Infections of cerebrospinal fluid shunts

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INTRODUCTION

Cerebrospinal fluid (CSF) shunts are used in the setting of hydrocephalus to divert CSF to another part of the body for absorption. The approach to management of shunt infections is discussed here.

Indications for shunt placement and other issues related to hydrocephalus are discussed separately. (See "Hydrocephalus in children: Management and prognosis" and "Normal pressure hydrocephalus".)

General issues related to health care-associated meningitis and ventriculitis in adults, including post-neurosurgical infections and infections related to extraventricular drains, are discussed in detail elsewhere. (See "Health care-associated meningitis and ventriculitis in adults: Clinical features and diagnosis" and "Health care-associated meningitis and ventriculitis in adults: Treatment and prognosis".)

The management of bacterial meningitis in neonates, children, and adults is discussed in detail separately. (See "Bacterial meningitis in the neonate: Treatment and outcome" and "Bacterial meningitis in children older than one month: Treatment and prognosis" and "Initial therapy and prognosis of community-acquired bacterial meningitis in adults" and "Treatment of bacterial meningitis caused by specific pathogens in adults".)

SHUNT DEVICES

The proximal portion of the shunt catheter is most commonly placed in one of the cerebral ventricles but may also be placed in an intracranial cyst or the lumbar subarachnoid space. The distal portion of the shunt can be internalized or externalized. Internalized shunts most commonly drain into the peritoneum (ventriculoperitoneal [VP] shunt), although, less commonly, they drain into the vascular space (ventriculoatrial [VA] shunt) or the pleural space (ventriculopleural shunt).

Externalized devices (ventriculostomy catheters, also called external ventricular drains [EVDs]) are temporary devices typically placed in the setting of acute hydrocephalus for intracranial pressure monitoring and therapeutic diversion of CSF. They may also be placed for interim management of hydrocephalus during antibiotic therapy for an infected internalized device that has been removed. (See "Health care-associated meningitis and ventriculitis in adults: Clinical features and diagnosis", section on 'Ventricular catheter infection'.)

Other externalized CSF drainage devices such as Ommaya reservoirs (for administration of antimicrobial drugs or cancer chemotherapy) can also become infected. The proximal portion of these devices is typically placed in the intraventricular space but may also be placed in an abscess cavity or tumor. The distal portion of the device is a reservoir placed under the scalp (less commonly in the lumbar space) and accessed via a needle when needed. (See "Health care-associated meningitis and ventriculitis in adults: Clinical features and diagnosis", section on 'Infection of other CNS devices'.)

INCIDENCE AND RISK FACTORS

The rate of internalized CSF shunt infection in most studies has ranged from approximately 5 to 15 percent [1-11]. Infections are most likely to be diagnosed during the initial month after placement [3,11,12].

Other risk factors for CSF shunt infection include [4,12-14]:

- Patient factors:
  - Premature birth, especially when associated with intraventricular hemorrhage
  - Younger age
  - Previous shunt infection

- Certain causes of hydrocephalus (more likely after purulent meningitis, hemorrhage, or myelomeningocele)

- Procedural factors:

  - Less experienced neurosurgeon
  - Higher number of people traversing the operating theater during shunt placement
  - Exposure to perforated surgical gloves
  - Intraoperative use of a neuroendoscope
  - Longer duration of the shunt procedure
  - In those with ventriculoatrial (VA) shunting, insertion of the catheter below the level of the T7 vertebral body
  - Improper patient skin preparation
  - Shaving of skin
  - Exposure of large areas of the patient's skin during the procedure
  - Shunt revision, particularly if the patient has undergone ≥3 revisions
  - Gastrostomy tube placement

Incidence and risk factors for infections related to external ventricular drains are discussed elsewhere. (See "Health care-associated meningitis and ventriculitis in adults: Clinical features and diagnosis", section on 'Ventricular catheter infection'.)

MICROBIOLOGY AND PATHOGENESIS

Shunt infections most frequently develop via colonization of the shunt with skin flora. This may occur at the time of shunt placement or postoperatively via breakdown of the wound or overlying skin. Early infection with skin flora is the most common type of CSF shunt infection; approximately one half of all shunt infections are due to coagulase-negative staphylococci and one third are due to *Staphylococcus aureus* [2,15-20]. Diphtheroids (such as *Cutibacterium* [formerly *Propionibacterium*] *acnes* and *Corynebacterium jeikeium*) can also cause shunt infection. (See "Infection due to coagulase-negative staphylococci: Epidemiology, microbiology, and pathogenesis".)

Shunt infections may also develop via direct contamination of the distal end of the shunt or via hematogenous seeding. Distal-end contamination of ventriculoperitoneal shunts occurs in the setting of bowel perforation or peritonitis, whereas contamination of externalized devices occurs via catheter irrigation or tracking of microorganisms along the exit site. These infections tend to occur months after shunt placement and account for about 10 to 15 percent of shunt

infections. They may be due to a variety of organisms including streptococci, gram-negative bacteria (including *Pseudomonas aeruginosa*), anaerobes, mycobacteria, and fungi [21-34].

CLINICAL MANIFESTATIONS

CSF shunt infections can present with few or no symptoms [3,4]. In some cases, symptoms develop only when infection has caused shunt obstruction and subsequent malfunction with clinical signs of increased intracranial pressure (eg, headache, nausea/vomiting, lethargy, or altered mental status). Meningeal symptoms may not be observed because communication between the infected ventricles and the meninges is usually absent (this is the reason for the shunt). Fever may or may not be present.

Another reason that the clinical manifestation may be subtle or absent is that commonly implicated pathogens, such as coagulase-negative staphylococci and *C. acnes*, are indolent, cause minimal inflammation, and are primarily pathogenic when prosthetic material is present [4]. In some cases, there may be only mechanical blockage as a result of biofilm formation in or on the catheter [4,35,36].

Symptoms may also present with localization to the distal internal (ventriculoperitoneal [VP], ventriculopleural, or ventriculoatrial [VA] shunts) or external end of the shunt:

- VP shunt infections may manifest with symptoms of peritonitis, including fever, abdominal pain, and anorexia. Large loculated pockets can develop in the peritoneum because of diminished CSF absorption in the setting of inflammation [37]. (See "Spontaneous bacterial peritonitis in adults: Clinical manifestations".)

- In patients with ventriculopleural shunts, symptoms and signs of pleuritis in the absence of another etiology are suggestive of shunt infection [4].

- VA shunt infections may present with fever and evidence of bloodstream infection, which may develop via entry of infected CSF into the bloodstream or from an infected thrombus at the catheter tip. Subsequent endocarditis and its concomitant sequelae can occur, including septic pulmonary emboli and antibody-mediated sequelae such as glomerulonephritis and dermatologic manifestations [38]. (See "Clinical manifestations and evaluation of adults with suspected left-sided native valve endocarditis".)

- Distal external shunt infections typically present as evidence of soft tissue infection with swelling, erythema, tenderness, or purulent drainage.

DIAGNOSTIC CRITERIA

The diagnostic criteria for CSF shunt infections are the same as for health care-associated meningitis or ventriculitis, which are listed in the table (table 1) and discussed in detail elsewhere. (See "Health care-associated meningitis and ventriculitis in adults: Clinical features and diagnosis", section on 'Diagnosis'.)

DIAGNOSIS

If clinical manifestations suggest the possibility of infection, a diagnostic evaluation should be initiated with CSF analysis, blood cultures, and imaging.

Cerebrospinal fluid — Direct aspiration of the CSF shunt is preferred over ventricular tap or lumbar puncture when possible [17,39]. The CSF should be examined for white cell count with differential, glucose and protein concentrations, Gram stain, and culture. CSF cultures are the most important test for establishing the diagnosis of CSF shunt infections and should be obtained before starting antibiotics. In some cases, other studies can be useful, as discussed below. (See "Clinical features and diagnosis of acute bacterial meningitis in adults", section on 'Cerebrospinal fluid analysis' and "Bacterial meningitis in children older than one month: Clinical features and diagnosis", section on 'Interpretation'.)

Cell count and differential — Interpretation of CSF parameters can be challenging, and no single clinical or laboratory parameter, including fever, leukocytosis, CSF pleocytosis, or CSF protein and glucose, can reliably predict or exclude a shunt infection [4,40]. Central nervous system (CNS) device-related infections often manifest with less inflammation than bacterial meningitis; as a result, cell count abnormalities may be subtle and difficult to distinguish from postoperative inflammation. In a retrospective report of 11 pediatric shunt infections, for example, 5 had CSF white blood cell (WBC) counts less than 12/microL [41].

The WBC differential may be a useful clue to CSF shunt infections [41,42]. In one report of 129 shunt placements, a WBC count differential in CSF with >10 percent neutrophils was 90 percent sensitive for predicting infection; the negative predictive value was 0.99. The presence of eosinophils in CSF is controversial with regard to infection specificity. While some studies indicate that the presence of eosinophils is rare in the setting of infection and should raise the possibility of inflammation due to shunt malfunction [41,42], another study found that CSF eosinophilia of >8 percent of the differential count was associated with indolent infection [43]. A study that used >1 percent eosinophils as the cutoff demonstrated an association with both

infection and a variety of noninfectious entities [44] and has prompted continued controversy regarding the utility of CSF eosinophilia in the diagnosis of infection [45].

Gram stain and culture — CSF culture is the most important test for establishing a diagnosis of CSF shunt infection; it is critical for both pathogen identification and in vitro susceptibility testing to define an optimal treatment regimen. Ideally, CSF cultures should be obtained prior to starting antibiotic therapy. In one study of 326 children and adults, obtaining CSF prior to antibiotics increased the likelihood of a positive Gram stain (26 versus 13 percent) and CSF culture (66 versus 49 percent) [46]. A negative CSF Gram stain or culture does not exclude infection, particularly in patients who have received recent antibiotics [4].

If initial cultures are negative, they should be held for at least 10 days to increase the chance of recovering a slow-growing organism such as *C. acnes* [4]. If the initial CSF culture is negative and infection is considered likely, the CSF culture should be repeated. Positive cultures from the thioglycolate broth only should be interpreted with caution as they may represent a contaminant rather than infection, but, in patients who have received antibiotics, they could represent infection.

If a CSF shunt is removed in a patient suspected of having infection, the shunt components should be cultured [4]. However, if it is removed for a reason other than infection, cultures of the shunt components are **not** recommended. A positive CSF culture in a patient with pleocytosis and/or hypoglycorrhachia, or an increasing cell count, and clinical findings suspicious for ventriculitis or meningitis is indicative of CSF shunt infection.

If a patient with CSF shunt malfunction but no signs or symptoms suggestive of infection undergoes a CSF culture and that culture is positive, it could be a contaminant, but infection should also be considered [4]. In this situation, the CSF culture should be repeated. If the repeat culture grows the same organism, it is usually indicative of true infection.

Other tests — Other tests can be helpful when Gram stain and culture results are negative or are inconclusive in establishing a diagnosis of CSF shunt infection:

- **CSF lactate, CSF procalcitonin, and serum procalcitonin** – An elevated CSF lactate or CSF procalcitonin (or the combination of both tests) may aid in the diagnosis of bacterial CSF shunt infection [4,47-49]. As an example, an elevated serum procalcitonin may be helpful for differentiating between CSF abnormalities due to surgery or intracranial hemorrhage and those due to bacterial infection since serum procalcitonin is often elevated in the setting of bacterial infection [4]. However, further study of the utility of these tests in patients with CSF shunt infections is necessary since some processes can cause both CSF lactate and serum procalcitonin elevations. In addition, in some studies, the use of these

tests has been conflicting. Thus, elevated CSF lactate and serum procalcitonin should be considered adjuncts to clinical and other lab tests. When the prior probability of infection is low, a positive result might prompt reconsideration, but when it is high, a negative result should not dismiss the diagnosis. (See "Cerebrospinal fluid: Physiology and utility of an examination in disease states", section on 'Lactate'.)

- **CSF molecular tests** – Nucleic acid amplification tests can be helpful for detecting a specific pathogen and decreasing the time to making a diagnosis [4]. The methodology to conduct broad-range 16S (bacterial) rRNA polymerase chain reaction is becoming increasingly available in many centers. (See "Molecular diagnosis of central nervous system infections".)

- **CSF beta-D-glucan and galactomannan** – 1,3-beta-D-glucan, a cell wall component of many fungi including *Candida* and *Aspergillus* spp, is detected by the beta-D-glucan assay. Galactomannan is a polysaccharide that is a major constituent of *Aspergillus* cell walls and that is also present in the cell walls of certain other fungal species. Although most studies of the beta-D-glucan and galactomannan assays have involved testing serum specimens, some studies have suggested that they may be helpful for diagnosing fungal CNS infections. When fungal CSF shunt infection is suspected, it is reasonable to send CSF beta-D-glucan and galactomannan assays [4]. (See "Diagnosis of invasive aspergillosis", section on 'Beta-D-glucan assay' and "Diagnosis of invasive aspergillosis", section on 'Galactomannan antigen detection' and "Clinical manifestations and diagnosis of candidemia and invasive candidiasis in adults", section on 'Beta-D-glucan assay' and "Approach to the patient with chronic meningitis", section on 'CSF examination and other laboratory testing'.)

Blood cultures — Blood cultures should be obtained along with CSF analysis when a CSF shunt infection is suspected and should be collected before antibiotics are started. Their yield is much higher in the setting of ventriculoatrial (VA) shunts than ventriculoperitoneal (VP) shunts (95 versus 20 percent in one series) [17]. Careful interpretation of positive blood cultures is necessary, particularly when only one set of cultures is positive and it grows skin flora.

Imaging — Neuroimaging studies should be performed to look for evidence of ventriculitis or CSF obstruction (see "Hydrocephalus in children: Management and prognosis", section on 'Shunt malfunction'). Magnetic resonance imaging with gadolinium and diffusion-weighted imaging is the most useful modality for evaluating patients with possible CSF shunt infections [4].

Abdominal imaging (computed tomography or ultrasound) may be useful to identify CSF loculations at the distal end of VP shunts.

TREATMENT

There are no randomized trials addressing optimal treatment of CSF shunt infections. Management of CSF shunt infection should include removal of the device, external drainage, parenteral antibiotics, and shunt replacement once the CSF is sterile [4,50-53]. If device removal is not feasible, intraventricular antibiotics may be useful [4]. (See 'Adjunctive intraventricular antibiotics in selected cases' below.)

In 2017, the Infectious Diseases Society of America (IDSA) published guidelines for the management of healthcare-associated ventriculitis and meningitis [4]. Our recommendations are generally in keeping with the IDSA guidelines.

Device removal — Optimal management of CSF shunt infection should include complete removal of the device, external drainage, and subsequent shunt replacement once CSF is sterile [4,51,52,54,55]. Removal of hardware is a critical part of management because, as noted above, some of the pathogens that cause CSF shunt infections form biofilms on prosthetic material, and antimicrobials are not able to eliminate organisms associated with biofilms and prosthetic material.

In one retrospective review of 50 CSF shunt infections, for example, 22 patients were treated with shunt removal, external drainage, and antibiotics; 17 patients were managed with shunt removal followed by immediate shunt replacement and antibiotics; and 11 patients received antibiotics without shunt removal [52]. The response rates were 95, 65, and 35 percent, respectively. In a cohort study that included 86 episodes of ventriculoperitoneal shunt infection, the only risk factor associated with treatment failure by multivariate analysis was shunt retention (odds ratio [OR] 46.04; 95% CI 5.30-399.88) [55]. Failure occurred more frequently among those who had one-stage shunt replacement compared with those who had two-stage shunt exchange (68 versus 11 percent; OR 17.88, 95% CI 4.33-73.85).

Management of intracranial pressure during the interval of device removal requires careful coordination between neurosurgeons and infectious disease consultants, particularly in shunt-dependent patients who require external drainage to control intracranial hypertension.

The management of the rare patient who cannot undergo hardware removal is discussed below. (See 'Duration of antibiotics' below.)

Antibiotic therapy

Systemic antibiotics

Empiric therapy — Parenteral antibiotic selection should be guided by the results of CSF Gram stain and culture. Pending these results, for adults, we recommend empiric therapy, taking into account local in vitro susceptibility results and bacteria previously isolated from the patient [4]. For most adults, we give vancomycin (table 2) and an agent to cover gram-negative bacilli, including *P. aeruginosa*. For adults, an agent to cover healthcare-associated gram-negative bacilli (ceftazidime [2 g intravenously (IV) every 8 hours], cefepime [2 g IV every 8 hours], or meropenem [2 g IV every 8 hours]) is appropriate. For adults with severe beta-lactam allergies (eg, anaphylaxis) and for whom meropenem is contraindicated, aztreonam (2 g IV every 6 to 8 hours) or ciprofloxacin (400 mg IV every 8 to 12 hours) should replace the cephalosporin or carbapenem.

For children, we recommend empiric therapy with vancomycin (15 mg/kg IV per dose every 6 hours; not to exceed 1 g per dose) and an agent to cover endogenous gram-negative pathogens (eg, cefotaxime, if available, [200 mg/kg IV per day in four divided doses; maximum daily dose 12 g] or ceftriaxone [100 mg/kg IV per day in two divided doses; maximum daily dose 2 g]). Infection with *P. aeruginosa* or other resistant gram-negative bacilli is uncommon in children. We therefore do not include an antipseudomonal agent as part of the empiric regimen for most children, unless there are specific risk factors. If a multidrug-resistant gram-negative bacillus is a concern, meropenem (40 mg/kg IV per dose every 8 hours; maximum 2 grams/dose or 6 grams/day) is appropriate. The doses recommended above are intended for patients with normal renal function; dosing must be adjusted in patients with renal dysfunction.

For patients known to be colonized or infected at other anatomic sites with a highly antibiotic-resistant pathogen, the empiric regimen should be adjusted to treat this pathogen [4].

Targeted therapy — Subsequent antibiotic therapy should be tailored to culture and susceptibility results.

Staphylococci — For gram-positive isolates, vancomycin monotherapy should be continued for methicillin-resistant pathogens, whereas methicillin-susceptible pathogens should be managed with nafcillin or oxacillin. Oral rifampin is not routinely added to the above regimens but may augment treatment in the setting of refractory cases [56]. We also include rifampin as part of a combination regimen for those whose infected central nervous system (CNS) hardware cannot be removed.

In the event that cultures are negative but there is still a strong suspicion of CNS infection, we recommend empiric vancomycin for presumed staphylococcal infection. The dosing is summarized in the table (table 2).

Vancomycin is the drug of choice for methicillin-resistant strains of *S. aureus* (MRSA) and coagulase-negative staphylococci that cause CSF shunt infections because it is the best studied and there is the most clinical experience with this agent. However, vancomycin has poor CSF penetration (1 percent in uninflamed meninges; 5 percent in inflamed meninges) [54,57-59]. In contrast, nafcillin and oxacillin have good CSF penetration in the setting of meningeal inflammation and are the drugs of choice for methicillin-susceptible strains of *S. aureus* (MSSA) that cause CSF shunt infections. Patients with MSSA infection who have an IgE-mediated allergy to penicillins can either be desensitized to nafcillin or oxacillin or receive vancomycin as an alternative agent [4]. Cefazolin should **not** be used for MSSA meningitis because it does not adequately penetrate into the CNS.

Nafcillin and oxacillin are also the drugs of choice for the small proportion of coagulase-negative *Staphylococcus* strains that are confirmed to be methicillin-susceptible strains by specialized testing, such as using a gene probe for the *mecA* gene. If such specialized testing is not available, then vancomycin should be used because of the high frequency of methicillin-resistant strains and because of concerns about heteroresistance (subpopulations within a bacterial population that have varying degrees of phenotypic resistance) with coagulase-negative staphylococci that may not be detected on routine susceptibility testing. (See "Overview of antibacterial susceptibility testing", section on 'Basic concepts of antimicrobial resistance'.)

For MRSA isolates with a vancomycin minimum inhibitory concentration (MIC) ≥1 mcg/mL, an alternative agent should be considered in patients who have not had the appropriate clinical or microbiologic response [4]. The IDSA guidelines recommend linezolid, daptomycin, or trimethoprim-sulfamethoxazole (TMP-SMX) as alternative agents when a beta-lactam or vancomycin cannot be used for staphylococcal meningitis and ventriculitis [4]. Among the alternative agents for staphylococcal meningitis (including MRSA), we generally favor linezolid in adults. The linezolid dose for adults is 600 mg IV or orally every 12 hours. However, the manufacturer states that empiric linezolid use in children with CNS infections is not recommended due to inconsistent concentrations in the CSF. Case reports have described successful treatment with linezolid of staphylococcal and vancomycin-resistant enterococcal CNS infections, including CSF shunt infections, despite the fact that linezolid is not bactericidal [60,61].

Because there is limited experience with alternative agents, CSF penetration is something of a proxy for potential utility in CNS device infections. Linezolid has good CSF penetration of approximately 66 percent [54,62-64], and TMP-SMX has moderately good CSF penetration (13 to 53 percent for TMP and 17 to 63 percent for SMX) [54,65,66]. In a rabbit meningitis model, CSF daptomycin penetration was 5 to 6 percent and achieved adequate concentrations [54,67,68]. Case reports and case series of patients with CNS infections caused by MRSA have evaluated linezolid [61,69-72], TMP-SMX [54,65,73], and daptomycin usually combined with rifampin as alternative regimens [74,75]. Although there are insufficient data regarding the efficacy of these regimens for the treatment of meningitis caused by MRSA, these agents (particularly linezolid) are reasonable alternatives when vancomycin cannot be used (eg, in patients with allergies) or a patient has failed clinically or microbiologically. Further studies could be helpful in establishing the benefit of these agents for the treatment of meningitis, but they will be difficult to perform given the infrequency of need and the challenge of making comparisons to existing agents.

Cutibacterium acnes — For *C. acnes* infection, penicillin G is the agent of choice [4]. Alternative agents include third-generation cephalosporins (ceftriaxone, cefotaxime), vancomycin, daptomycin, and linezolid. (See "Invasive Cutibacterium (formerly Propionibacterium) infections".)

Other causes — Treatment of gram-negative bacillary meningitis and *Candida* infections of the CNS is described in detail separately. (See "Treatment of bacterial meningitis caused by specific pathogens in adults", section on 'Gram-negative bacilli' and "Candida infections of the central nervous system", section on 'CNS shunts and other devices'.)

Adjunctive intraventricular antibiotics in selected cases — Adjunctive intraventricular antibiotics are not routinely necessary for treatment of CSF shunt infections. We generally reserve intraventricular antibiotics for infections that are refractory to appropriate systemic antibiotic therapy, infections caused by highly resistant organisms susceptible only to antimicrobials with poor CSF penetration, and infections in which the shunt cannot be removed. When we give intraventricular antibiotics, we use them as an adjunct to intravenous antibiotics (ie, in combination with intravenous therapy).

Administration, dosing, efficacy, and adverse effects of intraventricular antibiotics are discussed in detail elsewhere. (See "Health care-associated meningitis and ventriculitis in adults: Treatment and prognosis", section on 'Intrathecal and intraventricular therapy'.)

Duration of antibiotics — No randomized prospective trials have been performed to determine the optimal duration of antibiotic therapy for CSF shunt infections [4,50].

We generally favor the following durations of antibiotics, in accordance with the IDSA [4]:

- Infections caused by coagulase-negative staphylococci or *C. acnes* with no or minimal CSF pleocytosis, normal CSF glucose, and few symptoms or systemic features should be treated for 10 days.

- Infections caused by coagulase-negative staphylococci or *C. acnes* with significant CSF pleocytosis, low CSF glucose, clinical symptoms, or systemic features should be treated for 10 to 14 days.

- Infections caused by *S. aureus* or gram-negative bacilli with or without significant CSF pleocytosis, low CSF glucose, or clinical symptoms or systemic features should be treated for 10 to 14 days. Some experts treat infections caused by gram-negative bacilli for 21 days.

- For patients with repeatedly positive CSF cultures on appropriate antibiotics, treatment should be continued for 10 to 14 days following the last positive culture.

Decisions regarding antibiotic duration should be tailored to an individual patient's response to therapy; longer courses may be warranted in the setting of delayed or incomplete response.

In rare patients, complete device removal is not possible. In these cases, long-term oral suppressive antimicrobial therapy may be needed after completion of initial intravenous therapy.

Timing of new shunt placement — The optimal timing of new shunt placement has not been defined, but we generally favor the following approach, in accordance with the IDSA guidelines [4]; it should be noted that the timing of new shunt placement should be individualized based upon the isolated organism, the severity of the infection, and the improvement of CSF parameters and CSF sterilization in response to antibiotics [4]:

- For patients with coagulase-negative staphylococci or *C. acnes* infection **without** associated CSF abnormalities and with negative CSF cultures for 48 hours following externalization of the shunt, a new shunt can be placed as soon as the third day following removal of the infected shunt.

- For patients with coagulase-negative staphylococci or *C. acnes* infection **with** associated CSF abnormalities but with negative repeat CSF cultures, a new shunt can be placed after seven days of antibiotics. If repeat cultures are positive, antimicrobial treatment should be continued until CSF cultures remain negative for 7 to 10 consecutive days before a new shunt is placed.

- For patients with infection caused by *S. aureus* or gram-negative bacilli, a new shunt can be placed 10 days after CSF cultures are negative.

A period without antibiotics is **not** recommended to verify clearance of infection before a new shunt is placed [4]. Close follow-up after placement of a new shunt is important to ensure that the infection has been adequately treated.

Monitoring the response to therapy — Patients being treated for shunt infection should be monitored for a response to therapy using clinical parameters and CSF testing prior to replacing the shunt [4]. No data exist on the appropriate frequency of rechecking CSF cultures; we typically recheck them at 48- to 72-hour intervals. In patients without clear clinical improvement, additional CSF analysis should be performed. (See 'Cerebrospinal fluid' above.)

For patients who have an external ventricular drains (EVD) for an indication other than infection, daily CSF cultures and other CSF analysis are **not** recommended unless there is a clinical indication [4]. The rationale for this recommendation is that the results of such surveillance do not reliably predict infection and may increase the risk of iatrogenic infection. In one retrospective study, daily cultures did not identify infection before clinical signs and symptoms developed [76]. In a prospective study of patients with an external drainage device, CSF samples showed no significant differences in leukocyte count, protein concentration, glucose concentration, or CSF/blood glucose ratio between the patients in whom meningitis developed and a control group without EVD-associated meningitis during the first three days of infection or during the three days preceding the infection [77]. In addition, Gram staining had low sensitivity for detecting infection (18 percent on the first day of infection; 60 percent on the second day of infection). Thus, a positive Gram stain can be quite helpful, but a negative one is less useful.

In a prospective study of patients with EVDs in whom CSF was tested daily, the only parameter that correlated with a positive CSF culture was CSF cell count; peripheral white blood cell (WBC) count, CSF glucose, and CSF protein were not reliable predictors of infection [78]. Similarly, in a retrospective study of patients with EVDs that compared clinical and laboratory findings at the time of EVD insertion and at the time of documented infection, the two most reliable indicators of infection were increasing CSF pleocytosis (median WBC count 175/microL) and fever [79].

PREVENTION

Measures for prevention of CSF shunt infection include meticulous adherence to surgical and sterile technique (including topical antiseptic), short procedure times, and perioperative

antibiotic prophylaxis [80,81]. Antibiotic-impregnated catheters may be beneficial. Prophylactic catheter exchange is not recommended.

Antibiotic prophylaxis — Perioperative antibiotic prophylaxis is warranted in patients undergoing central nervous system (CNS) device placement [4,82-85]. Prolonged antibiotic prophylaxis for the duration of external ventricular drain (EVD) use is **not** recommended, as it has not been proven to be beneficial and might select for the emergence of resistant organisms [4].

For patients undergoing clean neurosurgical procedures, including CSF shunting procedures and intrathecal pump placement, we suggest cefazolin (2 g intravenously [IV] for adults <120 kg adults and 3 g IV for adults ≥120 kg; 30 mg/kg IV for children) given 60 minutes prior to the incision. Cefazolin should be redosed at four-hour intervals until the surgery is over given the relatively short (about two-hour) half-life of cefazolin (table 3). This approach is consistent with guidelines for antimicrobial prophylaxis for surgery that were published in 2013, representing the views of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America (IDSA), the Surgical Infection Society, and the Society for Healthcare Epidemiology of America [81].

However, other experts use a different approach to antibiotic prophylaxis. As an example, although we prefer to administer antibiotics only prior to and during the surgical procedure, some guidelines suggest antibiotics be continued for as long as 24 hours postoperatively, as this is the duration that has been studied [4]. In addition, some experts prefer vancomycin instead of or in addition to cefazolin. The rationale for using vancomycin alone or with cefazolin is that coagulase-negative staphylococci, many of which are oxacillin-resistant, are commonly implicated in CSF shunt infections. Also, some add vancomycin to cefazolin in patients who had prior methicillin-resistant *S. aureus* (MRSA) colonization or infection or when the patient is at increased risk of MRSA colonization (table 4). The dosing of vancomycin is 15 mg/kg (not to exceed 2 g) IV. It is important to note that vancomycin requires a prolonged infusion time and should be started two hours prior to the incision (compared with 60 minutes prior to the incision for most other agents) [81]. Only a single preoperative dose of vancomycin is necessary given its long half-life. (See "Methicillin-resistant Staphylococcus aureus (MRSA) in adults: Epidemiology", section on 'MRSA colonization'.)

The benefit of antimicrobial prophylaxis for intracranial ventricular shunts was demonstrated in a meta-analysis of 15 observational studies that found systemic prophylactic antibiotics decrease rates of CSF shunt infection (odds ratio 0.52, 95% CI 0.36-0.74) [82]. A second meta-analysis of nine studies (seven randomized clinical trials and two retrospective cohort studies)

showed similar findings, with the infection rate in the prophylactic antibiotic group being 5.9 compared with 10.7 percent in the control group (relative risk 0.55; 95% CI 0.38-0.81) [86].

Data regarding the possible benefit of antibacterial prophylaxis for EVDs are more limited, and only some studies have suggested a benefit [87]. Other studies have suggested no benefit, or even an association between antibiotic prophylaxis and the development of infections caused by resistant bacteria, but these studies had major limitations, such as being retrospective and underpowered to show a benefit [4].

To further reduce the risk of infection, some centers have advocated for the use of intrathecal antimicrobial administration in addition to intravenous antimicrobials as surgical site prophylaxis for new shunt placement [88,89]. However, given the absence of prospective, randomized trial data, we feel there is insufficient evidence to support the routine use of intrathecal antimicrobials as prophylaxis in patients with first-time shunt placement.

Antimicrobial prophylaxis for the prevention of surgical site infections is discussed in greater detail separately. (See "Antimicrobial prophylaxis for prevention of surgical site infection in adults".)

Antibiotic-impregnated catheters — We favor the use of antibiotic-impregnated devices as they are likely to reduce the incidence of CSF shunt and EVD infections [4]. Although available data has generally been judged to be low-certainty, meta-analyses have found a reduction in infections with these catheters [82,90-94]. In addition, in a multicenter, single-blinded, randomized trial of 1605 patients comparing antibiotic-impregnated or silver-impregnated versus standard ventriculoperitoneal (VP) shunts, the percentage of individuals requiring a revision for infection was lower in the antimicrobial shunt group compared to the standard shunt and silver shunt groups (2, 6, and 6 percent, respectively) [95].

No role for prophylactic catheter exchange — Prophylactic catheter exchange does not appear effective for preventing CSF shunt infection and is therefore not recommended [4,82,96,97]. As an example, in a trial of 103 patients with EVD randomly assigned to prophylactic catheter exchange or control groups, there was no difference in shunt infection rates (8 versus 4 percent, respectively) [96]. Similar lack of benefit was noted in a meta-analysis [82].

Combined interventions — Interventions that combine different prevention strategies appear to be effective in certain settings. The Hydrocephalus Clinical Research Network undertook an initiative in which centers agreed to develop an 11-step protocol to reduce CSF shunt infection rates; the protocol enforced sterile surgical techniques as well as the timing of antibiotic administration [98]. The infection rate decreased from 8.8 percent to 5.7 percent while using the

protocol (relative risk, reduction of 36 percent, with a number needed to treat of 33), indicating that use of a standardized protocol is effective in reducing CSF shunt infection rates. However, antibiotic-impregnated shunt catheters were not examined in this investigation, and a subsequent study failed to demonstrate a reduction in infection rate with use of the 11-step protocol when these catheters were used [99].

In patients requiring placement of an EVD, following adoption of a simple protocol that bundled evidence-based infection prevention and control measures, ventriculitis rates declined from 6.3 percent in the baseline period to 0.8 percent during a three-year follow-up period [100]. In a subsequent study that examined the same cohort and included an additional four years of follow-up, the infection rate declined to 0 percent [101]. If these results can be replicated in other medical centers, they could provide support for a new guideline in the prevention of EVD infection.

SUMMARY AND RECOMMENDATIONS

- **Epidemiology and microbiology** – The rate of cerebrospinal fluid (CSF) shunt infection is about 5 to 15 percent. Risk factors include intraventricular hemorrhage, subarachnoid hemorrhage, and cranial fracture with CSF leak. (See 'Incidence and risk factors' above.)

  Skin flora account for the majority of infections associated with internalized or externalized CSF shunt devices. Shunt infections may also develop from the distal ends of internalized devices, leading to peritonitis or bloodstream infection with a variety of pathogens. (See 'Microbiology and pathogenesis' above.)

- **Clinical presentation** – Symptoms may be subtle or absent. Patients may present with manifestations of increased intracranial pressure or with symptoms localized to the distal end of the device. (See 'Clinical manifestations' above.)

- **Diagnosis** – Diagnosis of CSF shunt infection can be challenging; CSF cell counts may be low and should be correlated with Gram stain and culture results.

  CSF cultures are the most important test for establishing the diagnosis of CSF shunt infections and external ventricular drain (EVD) infections and should be obtained before starting antibiotics.

  Blood cultures and imaging studies may be useful adjunctive tools. (See 'Diagnosis' above.)

- **Initial management**

- **Device removal** – For patients with CSF shunt infections, we recommend device removal (**Grade 1B**). Some patients may require external drainage to control intracranial hypertension. (See 'Treatment' above.)

- **Empiric antibiotic regimens** – For adult patients, we suggest empiric parenteral antibiotic therapy with vancomycin **plus** ceftazidime, cefepime, or meropenem (**Grade 2C**).

  For children, we suggest empiric parenteral antibiotic therapy with vancomyc**in plus** cefotaxime, ceftriaxone, or meropenem (**Grade 2C**).

  These regimens provide coverage of coagulase-negative staphylococc*i, Staphylococcus aureus*, and gram-negative pathogens. (See 'Empiric therapy' above.)

- **Subsequent management** – Subsequent antibiotic therapy should be tailored to culture and susceptibility results. The role for intraventricular antibiotics is discussed in detail elsewhere. (See 'Targeted therapy' above and "Health care-associated meningitis and ventriculitis in adults: Treatment and prognosis", section on 'Intrathecal and intraventricular therapy'.)

  The duration of antibiotic therapy depends upon the implicated pathogen. (See 'Duration of antibiotics' above.)

  Patients should be monitored for a response to therapy using clinical parameters. In addition, CSF cultures should be checked serially to ensure that they have become negative. (See 'Monitoring the response to therapy' above.)

  The timing of new shunt placement should be individualized based upon the isolated organism, the severity of the infection, and the improvement of CSF parameters and CSF sterilization in response to antibiotics. (See 'Timing of new shunt placement' above.)

- **Prevention of CSF shunt and device infection** – For CNS device placement, we recommend antibiotic prophylaxis (**Grade 1B**). We suggest cefazolin administered 60 minutes prior to incision and dosed every four hours during the procedure (**Grade 2C**). Alternative regimens, including the use of vancomycin, are reasonable (table 3). (See 'Antibiotic prophylaxis' above.)

  We suggest that antibiotic-impregnated CSF catheters be used (**Grade 2C**). (See 'Antibiotic-impregnated catheters' above.)

We suggest against prophylactic catheter exchange for prevention of infection (**Grade 2C**). Limited data suggest that prophylactic catheter exchange does not reduce infections. (See 'No role for prophylactic catheter exchange' above.)

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Topic 1286 Version 36.0

GRAPHICS

CDC surveillance definition for health care-associated meningitis and ventriculitis[1]

At least one of the following criteria:
1. Organism(s) identified from CSF by a culture or non-culture-based microbiologic testing method*
OR
2. The following features are present ▪ At least two of the following: • Fever (>38.0°C) or headache¶ • Meningeal sign(s) with no other recognized cause • Cranial nerve sign(s) with no other recognized cause ▪ And at least one of the following: • Increased white cells, elevated protein, and decreased glucose in CSF • Organism(s) seen on Gram stain of CSF • Organism(s) identified from blood by a culture or non-culture based microbiologic testing method • Diagnostic single antibody titer (IgM) or fourfold increase in paired sera (IgG) for organism

CDC: United States Centers for Disease Control and Prevention; CSF: cerebrospinal fluid.

* Only when testing is performed for purposes of clinical diagnosis or treatment, and not, for example, active surveillance culture/testing.

¶ For patients ≤1 year of age, this clinical criteria can be met by fever (>38.0°C), hypothermia (<36.0°C), apnea, bradycardia, or irritability without other recognized cause.

Reference:

1. *Centers for Disease Control and Prevention. CDC/NHSN Surveillance Definitions for Specific Types of Infections. Available at: https://www.cdc.gov/nhsn/pdfs/pscmanual/17pscnosinfdef_current.pdf (Accessed on January 30, 2023).*

Graphic 140116 Version 1.0

Approach to vancomycin dosing for adults with normal kidney function*

Loading dose (for patients with known or suspected severe *Staphylococcus aureus* infection)¶	Load 20 to 35 mg/kg (based on actual body weight, rounded to the nearest 250 mg increment; not to exceed 3000 mg). Within this range, we use a highe dose for critically ill patients; we use a lower dose for patients who are obese and/or are receiving vancomycin via continuous infusion.
Initial maintenance dose and interval	Typically 15 to 20 mg/kg every 8 to 12 hours for most patients (based on actual body weight, rounded to the nearest 250 mg increment). In general, the approach to establishing the vancomycin dose/interval is guided by a nomogram.Δ
Subsequent dose and interval adjustments	Based on AUC-guided (preferred for severe infection)[1] or trough-guided serum concentration monitoring.◇

AUC: area under the 24-hour time-concentration curve.

* Refer to the UpToDate topic on vancomycin dosing for management of patients with abnormal kidney function.

¶ For patients with known or suspected severe *S. aureus* infection, we suggest administration of a loading dose to reduce the likelihood of suboptimal initial vancomycin exposure. Severe *S. aureus* infections include (but are not limited to) bacteremia, endocarditis, osteomyelitis, prosthetic joint infection, pneumonia warranting hospitalization, infection involving the central nervous system, or infection causing critical illness.

Δ If possible, the nomogram should be developed and validated at the institution where it is used to best reflect the regional patient population. Refer to the UpToDate topic on vancomycin dosing for sample nomogram.

◇ Refer to the UpToDate topic on vancomycin dosing for discussion of AUC-guided and trough-guided vancomycin dosing. For patients with nonsevere infection who receive vancomycin for <3 days (in the setting of stable kidney function and absence of other risk factors for altered vancomycin kinetics), vancomycin concentration monitoring is often omitted; the value of such monitoring prior to achieving steady state (usually around treatment day 2 to 3) is uncertain.

Reference:

1. *Rybak MJ, Le J, Lodise TP, et al. Therapeutic Monitoring of Vancomycin for Serious Methicillin-Resistant Staphylococcus Aureus Infections: A Revised Consensus Guideline and Review by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the Society of Infectious Diseases Pharmacists. Am J Health Syst Pharm 2020; 77:835.*

Graphic 128911 Version 5.0

Antimicrobial prophylaxis for neurosurgery in adults

Nature of operation	Common pathogens	Recommended antimicrobials	Usual adult dose*	Redose interval¶
Elective craniotomy Cerebrospinal fluid shunting procedures Implantation of intrathecal pumps	*Staphylococcus aureus*, *S. epidermidis*	Cefazolin	<120 kg: 2 g ≥120 kg: 3 g	4 hours
		OR vancomycinΔ	15 mg/kg IV (max 2 g)	12 hours
		OR clindamycin	900 mg IV	6 hours

IV: intravenous.

* Parenteral prophylactic antimicrobials can be given as a single IV dose begun within 60 minutes before the procedure. If vancomycin is used, the infusion should be started within 60 to 120 minutes before the initial incision to have adequate tissue levels at the time of incision and to minimize the possibility of an infusion reaction close to the time of induction of anesthesia.

¶ For prolonged procedures (>3 hours) or those with major blood loss, or in patients with extensive burns, additional intraoperative doses should be given at intervals one to two times the half-life of the drug (cefazolin every four hours, clindamycin every six hours, vancomycin every 12 hours) for the duration of the procedure in patients with normal renal function.

Δ Use of vancomycin is appropriate in hospitals in which methicillin-resistant *S. aureus* (MRSA) and *S. epidermidis* are a frequent cause of postoperative wound infection, in patients previously colonized with MRSA, or for those who are allergic to penicillins or cephalosporins. Rapid IV administration may cause hypotension, which could be especially dangerous during induction of anesthesia. Even when the drug is given over 60 minutes, hypotension may occur; treatment with diphenhydramine and further slowing of the infusion rate may be helpful. For procedures in which enteric gram-negative bacilli are common pathogens, many experts would add another drug such as an aminoglycoside (such as gentamicin 5 mg/kg IV), aztreonam (2 g IV), or a fluoroquinolone (such as ciprofloxacin 400 mg IV or levofloxacin 500 mg IV).

Adapted from:

1. Antimicrobial prophylaxis for surgery. Med Lett Drugs Ther 2016; 58:63.

2. Bratzler DW, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt) 2013; 14:73.

Graphic 87202 Version 10.0

Risk factors for methicillin-resistant *Staphylococcus aureus* (MRSA) infection in adults

Health care exposures during the prior 12 months:
▪ Recent hospitalization
▪ Residence in a long-term care facility
▪ Recent surgery
▪ Hemodialysis
Patient-specific risk factors:
▪ Known MRSA colonization or past infection with MRSA
▪ Recent close contact with a person colonized or infected with MRSA
▪ HIV infection
▪ Injection drug use
▪ Homelessness
▪ Men who have sex with men
▪ Antibiotic use within prior 6 months
Environmental exposures associated with outbreaks of MRSA skin abscesses*:
▪ Incarceration or working as prison guard
▪ Military service
▪ Attending schools or living in communities with high colonization rates
▪ Living in crowded conditions
▪ Attending or working in childcare centers
▪ Playing contact sports or sharing sporting equipment
▪ Sharing needles, razors, or other sharp objects

This list of risk factors is based on observational studies performed in different regions of the world. MRSA risk factors for individual countries may vary depending on local MRSA epidemiology.

MRSA: methicillin-resistant *Staphylococcus aureus*.

* These exposures are generally not associated with other types of MRSA infections, including cellulitis without abscess.

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