Catheter associated infection idsa guidelines

Table 1. Empiric Treatment for CA-UTIs

Severity of Illness	1st-Line Therapy[a]
Mild-to-moderate[b]	Ciprofloxacin 500 mg po or 400 mg IV q12h Levofloxacin 500-750 mg IV/po q24h Ceftriaxone 1 g IV daily
Severe[c,d]	Cefepime 2 g IV q12h Ceftazidime 2 g IV q8h Imipenem 500 mg IV q6h Doripenem 500 mg IV q8h Meropenem 1 g q8h Piperacillin-tazobactam 3.375-4.5 g IV q6h

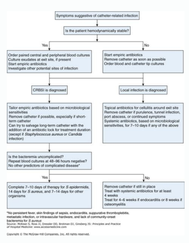
[a] Dosing adjustments may be necessary in reduced renal function. [b] Patient not from LTC facility, not pregnant, has low fluoroquinolone resistance. [c] Patient recently received fluoroquinolone or from LTC facility, severely ill, shows gram-positive cocci upon Gram stain. [d] Add vancomycin per Gram stain results; loading dose 25-30 mg/kg, then 15 mg/kg IV q12h.
CA: catheter-associated; LTC: long-term care.
Source: Reference 16 and Johns Hopkins ABX Guide [database]. http://Hopkins-abxguide.org. Accessed July 12, 2010.


Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America

Enterobacteriaceae — *Escherichia coli*
Klebsiella spp *(K. oxytoca, K. pneumoniae)*
Serratia spp *(S. marcescens)*
Citrobacter spp *(C. koseri)*
Enterobacter spp *(E. cloacae)*
Providencia stuartii
Morganella morganii
Proteus spp *(P. mirabilis)*

Non-Enterobacteriaceae — *Pseudomonas aeruginosa*

Gram-positive cocci — Coagulase-negative staphylococci
S. saprophyticus
S. epidermidis (usually a contaminant)
S. lugdunensis (usually a contaminant)
Coagulase-positive staphylococci
Staphylococcus aureus
Enterococcus spp
E. faecalis
E. faecium
Group B streptococci



the basis of our surveillance data and in the era of antimicrobial stewardship, it is reasonable to consider anti-staphylococcal therapy alone as empiric treatment for septic patients receiving TPN in our center. We suggest that empiric treatment for CR-BSI in patients receiving TPN should be guided primarily by local epidemiological data.

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IDSA Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Bloodstream Infection

To the Editor—The recently published Infectious Diseases Society of America (IDSA) clinical practice guidelines for the diagnosis and management of intravascular catheter-related bloodstream infection (CR-BSI) [1] is a welcome updated document that is likely to be very useful to many clinicians caring for febrile patients with intravascular catheters. One issue that I believe the authors could have addressed more clearly revolves around drawing blood cultures through vascular catheters when CR-BSI is suspected. Specifically, the guidelines suggest that for suspected CR-BSI, paired blood samples, one set drawn from the catheter and another set through a peripheral vein, should be obtained while simultaneously stressing that the diagnosis of CR-BSI without removal of the catheter is only possible by performing quantitative blood cultures or calculating the differential time to positivity [1]. In addition, the guidelines affirm that definite diagnosis of CR-BSI requires the growth of the same organism from a peripheral (not catheter) blood culture and catheter tip culture, and that the management of patients with a positive blood culture from an intravascular catheter and a negative result from peripheral blood draw remains an "unresolved issue" [1]. Collectively, these statements suggest that, without availability of quantitative blood cultures (as is the case in most laboratories [2]) or calculation of the differential time to positivity (also not widely embraced [3]), or the presence of patient factors impacting peripheral venous puncture (eg, patient preference or difficult venous access), routine culturing of blood samples obtained from intravascular catheters cannot be regarded as a preferred practice in the evaluation of CR-BSI. In fact, given the higher likelihood of contamination associated with catheter-drawn blood cultures [3, 4], with their attendant additional unnecessary cost of care [5] and their relatively poor positive predictive value for CR-BSI [6–8] without greater negative predictive values compared with those of peripheral blood cultures [8], the "2 sets (1 peripheral)" practice should generally be avoided [3, 4] instead of encouraged as was done throughout the document [1]. The guidelines' recommendation to study the frequency of compliance with such practice as a "performance measure" for evaluation of CR-BSI further implies that it should be adopted universally by health care facilities, seemingly without regards to laboratory capabilities or patient factors.

This is not a trivial issue. On the basis of my experience of >20 years at a large tertiary care community teaching medical center, the "knee-jerk" response of many clinicians to fever in a patient with a central venous line is often to order 2 sets of blood cultures, 1 through the intravascular catheter and another peripherally, even though no quantitative blood culture or differential time to positivity services are available. When I ask the ordering physician about the rationale for such practice, they often respond that "a positive blood culture from the line and a negative one from peripheral draw means the line is infected." I hope that future guidelines avoid the "1 size fits all" approach to the evaluation of CR-BSI and seize the opportunity to dispel, not perpetuate, this practice myth in many centers.

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Published CID, 2/14/2017 Clinical Infectious Diseases, Volume 64, Issue 6, 15 March 2017, Pages e34–e65, 14 February 2017 Allan R. Tunkel, Rodrigo Hasbun, Adarsh Bhimraj, Karin Byers, Sheldon L. Kaplan, W. Michael Scheld, Diederik van de Beek, Thomas P. Bleck, Hugh J.L. Garton, Joseph R. Zunt For full document, including tables and references, please visit the Oxford University Press website. PDF The Infectious Diseases Society of America (IDSA) Standards and Practice Guidelines Committee collaborated with partner organizations to convene a panel of 10 experts on healthcare-associated ventriculitis and meningitis. The panel represented pediatric and adult specialists in the field of infectious diseases and represented other organizations whose members care for patients with healthcare-associated ventriculitis and meningitis (American Academy of Neurology, American Association of Neurological Surgeons, and Neurocritical Care Society). The panel reviewed articles based on literature reviews, review articles and book chapters, evaluated the evidence and drafted recommendations. Questions were reviewed and approved by panel members. Subcategories were included for some questions based on specific populations of patients who may develop healthcare-associated ventriculitis and meningitis after the following procedures or situations: cerebrospinal fluid shunts, cerebrospinal fluid drains, implantation of intrathecal infusion pumps, implantation of deep brain stimulation hardware, and general neurosurgery and head trauma. Recommendations were followed by the strength of the recommendation and the quality of the evidence supporting the recommendation. Many recommendations, however, were based on expert opinion because rigorous clinical data are not available. These guidelines represent a practical and useful approach to assist practicing clinicians in the management of these challenging infections. Keywords: ventriculitis; meningitis, cerebrospinal fluid shunts, cerebrospinal fluid drains, central nervous system infections Meningitis may not only be acquired in the community setting, but may be associated with a variety of invasive procedures or head trauma. The latter group has often been classified as nosocomial meningitis because a different spectrum of microorganisms (ie, resistant gram-negative bacilli and staphylococci) is the more likely the etiologic agents, and different pathogenic mechanisms are associated with the development of this disease. Although many of these patients present with clinical symptoms during hospitalization, ventriculitis and meningitis may develop after hospital discharge or even many years later. We, therefore, prefer the term "healthcare-associated ventriculitis and meningitis" to be more representative of the diverse mechanisms (that include placement of devices) that can lead to these serious illnesses. Summarized below are recommendations for the evaluation, diagnosis, and management of healthcare-associated ventriculitis and meningitis, specifically addressing the approach to infections associated with cerebrospinal fluid shunts, cerebrospinal fluid drains, intrathecal drug (eg, baclofen) therapy, deep brain stimulation hardware, and neurosurgery and head trauma. These infections may be difficult to diagnose because changes in cerebrospinal fluid parameters are often subtle, making it hard to determine if the abnormalities are related to infection, related to placement of devices, or following neurosurgery. Many of our recommendations are based on expert opinion because rigorous clinical data are not available and the likelihood that clinical trials will be conducted to answer some of these questions is low. Our goal was to develop guidelines that offered a practical and useful approach to assist practicing clinicians in the management of these challenging infections. The panel followed a process used in the development of other IDSA guidelines that included a systematic weighting of the strength of recommendations and quality of evidence using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system (Figure 1) [1–5]. A detailed description of the methods, background, and evidence summaries that support each recommendation can be found in the full text of the guidelines. I. What are the Typical Symptoms and Signs in Patients with Healthcare-Associated Ventriculitis and Meningitis? Cerebrospinal Fluid Shunts and Drains New headache, nausea, lethargy, and/or change in mental status are suggestive of cerebrospinal fluid (CSF) shunt infection (strong, moderate). Erythema and tenderness over the subcutaneous shunt tubing are suggestive of CSF shunt infection (strong, moderate). Fever, in the absence of another clear source of infection, could be suggestive of CSF shunt infection (weak, low). Symptoms and signs of peritonitis or abdominal tenderness in patients with ventriculoperitoneal shunts, in the absence of another clear etiology, are indicative of CSF shunt infection (strong, moderate). Symptoms and signs of pleuritis in patients with ventriculopleural shunts, in the absence of another clear etiology, are indicative of CSF shunt infection (strong, moderate). Demonstration of bacteremia in a patient with a ventriculoatrial shunt, in the absence of another clear source of bacteremia, is evidence of CSF shunt infection (strong, moderate). Demonstration of glomerulonephritis in a patient with a ventriculoatrial shunt is suggestive of CSF shunt infection (weak, low). New or worsening altered mental status in patients with external ventricular drains is suggestive of infection (weak, low). New fever and increased CSF white blood cell count in patients with external ventricular drains could be suggestive of infection (weak, low). Neurosurgery or Head Trauma New headache, fever, evidence of meningeal irritation, seizures, and/or worsening mental status are suggestive of ventriculitis or meningitis in the setting of recent trauma or neurosurgery (strong, moderate). Fever, in the absence of another clear source of infection, is suggestive of central nervous system (CNS) infection in the setting of recent head trauma or neurosurgery (weak, low). Intrathecal Infusion Pumps New fever and drainage from the surgical site in patients with intrathecal infusion pumps are suggestive of wound infection (weak, low). II. What are the Typical Cerebrospinal Fluid Findings in Patients with Healthcare-Associated Ventriculitis and Meningitis? Cell Count, Glucose, and Protein Abnormalities of CSF cell count, glucose, and/or protein may not be reliable indicators for the presence of infection in patients with healthcare-associated ventriculitis and meningitis (weak, moderate). Normal CSF cell count, glucose, and protein may not reliably exclude infection in patients with healthcare-associated ventriculitis and meningitis (weak, moderate). A negative CSF Gram stain does not exclude the presence of infection, especially in patients who have received previous antimicrobial therapy (strong, moderate). Culture CSF cultures are the most important test to establish the diagnosis of healthcare-associated ventriculitis and meningitis (strong, high). If initial CSF cultures are negative in patients with CSF shunts or drains with suspected infection, it is recommended that cultures be held for at least 10 days in an attempt to identify organisms such as Propionibacterium acnes (strong, high). If a CSF shunt or drain is removed in patients suspected of having infection, cultures of shunt and drain components are recommended (strong, moderate). If a CSF shunt or drain is removed for indications other than infection, cultures of shunt or drain components are not recommended (strong, moderate). Blood cultures are recommended in patients with suspected ventriculoatrial shunt infections (strong, high). Blood cultures may be considered in patients with ventriculoperitoneal and ventriculopleural shunts (weak, low). Single or multiple positive CSF cultures in patients with CSF pleocytosis and/or hypoglycorrhachia, or an increasing cell count, and clinical symptoms suspicious for ventriculitis or meningitis, is indicative of CSF drain infection (strong, high). CSF and blood cultures in selected patients should be obtained before the administration of antimicrobial therapy; a negative CSF culture in the setting of previous antimicrobial therapy does not exclude healthcare-associated ventriculitis and meningitis (strong, moderate). Neurosurgery or Head Trauma CSF pleocytosis with a positive culture and symptoms of infection are indicative of a diagnosis of healthcare-associated ventriculitis or meningitis (strong, high). Hypoglycorrhachia and elevated CSF protein concentrations are suggestive of the diagnosis of healthcare-associated ventriculitis or meningitis (weak, low). Growth of an organism that is commonly considered a contaminant (eg, coagulase-negative staphylococcus) in enrichment broth only or on just 1 of multiple cultures in a patient with normal CSF and no fever is not indicative of healthcare-associated ventriculitis or meningitis (strong, low). CSF cultures with multiple organisms from a single sample may be contaminants in patients with no symptoms of infection or CSF pleocytosis (weak, low). CSF cultures that grow Staphylococcus aureus or aerobic gram-negative bacilli are indicative of infection (strong, moderate). CSF cultures that grow a fungal pathogen are indicative of infection (strong, moderate). III. What Specific Tests of Cerebrospinal Fluid can be used to Confirm the Patient has Healthcare-Associated Ventriculitis and Meningitis? An elevated CSF lactate or an elevated CSF procalcitonin, or the combination of both, may be useful in the diagnosis of healthcare-associated bacterial ventriculitis and meningitis (weak, moderate). An elevated serum procalcitonin may be useful in differentiating between CSF abnormalities due to surgery or intracranial hemorrhage from those due to bacterial infection (weak, low). Nucleic acid amplification tests, such as polymerase chain reaction, on CSF may both increase the ability to identify a pathogen and decrease the time to making a specific diagnosis (weak, low). Detection of β-D-glucan and galactomannan in CSF may be useful in the diagnosis of fungal ventriculitis and meningitis (strong, moderate). IV. What is the Role of Imaging in Patients with Suspected Healthcare-Associated Ventriculitis and Meningitis? Neuroimaging is recommended in patients with suspected healthcare-associated ventriculitis and meningitis (strong, moderate). Magnetic resonance imaging with gadolinium enhancement and diffusion-weighted imaging is recommended for detecting abnormalities in patients with healthcare-associated ventriculitis and meningitis (strong, moderate). In patients with infected ventriculoperitoneal shunts and abdominal symptoms (eg, pain or tenderness), an ultrasound or computed tomography of the abdomen is recommended to detect CSF loculations at the shunt terminus (strong, moderate). V. What is the Empiric Antimicrobial Approach for Patients with Suspected Healthcare-Associated Ventriculitis and Meningitis? Vancomycin plus an anti-pseudomonal beta-lactam (such as cefepime, ceftazidime, or meropenem) is recommended as empiric therapy for healthcare-associated ventriculitis and meningitis; the choice of empiric beta-lactam agent should be based on local in vitro susceptibility patterns (strong, low). In seriously ill adult patients with healthcare-associated ventriculitis and meningitis, the vancomycin trough concentration should be maintained at 15–20 µg/mL in those who receive intermittent bolus administration (strong, low). For patients with healthcare-associated ventriculitis and meningitis who have experienced anaphylaxis to beta-lactam antimicrobial agents and in whom meropenem is contraindicated, aztreonam or ciprofloxacin is recommended for gram-negative coverage (strong, low). For patients with healthcare-associated ventriculitis and meningitis who are colonized or infected elsewhere with a highly antimicrobial-resistant pathogen, adjusting the empiric regimen to treat for this pathogen is recommended (strong, low). VI. Once a Pathogen is Identified, What Specific Antimicrobial Agent(s) Should be Administered? For treatment of infection caused by methicillin-susceptible S. aureus, nafcillin or oxacillin is recommended (strong, moderate). If the patient cannot receive beta-lactam agents, the patient can be desensitized or may receive vancomycin as an alternative agent (weak, moderate). For treatment of infection caused by methicillin-resistant S. aureus, vancomycin is recommended as first-line therapy (strong, moderate), with consideration for an alternative antimicrobial agent if the vancomycin minimal inhibitory concentration (MIC) is ≥1 µg/mL (strong, moderate). For treatment of infection caused by coagulase-negative staphylococci, the recommended therapy should be similar to that for S. aureus and based on in vitro susceptibility testing (strong, moderate). If the staphylococcal isolate is susceptible to rifampin, this agent may be considered in combination with other antimicrobial agents for staphylococcal ventriculitis and meningitis (weak, low); rifampin is recommended as part of combination therapy for any patient with intracranial or spinal hardware such as a CSF shunt or drain (strong, low). For treatment of patients with healthcare-associated ventriculitis and meningitis caused by staphylococci in whom beta-lactam agents or vancomycin cannot be used, linezolid (strong, low), daptomycin (strong, low), or trimethoprim-sulfamethoxazole (strong, low) is recommended, with selection of a specific agent based on in vitro susceptibility testing. For treatment of infection caused by Propionibacterium acnes, penicillin G is recommended (strong, moderate). For treatment of infection caused by gram-negative bacilli, therapy should be based on in vitro susceptibility testing with agents that achieve good CNS penetration (strong, moderate). For treatment of infection caused by gram-negative bacilli susceptible to third-generation cephalosporins, ceftriaxone or cefotaxime is recommended (strong, moderate). For treatment of infection caused by Pseudomonas species, the recommended therapy is cefepime, ceftazidime, or meropenem (strong, moderate); recommended alternative antimicrobial agents are aztreonam or a fluoroquinolone with in vitro activity (strong, moderate). For treatment of infection caused by extended-spectrum beta-lactamase–producing gram-negative bacilli, meropenem should be used if this isolate demonstrates in vitro susceptibility (strong, moderate). For treatment of infection caused by Acinetobacter species, meropenem is recommended (strong, moderate); for strains that demonstrate carbapenem resistance, colistimethate sodium or polymyxin B (either agent administered by the intravenous and intraventricular routes) is recommended (strong, moderate). Prolonged infusion of meropenem (each dose administered over 3 hours) may be successful in treating resistant gram-negative organisms (weak, low). For treatment of infection caused by Candida species, based on in vitro susceptibility testing, liposomal amphotericin B, often combined with 5-flucytosine, is recommended (strong, moderate); once the patient shows clinical improvement, therapy can be changed to fluconazole if the isolated species is susceptible (weak, low). For treatment of infection caused by Aspergillus or Exserohilum species, voriconazole is recommended (strong, low). VII. What is the Role of Intraventricular Antimicrobial Therapy in Patients with Healthcare-Associated Ventriculitis and Meningitis? Intraventricular antimicrobial therapy should be considered for patients with healthcare-associated ventriculitis and meningitis in which the infection responds poorly to systemic antimicrobial therapy alone (strong, low). When antimicrobial therapy is administered via a ventricular drain, the drain should be clamped for 15–60 minutes to allow the agent to equilibrate throughout the CSF (strong, low). Dosages and intervals of intraventricular antimicrobial therapy should be adjusted based on CSF antimicrobial concentrations to 10–20 times the MIC of the causative microorganism (strong, low), ventricular size (strong, low), and daily output from the ventricular drain (strong, low). VIII. What is the Optimal Duration of Antimicrobial Therapy in Patients with Healthcare-Associated Ventriculitis and Meningitis? Infections caused by a coagulase-negative staphylococcus or P. acnes with no or minimal CSF pleocytosis, normal CSF glucose, and few clinical symptoms or systemic features should be treated for 10 days (strong, low). Infections caused by a coagulase-negative staphylococcus or P. acnes with significant CSF pleocytosis, CSF hypoglycorrhachia, or clinical symptoms or systemic features should be treated for 10–14 days (strong, low). Infections caused by S. aureus or gram-negative bacilli with or without significant CSF pleocytosis, CSF hypoglycorrhachia, or clinical symptoms or systemic features should be treated for 10–14 days (strong, low); some experts suggest treatment of infection caused by gram-negative bacilli for 21 days (weak, low). In patients with repeatedly positive CSF cultures on appropriate antimicrobial therapy, treatment should be continued for 10–14 after the last positive culture (strong, low). IX. What is the Role of Catheter Removal in Patients with Cerebrospinal Fluid Shunts or Drains? Complete removal of an infected CSF shunt and replacement with an external ventricular drain combined with intravenous antimicrobial therapy is recommended in patients with infected CSF shunts (strong, moderate). Removal of an infected CSF drain is recommended (strong, moderate). Removal of an infected intrathecal infusion pump is recommended (strong, moderate). Removal of infected hardware in patients with deep brain stimulation infections is recommended (strong, moderate). X. How are Patients Monitored for Response to Treatment? Patients with healthcare-associated ventriculitis and meningitis should be monitored for response to treatment based on clinical parameters (strong, low). In patients with healthcare-associated ventriculitis and meningitis and an external drainage device, monitoring of CSF cultures is recommended to ensure that they become negative (strong, low). In patients with no definitive clinical improvement, additional CSF analysis is recommended to ensure that the CSF parameters have improved and the cultures become negative (strong, low). For external CSF drains not being used in the treatment of CSF shunt infection, daily CSF cultures and analysis are not recommended unless clinically indicated (strong, low). XI. In Patients with Cerebrospinal Fluid Shunts Who Develop Ventriculitis and Meningitis, When can a New Shunt be Reimplanted? In patients with infection caused by coagulase-negative staphylococci or P. acnes, with no associated CSF abnormalities and with negative CSF cultures for 48 hours after externalization, a new shunt should be reimplanted as soon as the third day after removal (strong, low). In patients with infection caused by a coagulase-negative staphylococcus or P. acnes, with associated CSF abnormalities but negative repeat CSF cultures, a new shunt should be reimplanted after 7 days of antimicrobial therapy (strong, low); if repeat cultures are positive, antimicrobial treatment is recommended until CSF cultures remain negative for 7–10 consecutive days before a new shunt is placed (strong, low). In patients with infection caused by S. aureus or gram-negative bacilli, a new shunt should be reimplanted 10 days after CSF cultures are negative (strong, low). A period off antimicrobial therapy is not recommended to verify clearing of the infection before shunt reimplantation (strong, low). XII. What is the Best Approach to Prevent Infection in Patients Who are Receiving Cerebrospinal Fluid Shunts? Periprocedural prophylactic antimicrobial administration is recommended for patients undergoing CSF shunt or drain insertion (strong, moderate). Periprocedural prophylactic antimicrobial administration is recommended for patients undergoing placement of external ventricular drains (strong, moderate). Prolonged antimicrobial prophylaxis for the duration of the external ventricular drain is of uncertain benefit and not recommended (strong, moderate). Use of antimicrobial-impregnated CSF shunts and CSF drains is recommended (strong, moderate). In patients with external ventricular drains, fixed interval exchange is not recommended (strong, moderate). Use of a standardized protocol for insertion of CSF shunts and drains is recommended (strong, moderate). XIII. Is there a Role for Prophylactic Antimicrobial Therapy in Patients Undergoing Neurosurgery or in those with Cerebrospinal Fluid Leak? For neurosurgical patients, perioperative antimicrobial agents are recommended to prevent infections of the incision (strong, high). In patients with basilar skull fractures and a CSF leak, prophylactic antimicrobial agents are not recommended (strong, moderate). In patients with basilar skull fractures and a prolonged CSF leakage (>7 days), an attempt to repair the leak is recommended (strong, low). In patients with basilar skull fractures and a CSF leak, pneumococcal vaccination is recommended (strong, moderate). Meningitis may be acquired in the community setting or may be associated with a variety of invasive procedures or head trauma. The latter group has often been classified as nosocomial meningitis because a different spectrum of microorganisms (eg, resistant gram-negative bacilli and staphylococci) is the more likely etiologic agents and because different pathogenic mechanisms are associated with the development of this disease. Although many of these patients present with clinical symptoms during hospitalization, ventriculitis and meningitis may develop after hospital discharge or even many years later. Therefore, the term "healthcare-associated ventriculitis and meningitis" is more representative of the diverse mechanisms that can lead to this serious illness. The following sections describe specific circumstances associated with healthcare-associated ventriculitis and meningitis. Cerebrospinal Fluid Shunts Cerebrospinal fluid (CSF) shunts are considered permanent catheters in which the proximal end of the shunt is in the cerebral ventricle, subdural space, an intracranial cyst, or the lumbar subarachnoid space; the distal end usually terminates in the peritoneal, pleural, or vascular space. Typically, part of the system (as a separate integrated component) is a pressure-regulating valve that is usually placed just outside the skull or as an integral part of the distal tubing [6]. Reservoirs for intermittent percutaneous access can also be added to the system or incorporated into the valve assembly. Additional hardware may include antisiphon valves and various connectors, allowing interconnection of more than 1 catheter or device. The case incidence of CSF shunt infection (ie, the occurrence of infection in any given patient) has ranged from 5% to 41% in various series, although the incidence is usually in the range of 4%–17% [7–14]. The operative incidence (ie, the occurrence of infection per procedure) has ranged from 2.8% to 14%, although most series have generally reported operative infection rates of less than 4% [15–17]. Factors associated with an increased risk of CSF shunt infection include premature birth (especially when associated with intraventricular hemorrhage), younger age, previous shunt infection, cause of hydrocephalus (more likely after purulent meningitis, hemorrhage, and myelomeningocele), less experienced neurosurgeon, higher number of people traversing the operating theater, exposure to perforated surgical gloves, intraoperative use of the neuroendoscope, longer duration of the shunt procedure, insertion of the catheter below the level of the T7 vertebral body in those with ventriculoatrial shunting, improper patient skin preparation, shaving of skin, exposure of large areas of the patient's skin during the procedure, and shunt revision (risk is especially high in those undergoing 3 or more revisions) [18, 19]. There are 4 mechanisms by which CSF shunts may become infected. The first, and most frequent, mechanism is colonization of the shunt at the time of surgery. This mechanism is suggested by the timing of most shunt infections and by the microorganisms that are isolated. In one study in adults with CSF shunt–associated infections, 62% occurred within the first month after shunt surgery and 72% were thought to be acquired intraoperatively [14]. The second mechanism is retrograde infection from the distal end of the shunt; for example, bowel perforation can lead to distal catheter contamination in patients with ventriculoperitoneal shunts. In addition, certain populations of patients with CSF shunts, such as those with myelomeningocele, may have undergone multiple intraabdominal procedures related to either bowel or bladder continence and may be at greater risk for shunt infection via this route. A third mechanism is through the skin, such as after insertion of a needle into the reservoir or the shunt to culture the CSF or assess patency, after injection of a drug into the ventricular reservoir, or after erosion of the catheter through the skin. The fourth mechanism is hematogenous seeding; patients with ventriculoatrial shunts have a foreign body (ie, the catheter) in the vascular system and are at continued risk of infection from bacteremia (with a retrograde infection). Patients with existing CSF shunts can also develop community-acquired bacterial meningitis unrelated to the shunt, and this may need to be considered in the appropriate clinical circumstance. Cerebrospinal Fluid Drains CSF drains are temporary catheters that divert CSF externally [20]. The proximal end is in the cerebral ventricle (ventricular drain), the subdural space, an intracranial cyst, or the lumbar subarachnoid space (lumbar drain). External ventricular drains are most useful for temporary management in patients with elevated intracranial pressure secondary to acute hydrocephalus caused by intracranial hemorrhage, neoplasm obstruction of the CSF circulation, or trauma. The distal end of the catheter is connected to a collecting system, which has a drip chamber, ports for measuring intracranial pressure, sampling and injection ports (used to obtain CSF and inject medications), and a collection bag. Drains are usually placed via 1 incision and then tunneled a distance subcutaneously before exiting through the skin. In patients with external ventricular drains, the incidence of ventriculitis has ranged from 0% to 22%. In a large metaanalysis of 35 studies that yielded 752 infections from 66706 catheter-days of observation [21], the overall pooled incidence of external ventricular drain–related CSF infection was 11.4 per 1000 catheter-days (95% confidence interval [CI], 9.3–13.5); for high-quality studies, the incidence was 10.6 per 1000 catheter-days (95% CI, 8.3–13). Factors associated with an increased risk of infection are intraventricular or subarachnoid hemorrhage, cranial fracture with CSF leak, catheter irrigation, craniotomy, and duration of catheterization. Although controversy exists regarding the relationship between the duration of catheterization and risk of infection, most studies consider extended catheter duration (usually exceeding 5 days) to be an important risk factor for subsequent infection [20]. However, in the metaanalysis cited above [21], studies in which patients had a mean catheter duration of less than 7 days had a pooled external ventricular drain infection rate of 19.6 per 1000 catheter-days, 12.8 per 1000 catheter-days for drains in place for 7–10 days, and 8 per 1000 catheter-days for drains in place for more than 10 days. Although infection is most likely introduced at the time of placement, retrograde infection is another mechanism of infection of CSF drains. Microorganisms may enter the device by tracking from the exit site alongside the device, gaining access to the fluid column that drains CSF, or they may be introduced from flushing of the tubing to maintain tubular patency. External lumbar drains, which may be placed to deal with complications of operative or post-traumatic transcutaneous CSF leak or to aid in the diagnosis of normal-pressure hydrocephalus (potentially a lower-risk group), have been associated with meningitis rates of up to 5%. The risk factors associated with these drains include disconnection of the external drainage system and the presence of other infections. In a study involving 233 consecutive patients who underwent placement of an external lumbar drain for normal-pressure hydrocephalus testing, the rate of meningitis was low (0.8%) [22]. The investigators in that study used a strict protocol that called for no surveillance testing of CSF, drainage of CSF for a maximum of 5 days, sterile reconnection after disconnection or fracture of the drain, and permanent removal of the drain after a second disconnection or fracture. Intrathecal Infusion Pumps Administration of drug therapy (eg, baclofen) via intrathecal infusion pumps has been successful for patients with intractable spasticity, most commonly in patients with cerebral palsy but also in patients with spasticity from multiple sclerosis, trauma, hereditary spastic paraplegia, and a variety of other conditions. Intrathecal opiate therapy has been used in the management of intractable pain, usually in patients with malignancy. The catheter is inserted in the lumbar region and passed intrathecally with the tip at the highest spinal cord level at which the drug is to be administered. Initially, the pumps were inserted subcutaneously in the abdomen, but this has been superseded in some centers, particularly those focused on pediatric patients, by placement below the abdominal fascia to decrease the risk of erosion through the skin. Once implanted, the device must be periodically refilled with the desired drug via transcutaneous puncture of the device. Few studies have evaluated the incidence of meningitis complicating use of intrathecal infusion pumps. Reported infection rates vary from 3.6% for those with subfascial placement of the pump to 20% for those with subcutaneous placement of the pump [23]. Infections are usually more common in pediatric series [24, 25]. Most reported infections are at the incision site; in one series, 3 of 49 patients developed meningitis in concert with an incisional infection, while 4 others had meningitis alone [26]. Another retrospective study identified infectious complications in 38 (18.4%) of 207 children with intrathecal infusion pumps delivering baclofen therapy [27]. Of these 38 patients, 25 had suspected or superficial infections and 13 had deep-seated infections, with 2 patients diagnosed with meningitis. In many reports, it is not possible to distinguish meningitis from local infections related to the infusion pump. The majority of infections occur within the first 2 months of surgery, but infections may occur years after implantation as access for drug refills may be needed every 3–6 months for the service life of the device [26, 28]. The majority of reported infections are caused by Staphylococcus aureus, but a variety of other organisms, including multiply drug-resistant gram-negative bacilli, have been recovered. Deep Brain Stimulation Hardware Deep brain stimulation, introduced in 1987 for the treatment of Parkinson's disease, is now being used for other conditions such as dystonia, essential tremor, and obsessive-compulsive disorder [29]. The stimulator consists of an intracranial lead, a connector, and a pulse generator that is implanted in the infraclavicular area [30]. The incidence of infections following implantation of deep brain stimulation hardware varies from 0.62% to 14.3% and can involve all 3 components of the device. The infection of the pulse generator is the most common, with infection usually caused by S. aureus, a coagulase-negative staphylococcus, or Propionibacterium acnes. These infections may occur after initial implant or after the battery is exchanged at a subsequent surgery. Brain stimulation for intractable focal epilepsy involves placement of a combination of cortical and depth electrodes intracranially. These electrodes are used to both sense abnormal electroencephalographic activity and to deliver patterned electrical stimuli to interrupt developing seizures. The electrodes are connected to a controller that is implanted in the skull. In initial trials of this system, involving 256 patients, 2% of patients had a post-operative superficial wound infection; most were treated successfully with antimicrobial therapy, but 1 patient required explantation of the system [31]. The mean follow-up period was 5.4 patient implant years (a total of 1389 patient implant years), during which 20 patients (7.8%) experienced a soft tissue infection at the implant site. Fourteen of these patients underwent removal of the stimulator. The organisms involved and their treatments were not reported. Neurosurgery or Head Trauma Ventriculitis and meningitis can be complications in patients who have undergone neurosurgery or head trauma. Because concern and evaluation of infection in the post-surgical and post-traumatic situations usually occur after a period of hospitalization, this phenomenon is termed "healthcare-associated," recognizing that there will be individual instances, such as in trauma, in which the contamination that led to infection occurred prior to the patient's entry into the healthcare system. The diagnosis may be difficult to establish since surgery and trauma can both induce CSF abnormalities that confound the usual diagnostic studies. These patients may also have fever for reasons unrelated to infection (eg, central fever, drug fever, thrombophlebitis, or chemical meningitis after posterior fossa surgery). Also, they are at increased risk of developing infection because of the risk associated with surgery (including surgery after head trauma), direct contamination of the central nervous system (CNS), and the increased risk of meningitis in patients with a CSF leak. In a study of 334 procedures in patients undergoing craniotomy, risk factors associated with post-craniotomy meningitis were use of CSF drain, CSF leak, and perioperative steroid use [32]. Healthcare-associated ventriculitis and meningitis is a problem at medical facilities that perform neurosurgery. In a review of all causes of meningitis at Massachusetts General Hospital between 1962 and 1988, 40% were classified as nosocomial in origin [33]. In another study of confirmed bacterial meningitis in adults who were hospitalized at an acute care teaching hospital in southern Taiwan, 48% of cases were classified as nosocomial infections [34]. In a recent epidemiological study of bacterial meningitis in the United States [35], the incidence of meningitis caused by nosocomial pathogens (eg, gram-negative bacilli and S. aureus) approached that caused by Neisseria meningitidis. These guidelines address the management of children and adults with healthcare-associated ventriculitis and meningitis with the objective to provide evidence-based guidelines to manage these infections. Practice Guidelines "Practice guidelines are systematically developed statements to assist practitioners and patients in making decisions about appropriate health care for specific clinical circumstances" [36]. Attributes of good guidelines include validity, reliability, reproducibility, clinical applicability, clinical flexibility, clarity, multidisciplinary process, review of evidence, and documentation [36]. Panel Composition The Infectious Diseases Society of America (IDSA) Standards and Practice Guidelines Committee (SPGC) collaborated with partner organizations to convene a panel of 10 experts on healthcare-associated ventriculitis and meningitis. The panel represented pediatric and adult specialists in the field of infectious diseases and represented other organizations whose members care for patients with healthcare-associated ventriculitis and meningitis, including the following: American Academy of Neurology, American Association of Neurological Surgeons (AANS), Congress of Neurological Surgeons (CNS), Neurocritical Care Society (NCS), and Society for Healthcare Epidemiology of America (SHEA). The AANS and CNS affirm the educational content and the AAN affirms the value of this document. These guidelines were reviewed and endorsed by NCS and SHEA. These guidelines were also reviewed and approved by the IDSA SPGC and the Board of Directors (BOD). Process Overview, Literature Selection, and Consensus Development Based on Evidence The panel followed a process used by IDSA in the development of other guidelines. The process included a systematic weighting of the quality of the evidence and the grade of the recommendation (Figure 1). [Approach and implications to rating the quality of evidence and strength of recommendations using the GRADE methodology. Available at: —Accessed July 2015]. The panel reviewed articles based on literature reviews (using PubMed and Medline); reviewed articles and book chapters (including references published in reviews and chapters); evaluated the evidence, which included analysis of source literature; and drafted recommendations. Panel members reviewed and approved questions. Subcategories were included for some questions based on specific populations of patients who may develop healthcare-associated ventriculitis and meningitis after the following procedures or situations: cerebrospinal fluid shunt placement, cerebrospinal fluid drain placement, implantation of intrathecal infusion pumps, implantation of deep brain stimulation hardware, and general neurosurgery and head trauma. Recommendations were followed by the strength of the recommendation and the quality of the evidence supporting the recommendation. Many recommendations, however, were based on expert opinion because rigorous clinical data are not available, and the likelihood that clinical trials will be conducted to answer some of these questions is low. For many of these recommendations, the grade was designated as "strong" and evidence was designated as "low" if there was consensus among the experts around specific recommendations. Drafts were reviewed by panel members, who provided input on the content as well as weighting and grading of the evidence. These guidelines represent a practical and useful approach to assist practicing clinicians in the management of these challenging infections. Guideline and Conflicts of Interest All panel members complied with IDSA policy on conflicts of interest, which requires disclosure of any financial or other interest that might be construed as constituting an actual, potential, or apparent conflict. They were provided IDSA's conflicts of interest disclosure statement and asked to identify ties to companies that develop products that might be affected by promulgation of the guideline. Information was requested regarding employment, consultancies, stock ownership, honoraria, research funding, expert testimony, and membership on company advisory committees. The panel decided on a case-by-case basis whether a conflict should limit member participation. Potential conflicts are listed in the Acknowledgments section. Future Revision Dates At annual intervals, the panel chair, SPGC liaison advisor, and SPGC chair will determine the need for guideline revisions by reviewing current literature. If necessary, the entire panel will be reconvened. When appropriate, the panel will recommend revisions to the IDSA SPGC, BOD, and other collaborating organizations for review and approval. I. What are the Typical Symptoms and Signs in Patients with Healthcare-Associated Ventriculitis and Meningitis? Cerebrospinal Fluid Shunts and Drains Recommendations New headache, nausea, lethargy, and/or change in mental status are suggestive of cerebrospinal fluid (CSF) shunt infection (strong, moderate). Erythema and tenderness over the subcutaneous shunt tubing are suggestive of CSF shunt infection (strong, moderate). Fever, in the absence of another clear source of infection, could be suggestive of CSF shunt infection (weak, low). Symptoms and signs of peritonitis or abdominal tenderness in patients with ventriculoperitoneal shunts, in the absence of another clear etiology, are indicative of CSF shunt infection (strong, moderate). Symptoms and signs of pleuritis in patients with ventriculopleural shunts, in the absence of another clear etiology, are indicative of CSF shunt infection (strong, moderate). Demonstration of bacteremia in a patient with a ventriculoatrial shunt, in the absence of another clear source of bacteremia, is evidence of CSF shunt infection (strong, moderate). Demonstration of glomerulonephritis in a patient with a ventriculoatrial shunt is suggestive of CSF shunt infection (weak, low). New or worsening altered mental status in patients with external ventricular drains is suggestive of infection (weak, low). New fever and increased CSF white blood cell count in patients with external ventricular drains could be suggestive of infection (weak, low). Evidence Summary The clinical features of CSF shunt infection can be quite variable and depend on the pathogenesis of infection, organism virulence, and type of shunt [14, 37–39]. Unlike the organisms that cause community-acquired bacterial meningitis, those that cause CSF catheter-associated ventriculitis, such as coagulase-negative staphylococci and P. acnes, are indolent, evoke minimal inflammation, and are primarily pathogenic in the presence of prosthetic material. Frequently, there may only be minimal ventriculitis without meningeal involvement or only mechanical blockage as a result of biofilm formation in or on the catheter [40, 41]. Therefore, the clinical symptoms of meningitis may be absent and the clinical presentation more subtle with a longer duration of symptoms. The most frequent symptoms in patients with CSF shunt infection are headache, nausea, lethargy, and change in mental status (seen in as many as 65% of infected patients). These symptoms occur as a result of shunt malfunction secondary to the infection. Fever is reported in as few as 14% to as many as 92% of cases, so the absence of fever cannot exclude the possibility of infection, although fever is typically present in the majority of patients. Pain, often related to infection at the peritoneal or pleural endings of the shunt, may be absent in as many as 60% of infections [42]. Clinically, individual symptoms are not typically both sensitive and specific [43, 44]. This is not surprising since the most common presenting complaints associated with a request for assessment of a CSF shunt for infection (ie, headache, nausea, vomiting, irritability, and fever) are present in a wide variety of other illnesses. Because the vast majority of shunt infections occur in the first few months after shunt surgery, the positive and negative predictive values of individual symptoms will change depending on when the shunt procedure was performed [45]. Symptoms and signs of a CSF shunt infection may be referable either to the proximal or distal portion of the shunt. Infection beginning in the proximal portion of the shunt (ie, the catheter within the CSF space) may result in ventriculitis or meningitis and may cause shunt obstruction or decreased function [38, 46]. Rarely, intracranial empyemas and abscesses may occur secondary to an incompletely treated infection or in the presence of hardware not removed as part of the treatment process. Symptoms of infection referable to the distal portion of the shunt are more specific to terminus location [46]. Infected shunts that terminate in the peritoneal or pleural space may lead to an inflammatory response in the absorbing tissue (ie, peritonitis or pleuritis). In patients with infected ventriculoperitoneal shunts, symptoms of peritonitis appear as the peritoneal inflammation becomes more severe and as fever, anorexia, and other signs and symptoms of an acute abdomen develop. With low-virulence organisms, localizing signs of peritonitis may be confined to abdominal tenderness and/or guarding. In the peritoneal cavity, host defense mechanisms attempt to limit the infection, often resulting in the encystment of the shunt catheter, fluid buildup within the cyst, and loculation of pockets of fluid within the abdomen. These fluid collections, often termed pseudocysts, can grow quite large because the loculated CSF is not absorbed within the cyst. Partial or complete shunt obstruction may result. However, pseudocyst formation may be the result of noninfectious etiologies (eg, local inflammatory response to the foreign body) that will resolve with reimplantation of the distal part of the catheter. Infected ventriculoatrial shunts may lead to bacteremia secondary to infected CSF directly entering the bloodstream, an infected thrombus or atrial mural vegetation at the end of the vascular catheter, or true bacterial endocarditis. However, the clinical presentation of an infected vascular shunt is usually nonspecific, with fever and lethargy often seen. One unique complication of a chronic vascular shunt is shunt nephritis [10, 38, 46], which is observed in 4%–14% of patients with infected ventriculoatrial shunts. The majority of isolated bacteria in patients with shunt nephritis are usually coagulase-negative staphylococci and S. aureus, although diphtheroids and other pathogens have been isolated. The pathogenesis of shunt nephritis is similar to that of subacute bacterial endocarditis, with deposition of immunoglobulin M and G antigen–antibody complexes in the renal glomeruli. The complement system is activated with subsequent depletion of circulating complement factors C3 and C4. Failure to detect this condition can lead to permanent kidney injury. However, some shunt infections are insidious and cause few or no symptoms, perhaps only an intermittent low-grade fever or general malaise. The patient may present with an unexplained occlusion of an open-ended peritoneal catheter or failure of peritoneal CSF

absorption. Cerebrospinal Fluid Drains Recommendations New or worsening altered mental status in patients with external ventricular drains is suggestive of infection (weak, low). New fever and increased CSF white blood cell count in patients with external ventricular drains could be suggestive of infection (weak, low). Evidence Summary Ventricular drains become infected from organisms that are introduced through the drainage system or through the skin site [47, 48]. Infections are more frequent with external ventricular drains than with CSF shunts and may be caused by hospital flora. The change in mental status that occurs in patients in whom meningitis or ventriculitis develops may be difficult to distinguish from the impaired level of consciousness that is a manifestation of the patient's underlying disease. In patients with CSF drain–related ventriculitis, symptoms and signs are not very useful in determining the underlying reason for drain placement; subarachnoid hemorrhage or tumor can also cause a similar neurologic presentation and these patients are often unresponsive in the intensive care unit and unable to report symptoms. Fever that occurs in these patients may also be from other sources of infection. In one study that compared the clinical and laboratory findings at the time of insertion of the external ventricular drain and at the time of documented infection, increasing CSF pleocytosis (median white blood cell [WBC] count of 175/mm3) and fever were the most reliable indicators of infection [49]. Neurosurgery or Head Trauma Recommendations New headache, fever, evidence of meningeal irritation, seizures, and/or worsening mental status are suggestive of ventriculitis or meningitis in the setting of recent trauma or neurosurgery (strong, moderate). Fever, in the absence of another clear source of infection, is suggestive of central nervous system (CNS) infection in the setting of recent head trauma or neurosurgery (weak, low). Evidence Summary The recognition of infectious meningitis or ventriculitis in patients who have had recent neurosurgery or head trauma can be difficult because patients may not be able to provide any history. Because there are little data on patients in this setting, this recommendation is based largely on studies of patients with bacterial meningitis in the community. The usual symptoms and signs of meningitis can also be due to a recent intracranial bleed or other procedures such as neurosurgery. Fever and altered mental status may be the only signs of infection [50]. Fever and peripheral leukocytosis are also classic findings in meningitis, but there may be many other causes of these findings in a hospitalized patient [51]. Signs of meningeal irritation, including nuchal rigidity, are seen in only 20%–30% of patients [52, 53]. A history of a device placed into the CSF, a craniotomy or trauma resulting in contamination of the CSF, and the absence of another cause for fevers or seizures makes this diagnosis more likely. Intrathecal Infusion Pumps Recommendation New fever and drainage from the surgical site in patients with intrathecal infusion pumps are suggestive of wound infection (weak, low). Evidence Summary The clinical presentation of patients with intrathecal infusion pump infections is not well documented in the literature. One retrospective case series described 45 (8%) infections in 571 baclofen pump surgeries [28]. Clinical features were present for 12 patients with infection caused by gram-negative organisms. The most common presentations were fever and drainage from the surgical site. Other series have reported similar rates of infection [54]. As in patients who have CSF shunts, symptoms can be divided into those indicative of local wound infection (eg, erythema, swelling, and purulent drainage at surgical sites) and those indicative of meningitis. Patients may present with either or both of these classes of symptoms. In one series of 19 infectious complications in 119 patients [23], one-third of patients had meningitic symptoms, and one-half of those occurred in the absence of symptoms at the surgical site, most occurred soon after surgery, implying infection occurring at surgery rather than as a result of a pump refill. II. What are the Typical Cerebrospinal Fluid Findings in Patients with Healthcare-Associated Ventriculitis and Meningitis? Cell Count, Glucose, and Protein Recommendations Abnormalities of CSF cell count, glucose, and/or protein may not be reliable indicators for the presence of infection in patients with healthcare-associated ventriculitis and meningitis (weak, moderate). Normal CSF cell count, glucose, and protein may not reliably exclude infection in patients with healthcare-associated ventriculitis and meningitis (weak, moderate). A negative CSF Gram stain does not exclude the presence of infection, especially in patients who have received previous antimicrobial therapy (strong, moderate) Evidence Summary The diagnosis of CSF shunt and CSF drain infections is difficult. Nonspecific laboratory parameters (eg, leukocytosis, elevation of erythrocyte sedimentation rate or C-reactive protein) have not been evaluated in the approach to diagnosis of these infections. In patients with suspected CSF shunt infection (ie, in those in whom evidence of infection is suspected and other sources of infection have been excluded), consultation with a neurosurgeon is necessary to access CSF for analysis. Note that CSF may not need to be obtained if another clear source of infection has been identified. Changes in CSF parameters may be subtle [14], thus making it hard to determine if the abnormalities are related to infection or secondary to the underlying reason for catheter placement or a result of neurosurgery [55, 56]. Although high CSF white blood cell counts correlate with the presence of infection, infection may be present even in patients with normal CSF white blood cell counts. CSF white blood cell counts and lactate concentrations were normal in approximately 20% of episodes in one study of adults with shunt-associated infection [14]. CSF eosinophilia (>8% of the differential count) has been associated with an indolent infection [57]. Using a looser definition of eosinophilia (ie, >1% of the differential count), another analysis noted a correlation of eosinophilia with CSF infection but also with subcutaneous (not transcutaneous) CSF extravasation, blood in the CSF, younger age at shunt insertion, and intraventricular hemorrhage as a cause of the hydrocephalus [58]. However, others have questioned the association between CSF eosinophil count and infection [59]. The cell count may be obscured by recent surgery during which blood spilled into the CSF or may have caused an inflammatory reaction, so-called chemical meningitis [55]. Attention should also be paid to the site of CSF sampling, as the CSF white blood cell count in samples obtained by shunt aspiration or from ventricular fluid tends to be lower than when CSF is obtained after lumbar puncture. Conversely, it should also be considered that in many patients with CSF shunts in the ventricular space, the lumbar cistern may not be in communication with the ventricular space, as is the case in obstructive hydrocephalus. In one cohort study of 230 consecutive patients with external CSF drains [56], CSF samples were collected daily and prospectively evaluated for the presence of bacteria using Gram stain and culture. In this study, lumbar catheters were placed in 125 patients (54.3%), ventricular catheters in 97 patients (42.2%), and more than 1 type of catheter in 8 patients (3.5%). The CSF was also analyzed for leukocyte count, protein concentration, glucose concentration, and ratio of CSF to blood glucose. External drainage–related bacterial meningitis developed in 22 patients (9.6%). Results from analyses of 1516 CSF samples showed no significant differences between the patients in whom external ventricular drain–related meningitis developed and a control group without external ventricular drain–related meningitis during the first 3 days of infection. Also, there were no significant differences during the 3 days preceding the infection with regard to leukocyte count, protein concentration, glucose concentration, and CSF-to-blood glucose ratio. The predictive and diagnostic values of the CSF parameters were evaluated using receiver operating characteristic curves. They could not establish a cutoff value with a sensitivity and specificity of at least 60% for any of the CSF parameters. In a prospective study that included 130 patients at a neurosurgical intensive care unit who received an external ventricular drain [60], daily CSF samples were obtained and examined for cell count and glucose and protein content. Bacteriological cultures were taken 3 times a week. Standard laboratory parameters, such as peripheral leukocyte count, CSF glucose, and CSF protein, were not reliable predictors for incipient ventricular catheter infection. The only parameter that significantly correlated with the occurrence of a positive CSF culture was the CSF cell count ($P < .05$). One prospective study evaluated the utility of cell index, which is the ratio of leukocytes to erythrocytes in CSF and of leukocytes to erythrocytes in peripheral blood, in predicting ventriculitis [61]. The study was limited to 13 patients with intraventricular hemorrhage who had external ventricular drains; 7 patients developed a culture-confirmed ventriculitis. Diagnosis by cell index was possible up to 3 days prior to conventional diagnosis. The results, however, have not been validated. The diagnostic accuracy of a Gram stain is a function of the number of microorganisms present, the type of meningeal pathogen, and the receipt of prior antimicrobial therapy [62]. A negative result of a CSF Gram stain does not exclude the likelihood of infection. The CSF Gram stain was positive in 65 (71%) of 91 cases in one study of patients with nosocomial meningitis [63]. Culture Recommendations CSF cultures are the most important test to establish the diagnosis of healthcare-associated ventriculitis and meningitis (strong, high). If initial CSF cultures are negative in patients with CSF shunts or drains with suspected infection, it is recommended that cultures be held for at least 10 days in an attempt to identify organisms such as Propionibacterium acnes (strong, high). If a CSF shunt or drain is removed in patients suspected of having infection, cultures of shunt and drain components are recommended (strong, moderate). If a CSF shunt or drain is removed for indications other than infection, cultures of shunt or drain components are not recommended (strong, moderate). Blood cultures are recommended in patients with suspected ventriculoatrial shunt infections (strong, high). Blood cultures may be considered in patients with ventriculoperitoneal and ventriculopleural shunts (weak, low). Single or multiple positive CSF cultures in patients with CSF pleocytosis and/or hypoglycorrhachia, or an increasing cell count, and clinical symptoms suspicious for ventriculitis or meningitis, is indicative of CSF drain infection (strong, high). CSF and blood cultures in selected patients should be obtained before the administration of antimicrobial therapy; a negative CSF culture in the setting of previous antimicrobial therapy does not exclude healthcare-associated ventriculitis and meningitis (strong, moderate). Evidence Summary CSF cultures from the shunt, reservoir, or drain are the most important tests for establishing the diagnosis of infection. The culture will usually be positive in patients with an infected device even when there is no pleocytosis or alterations in CSF chemistries. Positive cultures in only thioglycolate broth should be interpreted with caution but may be significant in the appropriate clinical circumstance (eg, in patients who have received prior antimicrobial therapy). CSF cultures may require several days to weeks of incubation before they can be called negative, especially for slow-growing organisms such as P. acnes, or the results may be negative in patients who have received previous antimicrobial therapy. A negative result of a CSF culture does not exclude the possibility of infection, and cultures should be repeated if initial cultures are negative and infection is considered likely. In a study of 245 children with bacterial meningitis, the sensitivity of the CSF culture decreased from 88% to 70% with any use of antimicrobial therapy ($P < .001$). The sensitivity further decreased to 59% if antimicrobial therapy was administered for >24 hours prior to the lumbar puncture, although patients with CSF shunts were specifically excluded from this study [64]. A similar study in patients with healthcare-associated ventriculitis and meningitis is currently lacking. However, one study of 86 cases of suspected nosocomial meningitis showed that use of broad-range 16S rRNA polymerase chain reaction (PCR) detected bacteria in approximately 50% of culture-negative cases [65]. Most of the patients who were PCR positive and culture negative had received previous antimicrobial therapy. Occasionally, CSF shunts may be tapped for evaluation of function in patients with no clinical evidence of infection and may be found to be culture positive. In this situation, contamination may be responsible for the positive culture, but true infection must be strongly considered. The shunt should be retapped; a positive culture with the same microorganism is usually indicative of true infection. Shunt failure in the absence of shunt infection is a common occurrence; shunt components are frequently removed during surgical procedures to revise the failed shunt. In the absence of clinical evidence of a CSF shunt infection, routine cultures of shunt components, when shunts are removed for other indications, is not recommended. In one study of 174 shunt revisions, 19 patients had positive shunt component cultures without signs of infection (ie, asymptomatic bacteriologic shunt contamination); only 1 patient was treated with antimicrobial therapy [66]. There was no increase in the risk of shunt malfunction in this group when compared to other patients with CSF shunts in the database at their institution. In patients with ventriculoatrial shunts, blood cultures should be performed because bacteremia is invariably present in patients with infected ventriculoatrial shunts (positive blood cultures in >90% of cases). This contrasts with infections in other types of CSF shunts in which the incidence of negative blood cultures approaches 80% [38]. Blood cultures may be considered in these patients, although positive results should be interpreted cautiously in patients with nonvascular CSF shunts and may represent a contaminant or another source of infection. In patients with lumbar or ventricular drains, definite infection is defined as a positive CSF culture (obtained from the ventricular or lumbar catheter) associated with CSF pleocytosis [20, 47]. Progressively decreasing CSF glucose and increasing CSF protein accompanied by advancing CSF pleocytosis, in the absence of positive CSF cultures or positive Gram stain, characterizes a suspected infection in the absence of another etiology. A contaminating microorganism is defined as an isolated positive CSF culture and/or positive Gram stain with a normal CSF cell count, CSF glucose, and CSF protein. Lozier et al [20] proposed a classification system for determination of ventriculostomy infection in the presence of ventriculitis. Cases with positive CSF cultures were classified as contaminant, colonization, suspected ventriculostomy-related infection, ventriculostomy-related infection, and ventriculitis. The definition of ventriculitis included "clinical signs of meningitis" such as neck stiffness and photophobia, which are often absent because organisms such as a coagulase-negative staphylococcus and P. acnes are indolent and may not cause significant inflammation. In addition, patients with subarachnoid hemorrhage can have symptoms that mimic meningitis. The classification we propose for patients with ventricular drains is a modification, as follows: Contamination: An isolated positive CSF culture or Gram stain, with normal CSF cell count and glucose and protein concentrations and with lack of clinical symptoms suspicious for ventriculitis or meningitis. Colonization: Multiple positive CSF cultures or Gram stain, with normal CSF cell count and glucose and protein concentrations and with lack of clinical symptoms suspicious for ventriculitis or meningitis. Infection: Single or multiple positive CSF cultures with CSF pleocytosis and/or hypoglycorrhachia, or an increasing cell count, and clinical symptoms suspicious for ventriculitis or meningitis. The Centers for Disease Control and Prevention's National Healthcare Safety Network (CDC/NHSN) definition of healthcare-associated ventriculitis or meningitis includes at least 1 of the following criteria (CDC/NHSN Surveillance Definitions; January 2015) [67]: Organism cultured from CSF At least 2 of the following symptoms with no other recognized cause in patients aged >1 year: fever >38°C or headache, meningeal signs, or cranial nerve signs, or at least 2 of the following symptoms with no other recognized cause in patients aged ≤1 year: fever >38°C or hypothermia 7500/mm3 or if the CSF glucose is 1 week) was more suggestive of infectious meningitis in one study [55], although a limitation of this study was that there was no single variable that could be used to accurately distinguish between bacterial and aseptic meningitis at the time of presentation. The most common CSF contaminants are coagulase-negative staphylococci. In a study of pediatric patients who had daily cultures, more than half of the positive cultures were thought to be contaminants, and a coagulase-negative staphylococcus was isolated in more than half of those with positive cultures [47]. It was thought to be a contaminant in 15 positive cultures and a true pathogen in only 3 cultures. However, a coagulase-negative staphylococcus is also one of the more common causes of infection in patients who have had recent surgery or who have external ventricular drains. Clues to this organism being a contaminant included light growth, growth only in enrichment broth, and growth of the organism in a minority of cultures. All patients with predefined "true infections" in this study had fever and a peripheral leukocytosis. However, these results have not been validated in other cohorts. When cultures are collected from a drainage device (eg, an external ventricular drain or a lumbar drain), the absence of any change in CSF parameters (eg, cell count, glucose, protein) suggests contamination. Ideally, cultures should be collected from the injection site and sampling port of an external ventricular drain rather than the drainage bag in order to decrease the risk of contamination. Similarly, with a lumbar drain, the sampling port is the preferred site for obtaining CSF. The majority of reports of healthcare-associated meningitis identified a single pathogen with each episode of meningitis. While sequential infections may be seen in a patient who has a drainage device for a long period of time, it would be unusual to develop an infection with multiple organisms simultaneously unless there was an obvious route of infection from a contaminated source (eg, after head trauma with open fracture). In the absence of a likely source, changes in the CSF, or symptoms of infection, this may represent contamination from the time of CSF collection. If there is a question of whether or not the culture represents contamination, it is reasonable to collect additional CSF to evaluate CSF parameters and repeat cultures in order to determine the significance of the result. Healthcare-associated fungal ventriculitis and meningitis is much less common than that caused by bacteria; however, it may be seen after surgery or other invasive procedures or trauma. In the post-operative setting, Candida species are the most likely pathogen. This organism has been implicated in premature infants and in 5% of cases following neurosurgery [69]. Other fungal pathogens have also been isolated after traumatic head injuries, including Aspergillus [70] and Cryptococcus neoformans [71]. The underlying host defect may also affect the epidemiology. In a review of oncology patients at Memorial Sloan-Kettering Cancer Center with meningitis between 1993 and 2004 [72], 7% of patients were infected with C. neoformans and 1% with Candida albicans; 78% of these patients had prior neurosurgery. In a multistate outbreak of fungal meningitis in September 2012 as a result of contaminated methylprednisolone made at a single compounding pharmacy in Massachusetts [73–75], the index patient was infected with Aspergillus fumigatus, but most of the subsequent infections were caused by Exserohilum rostratum. Of the 749 patients with infections, meningitis was seen in 233 (31%) cases. Another 151 patients (20%) had meningitis and a concurrent spinal or paraspinal infection. In addition, a large number of patients had epidural infections without meningitis [74]. III. What Specific Tests of Cerebrospinal Fluid can be used to Confirm the Patient has Healthcare-Associated Ventriculitis and Meningitis? Recommendations An elevated CSF lactate or an elevated CSF procalcitonin, or the combination of both, may be useful in the diagnosis of healthcare-associated bacterial ventriculitis and meningitis (weak, moderate). An elevated serum procalcitonin may be useful in differentiating between CSF abnormalities due to surgery or intracranial hemorrhage from those due to bacterial infection (weak, low). Nucleic acid amplification tests, such as polymerase chain reaction, on CSF may both increase the ability to identify a pathogen and decrease the time to making a specific diagnosis (weak, low). Detection of β-D-glucan and galactomannan in CSF may be useful in the diagnosis of fungal ventriculitis and meningitis (strong, moderate). Evidence Summary Lactate An elevated CSF lactate concentration of more than 3.5 to 4.2 mmol/L occurs more frequently in bacterial than in aseptic meningitis. Two large metaanalyses have concluded that elevated CSF lactate concentration is better than the CSF WBC count, glucose, or protein in differentiating bacterial meningitis from aseptic meningitis (sensitivity of 93% and 97% and specificity of 96% and 94%, respectively) [76, 77]. However, the studies in these metaanalyses mostly equated aseptic meningitis with viral meningitis, and few post-surgical or post-trauma patients were included. In patients with healthcare-associated ventriculitis and meningitis, CSF lactate concentrations, using a cutoff of 4 mmol/L, are both sensitive (88%) and highly specific (98%) in making the diagnosis of bacterial meningitis following neurosurgery [78]. The positive predictive value was 96% and the negative predictive value was 94%; this study included patients who had a lumbar puncture performed within 40 days of neurosurgery. However, the evidence is conflicting. In a prospective study of 16 patients with an intraventricular hemorrhage who had an external ventricular drain, the CSF lactate was elevated in all 3 patients with infection. In 11 of 13 patients without infection it was 1 ng/mL had a proven CSF infection. The mean procalcitonin concentration with a positive CSF culture was 4.7 ± 1.0 vs 0.2 ± 0.01 ng/mL ($P < .0001$). The sensitivity and specificity of this cutoff were both 100%. In this study, the CSF lactate in 34 patients with a positive culture compared to those with a negative culture was 42 mmol/L vs 34 mmol/L ($P = .76$) [83]. The CSF lactate in the group with negative cultures was higher than would be expected in patients without bacterial meningitis. This may be due to the large number of patients who had an intracranial hemorrhage. In a more recent observational prospective study of 36 adult patients with severe head trauma and an external ventricular drain [84], patients with negative CSF cultures had a mean serum procalcitonin concentration 100 mL/day, every other day if the drainage is 50–100 mL/day, and every third day if drainage is 38.5°C) and peripheral leukocytosis (>11000/mm3) on the day the infection was identified, and 1 had a change in CSF appearance. A prospective study also demonstrated no value of routine analysis of CSF for prediction and diagnosis of external drain–related bacterial meningitis [56]. Another study assessed whether the incidence of ventriculitis changed when CSF sampling frequency was reduced to once every 3 days [152]. In that study, a prospective sample of external ventricular drain–treated patients was compared to a historical comparison group at 2 tertiary hospital intensive care units. The incidence of ventriculitis decreased from 17% to 11% overall and, in those with proven ventriculitis, from 10% to 3% once sampling frequency was reduced. XI. In Patients with Cerebrospinal Fluid Shunts who Develop Ventriculitis and Meningitis, When can a New Shunt be Reimplanted? Recommendations In patients with infection caused by coagulase-negative staphylococci or P. acnes, with no associated CSF abnormalities and with negative CSF cultures for 48 hours after externalization, a new shunt should be reimplanted as soon as the third day after removal (strong, low). In patients with infection caused by a coagulase-negative staphylococcus or P. acnes, with associated CSF abnormalities but negative repeat CSF cultures, a new shunt should be reimplanted after 7 days of antimicrobial therapy (strong, low); if repeat cultures are positive, antimicrobial treatment is recommended until CSF cultures remain negative for 7–10 consecutive days before a new shunt is placed (strong, low). In patients with infection caused by S. aureus or gram-negative bacilli, a new shunt should be reimplanted 10 days after CSF cultures are negative (strong, low). A period off antimicrobial therapy is not recommended to verify clearing of the infection before shunt reimplantation (strong, low). Evidence Summary Once the infected CSF shunt has been removed, the optimal timing of shunt reimplantation is unclear. Early placement may increase the risk of relapse, but a delay in reimplantation may increase the risk of secondary infection of the external ventricular drain. The timing of reimplantation should be individualized based on the isolated organism, severity of ventriculitis, and improvement of CSF parameters and CSF sterilization in response to antimicrobial therapy. The total duration of antimicrobial therapy (see Question VIII) is difficult to separate from the timing of shunt reimplantation. Some authorities extend antimicrobial therapy for several days after shunt reimplantation, whereas others decide on total duration of therapy based on obtaining negative CSF cultures and do not extend antimicrobial therapy beyond the time of shunt reimplantation. In patients with shunt infection caused by coagulase-negative staphylococci and with normal CSF findings, the presence of negative CSF cultures for 48 hours after externalization generally confirms that removal of the hardware affected a cure and that the patient can have a new shunt placed on the third day after removal. If the coagulase-negative staphylococcus was isolated in association with CSF abnormalities (eg, CSF pleocytosis, abnormal chemistries), a true infection was likely present. If repeat cultures are negative, 7 days of antimicrobial therapy are usually recommended before shunt placement. However, if repeat cultures are positive, antimicrobial treatment is continued until CSF cultures remain negative for 7–10 consecutive days before a new shunt is placed. This approach is also recommended for infection caused by P. acnes [131]. For shunt infections caused by S. aureus or gram-negative bacilli, 10 days of antimicrobial therapy with negative cultures are recommended before shunt placement [18, 153], although some authorities would consider a 21-day course of therapy when gram-negative bacilli are isolated. Some experts also suggest a 3-day period off antimicrobial therapy in order to verify clearing of the infection before shunt reimplantation; this observation period is optional and not routinely recommended. However, these recommendations have not been rigorously studied, and some patients may require a longer duration of antimicrobial therapy before a new CSF shunt is placed. Furthermore, significant variations have been observed in the duration of antimicrobial therapy in patients with CSF shunt infections [141, 150]. Careful follow-up after reimplantation is also critical to ensure that the patient has been cured. Regardless of the manner of treatment, CSF shunt infection can recur. In one study [141], the recurrence rate was 26%, with two-thirds of cases caused by the same microorganism. The recurrence rate in patients with S. epidermidis shunt infection was 29%. In a recent study in children, risk factors identified for reinfection were those with complex shunts (multiple shunts placed or any single shunt with multiple catheters together), an atrial shunt, any complication after the first infection (ie, shunt malfunction, hemorrhage, CSF leak), or intermittent negative cultures defined as positive CSF cultures clearing and then returning over the course of treatment [142]. XII. What is the Best Approach to Prevent Infection in Patients Who are Receiving Cerebrospinal Fluid Shunts? Recommendations Periprocedural prophylactic antimicrobial administration is recommended for patients undergoing CSF shunt or drain insertion (strong, moderate). Periprocedural prophylactic antimicrobial administration is recommended for patients undergoing placement of external ventricular drains (strong, moderate). Prolonged antimicrobial prophylaxis for the duration of the external ventricular drain is of uncertain benefit and not recommended (strong, moderate). Use of antimicrobial-impregnated CSF shunts and CSF drains is recommended (strong, moderate). In patients with external ventricular drains, fixed interval exchange is not recommended (strong, moderate). Use of a standardized protocol for insertion of CSF shunts and drains is recommended (strong, moderate). Evidence Summary There have been numerous studies on specific surgical techniques to minimize the possibility of infection in patients undergoing CSF shunt placement; however, there are significant methodological limitations to these studies. Much of what is recommended is based on described risk factors for shunt infection. In one prospective, randomized controlled study of 61 patients undergoing 84 shunt procedures, the shunt infection rate was reduced in those who received antimicrobial-impregnated sutures (4.3% vs 21%; $P = .038$) [154], although there was a high rate of infection in the control group. There is some evidence that double gloving may decrease CSF shunt infection rates [155], and good surgical techniques [156] and adherence to infection control measures are important. There appears to be relatively strong evidence for the use of prophylactic antimicrobial therapy prior to shunt insertion surgery, although the clinical trials supporting this recommendation generally predate the use of antimicrobial-impregnated catheters. The latter have been less well studied to date but appear promising. Studied interventions are detailed in the following sections. Antimicrobial Prophylaxis Evidence supports the use of periprocedural prophylactic antimicrobial administration for patients undergoing CSF shunt insertion and placement of external ventricular drains. Although no randomized studies of periprocedural prophylactic antimicrobial agents for CSF shunt placement have been adequately powered to clearly establish efficacy, several metaanalyses have concluded that this approach decreases infection rates by approximately 50% [157, 158]. A Cochrane database review indicated that the odds ratio for decreased infection was 0.52 (95% CI, 0.36–0.74) [159]. The antimicrobial agent should be given before incision to achieve adequate tissue concentrations and should be continued for as long as 24 hours postoperatively, as studies included in these analyses generally administered therapy for this duration. With respect to CSF drain infection prevention, one review [20] that cited 10 studies addressed the use of prophylactic antimicrobials [47, 68, 160–167]. One study with 102 ventriculostomies in 70 patients [165] included 44 patients who received antimicrobials and 26 who did not. This study showed a decrease in ventriculitis rates from 27% to 9%. Eight subsequent studies did not show a difference [20, 47, 160–162, 168], with the caveat that they were underpowered for an event rate of 1%–10%. A recent large review of 35 studies published from 1972 to 2013 noted that about half of these studies describe the use of periprocedural antimicrobial therapy [21], but did not assess the efficacy of this practice. Some studies also showed that use of prophylactic antimicrobials resulted in development of ventriculitis due to resistant organisms [162, 167]. In one study, patients in the prophylactic antimicrobial arm developed ventriculitis caused by MRSA and Candida spp. [163]. In another study, rates of gram-negative ventriculitis were higher in patients who received prophylactic antibiotics [160]. However, conflicting reports have been published. In a Brazilian prospective study [169], prophylactic antimicrobials were used in 75% of the patients, and there was no significant difference in ventriculitis when compared to those who did not receive antimicrobials. Another study from the Netherlands also did not show a difference in percentage of patients who developed ventriculitis [170]. The limitations of these studies were that most of them were retrospective, underpowered, used different definitions for ventriculitis, and did not all report adverse effects (eg, adverse reactions to antimicrobials and infections with resistant organisms). Prolonged Prophylactic Systemic Antimicrobials for External CSF Drains Although the use of periprocedural prophylactic antimicrobial agents for placement of external ventricular drains is generally accepted, the use of prophylactic prolonged systemic antimicrobials for the duration of external CSF drainage is more controversial. One study noted that the infection rate was 3.8% in those who received prophylactic antimicrobials for the duration of external ventricular drain placement and 4.0% for those who received only periprocedural antimicrobial therapy [160]. This suggests that prophylactic antimicrobial agents throughout drainage did not significantly decrease the rate of ventriculitis and might select for emergence of resistant organisms. In contrast, another study demonstrated the benefit of prophylactic antimicrobial agents (2.6% CSF infection rate vs 10.6% in those who only received periprocedural antimicrobials; $P = .001$) [163]. It is important to note that the infections in those who received prophylactic antimicrobials were caused by more drug-resistant virulent pathogens and that the mortality rate was higher (66% vs 41%). In a pooled estimate of 9 studies, the CSF infection rate was 8.1% in those who received periprocedural antimicrobials and 5.3% in those who received antimicrobial therapy for the duration of external drainage [20, 168]. This led to a recommendation to maintain prophylactic antimicrobial therapy in all patients while the external ventricular drain is in place, although this is not the practice in all clinical facilities. One randomized study that compared placebo to trimethoprim-sulfamethoxazole did not show a significant difference in the rate of ventriculitis between the 2 groups [171]. A second randomized study that compared periprocedural antimicrobials only (intravenous ampicillin/sulbactam) to prolonged antimicrobials (ampicillin/sulbactam and aztreonam) revealed that the patients who received prolonged ampicillin/sulbactam and aztreonam had a significantly lower rate of ventriculitis (3 of 115, 3%) than those who received only periprocedural ampicillin/sulbactam (12 of 113, 11%; $P < .05$) [163]. The limitations of this study were that it did not provide a clear definition of ventriculitis and the duration that the external ventricular drain remained in place was not specified for both groups. Another important finding in this study was that infections caused by resistant organisms such as MRSA and Candida species were higher in the prolonged antimicrobial arm. The mortality rate in the prolonged antimicrobial arm was 66% (2 of 3) when compared to the periprocedural antimicrobial arm, which had a 41% mortality rate (5 of 12). In a systematic review that pooled data from 2 randomized studies and 4 observational studies [172], there was a reduced relative risk of 0.45 with use of prophylactic prolonged systemic antimicrobials, although there were significant methodological limitations and heterogeneity in the pooled studies. The definitions of ventriculitis were variable, the type and dose of antimicrobials were different, adverse effects were not well studied, and most of the studies were retrospective and prone to bias. In light of these findings and based on the availability of an efficacious alternative (ie, antimicrobial-impregnated catheters; see below), the use of prophylactic prolonged systemic antimicrobials for prevention of infection in patients with external ventricular drains is not recommended, although prolonged use does remain the practice in some centers. In a recent study in patients with antimicrobial-impregnated external ventricular drains who also received prolonged systemic antimicrobial therapy, the addition of prolonged systemic therapy did not reduce the incidence of catheter-related ventriculitis but was associated with a higher rate of nosocomial infections (bloodstream infections and ventilator-associated pneumonia) and increased cost [173]. Antimicrobial-Impregnated Catheters Antimicrobial-impregnated catheters for CSF shunts and drains have been under development for several decades and, more recently, have been introduced into clinical practice. They are typically impregnated with either minocycline or clindamycin, combined with rifampin. In one randomized study that included 110 patients who underwent placement of CSF shunts impregnated with clindamycin and rifampin, there was a trend toward a decrease in infection rate from 16.6% to 6% ($P = .084$) [174]. However, the study was hampered by a small number of patients and a high infection rate in the control group. Other noncontrolled studies in patients with CSF shunts have led to mixed results, some supporting [175, 176] and others disputing [177, 178] these findings. In a metaanalysis of pooled data from 12 studies that compared antimicrobial-impregnated to nonantimicrobial-impregnated ventriculoperitoneal shunts, there was a statistically significant decrease in infections in patients who had received antimicrobial-impregnated shunts (risk ratio, 0.37; $P < .0001$) [179]. In another systematic literature review of 5613 shunt procedures, use of antimicrobial-impregnated shunt catheters was associated with a decreased risk of shunt infection (3.3% vs 7.2%; $P < .00001$) [180], with significant differences in both children and adults. Use did not appear to be associated with emergence of antimicrobial-resistant infections. Use of antimicrobial-impregnated shunts has not only reduced the incidence of CSF shunt infections but also has resulted in significant hospital cost savings [181]. In a study that compared the effectiveness of antimicrobial-impregnated shunt catheters in treatment of 12589 consecutive cases from 287 hospital systems in adult and pediatric patients with hydrocephalus [182], antimicrobial-impregnated catheter use was associated with a significant reduction in infection in both adult (2.2% vs 3.6%; $P = .02$) and pediatric (2.6% vs 7.1%; $P < .01$) patients. Reduced infection was demonstrated regardless of hospital size, annual shunt volume, hospital location, or patient risk factors. Similar results have been noted in patients who received antimicrobial-impregnated external ventricular drains. A randomized study of 306 patients who had placement of external ventricular drains impregnated with minocycline and rifampin showed a decrease in the CSF infection rate from 9.4% to 1.3% compared to those who received uncoated external ventricular drains [183]. The mean duration of external ventricular drain placement in both arms was similar. However, 95% of participants in both arms also received prolonged prophylactic antimicrobials; the antimicrobials were not specified. Pooled data from 5 studies in one metaanalysis showed a statistically significant benefit for antimicrobial-impregnated external ventricular drains (risk ratio, 0.31; $P = .009$) [179]. Sonabend et al [172] conducted a systematic review of studies that used antimicrobial-impregnated external ventricular drains. One randomized, controlled trial [183] and 3 cohort studies [184–186] that assessed the efficacy of antimicrobial-coated external ventricular drains for ventriculitis prevention were included in the metaanalysis. A pooled analysis of these studies showed a relative risk of 0.19 (95% CI, 0.07–0.52) with antimicrobial-coated external ventricular drains. Ventriculitis developed in 2 patients (1.3%) in the intervention group and in 13 patients (9.6%) treated with the standard uncoated external ventricular drains ($P = .0012$). The organism most commonly isolated from CSF samples of control patients was coagulase-negative staphylococcus, whereas CSF cultures from patients in the treated group grew E. faecalis, S. aureus, and Enterobacter aerogenes. The study did not provide a clear definition of colonization or contamination rates vs a definite infection. In another study that compared 47 children treated with a clindamycin and rifampin–coated external ventricular drain to 44 children who were treated with a standard external ventricular drain [186], CSF cultures were positive in 14 of 44 control patients (31.8%) and in only 1 of 47 patients (2.1%) treated with a coated catheter, demonstrating a statistically significant decrease in ventriculitis with the use of an antimicrobial-coated catheter ($P < .05$). In another study that compared prolonged antimicrobial prophylaxis (ampicillin/sulbactam and ceftriaxone) to antimicrobial-coated external ventricular drains with clindamycin and rifampin [187], the interim data analysis demonstrated that no ventriculitis occurred in either group. Allergic or systemic complications directly related to the antimicrobial agents in antimicrobial-impregnated catheters have been rare. When used for CSF shunt insertions, antimicrobial-impregnated catheters have not been associated with an increased risk of late CSF shunt infections when compared to historic controls [188]. Elective Fixed Interval Revision The greatest risk related to the external ventricular drain is that of secondary infection [20]. A longer duration of drain placement appears to increase the risk. Three studies have shown that the risk of infection does increase with catheter duration [47, 56, 166]. This was also confirmed in another review that demonstrated that longer duration of external ventricular CSF drain placement increased the risk of infection [189], although the risk may plateau over time. Prophylactic catheter exchange has been advocated to reduce this risk. However, prophylactic catheter exchange performed every 5 days does not significantly decrease the likelihood of CSF infection [190, 191]. In one study in 103 patients who required external ventricular drains for more than 5 days [191], the CSF infection rate was 7.8% for the group that underwent catheter exchange every 5 days and 3.8% for the no-change group ($P = .5$). This suggests that a single external ventricular drain can be used for as long as clinically indicated unless a change is necessary because of CSF infection or catheter malfunction. In addition, no significant difference was found in intensive care unit stay, ward stay, or clinical outcome between the 2 groups. Thus, in addition to use of antimicrobial-impregnated catheters, the infection risk can be lowered by prompt removal of the external ventricular drain when no longer needed, but not with prophylactic catheter exchange at a set interval. While not clearly demonstrated in the medical literature but by extrapolating from studies with other indwelling catheters, it seems likely that attention to maintaining a sterile, closed system with avoidance of injections into the system and surveillance of the draining CSF will also minimize the likelihood of infection. Combined Interventions Many of the studies on prevention of CSF shunt infections detailed above examined single interventions to determine effects on infection rates. However, use of "practice bundles" may also be valuable in development of standardized protocols for CSF shunt insertion. The Hydrocephalus Clinical Research Network recently undertook an initiative in which centers agreed to develop an 11-step protocol in an effort to reduce CSF shunt infection rates. This was a collaboration of pediatric neurosurgical centers and included all children who received shunts or revisions [192]. The initiative involved 21 surgeons and included 1571 procedures in 1004 children. Overall protocol compliance was about 75%, and another 20% followed 10 of the 11 steps. The network infection rate decreased from 8.8% prior to the protocol to 5.7% while using the protocol ($P = .0028$; relative risk reduction, 36%), indicating that use of a standardized protocol and reduction in variation by adherence to a common protocol are effective at reducing CSF shunt infection rates. Only proper hand-washing technique by all team members emerged as an independent predictor of decreased infection rates. Factors associated with increased infection were use of BioGlide catheters and use of antiseptic cream by any member of the surgical team. However, the nature of the study precluded identification of individual items of the bundle with certainty. Identification of other factors that are associated with infection may lead to addition of new interventions to the protocol in order to further reduce infection rates in the future. In patients with external ventricular drains, adherence to a checklist for insertion that included hand hygiene, appropriate skin preparation with povidone iodine, allowance of the skin preparation to completely dry before insertion, use of all 5 maximal sterile barriers (sterile gloves, sterile gown, cap, mask, and large sterile drape), and adherence to the policy for external ventricular drain maintenance led to a decline in infection rates from 16 per 1000 external drain catheter days to 4.5 per 1000 catheter days [193]. This infection rate further decreased to 1.3 per 1000 catheter days. Initiation of this protocol eventually resulted in no infections over a 25-month period. However, this study, as with many similar nonrandomized comparisons of care protocols, begins with an awareness of a recent increase in infection rates, making some of the achieved improvement possibly due to regression of the mean. XIII. Is there a Role for Prophylactic Antimicrobial Therapy in Patients Undergoing Neurosurgery or in those with Cerebrospinal Fluid Leak? Recommendations For neurosurgical patients, perioperative antimicrobial agents are recommended to prevent infections of the incision (strong, high). In patients with basilar skull fractures and a CSF leak, prophylactic antimicrobial agents are not recommended (strong, moderate). In patients with basilar skull fractures and a prolonged CSF leakage (>7 days), an attempt to repair the leak is recommended (strong, low). In patients with basilar skull fractures and a CSF leak, pneumococcal vaccination is recommended (strong, moderate). Evidence Summary While perioperative antimicrobial agents have been shown to decrease the risk of cranial wound infections [194–197], they have not been shown to decrease the risk of post-craniotomy meningitis [194, 195] or of meningitis after placement of a CSF shunt [198]. For prophylaxis against cranial wound infections, the first dose of antimicrobials should be given within 1 hour of surgery and should be discontinued within 24 hours after surgery [199]. Patients with traumatic injuries that result in a basilar skull fracture or CSF leak deserve special consideration. The overall infection rate of meningitis has been reported to be 1.4% [200]. However, in those who have depressed cranial fractures (up to 6% of patient with head injuries) [201], the infection rate is as high as 10.6% [202]. In a review of 51 patients with post-traumatic CSF leaks that did not resolve in 24 hours, the risk of meningitis was decreased from 21% to 10% with the use of prophylactic agents [203]. However, in another study of patients with traumatic pneumocephalus, the administration of ceftriaxone did not appear to decrease the risk of bacterial meningitis [204]. A Cochrane systematic review evaluated 208 participants from 4 randomized studies who were considered suitable for inclusion in the metaanalysis [205]. There were no significant differences between antimicrobial prophylaxis groups and control groups in terms of reduction of the frequency of meningitis, all-cause mortality, meningitis-related mortality, and the need for surgical correction in patients with CSF leakage. Leakage of CSF is the major risk factor for the development of meningitis, although most leaks that occur after trauma are unrecognized [200, 206]. Most leaks resolve spontaneously within 7 days, but surgical intervention is indicated if leakage persists. Since Streptococcus pneumoniae is an important pathogen in the setting of head trauma and a CSF leak [207, 208], it is reasonable to try to prevent infections with this organism using pneumococcal vaccination, although clinical studies assessing the efficacy of this approach are lacking. Nevertheless, specific recommendations exist for both adult and pediatric patients with CSF leaks. For unimmunized children aged 6–18 years and adults aged ≥19 years with CSF leak, the 13-valent pneumococcal conjugate vaccine should be administered first followed at least 8 weeks later with the 23-valent pneumococcal polysaccharide vaccine [209, 210]. The Advisory Committee on Immunization Practices recently recommended both the 13-valent pneumococcal conjugate vaccine and the 23-valent pneumococcal polysaccharide vaccine, administered in series, with the polysaccharide vaccine given 6–12 months after the conjugate vaccine in all pneumococcal vaccine-nave adults aged ≥65 years [211]. Acknowledgments The expert panel expresses its gratitude for thoughtful reviews of an earlier version by Drs Naomi O'Grady, Richard Whitley, William E. Whitehead, and Ram Yogev. The panel thanks Vita Washington for her guidance and preparation of the manuscript. Financial support Support for these guidelines was provided by the IDSA. Potential conflicts of interest The following is a reflection of what has been reported to the IDSA regarding potential conflicts of interest (COI). In order to provide thorough transparency, the IDSA requires full disclosure of all relationships, regardless of relevancy to the guideline topic. Such relationships as potential conflicts of interest are determined by a review process that includes assessment by the SPGC chair, the SPGC liaison to the development panel, and the BOD liaison to the SPGC, and, if necessary, the COI Task Force of the Board. This assessment of disclosed relationships for possible COI is based on the relative weight of the financial relationship (ie, monetary amount) and the relevance of the relationship (ie, the degree to which an association might reasonably be interpreted by an independent observer as related to the topic or recommendation of consideration). The reader should be mindful of this when the list of disclosures is reviewed. A. T. received royalties from UpToDate and Elsevier and honoraria from ACP and Merck. A. B. received research support from Cubist. R. H. has received personal fees for speaker bureau participation with Pfizer, Medicine's Company and Biofire; he has served as a consultant for Biomeriaux. S. K. served as a consultant for Pfizer; received royalties from UpToDate and Elsevier; and received research grants from Pfizer, Forest Laboratories, Cubist, and Merck. W. M. S. received research grants from the National Institutes of Health, Pfizer, and Wyeth. D. v. d. 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