CONSERVATIVE MANAGEMENT OF PATIENTS WITH CEREBROSPINAL FLUID SHUNT INFECTIONS

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OBJECTIVE: In patients with cerebrospinal fluid (CSF) shunt infection, removal of the shunt and antibiotic administration is the current standard of care. In 1986, we developed a protocol for the conservative management of patients with infected but functioning shunts. Treatment was based on the administration of a combination of intraventricular and systemic antibiotics. Intraventricular antibiotics were instilled via a separate access device. The purpose of this report is to describe our experience with this therapeutic intervention.

METHODS: An observational study of all patients treated for CSF shunt infection between 1986 and 2003 was undertaken. Cure was defined by sterile CSF after completion of therapy and sterile shunt components at next revision or long-term freedom from recurrent infection (follow-up period, 6–88 mo).

RESULTS: In total, 43 of 122 patients with CSF shunt infections were treated conservatively according to our protocol. Overall, 84% of these patients were cured, with a 92% success rate for patients with infections caused by bacteria other than *Staphylococcus aureus*. This included 30 coagulase-negative staphylococcal infections, of which two were treatment failures. We abandoned conservative treatment of patients with *Staphylococcus aureus* infections after early experience demonstrated that the success rate (four treatment failures in seven patients) was markedly lower than that for other pathogens. During the treatment and follow-up periods, there were three deaths, two of which were unrelated to shunt infection; treatment failure could not be completely excluded in the remaining patient. There was no toxicity related to intraventricular antibiotic administration. The incidence of shunt blockage among patients who were treated conservatively was not significantly different from that among a large cohort of patients with uninfected shunts. Ten patients received part of their courses of treatment as outpatients.

CONCLUSION: The success rate of conservative management of patients with CSF shunt infections caused by coagulase-negative staphylococci is comparable with those in the published literature for patients treated conventionally. This form of management avoids surgical intervention, with its attendant risks, and is safe.

KEY WORDS: Adverse event, Infection, Outpatient therapy, Ventricular access device, Ventriculoperitoneal shunt

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Of the complications associated with cerebrospinal fluid (CSF) shunt implantation, infection is one of the most important, both clinically and numerically. The incidence of shunt infection has varied widely from 1.5 to 39%, although more recently rates of 10 to 15% have been reported (6, 25). The most common pathogens are coagulase-negative staphylococci (CoNS) (50–90%), followed by *Staphylococcus aureus* (13–27%), and a miscellany of other organisms, including aerobic Gram-negative bacilli (AGNB) (10–20%), streptococci (8–10%), and *Propionibacterium spp*. The options for managing patients with shunt infections include the following: 1) a two-stage procedure whereby the entire colonized shunt is removed, CSF is drained externally, either by implantation of an external ventricular drain (EVD) or by regularly tapping the ventricles, antibiotics are administered by the systemic or intraventricular route or both, and the shunt is replaced when the CSF is sterile; 2) a one-stage procedure whereby the colonized shunt is removed and immediately replaced with a new shunt, followed by a course of antibiotics (either systemic, intraventricular, or both); and 3) antibiotic therapy alone, ad-

ministered either systemically, intraventricularly, or by both routes.

Variations on the above options, with exteriorization of the distal shunt catheter and the administration of systemic and intraventricular antibiotics for between 2 and 4 weeks, followed by revision of either the distal catheter alone (31) or the entire shunt system (26), have also been described.

The efficacies of one or more of the three principal options have been evaluated in several studies. However, the efficacies of all three major categories of intervention were compared in only seven of these studies and only one (in which very small numbers of patients were evaluated) was a randomized trial (21). There have been two reviews of these studies. Yogev (44) assessed 18 studies and reported cure rates of 96, 65, and 36% for the two-stage procedure, the one-stage procedure, and conservative management, respectively. A more recent analysis of the three approaches considered 17 studies and found similar cure rates (88, 64, and 34%, respectively) (36). It is clear from these analyses that a combination of complete removal of the shunt, external drainage of CSF, and antibiotic therapy is the most effective option and, according to a recent survey by Whitehead and Kestle (42), is the standard of care, at least among pediatric neurosurgeons. The poorest results have been observed with antibiotic treatment alone (34–36%) (36, 45), although cure rates associated with instillation of the drugs directly into the ventricles (with or without systemic therapy) have consistently been higher than those associated with systemic administration alone (18, 23, 31, 37).

Analysis of the literature has revealed a number of explanations for the low cure rates resulting from conservative management of patients with shunt infections. First, the predominant causes of shunt infections, staphylococci, adhere to the shunt and form microcolonies, which are often coated with bacterially-produced "slime" (3). A combination of reduced susceptibility to antibiotics while the organisms are in this sessile state and reduced penetration of these drugs into the slime is a major factor in the failure of attempts at eradication (46). Second, when antibiotics are administered by the parenteral route, the penetration of β-lactams and glycopeptides into the CSF is poor, especially when the meninges are minimally inflamed, as is often the case in patients with shunt infections, thereby resulting in subtherapeutic concentrations at this site (17, 20, 45). Third, there is an active transport system in the CSF compartment that ensures that the concentrations of β-lactams do not remain in the therapeutic range sufficiently long to be effective, even when the drugs have been given by the intraventricular route (41). Fourth, some patients received antibiotics (chloramphenicol and macrolides), which have only bacteriostatic activities; the CSF being a region of impaired host defenses, bactericidal antibiotics are necessary to facilitate cures (37). Fifth, in the past, some patients with infections caused by methicillin-resistant staphylococci were treated with cephalosporins, owing to a failure to appreciate that methicillin-resistant strains are also resistant to cephalosporins (30). Finally, in many cases, intraventricular antibiotics were instilled via the shunt reservoir. Most shunts rely on percutaneous pressure to occlude the valve and distal catheter while instilling antibiotics. Failure to adequately occlude the distal catheter could easily result in subtherapeutic concentrations in the ventricles. Furthermore, some valve types, in which the reservoir is located distal to the valve, would clearly preclude intraventricular administration, with antibiotics reaching the peritoneal catheter only (10).

In the light of this knowledge, which characteristics define the antibiotic regimen that would have the greatest likelihood of curing patients with shunt infections caused by staphylococci without concurrent removal of the shunt? 1) Because at least 60% of CoNS causing such infections are methicillin-resistant, a glycopeptide (vancomycin or teicoplanin), to which the overwhelming majority of such strains will be susceptible, would be the drug of choice. 2) Owing to the poor and unpredictable penetration of systemically administered glycopeptides into the CSF compartment, especially when there is minimal meningeal inflammation, the concentrations of these drugs should be maximized by instilling them directly into the ventricles. Ideally, a reservoir should be implanted to facilitate both the administration of the antibiotics and sampling of CSF for culture and assay; the use of such a reservoir also ensures distribution of the antibiotic throughout the ventricular system. Glycopeptides have the additional advantages of being eliminated slowly from the CSF and of being extremely safe when administered by the intraventricular route. A report of a patient who developed CSF eosinophilia that was not associated with clinical sequelae after the administration of intraventricular vancomycin is the only published evidence of toxicity attributable to this form of therapy (19). In our institution to date, more that 500 patients have received courses of intraventricular vancomycin (predominantly for the treatment of EVD-associated infections) without experiencing any adverse effects. 3) The regimen should include rifampicin, which can be given either orally or intravenously. This drug has been shown to penetrate slime, to attain bactericidal levels at the surfaces of infected implants (12), and to reduce viable counts within the slime to undetectable levels (38). In vitro susceptibility studies and animal experiments have shown that the antistaphylococcal activity of rifampicin is superior to that of the other drugs tested, including vancomycin (43). The addition of rifampicin to conventional antistaphylococcal antibiotics has also been shown to increase CSF bactericidal concentrations in patients with CSF shunt infections caused by *Staphylococcus epidermidis*, and, when used in combination with vancomycin, it improves the cure rates associated with device-related infections (prosthetic valve endocarditis and orthopaedic implant infections) in both animals and humans (2, 5, 12, 22, 32, 47). We describe here our experience over the past 17 years of treating patients with shunt infections without shunt removal.

PATIENTS AND METHODS

Study Design

This was an observational study of all patients treated for CSF shunt infections between 1986 and 2003. Patients man-

aged conservatively were prospectively monitored by the senior author (EMB). Supplementary data were collected retrospectively; these data included clinical and operative details of patients who were not treated conservatively (identified through a combination of the senior author's records and interrogation of the hospital clinical-coding database) and supplementary clinical data and extended follow-up data of the patients treated conservatively.

Patients

Consecutive patients with proven shunt infections and functioning shunts were eligible for inclusion. There were no age restrictions, and the only other requirement for enrollment was that patients should have a separate, subcutaneous, ventricular access device (VAD) (such as an Ommaya reservoir) at the time of presentation. The administration of intraventricular antibiotics via a separate VAD is an essential component of our protocol. Therefore, to meet the inclusion criteria for in situ treatment of the shunt infection, if such a device were not already present, it was implanted before treatment was started. The exclusion criteria were as follows: shunt blockage or suspected shunt blockage at presentation, other shunt malfunction at presentation requiring surgical intervention, redundant shunt, concurrent abscess or empyema at presentation, external shunt infection, abdominal pseudocyst, peritonitis secondary to bowel perforation, loculated hydrocephalus, fungal infection, and infection caused by the bacteria most commonly associated with community-acquired meningitis (*Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae*), which, by convention, are managed using systemic therapy without shunt removal (9, 24, 28, 29, 33).

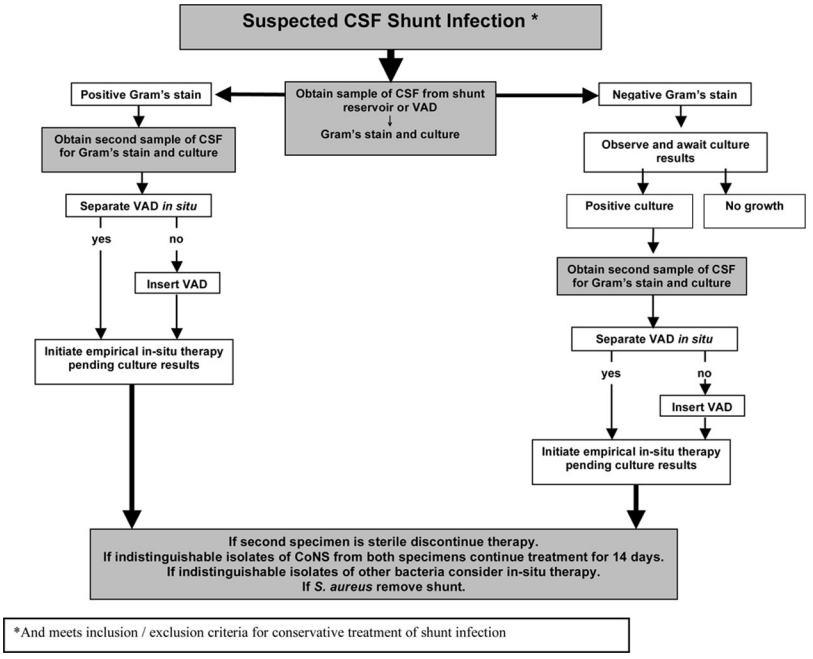

FIGURE 1. *Algorithm for conservative management of patients with clinically suspected shunt infection.*

Diagnosis

The diagnosis of shunt infection was based on the isolation of the same bacterium from at least two consecutive samples of CSF. In the event of a positive CSF, Gram's stain, treatment was initiated immediately after the second specimen was obtained but before the final culture results for that specimen were available. If the second specimen was subsequently shown to be sterile and there were doubts on clinical grounds about the reliability of the diagnosis, treatment was discontinued. CSF specimens were processed according to standard laboratory procedures. A management algorithm for patients with clinically suspected shunt infection is shown in *Figure 1*.

Antibiotics

Patients with staphylococcal infections were treated with intraventricular vancomycin and rifampicin (20 mg/kg in two divided doses daily to a maximum of 600 mg twice a day) by either the parenteral or oral route if isolates were confirmed to be susceptible. A formulation of vancomycin without preservative was used for intraventricular administration, and the dosage was based on the estimated volume of distribution of the CSF, with the aim of achieving concentrations of between 50 mg/L and 80 mg/L. The drug was instilled through a separate VAD, not the shunt reservoir. Approximately 5 ml of CSF were aspirated into a syringe containing the vancomycin, and the contents of the syringe were then flushed back into the ventricular system. To ensure that the entire dose was instilled, CSF was re-aspirated into the same syringe and flushed back. Doses were normally administered once daily. However, patients who made a good clinical response within a few days of therapy being initiated and who lived locally were allowed home, returning to the hospital on a daily basis for intraventricular instillation of antibiotics. In some cases, the dosages were doubled and patients returned to the hospital on alternate days.

The volume of distribution was determined, and the patency of the shunt was assessed 24 hours after the first dose. Just before the second dose was due to be given, a 2 ml sample of CSF (the trough) was aspirated, and the vancomycin was instilled into the CSF compartment. Between 15 and 30 minutes later, a second sample of CSF (the peak) was obtained. To eliminate sampling errors in the measurement of CSF antibiotic concentrations owing to the "dead space" of the reservoir itself, an initial 2 ml sample of CSF was obtained and discarded, followed by aspiration of the actual trough or peak specimen, which was submitted for analysis. The concentrations of vancomycin in both samples were determined, and the volume of distribution was calculated according to the following formula: vancomycin dosage (mg)/X

(mL) = peak vancomycin concentration − trough vancomycin concentration/1000 ml, where X is the volume of distribution.

The targeted trough and peak concentrations were 10 mg/L or less and 50 to 80 mg/L, respectively. If the peak concentration was outside this range a dosage adjustment was made. For example, if 10 mg had been instilled (based on an estimated volume of distribution of 150 ml) and the (peak − trough) concentration of vancomycin in the CSF was 120 mg/L, then 10 mg/X (mL) = 120 mg/1000 ml. The volume of distribution is actually only 80 ml and has, therefore, been overestimated. The dosage should be reduced to 5 mg. If the trough concentration is markedly in excess of 10 mg/L, either the shunt is not functioning or there has been a sampling error, unless the peak concentration is markedly in excess of 80 mg/L, in which case there is a need for a dosage adjustment.

Patients with infections caused by enterococci received a combination of vancomycin and gentamicin. The vancomycin dosage and administration were the same as those described above for staphylococci. A formulation of gentamicin without preservative was administered once daily according to the same technique used for vancomycin, with the aim of achieving peak concentrations of between 5 mg/L and 10 mg/L and trough concentrations 2 mg/L or less.

Patients with infections caused by AGNB, other than *Pseudomonas aeruginosa,* were given systemic therapy comprising a third-generation cephalosporin (either cefotaxime or ceftriaxone) in maximum dosage, assuming that the pathogen was susceptible, and once daily intraventricular gentamicin. Those with infections caused by *Pseudomonas aeruginosa* received parenteral ceftazidime in maximum dosage and once daily intraventricular gentamicin. The dosages of gentamicin for patients with either pseudomonas or nonpseudomonas infections were calculated to achieve peak concentrations of between 15 mg/L and 20 mg/L and trough concentrations 2 mg/L or less. The total duration of therapy of all antibiotics was 2 weeks.

Laboratory Investigations

Determination of the trough concentrations of intraventricular vancomycin and gentamicin was repeated after 1 week, principally to confirm that the shunt was still functioning. Samples of CSF for culture were obtained every 3 to 4 days during treatment courses and approximately 1 week and 1 month after completion of therapy.

Definition of Cure

Cure was defined as sterile CSF and the absence of clinical evidence of infection during follow-up or, in the event of shunt revision, sterile CSF and explanted shunt components. Patients in whom the shunt had not been revised were followed for a minimum of 6 months. Reinfection (the isolation of an organism distinguishable from the original pathogen) did not constitute treatment failure.

Statistical Analysis

Survival between any two groups was determined by the Kaplan-Meier method, and significance between the two groups was ascertained with the log rank test.

RESULTS

Of 122 consecutive episodes of suspected shunt infection, 44 (36%) in 40 patients fulfilled the inclusion criteria and were managed conservatively. Details of excluded patients are shown in *Table 1*. Forty-three of the 44 episodes involved ventriculoperitoneal shunts, the exception being a patient with a ventriculoatrial shunt. One patient was classified as a protocol violation because the antibiotic was administered via the shunt reservoir. Therefore, 43 episodes in 39 patients were evaluated. The 39 patients comprised 16 adults (age range, 21–64 yr) and 23 children (age range, 4 mo–14 yr). Ten (26%) patients required implantation of a VAD to facilitate intraventricular therapy. There were no complications related to insertion. However, one of the 10 VADs subsequently became blocked, possibly resulting from suboptimal positioning of the ventricular catheter, and revision was undertaken during the course of treatment; unfortunately, confirmatory postoperative imaging was not available. The CSF Gram-stain findings and the pathogens are summarized in *Tables 2* and *3*, respectively.

Patients received antibiotic therapy for between 7 and 21 days (median, 14 d), but most (41) patients were given these drugs for between 13 and 18 days; the patient who was treated for only 7 days died before completing therapy. One patient whose pathogen (an enterococcus) was initially mistakenly identified as a CoNS was treated with vancomycin and rifampicin. After 1 week, the mistake was recognized, the rifampicin was discontinued, and gentamicin was instilled with vancomycin into the ventricles for a further 2 weeks. The patient, therefore, received treatment for a total of 21 days. The median hospital stay from the time infection was diagnosed was 16 days (range, 4–60 d). Several of the patients were already inpatients at the time of diagnosis, and some of these had significant comorbidities that were unrelated to the shunt infection. The overall duration of stay was skewed by such ″outliers,″ whose stay was protracted for reasons other than the shunt infection (e.g., head injury rehabilitation, neurological disability from subarachnoid hemorrhage, etc.). Ten patients received part of their courses of therapy as outpatients for periods ranging from 6 to 10 days; the duration of hospital stay of one of these patients was only 4 days.

Patients were followed up for between 6 and 128 months. The outcomes are shown in *Table 3*. Overall, 84% of patients (93% of those with infections caused by CoNS) were cured with conservative therapy. There were five outright failures (three patients with infections caused by *S. aureus*, one with an infection caused by *Staphylococcus lugdunensis*, a CoNS whose virulence more closely resembles that of *S. aureus* [15, 39], and one with infection caused by *P. aeruginosa*) and one presumed

TABLE 1. Patients with shunt infections who were excluded from analysis (shunt removed or externalized unless otherwise stated)[a]

Excluded shunt infections	No. of shunt infections
Shunts blocked at presentation	15
Shunts externalized (suspected blockage)	5
S. aureus infection (shunt patent at presentation)	14 (includes 7 MRSA infections)
Wound breakdown/"external" infection	7
Complex/multiloculated hydrocephalus	5
Abdominal pseudocyst	5
Protocol violation	4
Bowel perforation	3
Candida infection	2
Redundant shunt, after endoscopic third ventriculostomy	2
Redundant shunt, arrested hydrocephalus	2
Shunt overdrainage (overriding sutures at presentation)	1
Associated intracranial abscess/empyema at presentation	2
Subcutaneous abscess involving shunt at presentation	2
Co-existent cryptococcal meningitis	1
Unknown (case notes destroyed or missing)	7
Pneumococcal shunt infection[b]	1
Total	78

[a] MRSA, methicillin-resistant *Staphylococcus aureus*.
[b] Treated in situ, but as this is standard of care it is not included in analysis.

TABLE 2. Cerebrospinal fluid Gram-stain findings for patients treated in situ[a]

CSF Gram-stain result	No. of patients
No organisms seen	10
Gram-positive cocci	27
Gram-negative bacilli	2
Mixed	1
Not recorded	3
Total	43

[a] CSF, cerebrospinal fluid.

relapse (an 8-mo-old child who presented with a CoNS shunt infection 4 mo after successful treatment of an infection caused by a strain of CoNS with the same susceptibility pattern). A patient with an *S. aureus* infection who relapsed was cured after a second attempt at in situ therapy. In the light of the high failure rate (four of seven episodes) in patients with infections caused by *S. aureus*, we abandoned efforts to treat such patients with retention of the shunt.

Six patients also had "redundant" ventricular catheters in addition to their functioning shunt systems at the time of presentation. Of these, four were successfully treated conservatively; the infections in the two failures were caused by *S. aureus*.

Mortality

There were three deaths during the treatment and follow-up periods. A 51-year-old malnourished and severely debilitated patient died of infection (staphylococcal pneumonia and pulmonary abscess complicated by multiorgan failure) that was unrelated to the shunt while undergoing in situ treatment; there was no postmortem evidence of CSF or shunt infection/colonization. A second patient died of gross hydrocephalus associated with shunt blockage 17 months after successfully undergoing in situ treatment. The remaining death occurred in a 43-year-old severely debilitated patient who had undergone resection of a cranial base chordoma. She developed a persistent CSF leak and postoperative hydrocephalus that failed to respond to lumbar drainage and direct surgical closure/packing of the fistula. The leak and hydrocephalus were eventually controlled by a combination of ventriculoperitoneal shunt implantation and further surgical packing. However, she subsequently developed a shunt infection caused by *P. aeruginosa* for which she received in situ treatment; after completion of the course of therapy, her CSF was sterile. The CSF leak persisted intermittently but, in view of her poor condition, further treatment was not pursued. She died of a recurrent episode of meningitis. The possibility of treatment failure could not be completely excluded.

Shunt removal/revision for catheter blockage was undertaken in respect of two patients while they were being managed conservatively and in respect of four patients within 3 months of completing conservative therapy. However, when the patients who underwent conservative management were compared with a large cohort of consecutive, uninfected patients with shunts at this institution, the blockage-free survival times were not significantly different ($P = 0.69$, log rank test) (*Fig. 2*). No patient suffered adverse events that could be attributed to the administration of intraventricular antibiotics.

DISCUSSION

We have evaluated cure rates associated with conservative management of patients with infected but functioning CSF shunt systems (excluding patients with external shunt infections, fungal infections, concurrent abscess or empyema at

TABLE 3. Infecting organisms treated with conservative therapy[a]

Organism	No. of infections	Successful eradication (%)
CoNS	30	28 (93)[d]
S. aureus	7	3 (43)
Enterococcus spp.	3[c]	3
Klebsiella oxytoca	1	1
Propionibacterium spp.	2[b]	2
Streptococcus sanguis	1	1
P. aeruginosa	1	0

[a] CoNS, coagulase-negative staphylococci.
[b] One combined with CoNS infection
[c] One combined with CoNS infection
[d] One *S. lugdunensis* and one *S. epidermidis* infection.

presentation, peritonitis secondary to bowel perforation, pseudocyst formation, or loculated hydrocephalus). We have demonstrated that, contrary to previous experience, cure rates of shunt infections caused by bacteria other than *S. aureus* are comparable with those associated with the current standard of care: removal of the infected shunt, external drainage and antibiotic therapy, followed by implantation of a new shunt (42). Earlier attempts to treat patients without shunt replacement were largely unsuccessful (cure rates of approximately 35%) (36, 44), probably because the antibiotic regimens and the routes of administration were suboptimal. We attribute our success in the treatment of patients with infections caused by the predominant pathogens, CoNS, to a regimen that comprises instillation of vancomycin directly into the ventricular system via a separate VAD, combined with the systemic administration (either oral or parenteral) of rifampicin. Initial concerns that this regimen was merely sterilizing the CSF, but was failing to eradicate the sessile variant of the pathogen from the protective "slime" that coated the shunt system have been allayed. The low relapse rate and the observation that shunts that were subsequently removed owing to mechanical failure were sterile suggest that pathogens are eradicated, both from the CSF and from the shunt. Sterilization of the shunt

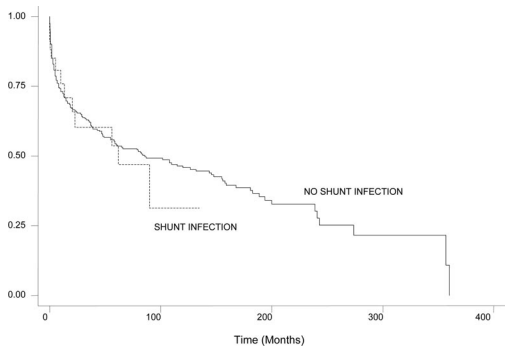

FIGURE 2. *Kaplan-Meier CSF shunt blockage-free survival estimates, by infection (P = 0.69, log rank test).*

may be attributed to the use of rifampicin, which has been shown to exhibit excellent penetration into slime (12). It has been demonstrated that there is variability in terms of bacterial adherence among strains of *S. epidermidis* (34) (i.e., highly-adherent strains are more difficult to eradicate with in situ therapy, and this may account for the single treatment failure among the patients with *S. epidermidis* CSF shunt infections).

Another concern is that management of patients with shunt infections without removal of the devices may predispose the patients to mechanical obstruction of the shunts because of accumulation of debris or slime in the catheter or valve at some time in the future. However, we have shown that the half-lives of shunts that have been infected do not differ significantly from those that have not been infected in patients from the same institution. Nonetheless, the survival curve on which the comparison is based should be interpreted with caution. The noninfected cohort included only patients with nontumoral hydrocephalus with onset in childhood, whereas the infected shunt group comprised patients with tumoral hydrocephalus and some with adult-onset hydrocephalus. Moreover, the noninfected cohort was studied over a longer time-frame (1973–2003) than the infected cohort (1986–2003). Although there is slight divergence of the curves after approximately 10 years of follow-up, the differences are not significant and predominantly reflect the very small number of patients in the infected group remaining for follow-up at 10 years. We think any small differences between the two groups at the extreme of follow-up, which were not detected because of the relatively small sample size of the infected cohort, would not be clinically significant.

Our results are most convincing for CoNS. These findings cannot be extrapolated to other pathogens owing to the small numbers of patients with infections caused by these organisms. However, on the basis of our experience, infections caused by *S. aureus* (four of seven treatment failures) are less amenable to conservative management. We do not know why this is the case, although others have reported that the failure rates for patients with catheter-related bloodstream infections caused by this bacterium who are managed with retention of the line are also high (4, 11, 40). For this reason, we have abandoned efforts to retain the shunts in respect of patients with infections caused by *S. aureus.* With regard to infections caused by AGNB, our experience (two infections, one of which was a failure) is too limited to allow us to draw meaningful conclusions. In common with *S. aureus*, some authorities have reported low success rates in patients with device-related infections caused by AGNB (16).

The optimal duration of antibiotic therapy of patients with shunt infections has not been determined. We have adopted a 2-week course, but this was based on convention rather than clinical or experimental evidence. Our view is that 2 weeks is an arbitrary duration, and we suspect that patients can be treated successfully after the administration of antibiotics for shorter periods (e.g., 1 week), although this would need to be confirmed by clinical trials.

The current standard of care, shunt removal, EVD drainage, antibiotic therapy, followed by new shunt insertion requires two surgical procedures at up to three operative sites (old shunt site, new EVD site, new shunt site). The removal of redundant, retained proximal catheters can be particularly hazardous, primarily because of the risk of intraventricular hemorrhage from avulsed choroid plexus (13). The potential surgical morbidity arising from this protocol is, therefore, not insignificant. In our series, four (9%) patients avoided removal of such redundant, retained catheters. Therefore, provided the infection is successfully eradicated, a conservative management protocol should be associated with a lower incidence of morbidity. Furthermore, the requirement for a prolonged hospital stay and at least two operative procedures comes at a high cost in financial terms, with recent estimates of $50,000 for the treatment of a patient with a shunt infection (8). Conservative management of patients with shunt infections could result in a substantial cost saving, not only because of the reduction in the number of surgical procedures and implants but also because of the potential for at least part of the treatment course to be administered on an outpatient basis.

There are three limitations of this study. First, it was an observational rather than a randomized controlled trial. However, we have evaluated more than 40 patient episodes, and the results are comparable with those reported consistently by investigators who have evaluated the various management options. This includes the current standard of care, shunt removal, administration of antibiotics, and insertion of a new shunt in studies, only one of which was a randomized controlled trial (21), which suffered from several methodological flaws (9). Second, the management of some patients (i.e., those who do not have VADs in situ [26% of patients in our series]) was not, in the strictest sense, conservative because these patients underwent surgical procedures (i.e., implantation of VADs to allow intraventricular antibiotics to be administered). In institutions where routine insertion of a VAD is not practiced, a greater proportion of patients treated according to our protocol would have had to undergo an operative procedure. However, the implantation of a VAD is probably associated with a lower incidence of morbidity, compared with the removal of an infected shunt system (particularly with associated retained, redundant proximal catheters). In many institutions, including our own, it is routine practice for patients to undergo placement of a separate VAD, either at the time of any previous endoscopic surgical management of the hydrocephalus or at the time of shunt insertion. The VAD may then be used to facilitate the diagnosis of shunt malfunction and sampling of CSF and to provide emergency ventricular access in the event of acute shunt failure (1, 7, 14, 27, 35). In patients with functioning shunts, the presence of slit-like ventricles may undermine accurate placement of VADs. In such situations, we advocate using either ultrasound or image-guidance to facilitate implantation of ventricular catheters. Finally, the product licenses for vancomycin and gentamicin do not extend to intraventricular instillation, although this route of administration is used extensively by neurosurgeons.

CONCLUSIONS

We think our results demonstrate that the conservative management of patients with CSF shunt infections caused by CoNS who have functioning shunt systems is as effective as the current standard of care, with the potential advantages of reductions in surgical morbidity rates, durations of hospital stay, and overall treatment costs and is worthy of further evaluation in a prospective, randomized, controlled trial. Furthermore, the instillation of antibiotics into ventricular CSF is safe. To the best of our knowledge, no clinically significant toxicity has ever been reported after the intraventricular administration of vancomycin, and we have not observed any adverse effects associated with the therapeutic instillation of this drug into the CSF compartments of more than 500 patients over approximately 20 years. In situ therapy is not suitable for patients with infections caused by *S. aureus*, and there are insufficient numbers in the current series to enable us to draw reliable conclusions regarding the efficacy of conservative management in patients with CSF shunt infections caused by organisms other than CoNS.

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COMMENTS

This is an extremely provocative study of 43 patients with infected but functioning cerebrospinal fluid (CSF) shunts treated with systemic and intraventricular antibiotics, rather than the traditional method of shunt removal, period of external drainage, and reinternalization. The patients were treated over a 17-year period. The intraventricular antibiotics were administered via a separate subcutaneous Ommaya reservoir with the dosage of antibiotic adjusted according to peak and trough levels. Some of the patients were managed as outpatients for part of their treatment.

Overall, 84% of the patients were cured of their shunt infection. Twenty-nine of 32 patients without *Staphylococcus aureus* infection were cured (92%). The authors abandoned *S. aureus* infections when 4 of 7 patients failed. The numbers with gram negative and other infections are small, but there were a number of treatment successes. Three patients died, two unrelated to shunt infection, and one from meningitis related to a persistent CSF leak.

This study contravenes conventional wisdom and the reported literature. The authors, however, have delivered the antibiotics via a separate intraventricular catheter/reservoir and have carefully monitored the dosage. Their results appear to be at least as good as conventional treatment. However, they do exclude subsequent infections with other organisms, which would normally be included in shunt infection studies. Twenty-six percent of their patients required an additional operative procedure, an Ommaya reservoir insertion, which presumably would have to be removed (and reinserted) if the treatment failed. According to their algorithm, a patient presenting without a subcutaneous reservoir would have one placed pending organism identification. If the organism proved to be *S. aureus*, then the shunt and reservoir would have to be removed and an extraventricular drain placed. Rather than decrease the number of operative procedures, as the authors maintain is the accomplishment of their treatment, this would increase by one the number of procedures over conventional treatment, albeit in this smaller subgroup.

This treatment focuses on a select group of shunt infection patients who were monitored very carefully. It is simplified by having a separate indwelling CSF reservoir at presentation, which is not placed at most institutions routinely. Shunt infection remains a persistent problem and the authors have challenged us to explore other treatment strategies.

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The present standard for the treatment of patients with shunt infections includes removal of the complete system, placement of an external ventricular drain, followed by intravenous antibiotics with or without the addition of intrathecal antibiotics and a second surgical intervention to replace their system. In this observational study, the patients with CSF documented shunt infections were treated conservatively, in that they did not immediately remove the infected shunt but treated the infection medically according to a protocol that included intraventricular vancomycin and either oral or parenteral rifampicin. Measures of peak and trough levels of CSF vancomycin were performed in order to optimize the volume of distribution for treatment and with a total therapeutic duration of 2 weeks. The authors' results showed that they were able to successfully treat patients without *S. aureus* infection, specifically those with coagulase-negative *Staphylococcal* infections. Not only was it possible to sterilize the CSF in these previously infected patients, but there also was no increase in the shunt malfunction rate of these treated systems. The ability to treat these patients conservatively without surgical intervention would be ideal. The authors have identified a population of patients that tend to do well with conservative treatment and with the potential for treatment at home. This could potentially allay hospital costs and avoid complications of surgery if successful. A unique aspect of the study is the use of the rifampicin, which has not been a routine antibiotic medication in the treatment of CSF shunt infections. Through meticulous monitoring, optimizing treatment, and specifying antibiotics, a significant number of patients would seem to do well with this conservative approach. Obviously, further trials as to duration of management would be necessary to define the optimal population and time period. In addition, for the less successful pathogens in this study, it should be considered whether another conservative regimen could be successfully developed, though this will depend on antibiotic CSF penetrance and success in eliminating those pathogens from the infected shunt hardware.

P. David Adelson
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This provocative and somewhat exciting paper revives the discussion brought about by McLaurin in the mid-seventies on the possibility of eradicating a CSF infection in subjects harboring an infected CSF shunt device by means of systemic and local (antibiotic injection into the drainage apparatus) antibiotic therapy. In the following years, inconsistent results led nearly all the neurosurgeons to adopt the more aggressive policy of removing the infected CSF shunt, placing an external ventricular drainage (EVD) to be used to control ICP and administering the antibiotic therapy intraventricularly, and reinserting the CSF shunt apparatus once the CSF infection was cured. Such a current standard procedure bears the risk of secondary contamination via the EVD and has several disadvantages, namely the patient's discomfort and the long hospitalization that is required in some cases. At the first glance, the results obtained by the authors in their patient with infected CSF shunts treated with systemic and intraventricular antibiotics, via an Ommaya reservoir, rather than the traditional protocol of shunt removal, period of external drainage, and shunt replacement, appear to provide an excellent therapeutics option. Indeed, 85% of their patients with infected shunts were cured.

There are, however, some limitations to be kept in mind before assuming the possibility of a wide application of this type of management of infected CSF shunts.

The first limitation, though of minor importance, is that the series is somewhat selective, as the authors excluded the subjects with an infection due to *S. aureus* as 4 out of 7 cases with such an infection failed.

The second and third limitations are, in my opinion, relevant. The second limitation concerns the necessity of a perfectly functioning CSF shunt in order to apply the authors' protocol. In many instances, however, an occlusion of the CSF shunt system is the presenting shunt complication leading to the diagnosis of an infected CSF shunt device. The third limitation is that the application of the protocol implies the presence of an Ommaya reservoir. Such a necessity is not a problem for the authors, who apparently are used to placing a separate reservoir in their patients during the insertion of a CSF shunt device. This policy, however, is not adopted in all the neurosurgical centers. Consequently, in order to evaluate the possibility of a wide adoption of the authors' protocol, it should be discussed whether the presence of the two devices and its associated infective and surgical risk are justified to treat possible future complications of an extrathecal CSF diversion in procedure.

Concezio Di Rocco
Rome, Italy

FUTURE MEETINGS—CONGRESS OF NEUROLOGICAL SURGEONS

The following are the planned sites and dates for future annual meetings of the Congress of Neurological Surgeons:

2006	Chicago, IL	October 7–12
2007	San Diego, CA	September 15–20
2008	Orlando, FL	September 20–25

FUTURE MEETINGS—AMERICAN ASSOCIATION OF NEUROLOGICAL SURGEONS

The following are the planned sites and dates for future annual meetings of the American Association of Neurological Surgeons:

2006	San Francisco, CA	April 22–27
2007	Washington, DC	April 14–19
2008	Chicago, IL	March 29–April 3
2009	San Diego, CA	May 2–7