients with functional or anatomic asplenia
Bacillus anthracis	Contact with infected animals or animal products	Edematous pruritic lesion with central eschar; spore-forming organism
	Target of bioterrorism	
Francisella tularensis	Contact with or bite from infected animal (particularly cats) or arthropod bites (particularly ticks)	Ulceroglandular syndrome characterized by ulcerative lesion with central eschar and localized tender lymphadenopathy; constitutional symptoms are often present
Mycobacterium marinum	Contact with fresh water or salt water, including fish tanks and swimming pools	Lesion often trauma-associated and often involving upper extremity; papular lesions become ulcerative at site of inoculation; ascending lymphatic spread can be seen ("sporotrichoid" appearance); systemic toxicity usually absent
Mycobacterium fortuitum	Exposure to freshwater footbaths/ pedicures at nail salons; infection following augmentation mammoplasty and open heart surgery	Multiple boils; razor shaving strongly associated

H CONT. eczema, lymphedema, lipodermatosclerosis, erythromelalgia, deep venous thrombosis, erythema nodosum, hypersensitivity reaction, and thrombophlebitis. H

KEY POINTS

- Cellulitis associated with purulent drainage or exudate is typically caused by methicillin-resistant *Staphylococcus aureus*, whereas nonpurulent cellulitis is usually caused by β-hemolytic streptococci.
- HVC Skin infection is usually diagnosed clinically; radiography should be reserved for when the diagnosis is uncertain, necrotizing fasciitis is suspected, or when an associated abscess or foreign body is a concern.

Community-Associated Methicillin-Resistant *Staphylococcus aureus*

Community-associated MRSA (CA-MRSA) infections commonly present as a purulent SSTI such as a furuncle, which is infection of the hair follicle that extends into the dermis and subcutaneous tissues. Healthy young persons can become infected, especially in conditions of crowding, suboptimal hygiene (sharing of contaminated items, including razors and towels), and frequent antibiotic use. Outbreaks have been reported on athletic teams, in correctional facilities and day care centers, and among military recruits and men who have sex with men. MRSA is responsible for almost 60% of SSTIs in patients seen in the emergency department. The increased prevalence of CA-MRSA has affected the treatment of SSTIs, and the Infectious Diseases Society of America (IDSA) has published evidence-based clinical practice guidelines to inform when empiric treatment for CA-MRSA is appropriate.

H The primary treatment of a cutaneous abscess is incision and drainage. Antibiotics generally are recommended only when the response to incision and drainage is inadequate; in extensive disease or rapid progression with associated cellulitis; in immunodeficiency and other comorbidities; for very young or very old patients; with clinical signs of systemic illness; when involved areas are challenging to drain, such as the genitalia, hands, or face; and in the presence of associated

H CONT. septic phlebitis. Outpatients with purulent cellulitis can be treated empirically for CA-MRSA with a 5- to 10-day course of oral antibiotics, such as trimethoprim-sulfamethoxazole or doxycycline. Linezolid is another treatment option, although its expense and similar efficacy to other agents limit its use to very few clinical situations. Outpatient oral antibiotic therapy for nonpurulent cellulitis should include a β-lactam antibiotic, such as cephalexin or dicloxacillin, which is effective against β-hemolytic streptococci. When coverage of both CA-MRSA and β-hemolytic streptococci is desired, outpatient oral options include clindamycin alone or trimethoprim-sulfamethoxazole or doxycycline in combination with a β-lactam agent, such as amoxicillin; linezolid is also an option in specific patients. Patients who require hospitalization for complicated SSTIs (deep soft tissue infections and abscesses, cellulitis, necrotizing infection, trauma-associated wound infection, postsurgical wound infection, infected burn/ulcer) should receive surgical evaluation for debridement in addition to empiric broad-spectrum antibiotic coverage that includes MRSA agents, such as vancomycin, daptomycin, or, in specific patients, linezolid. Rifampin is not recommended for MRSA treatment, even in an adjunctive role. Ceftaroline is a fifth-generation cephalosporin approved for treatment of SSTIs, including those associated with MRSA. It is recommended as empiric antibiotic therapy for purulent skin infections in immunocompromised hosts or immunocompetent patients with signs of systemic infection. It costs considerably more than vancomycin but less than daptomycin, linezolid, or telavancin, all of which are recommended as empiric treatment for these patients. H

KEY POINTS

HVC • In community-associated methicillin-resistant *Staphylococcus aureus* infections, the primary treatment of a cutaneous abscess is incision and drainage.

HVC • Antibiotic therapy generally is recommended for community-associated methicillin-resistant *Staphylococcus aureus* infections only if primary treatment is inadequate, if disease is extensive or marked by rapid progression and associated cellulitis, if immunodeficiency and other comorbidities are present, if the patient is very young or very old, if clinical signs of systemic illness are noted, if involved areas are challenging to drain, or if septic phlebitis is present.

H Necrotizing Fasciitis

Necrotizing fasciitis (NF) is a potentially lethal necrotizing skin infection. Type I NF refers to a polymicrobial infection comprising aerobic and anaerobic gram-positive and gram-negative organisms. Type II NF is a monomicrobial infection typically caused by *Streptococcus pyogenes*, although *S. aureus*, *Vibrio vulnificus*, or *Streptococcus agalactiae* can be causative. Patients who are immunocompromised, particularly those with liver disease, are at increased risk for infection with *V. vulnificus* in the correct clinical setting (see Table 6). Type III NF (gas gangrene or clostridial myonecrosis) usually develops after surgery or other significant trauma and is primarily caused by *Clostridium perfringens*.

Necrotizing fasciitis usually arises from skin damage or trauma, although a portal of entry is not always apparent. It is more common in patients who have comorbidities, including diabetes mellitus, cancer, injection drug use, liver disease, and immunosuppression, but may occur in healthy young patients.

Cutaneous manifestations can initially resemble less complicated cellulitis. Clues to a potential underlying necrotizing process include systemic toxicity with fever, chills, altered mental status, and hypotension. The pain may be disproportionate to the physical examination findings, and loss of sensation may later result from cutaneous nerve destruction. Skin changes can evolve rapidly and become ecchymotic, vesiculobullous, and gangrenous in appearance. "Woody" induration and crepitus on palpation of the involved areas are characteristic.

Clinical suspicion is important and laboratory evaluation, although nonspecific, may be helpful. Six independent laboratory indicators that, when added together, are associated with an increased likelihood of necrotizing fasciitis are C-reactive protein (≥15.0 mg/dL [150 mg/L]), total leukocyte count (>15,000-25,000/μL [15-25 × 10^9/L]), hemoglobin (<11-13.5 g/dL [110-135 g/L]), sodium (<135 mEq/L [135 mmol/L]), creatinine (>1.6 mg/dL [141 μmol/L]), and glucose (>180 mg/dL [10 mmol/L]).

Plain radiographs of the affected area may demonstrate subcutaneous gas; MRI with contrast is quite sensitive and can help determine the extent of infection. Blood cultures may be useful in identifying the causative agent, but early surgical exploration is the gold standard for diagnosis and treatment. Cultures of intraoperative tissue specimens help direct antibiotic management; repeated surgeries are often necessary for source control.

Empiric broad-spectrum antibiotics are recommended for patients suspected of having NF. Initial coverage should target aerobic and anaerobic gram-positive and gram-negative bacteria, including MRSA. Appropriate regimens include an anti-MRSA agent, such as vancomycin or daptomycin, linezolid plus imipenem (or meropenem), or piperacillin-tazobactam. In type II NF secondary to GABHS and type III NF secondary to clostridial species, penicillin and clindamycin are recommended. Clindamycin is included because it inhibits toxin production and remains effective even in the presence of a high inoculum of bacteria. Discontinuation of antimicrobials is reasonable when surgical debridement is no longer required and the patient is clinically stable. No absolute recommendations exist for the use of adjunctive intravenous immune globulin (IVIG) in streptococcal necrotizing fasciitis, although some infectious disease experts recommend its use in patients with associated toxic shock syndrome (see following). Doxycycline plus ceftazidime is recommended for *Vibrio vulnificus*-associated NF, and doxycycline plus ciprofloxacin is recommended for *Aeromonas hydrophila*-associated NF. H

KEY POINTS

- Clues to a potential underlying necrotizing process include systemic toxicity with fever, chills, altered mental status, and hypotension; pain may be disproportionate to physical examination findings, and loss of sensation may occur because of cutaneous nerve destruction.
- Early surgical exploration is the gold standard for diagnosis and treatment of necrotizing fasciitis.

Toxic Shock Syndrome

S. aureus and *S. pyogenes* can produce toxins called super antigens that stimulate cytokine production, resulting in the systemic signs of toxic shock syndrome (TSS) (**Table 7**, **Table 8**). TSS secondary to *S. aureus* (including MRSA) may be associated with tampon use during menstruation, the presence of wounds, a history of injection drug use, burns, nasal packings, or catheters. Bacteremia is present in about 5% of cases. *S. pyogenes*–associated skin infections (particularly NF) can also produce a toxic shock–like syndrome. Bacteremia is present in about 60% of cases.

Early management consists of adequate resuscitation to maintain tissue perfusion, identification of the cause and focus of infection, and source control, which typically involves surgical debridement. Empiric antimicrobial agents are the same as those used in NF. When identified, pathogen-directed therapy for *S. pyogenes* consists of penicillin plus clindamycin. Methicillin-sensitive *S. aureus*–associated TSS therapy consists of nafcillin or oxacillin plus clindamycin; if TSS is associated with MRSA, vancomycin plus clindamycin or linezolid can be used. Some experts recommend the use of adjunctive IVIG for TSS, although data are limited. Neutralizing antibodies to streptococcal toxins in IVIG provide the rationale for its use.

Hyperbaric oxygen treatment has also been used adjunctively. Droplet precautions are recommended until effective antibiotic therapy has been administered for 24 hours to prevent transmission of group A streptococcal infection to others; contact precautions are also recommended if the wound is draining. Antibiotic prophylaxis against invasive group A streptococcal infections among household contacts of patients with streptococcal TSS-like syndrome may be considered in older adults or in patients with comorbidities, such as diabetes mellitus, HIV infection, cancer, varicella infection, heart disease, steroid use, and injection drug use. Benzathine penicillin G plus rifampin, clindamycin, or azithromycin is recommended.

TABLE 7. Diagnostic Criteria for Staphylococcal Toxic Shock Syndrome

Fever >38.9 °C (102.0 °F)
Systolic blood pressure <90 mm Hg
Diffuse macular rash with subsequent desquamation, especially on palms and soles
Involvement of three of the following organ systems:
Gastrointestinal (nausea, vomiting, diarrhea)
Muscular (severe myalgia or fivefold or greater increase in serum creatine kinase level)
Mucous membrane (hyperemia of the vagina, conjunctivae, or pharynx)
Kidney (blood urea nitrogen or serum creatinine level at least twice the upper limit of normal)
Liver (bilirubin, aspartate aminotransferase or alanine aminotransferase concentration twice the upper limit of normal)
Blood (platelet count <100,000/μL [100 × 10^9/L])
Central nervous system (disorientation without focal neurologic signs)
Negative results on serologic testing for Rocky Mountain spotted fever, leptospirosis, and measles; negative cerebrospinal fluid cultures for organisms other than *Staphylococcus aureus*

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TABLE 8. Diagnostic Criteria for Streptococcal Toxic Shock Syndrome

Definite case:
Isolation of GABHS from a sterile site
Probable case:
Isolation of GABHS from a nonsterile site
Hypotension:
The presence of two of the following findings:
Kidney (acute kidney injury or failure)
Liver (elevated aminotransferase concentrations)
Skin (erythematous macular rash, soft tissue necrosis)
Blood (coagulopathy, including thrombocytopenia and disseminated intravascular coagulation)
Pulmonary (acute respiratory distress syndrome)

GABHS = group A β-hemolytic streptococci.

KEY POINT

- Early management of toxic shock syndrome consists of adequate resuscitation to maintain tissue perfusion, identification of the cause and focus of infection, and source control, which typically involves surgical debridement.

Animal Bites

Animal bites, most of which are caused by cats and dogs, account for 1% of all visits to the emergency department; up