Cerebrospinal fluid shunt infections in children over a 13-year period: anaerobic cultures and comparison of clinical signs of infection with Propionibacterium acnes and with other bacteria

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Object. Shunt infections represent a major problem with risk for sequelae and even death. The aim in this retrospective study was to analyze the incidence, origin, and clinical presentation of shunt infections, with special reference to the results of cultures for anaerobic organisms performed in addition to the usual tests, to prolonged incubation times, and to infections caused by Propionibacterium acnes.

Methods. The medical records of 237 hydrocephalic children (age range 0–15 years) in whom operations were performed by a pediatric surgeon at Uppsala University Hospital during a 13-year period were reviewed.

Results. Thirty-four verified or suspected intraventricular shunt infections and 5 distal catheter infections occurred after 474 operations. Skin bacteria, such as coagulase-negative staphylococci ([CoNS], 19 patients), Staphylococcus aureus (7 patients), and P. acnes (6 patients) predominated. The addition of anaerobic cultures and prolonged incubation times increased the verification of shunt infection by more than one third. Children with P. acnes infection were significantly older, had a lower body temperature, fewer cerebrospinal fluid (CSF) leukocytes, a higher CSF/blood glucose ratio, more distal catheter infections, and other sources of infection. Four had an abdominal pseudocyst. Children < 1 year of age and infected with CoNS were more affected than older children with systemic and local symptoms. In children with distal catheter infection and growth of propionibacteria at the time of the distal catheter and valve replacement, no follow-up antibiotic treatment was necessary.

Conclusions. Addition of anaerobic cultures and prolonged incubation times led to an increase in the detection of shunt infections. Infections caused by propionibacteria often result in mild symptoms that may be overlooked if adequate anaerobic cultures are not obtained. (DOI: 10.3171/PED/2008/1/5/366)

Key Words • anaerobic bacteria culture • antibiotic therapy • cerebrospinal fluid shunt infection • children • drug concentration • propionibacteria

Infection of CSF shunts is one of the most common infections faced by pediatric neurosurgeons, with an incidence in recent studies of 8–12%.3,10 Skin bacteria, such as CoNS and Staphylococcus aureus, cause most CSF shunt infections,5,9,14,19,24 with gram-negative bacteria being responsible for ~20% of cases.21 Propionibacterium acnes, which outnumbers other skin bacteria by 10- to 100-fold, has also been established as a pathogen,11,16,20,26 but causes only a small percentage of CSF shunt infections.6 Nevertheless, a diagnosis of P. acnes shunt infection is associated with difficulties. Contamination may occur, the clinical relevance of these bacteria has often been questioned,6,28 and infections may have been missed because the CSF was not cultured for anaerobic bacteria or the incubation time was not prolonged enough to demonstrate growth.

In the early 1990s, an institutional protocol for the management of shunt infection in children was developed at the Department of Pediatric Surgery at our hospital. Besides conventional cultures, this protocol stated that both CSF and the tip of the distal catheter should be routinely cultured for anaerobic bacteria and that the observation time in the laboratory for both aerobic and anaerobic bacteria cultures should be continued for at least 7 days. The purpose of this retrospective study was to analyze the incidence, origins, and clinical presentation of shunt infections, with special reference to the result of the addition of anaerobic and prolonged cultures and infections caused by P. acnes.

The standard protocol for treatment of intraventricular in-
infections included shunt externalization proximal to the valve in combination with systemic and intraventricular antibiotic treatment for 1–2 weeks until shunt replacement. The result of this treatment regimen has been described in detail elsewhere.1 Regarding distal catheter infections, the protocol stated that externalization of the shunt at the thoracic level—in combination with systemic antibiotics—was sufficient before placement of a new shunt system, which was to be done after 1–2 weeks. A secondary aim of the present study was to report the treatment effect in patients with distal catheter infections.

**Clinical Materials and Methods**

The medical records of all children with hydrocephalus who were treated by a pediatric surgeon at the Departments of Pediatric Surgery or Neurosurgery, Uppsala University Hospital, during a 13-year period (January 1992–December 2004) were reviewed, focusing particularly on shunt infection.

In children with suspected infection, externalization of the ventricular catheter was done and the distal catheter tip was sent for culturing. In children in whom the suspicion was mild, only the distal catheter was externalized at the thoracic level. If an intraventricular infection was then verified, the ventricular catheter was externalized, whereas in the case of a distal catheter infection, the catheter externalization at the thoracic level was continued. The CSF was obtained from the externalized catheter for culture and analysis of its glucose and leukocyte content. In addition, the levels of blood glucose, WBC count, and serum CRP were determined.

The samples were obtained at the time of catheter externalization. The CSF was transferred to a sterile test tube. In addition, 2 ml was inoculated into an anaerobic blood culture bottle. The distal catheter tip was placed in a sterile test tube. In the laboratory, CSF was inoculated on horse blood agar, chocolate agar (Colombia blood agar, Acumedia), and anaerobic blood agar (Fastidious anaerobic agar, Lab M, Ltd.) and incubated for 2–4 days at 36°C. The bottle cultures were supplemented with 5% Fildes (Becton, Dickinson and Co.) and incubated for 7–10 days at 36°C. The distal catheter tip was transferred to a tryptic soy broth (Becton, Dickinson and Co.) supplemented with 20% horse serum, which was incubated in the same way as the bottle. In case of growth in any of the cultures, the bacteria were diagnosed according to the ordinary routines of the laboratory. Agar and broth used at our laboratory are controlled for contamination according to the Swedish Board for Accreditation and Conformity Assessment (ISO 15189).

For the diagnosis of shunt infection, the criteria used in the present study were slightly modified from those used in a recent study by Wang et al.5 Intraventricular shunt infection was defined as follows: 1) growth of bacteria from the catheter tip or CSF; and 2) presence of either a glucose ratio (CSF/blood) of < 0.45, a CSF glucose concentration of < 2.5 mmol/L, or a CSF leukocyte count of > 250 × 10^6/L. Distal catheter infection was defined as bacterial growth from the distal catheter CSF in combination with either a positive culture from the tip or a repeated positive CSF culture in the presence of normal glucose and leukocyte concentration (< 5 × 10^3/L). Shunt infections with CSF leukocyte counts in the interval of 5–250 × 10^6/L and normal or unavailable glucose values were classified as suspected intraventricular infections, whereas cases in which the CSF leukocyte count was normal and glucose values were unavailable were considered unclassifiable.

In patients with shunt infection, the origin of hydrocephalus, age at onset of infection, clinical presentation, causative agent, suspected source of infection, and time from presumed contamination to verified infection were recorded. Furthermore, treatment and the results of treatment of the distal catheter infections were reviewed. Cure was defined as sterilization of CSF and resolution of clinical symptoms. Relapse was defined as infection with the same causative agent within 2 years after shunt replacement and withdrawal of antibiotic treatment.

In the children with distal catheter infection, CSF was collected for antibiotic concentration analysis at 2 hours after intravenous injection of the drugs. Meropenem, cefotaxime, and trimethoprim concentrations were analyzed using microbiological methods.

**Statistical Analysis**

The Mann–Whitney test was used for the analysis of differences in age, time from contamination to verified infection, temperature, CRP, blood, and CSF leukocytes at admission between infections caused by *P. acnes* and other causative bacteria. Differences in the type of infection, origin of hydrocephalus, presumed source of infection, proportion of patients demonstrating local symptoms, and pathological CSF glucose concentration were demonstrated using the Fisher exact test.

**Results**

During the study period, 474 shunt operations, of which 145 (31%) constituted initial insertions, were performed in 237 children whose ages ranged from 0 to 15 years (Fig. 1). The most common reason for acute shunt revision was obstruction due to a short or disconnected catheter. There were 39 shunt infections (8.2% of the total number of shunt operations) in 35 children. One child had 3 and 2 children had 2 separate shunt infections with different bacteria. In 8 cases, there was a clinical suspicion of infection that led to externalization, but after 3 repeated negative cultures, infection was considered to be ruled out. In 4 of these 8 patients demonstrating resorption difficulties a ventriculoatrial shunt was placed, whereas the others received a new ventriculoperitoneal shunt. At their follow-up visit after 2 years, none of them had shown signs of infection.

In 30 cases the shunt infections were classified as intraventricular, in 5 as distal catheter infection, in 4 as suspected intraventricular, and in none as unclassified. Causative bacteria in relation to patient age and type of infection are shown in Table 1. In all patients, the same bacteria were isolated from both the catheter tip and the CSF. The addition of anaerobic bacteria cultures resulted in growth of *P. acnes* in 6 children, and prolongation of cultures for ≥ 4 days resulted in growth of CoNS in 5 cases and *P. acnes* in 1 case. Skin bacteria, such as CoNS, *S. aureus*, and *P. acnes*, caused 82% of the shunt infections. Propionibacteria were found in 6 cases, resulting in an incidence of 1.3% of all operations. These children were older than those infected by other bacteria (p < 0.001), and the type of infection was significantly different, with intraventricular infection in only 1 case and distal catheter infection in 5 cases (p < 0.001). In con-
contrary, the risk of intraventricular infection caused by the other skin bacteria (CoNS and *S. aureus*) was higher in children < 1 year of age.

In children with hydrocephalus caused by hemorrhage, aqueductal stenosis, or myelomeningocele, the risk of shunt infection was higher than it was when the hydrocephalus was caused by other conditions, such as Dandy–Walker cyst, arachnoidal cyst, encephalocele, or meningitis (Table 2). A different distribution in the cause of hydrocephalus in relation to that of other bacteria could not be demonstrated for infections caused by propionibacteria. The risk for shunt infection at initial insertion and acute revision for proximal or distal obstruction was of a similar magnitude, at 9 (6.2%) of 145 and 10 (5%) of 197, respectively. Presumed sources of the shunt infections are shown in Table 3. Initial shunt insertions, shunt revisions, and bacteremia were the most common sources. Contamination at initial insertion (9 patients) was found in 3 children with unhealed wounds after myelomeningocele surgery, and in 1 of them the necrotic wound was simultaneously revised. In 2 children the initial insertion was performed at the same time as an operation for inguinal hernia. In the other 4 children, no obvious explanation was identified. The revisions were acute operations with no other notable risk factor for infection. Infected wounds included pressure necrosis over the valve (2 wounds), penetrating ligature, CSF leakage from the frontal flap, infected wound on the hand, and penetrating metal implant after simultaneous kyphosis correction and myelomeningocele repair (1 wound each). Other sources included antisiphoning device implantation (1 wound), puncture of the valve (2 wounds), and laparotomy (1 wound).

Causative bacteria in relation to the presumed source of infection are shown in Table 3. Infections by CoNS, *S. aureus*, and *P. acnes* were predominantly the result of surgical procedures. In 1 infection that occurred after the initial shunt insertion, which was performed at the same time as an operation for inguinal hernia, enterococci were isolated. In children in whom the shunt infection was secondary to bacteremia, a wider range of bacteria was seen. Not only CoNS and *S. aureus*, but also *β*-hemolytic streptococci group G and gram-negative rods, such as *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Haemophilus influenzae* were encountered. The presumed source of *P. acnes* infection was significantly different from that of other bacteria (*p* < 0.01). The infections that occurred after distal revision or valve puncture in this study were all caused by *P. acnes*. No cases of *P. acnes* infection were seen after the initial insertion or were secondary to bacteremia.

In 38 of the 39 infections, the time from presumed contamination to manifest infection varied between 1 and 28 days.

### Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CoNS</th>
<th><em>S. aureus</em></th>
<th>Propionibacteria</th>
<th>Enterococci</th>
<th><em>E. coli</em></th>
<th>Other Gram-Negative Rods</th>
<th>β-Hemolytic Streptococci</th>
<th>All Bacteria</th>
<th>No. of Ops</th>
<th>Risk of Infection (%)</th>
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<td>3</td>
<td>1</td>
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*AS = aqueductal stenosis; MMC = myelomeningocele.*
Propionibacterium acnes shunt infection

TABLE 3

<table>
<thead>
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<th>Presumed source of infection and time from contamination to verified infection in relation to causative bacteria*</th>
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<td>Suspected Source of Infection</td>
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<tr>
<td>other sources</td>
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<tr>
<td>bacteremia</td>
</tr>
<tr>
<td>total</td>
</tr>
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</table>

* Individual times from contamination to infection.
† One patient had intraventricular infection.

months, with a median interval of 3 weeks (in the 39th infection, the time from contamination to infection was 52 weeks; Table 3). The longest interval was seen in a child with CoNS infection, in whom a laparotomy had been performed 52 weeks earlier. The shunt had been inserted 11 years earlier, and no other possible source of infection could be identified. In infections caused by propionibacteria, the median time from presumed contamination to manifest infection was 9 weeks (range 1–28 weeks). This was longer than corresponding values for other bacteria (median 4 weeks, range 0.5–52 weeks), although statistical significance was not reached (p = 0.06).

Symptoms and laboratory parameters at admission in relation to causative bacteria are shown in Table 4. All infections caused by CoNS in children < 1 year of age were intraventricular and the children were severely affected with systemic symptoms. Of 11 children, 8 demonstrated obvious local symptoms. In the 8 children > 1 year of age, the body temperature was lower and none of them showed local symptoms. Two children with intraventricular infection, ages 5 weeks and 9 years, had also developed an intrabdominal pseudocyst due to the infection. All children with infections caused by S. aureus had systemic symptoms, and all but 1 had local symptoms. Infections caused by gram-negative rods or β-hemolytic streptococci were all associated with systemic symptoms, whereas local symptoms were found only in the patient with streptococcal infection. In the child with enterococcal infection, there were signs of local infection, whereas systemic symptoms were not pronounced. All children with P. acnes infection showed signs of distal catheter obstruction. Four of them had an abdominal pseudocyst but only 1 presented with abdominal pain. Body temperature was significantly lower than in children with infections caused by other bacteria (p < 0.001). With the exception of 2 individuals (the child with intraventricular infection and systemic and local reactions, and another child with a ventriculoatrial shunt and a history of unexplained fever after puncture of the valve), there were no systemic or local signs in children infected by propionibacteria. The number of WBCs in the CSF was lower (p < 0.05), and decreased glucose ratios or concentrations were less often seen in patients with P. acnes infection (p < 0.001). The CRP and blood leukocyte counts were increased in most of the children with propionibacteria infection but did not differ significantly from those of the others.

Treatment of the Children With Distal Catheter Infection

In the 5 children with distal catheter infection, all of whom showed growth of P. acnes, the distal catheters were externalized at the thoracic level, and according to the protocol these patients were only treated with systemic antibiotics. This treatment involved meropenem (2 patients), cefotaxime, intravenous trimethoprim/sulfamethoxazole, or oral rifampicin and fusidic acid (1 patient each for the last 3 treatments). Despite susceptible bacteria and treatment for several days,

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* Conc = concentration; NA = not analyzed; norm = normal; temp = temperature.
† No data for 1 patient.
antibiotic concentrations were low, the sterilization rate was poor, and no cure was achieved (Table 5). Regardless of the continuous growth of bacteria in the CSF, the whole shunt system was replaced after 5–14 days of therapy in 4 children. In the fifth child, in whom 2 shunts were inserted, only the distal part and the valve of the infected shunt were replaced after 8 days of treatment. Perioperative treatment with cloxacillin (3 patients), vancomycin (1 patient), and meropenem (1 patient) was given intravenously, together with 1 dose of intraventricular vancomycin (4 patients). With the exception of 1 child who also received oral antibiotics on the 1st postoperative day, no further antibiotic treatment was given. Cultures from the central CSF (5 patients) and ventricular catheter tip (4 patients) at operation were all negative, whereas cultures from inside the valve were all positive (5 patients). Body temperature normalized and localized symptoms disappeared in the children with symptoms. All 5 children were followed for 2 years and no relapses occurred within this follow-up period.

Discussion

The criteria for the diagnosis of intraventricular shunt infection used in our study were slightly modified from those used in a recent study.22 In that study the criteria for intraventricular infection could be fulfilled also by an increase in lactate concentration. During most of the study period, CSF lactate analysis was not used as a routine method at our hospital laboratory, and therefore no values were recorded. We cannot exclude the possibility that lactate concentration would have constituted an additional parameter that would have been valuable for assessing intraventricular infection. Given the design of the study, however, the strict definitions based on CSF glucose and leukocyte values and the known correlation between lactate and the other CSF parameters, this most probably did not affect the results.

By the addition of cultures for anaerobic bacteria at every sampling occasion and prolongation of the incubation times for 1 week or longer, the number of positive cultures increased from 28 to 39. This corresponds to an increase in the detection of shunt infections by more than one third, which emphasizes the importance of these measures in the diagnosis of CSF shunt infection. A similar regimen has previously been proposed by others,2,6,16,18,23 but the relative increase in diagnostic value has to our knowledge not previously been evaluated. Some authorities have advocated that the cultures should be held for up to 14 days before being reported as negative.11,16 Our protocol initially stated 7 days, but in most cultures the observation time was increased to 10 days. After 2002 the observation time was 10 days in all cultures. The fact that no culture turned positive during the last 3 days and the absence of readmittance for shunt infection in the children with negative cultures together suggest that almost all clinical infections will turn positive within 1 week with the culture technique used.

By adding cultures for anaerobic bacteria, there is an increased risk of finding \textit{P. acnes} contamination from the skin. However, the risk of contamination that has been demonstrated after percutaneous puncture of the Rickham reservoir or the antechamber20,28 was minimized by using perioperative cultures of samples obtained at the shunt externalization after careful disinfection of the skin. The fact that the cultures from both the catheter tip and the CSF were positive indicates that the infection is not just an asymptomatic shunt contamination as discussed by Steinbok et al.22 In addition, the signs of shunt dysfunction and infection as well as the absence of other causative bacteria, in combination with the continuous growth of \textit{P. acnes} despite treatment, more or less rule out the possibility of contamination, thus indicating the clinical relevance of the \textit{P. acnes} infections found in the present study.

The optimization of the sampling technique as well as the inclusion of patients with distal catheter infection both contribute to a higher shunt infection rate than would otherwise have occurred. In spite of this, the incidence of shunt infection in the present study (8%) was in the lower range of that previously reported (2–22%).7,16,27 The 6 patients with a shunt infection caused by \textit{P. acnes} represent a risk of infection of 1.3%, which is of the same magnitude as that reported by Everett et al.11 (1.7%). Rekate et al.16 reported somewhat higher values, but in that study asymptomatic patients with a positive culture from either the CSF or the shunt components were also included. On the other hand, in the study by Everett et al., CSF pleocytosis was required for case definition, and if such a definition had been used in our study, the distal catheter infections would have been excluded and the risk of infection would have been only 0.2%.

Older patients, those with previous puncture of the valve, and those with revisions seem to be predisposed to shunt infections with \textit{P. acnes}. Previous surgery is considered to be the most common source for these bacteria,6,28 whereas puncture of the valve has seldom been reported. Nevertheless, as demonstrated in the study by Westergren et al.,28 there must be a high risk of transferring propionibacteria from the skin to shunt components, and in line with this, infection with \textit{P. acnes} after a diagnostic tap of a subdural hematoma has previously been demonstrated.6 Surprisingly, there were no infections after initial insertion. It can be speculated that this difference may be caused by the straight incision used at all revisions, whereas a cutaneous flap was used at the initial insertion, resulting in a longer distance between skin and shunt components. Propionibacteria have been reported to cause late-onset CF shunt infection29 and, therefore, a longer incubation time was to be expected. Time from presumed contamination to infection was longer than for the other infections, and 1 case fulfilled the criteria of late-onset infection after ≥ 6 months,28 but the difference found did not reach statistical significance, presumably due
to the small number of cases. The relative infrequency of infection after initial insertions in combination with longer incubation times may represent one of the reasons for the age distribution.

The clinical presentation was associated with milder symptoms with less fever, lower CSF leukocyte count, and higher glucose ratio. Propionibacteria have previously been shown to cause intraventricular infection. There are also some cases described in which blocked shunts and glomerulonephritis occurred. In our study, only 1 patient demonstrated the full clinical picture of an intraventricular infection, with pleocytosis and a low glucose ratio, and in this case the symptoms were not clearly distinguishable from those of the other bacteria. Most patients only demonstrated signs of distal catheter infection with catheter obstruction, and in 4 of them there was pseudocyst formation—a mild infection that is most compatible with the well-documented low virulence level of propionibacteria.

The recommended treatment of propionibacteria-related shunt infection has been removal of the shunt components in combination with administration of systemic antibiotics. The child with intraventricular infection was treated with externalization of the ventricular catheter, and vancomycin was delivered intravenously and intraventricularly for 6 and 10 days, respectively, after which replacement of the shunt was performed. In the cases with distal catheter infection, our study demonstrates that not even the high concentrations, probably because of the low grade of the inflammatory response. In the presence of a foreign body in the form of shunt components, this leads to a very poor sterilization rate. The important therapeutic measure seems to be removal of the shunt components. In our patients this was done in the event of positive cultures, which indicate that antibiotic treatment prior to surgery is most probably not necessary. Antibiotic treatment delivered periorientally seems to be sufficient, because there was no further antibiotic treatment in 4 of the 5 children and just 1 day of treatment in the fifth child, and yet there were no relapses within the 2-year follow-up period. Thus, our data support the suggestion by Thompson and Albright that CSF shunt infection caused by *P. acnes* can be treated with short-term perioperative antibiotics and replacement of the shunt components, at least in distal catheter infections.

In all children with distal catheter infection, bacterial growth was demonstrated in the valve at its removal. The valve seems to harbor these bacteria for a long time, and from there a low-grade infection at the distal end of the catheter may be sustained, with the gradual development of pseudocyst formation and shunt blockage. Furthermore, our data, which show persistent bacterial growth despite high doses of intravenous antibiotics, indicate that the propionibacteria will not be eliminated if antibiotics are prescribed for another infection, even if the bacteria are susceptible to the antibiotics administered. Given this fact, distal catheter/valve infection seems to be a more appropriate name. Although not shown in the present study, this infection, if undiagnosed, may explain relapses in distal catheter obstruction in patients in whom the shunt components have not been replaced. In all children in the present study, cultures from the central CSF and ventricular catheter tip obtained at operation were negative. This may suggest that removal of only the distal catheter and the valve may be sufficient in patients with distal catheter/valve infection, but this needs further investigation.

Although not an aim of this study, it was notable that most infections after initial insertion occurred in children with unhealed wounds or when concomitant inguinal surgery was performed. This may explain why the risk of infection at initial insertion and revision was the same, and probably these situations should be avoided. In this study, as in others, CoNS was the most common causative agent and the risk of shunt infection was higher in patients < 1 year of age. Of special interest is the finding that CoNS infections were considerably more aggressive in these children than in older children.

Conclusions

The addition of cultures for anaerobic bacteria and prolonged observation time of the cultures led to an increase in the diagnostic yield by more than one third. Infection with *P. acnes* resulted in a mild clinical picture that may easily be overlooked if adequate anaerobic cultures are not obtained. In most cases there were mild symptoms with a clinical picture of distal catheter obstruction, the most important treatment for which seems to be exchange of shunt components in combination with perioperative antibiotic treatment.

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