# Cerebrospinal Fluid Shunt Infection: Avoidance, Diagnosis and Treatment

Justin Ker, Min Wei Chen, David Low, and Wan Tew Seow

## Contents



J. Ker (✉) · M. W. Chen
Department of Neurosurgery, National Neuroscience Institute, Singapore, Singapore
e-mail: justinker@gmail.com; minwei.chen@mohh.com.sg

D. Low · W. T. Seow
Department of Neurosurgery, National Neuroscience Institute, Singapore, Singapore

Neurosurgical Service, KK Women's and Children's Hospital, Singapore, Singapore
e-mail: david.low.c.y@singhealth.com.sg; Seow.Wan.Tew@singhealth.com.sg


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**Abstract**

The treatment of hydrocephalus with cerebrospinal fluid (CSF) diversion is central to the work of the pediatric neurosurgeon. Hydrocephalus affects approximately 1 out of 500 births (Jenkinson et al., Trials 15:4, 2014), resulting in significant societal health-care costs and patient morbidity, especially in the pediatric population. One review of pediatric shunt infections reported that infection rates ranged from 3.0% to 27.6% (Prusseit et al., Pediatr Neurosurg 45(5):325–336). This chapter traces the epidemiology and pathophysiology of shunt infections, and places shunt infections in their microbiological context. Diagnosis, investigations, and treatment are explored, and a review of strategies to avoid shunt infections is discussed. These strategies include using different types of patient skin preparation, prophylactic antibiotics, and antibiotic-impregnated shunts.

**Keywords**

Infection · Antibiotics · Prophyilaxis · Antibiotic impregnated · Microbiology · Staphylococcus · Gram positive · Gram negative

## Introduction

Hippocrates, Galen, and medieval Arab physicians have described cases of hydrocephalic patients since ancient times, but the modern age of hydrocephalus treatment begins in the 1960s, when slit and diaphragm silicone valves were developed. The 1990s saw a resurgence of interest in endoscopic ventriculostomy, but shunt insertion remains the mainstay of CSF diversion.

Patients with shunt infections have double the mortality risk and may undergo 3 times the number of shunt-related operations, aside from the financial cost of revision shunt surgery (Edwards et al. 2015). Understandably, shunt infections are the most costly implant-related infections in the United States with the average hospital cost of treating a shunt infection estimated at $50,000 (Attenello et al. 2010). Long-term data from the pediatric Shunt Design Trial showed that the overall shunt survival was 62% at 1 year, 52% at 2 years, 46% at 3 years, and 41% at 4 years (Kestle et al. 2000). Shunt infection accounted for 8.1% of the failures in the study.

Children with shunt infections have a mortality rate of 10% and more long-term morbidity, in terms of cognitive deficits, reduced academic achievement, psychomotor retardation, and seizure disorders (Thompson and Hatley 2015). Therefore, there is a strong impetus for neurosurgeons to reduce the rates of shunt infections. Preventative strategies toward this aim are, however, highly institutional and even surgeon-based, as the evidence base for what constitutes effective clinical practice for preventing shunt infection is varied and heterogeneous. This chapter reviews the current understanding of how a shunt infection seeds and the pathophysiology of how it progresses. The investigation, diagnosis, and management of shunt infection will be discussed, in addition to an overview of preventative strategies employed by neurosurgeons.

## Epidemiology and Definition of Shunt Infection in Children

There is some variability in the published shunt infection rates due to the lack of a consensus definition of what constitutes a shunt infection. However, the most definitive diagnostic criterion is CSF culture-proven infection (Thompson and Hatley 2015).

The neurosurgical literature often quotes pediatric shunt infection rates of 15%. This figure references Choux's (Choux et al. 1992) 1992 study on 606 shunt operations carried out from 1978 to 1982. Interestingly in the same paper, Choux showed that after a perioperative management protocol was instituted, the incidence of shunt infection decreased to 1%. In terms of the time to presentation of infection, Choux states that 70% of infections appear 1 month after surgery, and 90% occur within 6 months. One of the largest studies of shunt infections is by Davis (Davis et al. 1999) on 2325 shunt operations and quotes an overall infection rate of 3.2%. A review of shunt infection rates in the literature found that the range varied from 3% to 28% (Prusseit et al. 2009), reflecting the variable populations studied and the lack of uniformity in the definition of shunt infection.

## Pathophysiology of Shunt Infection

Clinically, it is perhaps useful to consider the source of shunt infections as acquired (1) during the shunt surgery or (2) after shunt surgery from an external event such as peritonitis and intra-abdominal sepsis. Hematogenous bacterial dissemination can also occur from the respiratory and urinary tracts, as well as the ear, nose, and throat. The median time to shunt infection occurs at 3 weeks (Simon et al. 2012), and 12% of shunt infections occur at 1 year (Hayn 1994) (which have been termed "late infections"). The majority of shunt infections occur in the perioperative period and should thus be viewed as a surgical complication, which can be potentially mitigated.

During shunt surgery, bacteria can come from the (1) patient's own skin flora, (2) the surgeon, and (3) the operating room environment. It is a widely held belief that the majority of shunt infections originate from organisms in the patient's skin flora, although the evidence for this is not definitive. In an analysis of 466 shunt operations, an association between skin bacteria density and risk of shunt infection was found, although the authors also reported patient age as the only major factor influencing infection rate (Pople et al. 1992). Moreover, a study of 20 shunt infection cases showed that while the majority of infections were caused by typical skin commensals, in only 4 cases (20%) were the offending organisms *identical* to those originally grown from the skin (Shapiro et al. 1988). The evidence for bacterial contamination from the surgeon or the airborne operating room environment is even weaker. Given the high morbidity and prevalence of shunt infection, numerous studies have attempted to study what factors may mitigate the risk of shunt infection.

McGirt (McGirt et al. 2003) retrospectively reviewed 442 pediatric patients, of which 92 (or 11%) developed shunt infection. The risk factors were prematurity, previous shunt infection, and intraoperative use of a neuroendoscope, although the latter is tenuous. Kulkarni's (Kulkarni et al. 2001a) prospective study of 299 children with shunt infections had an infection rate of 10.4%. He found that postoperative CSF leak, prematurity of the patient, and the number of times the shunt was exposed to breached surgical gloves carried increased risk of infection. The largest study on risk factors to date is Simon's (Simon et al. 2014) multicenter prospective trial on 1036 children undergoing shunt placement. 102 children, or approximately 10% of the patients across 6 centers, developed shunt infection. After correcting for baseline characteristics, Simon demonstrated that prior shunt surgery had the strongest risk for having a shunt infection. When a patient undergoes two or more shunt operations, the risk of infection carries a hazard ratio of 13 (confidence interval 6.5 to 24.9) (Table 1).

## Microbiology

Half of shunt infections are caused by coagulase-negative staphylococci (Thompson and Hatley 2015). In this group *Staphylococcus epidermidis* is the most common offending organism. The next most common organism is *Staphylococcus aureus*, which accounts for 20% of cases. The remaining cases are caused by gram-positive rods and cocci or gram-negative rods. Of note, propionibacteria are also known to cause shunt infections, although they may be difficult to isolate as they grow slowly and require prolonged

**Table 1** Risk factors for shunt infection

| Study | Number of pediatric patients | Shunt infection rate | Risk factor | Relative risk or hazard ratio |
|---|---|---|---|---|
| McGirt et al. (2003) | 442 | 11% | Prematurity of patient | Relative risk 4.8 |
| | | | Prior shunt infection | Relative risk 3.8 |
| | | | Intraoperative use of neuroendoscope | Relative risk 1.6 |
| Kulkarni et al. (2001a) | 299 | 10.4% | Postoperative CSF leak | Hazard ratio 19 |
| | | | Prematurity | Hazard ratio 4.7 |
| | | | Number of times shunt system was exposed to breached surgical gloves | Hazard ratio 1.07 |
| Simon et al. (2014) | 1036 | 9.8% | 1 prior shunt revision | Hazard ratio 3.9 |
| | | | 2 or more prior shunt revisions | Hazard ratio 13 |

anaerobic culture. *Staphylococcus epidermidis* and *aureus* have been isolated from early infections, reflecting their likely inoculation during shunt surgery. Late infections may also result from a precipitating event intra-abdominal sepsis or hematogenous spread from other sources.

## Biofilm

The current understanding of how a shunt infection becomes established and propagates invokes the idea of the "biofilm" (Fux et al. 2006). Firstly, the implantation of a foreign body invokes an inflammatory host reaction, which causes the expression of host proteins that adhere to the foreign shunt tubing. Certain species of bacteria possess cell-surface adhesins or receptors that recognize and bind to the host proteins. After bacterial adhesion, the act of receptor binding triggers signals within the bacterial cell that cause it to express an extracellular substance. This substance is known as an exopolymer and is rich in glycoproteins and polysaccharides. The composite of bacterial colonies and exopolymer is referred to as a biofilm. The biofilm coats the shunt implant and becomes a sequestered microcosm for bacterial growth and replication, at the same time acting as a barrier to antibiotic entry. Preventing the establishment of the biofilm is the rationale behind the research of silver or antibiotic-coated ventricular catheters and shunt tubing systems. There are reports that the proliferation of these new catheters have altered the bacterial demographic responsible for shunt infections (Thompson and Hatley 2015).

Diagnosing and identifying a causative organism in a shunt infection can be a difficult task, fraught with false negatives. It is thought that biofilms have a role to play in this, as bacteria adhere to the biofilm on the device, which provides both a medium for growth and a form of protection, making detection difficult. The tenacity of this adherence is seen in a study by Tunney on hip prostheses retrieved from revision hip surgery (Tunney et al. 1999). Bacterial organisms were recovered and cultured in 22% of the prostheses after ultrasound sonification to dislodge the organisms. No bacteria were grown in prostheses that were not sonified, allowing the authors to conclude that current methods of detecting, culturing, and isolating bacteria grossly underestimate the degree of bacterial colonization.

In an attempt to clarify the pathophysiology of biofilm formation, Fux examined the biofilm in three patients with documented shunt infections using routine microscopy and culture, scanning electron microscopy (SEM), and polymer chain reaction (PCR) of 16S rDNA primer sequences (Fux et al. 2006). The explanted catheters from these three patients, as well as newly manufactured, unused shunt tubings, were examined under electron microscopy. In the newly manufactured shunt tubings, surface irregularities

were seen, which may predispose to biofilm formation. On the inner surface of one of these new shunts, sterile biofilms inoculated during the manufacturing process were detected.

In the three patients with the explanted catheters, biofilm was detected both on the inner and outer surfaces. In two of the patients, the biofilms contained a monomorphous bacterial population, while in the last patient, the biofilm contained both cocci and bacilli.

As Tunney above suggests, it is likely that biofilm and bacterial colonization of implants are under-detected. At the same time, there are no studies that demonstrate biofilm colonization inexorably leads to implant-related infection. The biofilm obviously acts as a source for bacteria to cause a systemic infection, but there may be un-elucidated host-immune and bacterial-signaling factors that tip the balance from colonization to infection.

It is difficult to eradicate biofilms once they have formed on implants, and the nature of the cellular biology of the bacterial interactions within the biofilm bears further study. The extracellular matrix component of the biofilm is believed to limit the bactericidal reach of the host's inflammatory cells and their secreted cytokines (Costerton et al. 1999). Some hypotheses suggest that the spatial heterogeneity of bacteria within different layers of the biofilm, nutritional gradients, and cell-to-cell signaling may explain the persistence of antibiotic-resistant populations of bacteria that continue to persist within the biofilm (Xu et al. 2000). The dead biofilm plaques found by Fux on new, unused shunts were surprising. Although no bacterial structures were identified, this finding raises questions regarding the adequacy of current sterilization techniques using alcohol and ethylene oxide.

## Clinical Presentation

Children with shunt infections can present in a myriad of ways, making diagnosis difficult. Shunt infection can mimic common pediatric infections such as otitis media, respiratory tract, and urinary tract infections, and it is important to exclude these other causes expeditiously. The severity of the shunt infection can also vary, from mild cognitive changes (decreased attentiveness or irritability) due to shunt malfunction to septic shock in the younger age group. A thorough history and clinical examination must be done to sieve out the correct diagnosis and to direct the appropriate set of investigations.

Fever remains the most common presenting symptom, which may be low grade and intermittent (Duhaime 2006). The clinician must have a high index of suspicion when a febrile child with recent shunt surgery presents and as 90% of shunt infections present within 6 months of surgery (Choux et al. 1992). In a retrospective series of 1000 pediatric patients with shunts, two predictors of shunt infection were shunt surgery in the past 90 days (adjusted odds ratio 2.4) and fever (adjusted odds ratio 8.4) (Rogers et al. 2012).

Shunt malfunction due to mechanical obstruction is seen frequently and can manifest in a variety of ways. Proximally, ventricular enlargement occurs if the valve is not functioning well and occluded by proteinaceous exudates. With ventricular enlargement, the signs and symptoms of raised intracranial pressure become apparent. Fluid accumulation along the tubing tract is sometimes seen as CSF attempts to find another diversionary path and is seen as a fullness along the tubing tract. It is worth noting that an infected shunt may continue to function, meaning that the child may not have signs of shunt blockage in spite of the infection.

Headache is another common presenting symptom, and this may be due to the infection itself or raised intracranial pressure from shunt blockage. Other non-specific symptoms such as lethargy and vomiting may be seen in up to half of patients with shunt infections. Neck stiffness or meningism may be present in children with more aggressive infections from gram-negative bacteria, which may progress to ventriculitis, brain abscess, or empyema.

More specific signs for shunt infection include frank wound infection, purulent discharge, or CSF leak at the cranial or abdominal wounds. Erythema tracking along the tubing is another strong indicator of shunt infection. In rare cases, the

**Table 2** Signs and symptoms of shunt infection

| **Proximal shunt infection** |
|---|
| Fever |
| Shunt blockage, symptoms of raised intracranial pressure: headache, nausea, vomiting, lethargy, malaise, weakness, slow cognition |
| Headache |
| Seizures |
| Meningism |
| Wound infection |
| Skin erythema along shunt tubing |
| **Distal shunt infection** |
| Abdominal pain/peritonitis |
| Abdominal mass |
| Intestinal obstruction |
| Chest pain/pleuritis |
| Glomerulonephritis |

tubing may erode through the skin, bowel, or oral cavity, and this necessitates externalizing and changing the shunt system.

Abdominal pain, swelling, or frank peritonitis can occur when the distal end of a ventriculo-peritoneal shunt is infected. Suspicion of possible shunt infection must be raised in a shunted child with appendicitis, especially if the appendix has perforated. The cause of these symptoms may be from loculi of infected CSF in the peritoneum or infected ascites.

Distal infections of ventriculo-pleural shunts may cause the child to experience chest pain and shortness of breath or to have pleural effusions. One rare complication of ventriculo-atrial shunt infection is glomerulonephritis, which can occur years after shunt surgery. This occurs via an immune-mediated mechanism and can present with rash, hematuria, and renal impairment. The most common offending organism is *Staphylococcus epidermidis* (Table 2).

## Diagnosis

The most definitive diagnostic criteria for shunt infection is a positive CSF culture of the offending organism (Thompson and Hatley 2015). However, there is no universally agreed definition of what constitutes a shunt infection. Some clinicians may define shunt infection to include shunt wound infection, positive culture from the shunt implant itself, or clinical suspicion in a patient without any positive cultures at all. At times, the CSF white cell count may be high, with elevated protein and low glucose but with a negative CSF culture. Such a scenario may reflect the effect of early intravenous antibiotic use before CSF cultures were taken.

In coming to a diagnosis, the clinician often has to amalgamate and weigh the patient's presenting symptoms, past history of neurosurgical operations, the findings on clinical examination, and the investigation results. Ideally, a CSF sample should be taken before commencement of treatment. Choosing an inappropriate investigation delays treatment, and this may be clinically disastrous for the pediatric patient should fulminant ventriculitis or meningitis develop.

The accurate diagnosis of shunt infections is paramount as it has significant implications in the subsequent management decisions and, ultimately, the patient's outcome (Hardie et al. 1986; Hunt and Holmes 1976; Sacar et al. 2006). Investigation results may guide the clinician to externalize the shunt to an external ventricular drain and partially exteriorize the abdominal portion of the shunt, both of which imply heightened infection risks, a lengthened duration of antibiotics, hospital stay, and the necessity of reoperation. The mainstay of diagnosing shunt infections is obtaining a CSF sample for examination and culture, while radiological investigations provide useful additional information.

## Investigations

### Hematological Investigations and CSF Studies

#### Serum C-Reactive Protein

Serum C-reactive protein (CRP) is an acute phase reactant that appears in the blood during inflammatory processes such as surgery and infection. Bayston, in a study of 268 pediatric patients, stated that CRP was reliably positive in patients with shunt infections and that CRP levels tended

**Table 3** Common laboratory investigations in diagnosing shunt infections

| Investigation | Remarks |
|---|---|
| Serum C-reactive protein (CRP) | 97% sensitive and 73% specific for shunt infection<br>Normally falls to baseline after the fifth postoperative day |
| CSF cell count | Elevated in infection<br>Normal values (The Royal Children's Hospital Melbourne, Division of Medicine, Clinical Practice Guideline on CSF Interpretation)<br>Less than 1 month old: <20 lymphocytes per $mm^3$<br>Infants to adults: <5 lymphocytes per $mm^3$ |
| CSF protein concentration | Elevated in infection<br>Normal values (The Royal Children's Hospital Melbourne, Division of Medicine, Clinical Practice Guideline on CSF Interpretation):<br>Less than 1 month old: <0.4 g/L<br>Infants to adults: <1.0 g/L |
| CSF glucose concentration | Low glucose is seen in bacterial infections<br>May initially be normal due to a time lag from the start of infection |
| CSF cultures | Organism can be identified in 86% of cases (Kontny et al. 1993)<br>Gram stain should also be done<br>Mycobacterial and propionibacterium may take up to 2 months to culture |
| Others: blood cultures, wound swab, urinalysis, chest X-rays | Blood cultures are often negative<br>Urinalysis and chest X-rays may exclude other causes of fever |

to fall 5 days after shunt surgery (Bayston 1979). Therefore, a persistently high CRP level in the appropriate clinical context is an indicator of a shunt infection. A meta-analysis examined the utility of CSF and serum CRP levels to distinguish bacterial from viral meningitis but found that the sensitivity ranged from 69% to 99% and the specificity ranged from 28% to 99%. However, in spite of the large ranges, the odds ratio for serum CRP in the diagnosis of bacterial meningitis was 150 (95% CI, 44–509) (Gerdes et al. 2009). Another study showed that among all indices including CSF glucose concentration, protein concentration, leukocyte count, blood leukocyte count, and serum CRP, only serum CRP was able to distinguish gram stain-negative bacterial infections from viral infections with sensitivity of 96% and specificity of 93% and a high negative predictive value of 99% (Sormunen et al. 1999). However, being a general acute phase reactant, other systemic infections can also elevate CRP, and these need to be ruled out.

## CSF Cell Count

CSF shunt infections and meningitis share the same abnormal findings when the CSF is examined. Classically, bacterial meningitis will demonstrate CSF with increased white cells, low glucose concentrations, and high protein concentrations.

CSF leukocytosis is the most consistent finding in shunt infections (Conen et al. 2008). The definition of leukocytosis varies depending on the patient's age (see Table 3), and the leukocyte differential count gives a clue as to the infective etiology. A predominantly neutrophilic count may indicate bacterial infections, while a predominantly lymphocytic count suggests viral infection. There are exceptions, and 10% of patients with acute bacterial meningitis can present with a lymphocytic predominance in the CSF.

CSF eosinophilia has been suggested as a marker shunt infection, although it can be seen in other forms of shunt pathology (Bayston and Rodgers 1994; Vinchon et al. 1992). McClinton studied 12 patients with shunt infection and 69 with shunt malfunction. He stated that a combination of fever, CSF leukocytosis, and eosinophilia greater than 5% was highly predictive of shunt infection (McClinton et al. 2001). The combination of these three parameters was 99% specific for shunt infection and had a positive predictive value of 93% and a negative predictive value of 95%.

Essentially, no single CSF or laboratory parameter can reliably indicate the presence of

a shunt infection. Various authors have published models which predict shunt infection based on the combination of several CSF or hematological parameters, in work similar to McClinton's. In clinical practice, however, these models are not used, and the diagnosis of shunt infection is still dependent on the clinician evaluating the full clinical picture of signs and symptoms, and having a low threshold of suspicion, while awaiting the results of the CSF cultures.

## CSF Shunt Tap

Obtaining CSF can be done ideally via a shunt tap or in some cases via a lumbar puncture. Shunt taps are more accurate in diagnosing infection as they obtain CSF samples directly from the shunt system. One retrospective study showed that shunt taps were able to identify a causative organism in 85.7% of patients with a shunt infection (Kontny et al. 1993). Another study, albeit in the adult population, showed that causative microorganisms were identified in 91% of specimens obtained from shunt tap as compared to 45% of specimens obtained via lumbar puncture (Hardie et al. 1986).

However, shunt taps have their pitfalls. False negatives can occur if patients are on long-term antibiotics or if infections present distal to the valve (e.g., infected pseudocysts or intra-abdominal abscesses). False positives can arise from to skin contaminants during the process of obtaining CSF samples, and therefore strict asepsis is crucial during the collection procedure. The most common pathogen of shunt infections is staphylococci (Odio et al. 1984). A retrospective review showed that isolation of coagulase-negative staphylococci only in broth medium and not in solid medium always represented contamination (Meredith et al. 1997). Another study showed that positive CSF cultures in the absence of clinical signs and symptoms of infection did not correlate with development of clinical infection, even after long-term follow-up (Steinbok et al. 1996). Therefore, a positive CSF culture also has to be taken in the appropriate clinical context.

A shunt tap is for CSF obtained percutaneously via the puncturing of the shunt valve. Almost all shunt valves have a built-in CSF reservoir for percutaneous access. Tapping the shunt is generally safe, but one contraindication is when the entry site has a localized infection. Puncturing the valve runs the risk of introducing infection into an otherwise sterile CSF environment. In such instances CSF can be obtained from a lumbar puncture. Relative contraindications would be in a coagulopathic patient, or in a patient without a recent CT or MRI brain scan.

In young children or infants, topical local anesthesia before tapping the shunt is applied. The skin area overlying the shunt valve reservoir is prepared aseptically, and a 23-gauge butterfly needle is used for the puncture. The opening pressure can be measured by connecting a manometer to the needle tubing. Once the tap has been completed, the needle is withdrawn and gentle pressure is applied over the puncture site for hemostasis.

## Newer Tests on the Horizon

CSF cultures take at least 48 h for a positive result and often take longer to yield an organism. Therefore, there is a need for tests which provide a faster result so that the appropriate management can be instituted earlier.

Latex agglutination has good sensitivity in detecting antigens of common meningeal pathogens and is rapid and simple to perform (Gray and Fedorko 1992). However, a negative antigen test does not rule out infection caused by other specific pathogen. Some studies have shown that the routine use of this investigation did not change clinical therapy or the hospital course due to false positives and false negatives and the low yield in culture-negative samples (Maxson et al. 1994; Hayden and Frenkel 2000; Kaiser et al. 2001). Limulus lysate assay is another test that has been purportedly useful in identifying gram-negative pathogens. A positive test indicates the presence of endotoxin; however this test is unable to distinguish between specific organisms and is not commonly used.

## Radiological Investigations

Radiological investigations are useful adjuncts in the diagnosis of shunt infections. Each radiological modality listed in Table 4 is suited to revealing

**Table 4** Radiological investigations and possible findings in shunt infections

| Modality | Possible finding |
|---|---|
| X-ray shunt series (skull, neck, abdominal X-rays to trace course of the shunt tubing) | Tubing breaks<br>Disconnections in the shunt system<br>Catheter migration |
| Ultrasound (cranial fontanelles) | Ventriculomegaly |
| Ultrasound (abdominal mass or cyst) | Intra-abdominal abscesses<br>Pseudocysts |
| CT brain | Ventricular enlargement<br>Transependymal CSF flow<br>Edema adjacent to catheter<br>Subgaleal fluid collections<br>Brain abscesses<br>Subcutaneous emphysema next to shunt tubing |
| CT abdomen | Intra-abdominal abscesses<br>Pseudocysts |
| MRI brain | Ventricular enlargement<br>Transependymal CSF flow<br>Edema adjacent to catheter<br>Subgaleal fluid collections<br>Leptomeningeal enhancement (meningitis)<br>Ventricular ependymal enhancement (ventriculitis)<br>Debris in the ventricle (ventriculitis)<br>Brain abscesses |
| Radionucleotide CSF shunt studies (Technetium Tc 99 m pentetate) | Sluggish CSF flow through the valve or tubing<br>Obstruction at a point in the shunt system |

shunt malfunction or infection, and it is important to remember that shunt malfunction can coexist with, or be independent of, shunt infection.

The decision to choose a specific modality predicates on several factors: the severity of the shunt infection (i.e., how much delay will the radiological investigation and waiting for the result cause), the availability of certain modalities such as radionucleotide shunt studies, and the amount of ionizing radiation the patient can be subject to. It is also worth noting that the radiological investigations often offer indirect evidence of shunt infection only and can delay antibiotic therapy. The clinician can institute early management of shunt infection without radiological guidance.

X-ray images of the shunt system are often taken soon after presentation as they are easily available. These shunt series consist of anterior-posterior (AP) and lateral X-ray images of the skull, neck, chest, and abdomen and allow the clinician to trace the course of the shunt tubing from the cranium into the chest or abdomen. Shunt series can reveal breakages or disconnections in the tubing system and can give an approximate position of the distal catheter and if it is kinked. Additionally, shunt series also demonstrate if there are any signs of chest infection or intestinal obstruction, which need to be excluded early.

Ultrasonography has the benefit of being cheap, available, and not involving ionizing radiation. If the fontanelles are still open, one can determine if the ventricles are grossly enlarged. In the case of abdominal ultrasound, abdominal masses or pseudocysts can be identified and delineated.

CT scans of the brain mainly inform the clinician regarding shunt functionality and are done as a baseline or prior to reinsertion of a ventricular shunt after externalization. With shunt blockage, the ventricular system of the brain will be enlarged and there may be transependymal CSF shift. There may also be evidence of infection with edema adjacent to the catheter, collections, or outright brain abscesses (Wallace et al. 2014). Less commonly, subcutaneous emphysema next to the shunt tubing is seen. CT scans of the abdomen are used to investigate pseudocysts, abdominal masses, and intra-abdominal sepsis.

MRI brain scans serve a similar function to CT brains. While not being necessary to diagnose a shunt infection, MRI scans show subtle signs of infection in leptomeningeal or ependymal

enhancement, indicating that meningitis or ventriculitis respectively is present (Wallace et al. 2014). Cellular debris in the ventricles, on diffusion-weighted imaging (DWI) sequences, is also indicative of ventriculitis. Some centers use a fast one-shot T2 sequence for pediatric patients. This can minimize motion artifacts and obviate the need to sedate young patients. With the advent of programmable shunts, the clinician also needs to check and reset the patient shunt settings after MRI scan, if the shunt valve is not MRI compatible.

Radionucleotide studies or shuntograms involve injecting a small amount of technetium (typically less than 0.4 ml and up to 1.5 millicurie into the shunt reservoir) with the patient in the supine position. The flow of the radioactive tracer as it disperses is then examined over 30 min to look for areas of sluggish flow, or no flow, indicating the area of blockage. As with CT and MRI brains, this modality does not definitively diagnose shunt infection and is only done in very select cases.

### Algorithm for Investigation

Given the spectrum of clinical presentation, patient age, neurosurgical history, and institution resources, it is not surprising that there is no single, unified way in which clinicians investigate suspected shunt infection. While there is a common suite of tests for suspected shunt infection, it is not clear which tests should be ordered at which specific time points in the patient's clinical course. Below is the treatment algorithm used at our institution for working up a patient with suspected shunt infection (Fig. 1).

## Treatment

Infected shunts are managed in several ways, as described in the current literature. Treatment aims are directed at the eradication of the inciting organism, the prevention of repeat infections, and the avoidance of potentially devastating complications.

Some practitioners externalize the distal catheter and commence a course of systemic antibiotics, while others remove the shunt entirely. The latter is accompanied by the insertion of a temporizing external ventricular drain and a prolonged course of antibiotics before reinserting the shunt. Other practices include the removal of the infected shunt with the immediate reinsertion of a new shunt while starting high-dose antibiotics. In the past, shunt infections were sometimes managed with antibiotic therapy alone (Schoenbaum et al. 1975), although this is becoming less common. Antimicrobial therapy as a single modality of treatment is often ineffective, as the common inciting organisms such as coagulase-negative staphylococci are multiresistant. In addition, systemic antibiotics have poor CSF penetration, and suboptimal concentrations affect the bacteria which have colonized the shunt due to the presence of biofilms and the active secretion of β-lactams into the CSF space (Spector and Lorenzo 1974).

## Shunt Removal

The earlier practices in the 1960s and 1970s of preserving parts of, or the whole, shunt proved to have poor long-term outcomes (Callaghan et al. 1961). Christensen et al. reviewed 20 studies and found that removal of the shunt in either one or two steps was more successful than salvage treatment by leaving the shunt in situ (Christensen et al. 1994). Successful treatment rate in a one-step revision (removal followed by immediate reinsertion) was 70%, while two-step revisions (shunt removal followed by external ventricular drain insertion before shunt reinsertion after 7–10 days) yielded successful treatment in up to 95% of cases.

Kestle et al. performed a multicenter pilot study investigating a pediatric population with a mean age of 5.4 years (26 days to 18 years) and found great variation in treatment practice. Of 70 pediatric patients with infected shunts, 17 patients had shunt externalization, 50 underwent shunt removal and external ventricular drain insertion, and 3 patients were treated with antibiotic treatment alone (Kestle et al. 2006). They found the reinfection rate to be 26% (18 patients). In adults, the variation in practice

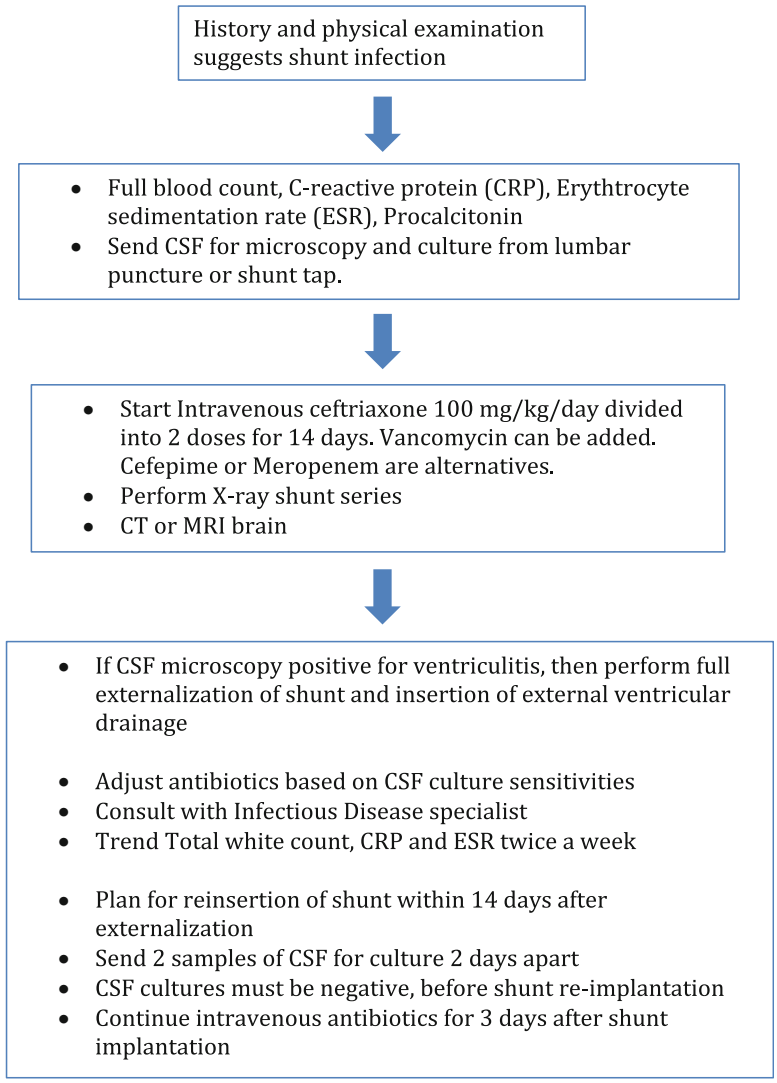


**Fig. 1** The investigation and management algorithm used at our institution

is also similar. In an 11-year retrospective review of adults with infected shunts, Conen et al. reported that shunt removal or shunt replacement was done in 81% of cases, compared to shunt retention and antibiotic therapy alone in 19% of cases. 13.3% of those treated with antibiotics alone had an unfavorable outcome (reinfection and death) compared to 1.6% in those who received some form of surgical treatment (Conen et al. 2008).

The only prospective randomized control trial published to date was performed in the 1980s by James et al. It showed that removal of an infected shunt, followed either by immediate shunt replacement with antibiotics, or interval EVD placement and antibiotics, was significantly better at treating shunt infections compared to antibiotics alone (James et al. 1980). Patients in one group (Group A) had shunt removal (with some externalized to an EVD), followed by intravenous and intraventricular antibiotics for 7 days. Patients in a second group (Group B) had their infected shunts removed and immediately replaced with a new one followed by daily intraventricular antibiotics for 3 weeks. In the third group (Group C), the shunt was not removed, but both intravenous and intraventricular antibiotics were given for 3 weeks. Each group had ten

patients, and in Groups A and B, all ten patients were cured, whereas in Group C, only three were cured. The mean hospital stay in Groups B and C were 9 and 23 days longer than the 24 days of Group A. It was also illustrated in the study that the type of surgical treatment did not seem to play a role in determining efficacy of treatment, as long as the infected shunt component was removed. This finding is also mirrored in a more recent cohort study by Kulkarni, specifically looking at risk factors of repeat shunt infections. The type of surgical treatment after initial shunt infection was not implicated in repeated shunt infection, as it did not reach statistical significance ($p = 0.58$) in survival analysis testing (Kulkarni et al. 2001b).

In 2009, the Infectious Diseases Society of America (IDSA) recommended the removal of infected shunts as the ideal treatment modality (Liu et al. 2009). A practice survey of the American Society of Pediatric Neurosurgeons by Whitehead and Kestle showed that 60–70% of practitioners removed the shunt and placed an EVD depending on the causative organism (Whitehead and Kestle 2001). In 1995, the British Society for Antimicrobial Chemotherapy recommended a regimen of shunt removal and placement of an external ventricular drain followed by intraventricular antibiotics (Bayston et al. 1995). They found this regimen successfully treated 100% of coagulase-negative staphylococci infections, once again emphasizing the need to remove shunt hardware once infected.

Tamber et al. conducted a literature review in 2014 on whether or not shunts should be removed during infection. From the 27 studies they examined, the authors recommended antibiotics with shunt partial externalization or full removal as a Class II recommendation (moderate clinical certainty). However, there is insufficient evidence to favor partial externalization over complete removal of the shunt, and the authors also found no evidence to recommend intraventricular antibiotic administration (Tamber et al. 2014).

At our institute, we favor the complete removal of the infected shunt, followed by external ventricular drainage and appropriate intravenous antibiotic therapy, which appear to be effective treatment modalities (Tunkel and Kaufman 2004; Kaufman 1997).

## Temporary CSF Diversion

The insertion of a temporary external drainage device is necessary after the removal of infected shunt components in order to manage any ongoing hydrocephalus. In the setting of temporary CSF diversion with the use of an external ventricular drain (EVD), it would be ideal to minimize the duration of the temporary drainage in order to minimize the risk of secondary nosocomial retrograde infections via the EVD.

In the multicenter pilot study by Kestle et al., 50 out of 70 patients with a shunt infection were initially treated surgically with shunt removal and EVD placement. Thirteen patients required an EVD insertion subsequently. The mean time required for a clear CSF sample to be obtained was 2.7 days after treatment initialization, while the mean time from a clear CSF sample to shunt reinsertion was 10.1 days (3–30 days) (Kestle et al. 2006).

EVD infection rates have been reported to be as high as 11% (Mayhall et al. 1984). Lo et al. found a mean time of 5.5 days (+/−0.7 days) from insertion to infection in a retrospective study of 199 patients (Lo et al. 2007). Another study by Hagel et al. found mean time to infection to be 6 days (1–11 days) (Hagel et al. 2014). Tsang et al. published a mean time to infection of 9.7 days (Tsang and Leung 2012). However in 2002, Lozier et al. did a multivariate analysis of a total of 2199 EVDs and reported no association between the risk of infection and duration of drainage (Lozier et al. 2002).

Based on the existing literature on risks of infection from the duration of an EVD, there is no conclusive evidence to direct what is an acceptable duration of a temporizing EVD. Compared to leaving an infected shunt in the patient, the risk of infection from a temporizing EVD appears to be less harmful. However, it would be logical to minimize the EVD duration and re-shunt the patient when feasible.

## Antibiotics

Definitive antibiotic treatment aims to achieve a sterile CSF and blood culture, prior to shunt reinsertion. This presumably minimizes the risk of shunt recolonization and repeat shunt infections. The management with appropriate antibiotics during this period is thus the cornerstone to successful treatment of infected shunts.

There is a wide variation in the duration, type, and route of antibiotic administration in the treatment of shunt infections. Some practitioners advocate treating shunt infections like bacterial meningitis, requiring 3–6 weeks of intravenous antibiotics, while some aim for successive sterile CSF cultures, before replacing the shunt.

The survey by the American Society of Pediatric Neurosurgeons found that after shunt removal, the duration of antibiotics varied significantly from 2 to 21 days for gram-positive infections and 5 to 24 days for gram-negative rod infections (Whitehead and Kestle 2001). Other studies showed similar variability in existing antibiotic treatment given similar clinical scenarios. The multicenter pilot study by Kestle et al. found antibiotic treatment time ranged from 4 to 47 days (mean of 16.5 days). In these studies, reinfection after treatment of a CSF shunt infection was not found to be related to the duration of antibiotic therapy (Kestle et al. 2006). Duration of antibiotics and timing of shunt replacement should be determined by the clinical state of the patient, the response to treatment as evidenced by sterile CSF studies, risk factors for repeat infections (e.g., immunocompromised states), and the type of offending organism (fungal infections vs. bacterial infections, gram positive vs. gram negative).

In selecting the appropriate type of antibiotic for treatment, empirical treatment is influenced by the hospital's local susceptibility patterns of common nosocomial strains. The choice of antibiotics is also determined by the local antibiotic policy at each institution. For example, empirical antibiotic treatment should include at least vancomycin in institutes with a high incidence of methicillin-resistant *Staphylococcus aureus* (MRSA). Once the results of CSF cultures are obtained, antibiotic regimens should be rationalized and narrowed based on the target bacteria's drug sensitivities and Minimum Inhibitory Concentration (the lowest concentration of an antibiotic that will inhibit the visible growth of a microorganism in a culture medium after incubation), in order to minimize drug resistance from emerging (Davison et al. 2000).

The use of intraventricular antibiotics is increasingly being studied due to the poor CSF penetration of intravenous antibiotics. Bayston et al. studied 50 patients with shunt- or EVD-associated ventriculitis and advocated the use of intraventricular vancomycin for 7–10 days before shunt replacement (Bayston et al. 1987). In 2013, Richard et al. did a systematic review of MEDLINE, Scopus, and the Cochrane database of studies between 1993 and 2012 (Richard et al. 2014). Their search results included eight studies, and they found the most common antibiotic regimen was intravenous and intrathecal vancomycin for gram-positive infections. However, there were no prospective randomized trials of antibiotic treatment. In vitro studies seem to suggest that these newer drugs have the potential to eliminate bacterial biofilms, thus negating the necessity for shunt removal. Bayston et al. used a continuous-perfusion model of shunt catheter biofilms to establish mature biofilms of methicillin-resistant *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Enterococcus faecalis*, and *Enterococcus faecium.* These were treated with either vancomycin or linezolid for 14 days. The biofilms were monitored, and the authors found that while the enterococci biofilms persisted, the staphylococci biofilms were eradicated entirely after 2 days and did not regrow (Bayston et al. 2012).

It should be noted that there are no comprehensive studies on the efficacy and pharmacokinetics of intraventricular drugs, and dosing is based on the individual institution's local policy. The use of antibiotics via the intraventricular route should always be balanced with the risk of neurotoxicity. Wombwell et al. reviewed the use of intrathecal vancomycin (Wombwell and Young 2014) as reported in the literature and reported several key points. Vancomycin is not metabolized in the CSF, and therefore its half-life is dependent on the diffusion and absorption from the CSF. The

rate of such a process in turn is influenced by the concomitant administration of intravenous vancomycin or the presence of an EVD. That gives rise to a wide variability in dosing. Initial intrathecal vancomycin dosing ranged from 5 to 50 mg/day in the available literature. Maintenance dosing then ranged from 5 to 10 mg/day with the aim of a CSF trough of 5 to 15 μg/ml. In terms of toxicities, adverse effects reports were limited and included changes in mental state, severe headaches, and vestibulocochlear nerve toxicity (Luer and Hatton 1993; Bayston et al. 1987; Golledge and McKenzie 1988).

There is no universal guideline for the type and duration of antibiotics in treating infected shunts. Most often, the antibiotic choice is guided by individual surgeon experience, individual institution protocols, and the patient's response to treatment. Clearly, the antibiotic choice selected is not based on a wide base of evidence. However, certain principles can be distilled from the varied treatment regimes in the literature: early commencement of empirical broad-spectrum antibiotics covering for common nosocomial pathogens, the tailoring of antibiotics once cultures and susceptibility tests are confirmed, and the shortest duration to achieve clearance of CSF with minimal toxicity.

## Fungal Shunt Infections

Less commonly, shunt infections occur due to atypical organisms such as fungi or viruses. Chiou et al. retrospectively analyzed fungal infections of shunts in eight premature babies. They recommended removal of the shunt and intravenous amphotericin B, reserving intrathecal amphotericin B, should the intravenous version prove ineffective (Chiou et al. 1994). Shapiro et al. also reported the successful treatment of seven premature babies with *Candida albicans* shunt infections. They used systemic amphotericin B in all patients and intraventricular amphotericin B in four patients (Shapiro et al. 1989). In these reports, the doses used were 1 mg/kg/day for children older than 4 months and 0.5–0.6 mg/kg/day for infants less than 4 months. Murphy et al. also reported the use of amphotericin B both intravenously and intrathecally to treat *Candida albicans* infections with good results. They treated the shunt infections surgically with externalization of the distal end followed by intravenous amphotericin B at 1 mg/kg/day and intrathecal amphotericin B at 1 mg once-daily doses (Murphy et al. 2000). Other antifungal drugs that have been reported with mixed results were flucytosine (Rodgers et al. 1978) and fluconazole in a premature infant (Cruciani et al. 1992).

## Avoidance

Shunt infection rates are often reported to be approximately in the region of 3–15% and even as high as 28% (Prusseit et al. 2009). The high morbidity and the impact on socioeconomic costs of treating shunt infections have led to efforts focused on preventing shunt infections.

Most of the studies in the available literature are based on historical controls with no randomized controlled double-blind studies to investigate individual factors. Nevertheless, possible factors which have been highlighted in many studies include decreasing the number of people in the operating room, shortening the duration of surgery, minimizing shunt hardware coming into contact with the skin, meticulous skin preparation, and use of prophylactic antibiotics and antibiotic-impregnated shunts (Faillace 1995; Mottolese et al. 2000; Kanev and Sheehan 2003).

Sarmey et al. did a systematic review identifying eight studies, most of which dealt with pediatric populations investigating various protocols to reduce shunt infection rates. They excluded antibiotic prophylaxis and the use of antibiotic-impregnated shunts. Although most studies demonstrated only Level 4 evidence and seven of the eight studies were based on historical controls, they found that reduction in infection rates ranging from 2.2% to 12.3% occurred with the implementation of a fixed shunt insertion protocol. Among the studies, surgical scrub with an antiseptic foam and failure to implement preoperative hair wash with 5% chlorhexidine gluconate were

independently associated with increased rates of shunt infections. For single-factor interventions, only antibiotic-impregnated sutures, no-shave policy, and double gloving with glove change prior to shunt handling resulted in significant reduction in shunt infection (Sarmey et al. 2015).

One way to avoid shunt infections is to tighten the criteria for inserting shunts, in order to avoid shunt insertion unless absolutely necessary. Chakraborty et al. (2008) reported that major studies of pediatric patients with myelomeningocele cited the shunt placement rate to be in the range of 63–91%. Using a more stringent criterion of repeated clinic and radiological reviews, Chakraborty et al. found that their 10-year shunt placement rate in 54 patients was 52%, which was lower than previously reported in the literature. They tolerated moderate ventriculomegaly and mild increases in ventricle size after myelomeningocele closure, and advocated a more critical evaluation of the need for shunt placement in children with myelomeningocele.

## Skin Preparation

Several studies have clearly established that shunt infections involving gram-positive bacteria account for most shunt infections and occur at the time of surgery. These pathogens come from the patient's own skin bacterial flora and fauna and often survive the skin preparation process (Pople et al. 1992; Shapiro et al. 1988; Bayston and Lari 1974). Bayston et al. showed that regardless of the solution used in skin prep, alcohol-based preparations are clearly superior in reducing the bacterial load (Bayston 1989). Darouiche et al. conducted randomized trials in 6 centers involving 849 patients, comparing alcohol-based chlorhexidine with povidone iodine in non-neurosurgical procedures. They found that the alcohol-based preparation significantly reduced superficial and deep wound infections (Darouiche et al. 2010). A Cochrane meta-analysis of randomized controlled trials by Dumville et al. also suggested that alcohol-based skin preparations are the most effective in preventing infections in clean surgical wounds (Dumville et al. 2013). Thus, there is substantial evidence available to suggest that the solution of choice for skin preparation to reduce bacterial load and wound contamination during skin incision should be an alcohol-based one. Whether this translates directly to reduced shunt infections per se is however not conclusive in the literature.

Regardless of skin preparation technique, the skin is only disinfected but not sterilized, and bacteria re-emerge from follicles, sweat glands, and contaminated skin edges within 20–30 min (Raahave 1976). Thus in an attempt to further reduce the bacterial load, other measures have been practiced. Gauze packs soaked in antibiotics like gentamicin or antiseptics (Tabara and Forrest 1982; Fitzgerald and Connolly 1984) and adhesive drapes which are impervious or iodine-impregnated barriers have been used to. A prospective randomized trial by Haliasos et al. compared Ioban™ (an iodine-impregnated adhesive barrier) with plain surgical drapes and found that only two cases of infection occurred in the plain drapes group (Haliasos et al. 2012). However, this result was not statistically significant due to the small sample size and, like other studies, shows that the use of these has either no effect or the positive results are influenced by selection bias (Jackson et al. 1971).

## Prophylactic Antibiotics

Bacterial contamination of shunts is now understood to occur mostly at the time of surgery, and therefore most surgeons advocate using prophylactic antibiotics for shunt operations. While some studies indicate that prophylactic antibiotics have no impact on shunt infection rates (George et al. 1979), most of the evidence in the literature supports the use of prophylactic perioperative antibiotics. Biyani et al. distributed a questionnaire on prophylactic antibiotics in pediatric shunt surgery (Biyani et al. 2006). Of the 45 medical centers that responded, the most common prophylactic antibiotic used was a first-generation cephalosporin (23 of 45 respondents), given at skin incision for 24 h.

A systematic review by Ratilal et al. in 2008 looked at randomized and quasi-randomized

studies involving the use of prophylactic systemic antibiotics. A search of the Cochrane database yielded 17 trials involving 2134 patients. The authors then performed subgroup analysis, comparing the type of internal shunt, the age of patient, and the duration of antibiotic administration. They found a statistically significant benefit (odds ratio 0.51, CI = 0.36, 0.73) of systematic prophylactic antibiotics in preventing shunt infections, regardless of age, duration of administration, or type of internal shunt used. They also found that there was uncertain benefit in giving antibiotics for more than 24 h after surgery (Ratilal et al. 2008).

Haines et al. pooled nine randomized clinical trials and found a statistically significant effect favoring antibiotic prophylaxis (approximately 50% reduction in infection risk). However this effect was lost once the baseline infection rate was 5% or below (Haines and Walters 1994). Subgroup analysis again showed that the type of antibiotic, duration of antibiotic administration, and age of patients did not have a significant effect on the pooled results.

Xu et al. published a systemic review of seven studies (both randomized and non-randomized studies), to assess the clinical efficacy of antibiotic prophylaxis in children who underwent shunt insertion. Of the 694 patients included, 287 patients were given prophylactic antibiotics, with the follow-up period ranging from 3 months to 30 months. Compared to the placebo or no-antibiotics group, the patients who received prophylactic antibiotics had a statistically significant reduction in infection rates with an odds ratio of 0.59 (CI = 0.38, 0.90) (Xu et al. 2015).

Despite the above studies, there are differing opinions. A report by the British Society for Antimicrobial Chemotherapy stated there is no consensus regarding the benefit of antibiotic prophylaxis in shunt surgery (Brown 1993), though it also states antibiotics probably have a protective effect in non-implantation neurosurgery. It also points out that surgeons will be hard pressed to arrive at an optimal choice of antibiotic and route of administration. One possible reason why prophylactic systemic antibiotics may have no effect on infection prevention is because the drugs rarely reach therapeutic levels in the CSF when administered intravenously. Those that do (e.g., rifampicin, chloramphenicol, or trimethoprim) are often bacteriostatic or have toxic side effects.

Finally, Klimo et al. carried out a systemic review on whether prophylactic antibiotics lower shunt infections in pediatric patients. Their pooled analysis of 9 studies revealed that patients given antibiotics had a 5.9% shunt infection risk, while this was 10.7% in the control group. The authors concluded with a Level 2 recommendation (moderate degree of clinical certainty) to prescribe preoperative antibiotics to lower shunt infections (Klimo Jr et al. 2014a).

Aside from intravenous antibiotics, some groups have also studied the intrathecal administration of antibiotics for prophylaxis. Ragel et al. published a single-center retrospective analysis of antibiotic prophylaxis and found that the infection rate with the use of intrathecal vancomycin plus gentamicin was 0.45%, compared to intrathecal gentamicin alone (5.4%) or no intrathecal antibiotic use (6.6%) (Ragel et al. 2006). Choksey et al. successfully achieved a shunt infection rate of 0.79% in a cohort of 126 patients, with the use of a strict sterile protocol that administered intrathecal prophylaxis. This protocol described the use of prophylactic intravenous benzylpenicillin and flucloxacillin at induction followed by irrigation of the shunt system with 5 mg of gentamicin and another 5 mg of gentamicin injected intrathecally (Choksey and Malik 2004).

Aside from antibiotic drugs, the use of prophylactic immunoglobulins has also been reported. Infants are at higher risk of shunt infections due to their biologically immature immune systems, and the instillation of immunoglobulins for this group of patients has been explored. In 1997, Ersahin et al. published a prospective randomized trial in 60 infants with ages ranging from 7 days to 11 months. The study group received prophylactic immunoglobulins (Sandoglobulin®) at a dose of 1 g/kg the night before surgery. Although their results did not reach statistical significance, there were zero infections in the study group, while the control group had an infection rate of 5.1% (Ersahin et al. 1997).

In summary, the scientific evidence suggests there are more benefits than risks with giving prophylactic antibiotics before shunt surgery. Prophylactic antibiotics covering gram-positive organisms such as first- or second-generation cephalosporins are most commonly used. In the case of MRSA positive patients, vancomycin is an alternative. A single dose before incision and administration for 24 h after surgery is adequate, and there is no evidence to support the use of antibiotics beyond that. Intrathecal or immunoglobulin prophylaxis has been investigated but the evidence does not support their routine use.

## Antibiotic-Impregnated Shunts

In recent years, there has been increasing interest in antibiotic-impregnated shunts. This is possibly because despite stringent aseptic techniques and antibiotic prophylaxis, shunt infections continue to persist. Aside from patient, surgeon, and environmental factors, the shunt implant itself is another possible vector implicated in shunt infections. Another argument for using antibiotic-impregnated shunts (AISs) is that systemic antibiotics do not penetrate the CSF adequately to treat the source of the infection if it originates from the shunt. There is also evidence that shunts arrive in the clinician's hands already adherent with biofilm (Fux et al. 2006), but it is unclear if this aseptic biofilm lowers the threshold for subsequent bacterial colonization and infection. With these considerations, there is an increasing number of published papers on the efficacy of AIS in preventing shunt infections.

During the manufacturing of antibiotic-impregnated shunts, a volatile solvent is used to expand the silicone molecular matrix to introduce the drug to be impregnated. Once the solvent is removed, the matrix reverts to its original volume, and the antibiotic drug is impregnated (Bayston and Milner 1981). The drug is then slowly released, with the rate of release being dictated by a diffusion gradient. Clindamycin and rifampicin are used to infuse AIS, and the duration of protective activity is for approximately 50 days (Bayston and Lambert 1997).

Evidence so far shows that the use of AIS catheters lowers the risk of early shunt infections, but longer-term data is yet unavailable. Sciubba et al. reported a reduction in pediatric shunt infection rates from 12% to 1.4% with the use of AISs, over a follow-up period of 6 months (Sciubba et al. 2005). The same group published a follow-up study in 2007 looking at late shunt infections beyond the initial 6-month follow-up. Of the 153 pediatric patients, mean follow-up was 21.7 months and none of them developed late shunt infections (Sciubba et al. 2007). Eymann et al. reported a single-center study of both adult and pediatric shunt infection rates for AISs from 2002 to 2006, compared to historical controls between 1998 and 2001. Overall infection rates were reduced from 5.8% to 1%, and a separate cost-benefit analysis showed that although AISs are more expensive, their use is more cost-effective if a 50% reduction in shunt infection is achieved, in institutions where the baseline shunt infection rate is more than 4% (Eymann et al. 2008).

A prospective randomized trial of 110 adult and pediatric patients by Govender et al. showed that AISs (with rifampicin and clindamycin) lowered overall shunt infection rates from 16.7% to 6%. They also showed that these shunts afford anti-staphylococcal protection during the early postoperative period and up to 9 months from surgery. None of the 6% of infected shunts were due to staphylococci (Govender et al. 2003). However, this study did not separate out the pediatric patients for analysis.

A retrospective review of adult and pediatric shunts in the UK shunt registry database by Richards et al. also reported an advantage in the use of AISs to prevent infections. They utilized a matched-pair study design, identifying 994 pairs from 2000 to 2006. Their review showed a 4.7% infection rate in standard shunts compared to 3% in AISs (Richards et al. 2009).

Kandasamy et al. also found in a multicenter study of pediatric patients in the UK a statistically significant benefit in the use of AISs in preventing shunt infections. However this was compared to historical controls, and in the three centers involved in the study, only results from the

London Great Ormond Street Pediatrics Unit were statistically significant. They also analyzed a subgroup of infants below the age of 1 and found similar results (Kandasamy et al. 2011).

More recently, Raffa et al. retrospectively analyzed the use of AISs in 48 infants under the age of 1. The minimum follow-up period was 1 year with a mean of 8 years. They showed that infection rates decreased from 34% to 9% with the use of these catheters. This effect was also observed in the subgroup analyses of high-risk children (preterm newborns, children with post-hemorrhagic or postinfectious hydrocephalus, and children with previous external ventricular drains) (Raffa et al. 2015).

In contrast, Hayhurst et al. reported no significant difference between the use of AISs and standard silicone shunts (9.8% vs. 10.4%). However, they detected a benefit in a subgroup analysis of neonates implanted with a de novo AIS, where infection rates were reduced from 27% to 10.7% (Hayhurst et al. 2008). Kan et al. also suggested no benefit in the use of AISs. They reviewed the results of a single surgeon who performed 80 shunt procedures using AISs, compared to 80 consecutive shunt procedures done before the introduction of antibiotic-coated catheters. Shunt infection rates were 5% in the AIS group compared to 8.8% in the control group, and this did not reach statistical significance ($p = 0.534$). Mean time to infection was also similar (Kan and Kestle 2007).

It is even more interesting to note that shunt infection rates of less than 1% can be achieved without the use of antibiotic-impregnated shunts. Pirotte et al. published in 2007 a prospective study of a strict surgical protocol using neither AISs nor laminar airflow operating theaters. This was imposed on a single surgical team involved in 115 shunt procedures in children who were followed up for a period ranging from 4 months to 70 months. The protocol involved uniform surgical technique, limited implant and skin manipulation, minimizing of human circulation in the operating theater, scheduling the surgery as the first case, avoiding postoperative CSF leak, double gloving, operative time of 30 min or less, and systemic antibiotic prophylaxis. They also did a subgroup analysis of high-risk groups including children with preoperative EVDs, CSF leak, meningitis, steroid use, and chemotherapy as well as infants less than 12 months. They reported that post protocol implementation, their shunt infection rates dropped from 17% to less than 1% (Pirotte et al. 2007). This has been demonstrated in other studies as reported by Choksey (Choksey and Malik 2004) and Choux (Choux et al. 1992).

A review of the conflicting literature was carried by Klimo et al., who published their results of their systemic review in 2014 (Klimo Jr et al. 2014b). Six Class III studies involving more than 3000 pediatric patients were included in the meta-analysis. Although four of the studies did not demonstrate statistical significance to advocate for AIS, the pooled analysis showed that the AIS group had a lower infection rate of 5.5%, compared to 8.6% for patients who were implanted with standard, non-antibiotic shunts. Patients with standard shunts were 1.96 times more likely to get a shunt infection compared to patients with AIS, and 24 AIS need to be implanted to avoid 1 case of shunt infection. Although the authors recommend using AIS, they also recognized that their recommendations are Class III (unclear degree of clinical certainty).

## Conclusion

Shunt infections remain a major source of morbidity for pediatric patients and have significant socioeconomic and psychosocial implications. Despite the presence of a substantial number of publications discussing this issue, it remains obvious that there are clearly no distinct preventative modalities and protocols to significantly reduce and prevent infections.

A major preventative measure to avoid shunt infections would be the complete avoidance of a shunt. As such, alternative treatments such as endoscopic third ventriculostomy and clear clinical indications before a decision is undertaken to insert a shunt are crucial.

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