Treatment of CSF shunt infections with intrashunt plus oral antibiotic therapy

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Infections of 12 cerebrospinal fluid (CSF) shunts in 11 children were treated with oral systemic antibiotic therapy plus daily intrashunt injections of antibiotics. Eight patients were infected with Staphylococcus epidermidis (four patients) or Staphylococcus aureus (four patients), and were treated with intrashunt vancomycin, plus oral trimethoprim/sulfamethoxazole (T/S), plus oral rifampin. One of these eight patients was later changed to a course of intrashunt cefapirin and oral cephalaxin plus oral rifampin. One patient with Micrococcus varians infection was treated with oral T/S and rifampin, without intrashunt therapy, another patient with Pseudomonas cepacia infection was treated with intrashunt kanamycin plus oral T/S, and a third with Corynebacterium sp. infection was treated with intrashunt vancomycin plus oral T/S. Eight of the 11 patients required some form of shunt surgery, the most common being temporary externalization of the peritoneal end of the catheter. Only two shunts were completely replaced (both were ventriculojugular shunts which were changed to ventriculoperitoneal shunts). Nine of 10 evaluable cases were considered cured of their infections. The patient treated with cephalosporins had an uncorrected shunt malfunction and relapsed 1 month after completing therapy. The authors have shown that CSF shunts infected with Staphylococci can be effectively cleared with daily intrashunt vancomycin plus systemic therapy with oral T/S and rifampin. Less common infections may also be amenable to this form of therapy. Revision surgery, if necessary, should be carried out during the antibiotic therapy.

KEY WORDS • shunt infection • vancomycin • rifampin • trimethoprim • Staphylococcus epidermidis • Staphylococcus aureus • antibiotics • infection

SHUNTING of cerebrospinal fluid (CSF) from the ventricular system to the vascular space or to another body cavity is a procedure which often allows patients with hydrocephalus to lead normal useful lives. However, a number of complications can occur with such procedures, the second most common of which is infection of the shunting apparatus.15 Infection rates reported in different series vary between 7% and 41%, depending on a number of different factors such as the age of the patient and the number of revisions for shunt malfunction. In an early series the mortality rates associated with CSF shunt infections ranged from 35% to 40%; more recent series have suggested a more stable infection rate of 10% to 15% and a reduced mortality rate from CSF shunt infection to 5% to 10% of those infected.7,16,24,25

Management strategies for CSF shunt infection can be divided roughly into two approaches,16 the first holds that all foreign bodies must be removed from an infection site and the infection cleared with antibiotics before new shunt materials can be placed. These patients thus require two operations and some temporary means of CSF pressure release while the infection is being treated. The second management strategy is to attempt sterilization of the CSF shunt while the mechanism remains in place, without any surgery directed at the infection. If a shunt malfunction is present, shunt revision is performed and if new shunt hardware is required it is replaced at the time of revision surgery. At this institution, management plans consistent with the latter philosophy have been followed with considerable success.5,14,18 In our more recent cases we have been investigating antibiotic concentrations in CSF and the antibacterial activity of patients' ventricular fluid against their own infecting organisms, the "CSF antibacterial titer."28

This paper describes the therapy of 11 patients with CSF shunt infections who were treated with oral antibiotic regimens supplemented by intrashunt junction of antibiotics. After success in three cases, which are detailed below, and because of the obvious benefits of oral antibiotic therapy compared to intravenous anti-
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Biotic therapy in small children, we applied this mode of therapy to an additional eight patients. The first patient treated in this manner was a patient with *Pseudomonas cepacia* infection of a CSF shunt, which we had been unable to eradicate with systemic antibiotics. The second patient had *Staphylococcus aureus* CSF shunt infection, which had been unresponsive to high-dose cephapirin and gentamicin therapy both systemically and into the shunt. The third patient was a young boy with a ventriculojugular (VJ) shunt infection with a *Micrococcus* species which had not responded to intravenous and intralshunt cephapirin and gentamicin therapy.

The trimethoprim/sulfamethoxazole (T/S) combination was chosen because of its *in vitro* activity against the patients' infecting organisms, and because of the good penetration of both components into the CSF. Rifampin is extremely potent against *Staphylococci*, and also penetrates the CSF concentrations that are effective against *Staphylococci*. However, resistance to rifampin develops rapidly when this agent is used alone. Vancomycin is also an excellent antistaphylococcal agent, but penetrates the CSF poorly when administered systemically. Meticillin and cephalosporin resistance is common in *Staphylococcus epidemidis* infections associated with implanted foreign devices; however, all of the organisms thus far reported have been susceptible to vancomycin.

**Clinical Material and Methods**

A reservoir is placed routinely in all ventricular shunts in this clinic. This consists of a plastic chamber between the ventricular catheter and the pumping device ("valve"). The reservoir is easily palpable beneath the scalp. To identify the bacteria in an infected shunt, fluid is aspirated from the ventricular system for analysis; after appropriate preparation of the overlying skin, a fine needle is introduced into the reservoir for ventricular fluid aspiration. When the bacteria is identified, the antibiotic is instilled back into the ventricle.

Standard methods for determining serum inhibitory and bactericidal titer were adapted for use with CSF. Fluid withdrawn from the CSF shunt reservoir underwent a serial twofold dilution in Mueller-Hinton broth, and each dilution received a 10⁶ inoculum of the patient's infecting organism. Growth was evaluated by inspection after 24 hours of incubation. The lowest dilution of CSF which inhibited visible growth of the patient's infecting organism was termed the inhibitory titer (CSF-IT). Tubes that showed no visible growth after 24 hours of incubation were subcultured onto antibiotic-free solid media for determination of the bactericidal titer (CSF-BT). The lowest dilution of CSF which killed at least 99.9% of the inoculated bacteria was designated the CSF-BT.

Since a basic principle of treating shunt infections in *vivo* has been to insure a well functioning shunt, revisions of the shunt system were sometimes necessary. Several types of procedures have been used to establish good CSF flow through the shunt system, including replacement of obstructed components, temporary externalization of the distal (peritoneal) end of the system, and, in two cases, replacement of the entire system. In addition to shunt revision, removal of unattached hardware left from previous operations was necessary in two patients.

**Case Reports**

**Case 1**

This 12-year-old girl with myelomeningocele had had numerous previous shunt procedures prior to her admission to the hospital in August, 1979, for urinary tract evaluation. At the time of admission she had a functioning VJ shunt in place, as well as a free floating catheter in the opposite lateral ventricle left behind from a previous shunt. While in the hospital she developed high fever and had positive blood and CSF cultures for *Pseudomonas cepacia*. The ventricular fluid also grew *Staphylococcus epidermidis*. The patient also had shunt nephritis with proteinuria, hematuria, and evidence of circulating immune complexes. Her most recent shunt surgery had been 2 years previously, in which time *Ps. cepacia* was also recovered from ventricular fluid.

She was initially started on chloramphenicol in a dose of 50 mg/kg/day (chloramphenicol had a minimum inhibitory concentration (MIC) of 4 µg/ml, and a minimum bactericidal concentration (MBC) of > 25 µg/ml for *Ps. cepacia*). On the 7th day of chloramphenicol therapy the patient's ventricular fluid was still positive for *Ps. cepacia*. Also on Day 7, the CSF shunt was replaced with a shunt catheter containing a reservoir, and intrashunt kanamycin injections were begun at 4 mg/day (kanamycin had an MIC of 16 µg/ml, and an MBC of 64 µg/ml). At that time chloramphenicol was discontinued and T/S was begun in divided doses totalling 20 mg trimethoprim, 100 mg sulfamethoxazole/kg/day (T/S had an MIC of 0.25/2.75 µg/ml, and an MBC of 2/38 µg/ml). One week later the free floating catheter in the right ventricle was removed. That catheter also was cultured positive for *Ps. cepacia*. Two weeks after shunt replacement, malfunction required the insertion of an external ventricular drain. At that time CSF fluid was cultured and found negative. A trial of external drain removal resulted in increased intracranial pressure which required repeated ventricular taps. Six weeks after therapy began the VJ shunt was changed to a ventriculoperitoneal (VP) shunt with a medium-pressure valve. Antibiotics were discontinued 4 days after shunt revision. Cultures of ventricular fluid taken at the time of shunt revision and 2 days later were negative. The patient had become afebrile 48 hours after beginning antibiotic therapy and remained so for the entire course. The shunt nephritis had resolved by the time of hospital discharge. This patient has been followed since late 1979, with no apparent recurrence of her CSF shunt infection.
**TABLE 1**

Clinical data in 11 patients with oral plus intrathecal therapy of CSF shunt infections*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Disease</th>
<th>Type of Shunt</th>
<th>Weeks Since Last Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12 yrs</td>
<td>meningomyelocele</td>
<td>VJ, FB</td>
<td>104</td>
</tr>
<tr>
<td>2</td>
<td>11 mos</td>
<td>astrocytoma</td>
<td>VP</td>
<td>26</td>
</tr>
<tr>
<td>3</td>
<td>2 yrs 10 mos</td>
<td>hydrocephalus</td>
<td>VJ</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>3 yrs</td>
<td>meningomyelocele</td>
<td>VP</td>
<td>“years”</td>
</tr>
<tr>
<td>5</td>
<td>14 yrs</td>
<td>hydrocephalus</td>
<td>VP, FB</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>2 mos</td>
<td>hydrocephalus</td>
<td>VP</td>
<td>2</td>
</tr>
<tr>
<td>7</td>
<td>12 yrs</td>
<td>hydrocephalus</td>
<td>VP</td>
<td>32</td>
</tr>
<tr>
<td>8</td>
<td>1 yr 3 mos</td>
<td>meningomyelocele</td>
<td>VP</td>
<td>4</td>
</tr>
<tr>
<td>9</td>
<td>3 yrs 6 mos</td>
<td>ependymoma</td>
<td>VJ</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>12 yrs</td>
<td>hydrocephalus</td>
<td>VP</td>
<td>4</td>
</tr>
<tr>
<td>11</td>
<td>3 yrs</td>
<td>hydrocephalus,</td>
<td>VP, CP</td>
<td>4</td>
</tr>
</tbody>
</table>

* CSF = cerebrospinal fluid; VJ = ventriculoujugular; FB = additional foreign body; VP = ventriculoperitoneal; CP = cyst-peritoneal.

**Case 2**

This 11-month-old girl had a supratentorial astrocytoma which was inoperable. A VP shunt had been placed in August, 1979, at the time of radiation therapy to the head. In March, 1980, the patient was admitted for evaluation of 2 weeks of daily fever spikes, as well as 24 hours of vomiting, diarrhea, and poor oral intake. Blood cultures and ventricular fluid cultures revealed *Staphylococcus aureus*. Since the patient was allergic to penicillin, she was begun on cephalaxin, 80 mg/kg/day with 50 mg cephalaxin injected into the shunt daily. Because of persistently positive cultures of *S. aureus*, gentamicin, 4 mg daily intrashunt, was added to the regimen. The gentamicin dose was then increased to 8 mg and the cephalaxin to 100 mg daily. Cultures of CSF remained positive for *Staphylococcus aureus*.

Because of persistently positive cultures, the antibiotic therapy was changed to vancomycin, 1 mg/day intrashunt, rifampin, 15 mg/kg/day, and T/S, 20/100 mg/kg/day, orally. The daily vancomycin dose was later increased to 2 mg. Because a fluid-filled cyst was demonstrated by abdominal echography, revision of the peritoneal end of the shunt was performed with replacement of the distal catheter in a different intraperitoneal position. After 14 days of oral rifampin and T/S and intrashunt vancomycin with persistently negative CSF cultures, the antibiotics were stopped. Aspiration of the ventricular fluid 48 hours later was negative for *Staphylococcus aureus*.

This patient required a number of subsequent admissions for increasing tumor size in the third ventricle. Shunt revisions were required on several occasions and on each occasion CSF cultures were negative. The patient died 15 months after her CSF shunt infection. Numerous CSF cultures were done in that 15-month period and at no time were cultures positive for bacteria. Autopsy was not performed.

**Case 3**

This boy, aged 2 years 10 months, had a long medical history, being the product of a 28-week pregnancy with multiple complications of prematurity. One of these was hydrocephalus secondary to intracranial hemorrhage which required CSF shunting. A VP shunt was later changed to a VJ shunt because of perforation of the umbilicus by the distal catheter. The shunt had been revised twice for lengthening prior to this admission, and 4 months before admission the patient had been treated for a *Micrococcus* CSF shunt infection with intravenous and intrashunt cephalaxin and gentamicin.

In May, 1980, he was admitted for evaluation of 4 days of fever and hematuria. Hypocomplementemic nephritis was demonstrated, and blood and CSF cultures were positive for *Micrococcus varians*. The patient’s intraventricular shunt and distal catheters were removed and he was begun on cephalaxin and gentamicin systemically. Intracranial pressure was controlled by emergency ventricular drainage inserted 2 days later. Because there was no access to the ventricular drain for intrashunt therapy, rifampin in a dose of 20 mg/kg/day and T/S in a dose of 20 and 100 mg/kg/day, respectively, was begun. Serum antibacterial titers on this regimen without intrashunt therapy were 1:2048 inhibitory and 1:8 bactericidal. After 18 days of therapy a VP shunt was placed, with a single dose of intraventricular vancomycin being given at the time of surgery. The patient was treated with an additional 2 weeks of oral therapy. This patient has not had a recurrence of his CSF shunt infection in 2 years.

In summary, this boy had a prior failure of systemic and intrashunt antibiotic therapy for a *Micrococcus* shunt infection. In this case, shunt removal and oral antibiotic therapy were successful in eradicating the infection.
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Summary of Cases

Twelve CSF shunt infections in 11 patients were treated with antibiotic regimens consisting of orally administered systemic antibiotics, supplemented in 10 instances with daily intrashunt injections of antibiotics. Four children were 12 or more years old, six were less than 3½ years old, and one was between 3½ and 12. Ten shunts were VP shunts and two were VJ shunts. Two patients had additional loose intraventricular catheters from prior shunting procedures. Shunts were required for hydrocephalus in six patients, meningomyelocele in three patients, and posterior fossa neoplasm in two patients (one astrocytoma, one ependymoma). One patient had two shunts; in addition to a shunt for hydrocephalus, he had a shunt from an arachnoid cyst to the peritoneal catheter, which was common to both shunts. Seven of the patients had recent shunt surgery within the month before the onset of the infection, and four patients had late-onset shunt infections occurring 6 months or more after the most recent shunt procedure (Table 1).

Seven of the eleven patients presented with fever and four were afebrile. Most patients had some disorder of central nervous system function, such as vomiting, lethargy, irritability, or increased frequency of seizures. The two patients with VJ shunts had shunt nephritis, and four patients had some external evidence of infection, such as erythema or redness over the shunt, or the presence of a large soft eschar over a previous operative site. Three patients had positive blood cultures including both patients with VJ shunts and the patient with astrocytoma. Two patients had prior failures of intravenous antibiotic therapy.

Initial examination of the CSF yielded inconsistent results (Table 2). Of the eight patients with CSF cell counts, four counts were above 200 cells/cu mm, and four were less than 100 cells. Most cells were polymorphonuclear leukocytes, although one patient (Case 2) had 15 mononuclear cells/cu mm. Protein values in the CSF ranged from 15 to 925 mg%, with a mean value of 218 mg%, but four values were less than 30 mg%. The glucose was clearly depressed in only one patient (Case 1: 1 mg%), with the remaining values ranging between 36 and 90 mg%.

Thirteen organisms were involved in the shunt infections: Staphylococcus epidermidis in five, Staphylococcus aureus in four, Micrococcus varians in one, Pseudomonas cepacia in one, and Enterococcus and Corynebacterium species in each one. Three patients had mixed shunt infections with two organisms (Table 3). There was little correlation between the species of organism and the elapsed time between the prior operative procedure and the onset of the shunt infection, although three of four S. aureus infections occurred within 1 month of the most recent surgery.

All 11 patients received oral antibiotics as their systemic therapy (Table 3). Each patient received oral T/S in doses designed to achieve serum concentrations of 75 to 150 μg/ml of sulfamethoxazole. The starting dose was 50 to 100 mg of sulfamethoxazole and 10 to 20 mg of trimethoprim/kg body weight/day. One patient (Case 8) was changed to oral cephalaxin, 57 mg/kg/day, after his S. epidermidis was found to be resistant to T/S. This patient had been receiving T/S prophylaxis for chronic urinary tract infection. Nine patients received oral rifampin in doses ranging between 10 and 20 mg/kg/day. Duration of oral therapy ranged from 14 to 45 days, with most patients receiving between 2 and 3 weeks of therapy.

Ten patients received intrashunt antibiotics (Table 3). One patient (Case 3) received only oral therapy because of the absence of a CSF shunt reservoir. Eight patients received intrashunt vancomycin every 24 hours for 2 to 3 weeks. One patient (Case 8) was changed from vancomycin to cephaandin, 100 mg intrashunt daily, when his oral therapy was changed to cephalaxin. The vancomycin dose for five patients was 10 mg intrashunt daily, while two received 20 mg daily and two received 1 or 2 mg daily. One patient (Case 11) received 10 mg into each of two shunts daily. One patient (Case 1) received kanamycin, 4 mg intrashunt daily, for 45 days.

Cerebrospinal fluid removed from the shunt reservoir 24 hours after intraventricular antibiotic administration was assayed for antibacterial titers against the patient’s infecting organism(s) in nine cases (Table 4). The inhibitory titers ranged between 1:8 and 1:2048 dilutions of CSF. Of the eight patients who had bactericidal titers performed, six achieved killing titers of greater than or
TABLE 4
Inhibitory and bactericidal titer of ventricular fluid*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Infecting Organism</th>
<th>Highest CSF Dilution Achieved</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Inhibitory</td>
</tr>
<tr>
<td>1</td>
<td><em>Ps. cepacia,</em></td>
<td>1:64</td>
</tr>
<tr>
<td></td>
<td><em>S. epidermidis</em></td>
<td>not done</td>
</tr>
<tr>
<td>2</td>
<td><em>S. aureus</em></td>
<td>1:128</td>
</tr>
<tr>
<td>3</td>
<td>Micrococcus varians</td>
<td>1:2048</td>
</tr>
<tr>
<td>4</td>
<td><em>S. epidermidis</em></td>
<td>1:16</td>
</tr>
<tr>
<td>5</td>
<td><em>S. aureus,</em></td>
<td>1:512</td>
</tr>
<tr>
<td></td>
<td>Enterococcus</td>
<td>1:256</td>
</tr>
<tr>
<td>6</td>
<td><em>S. epidermidis</em></td>
<td>1:64</td>
</tr>
<tr>
<td>7</td>
<td>Corynebacterium, group 3</td>
<td>1:128</td>
</tr>
<tr>
<td>8</td>
<td><em>S. epidermidis</em></td>
<td>a) 1:8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>b) 1:1024</td>
</tr>
<tr>
<td>9</td>
<td><em>S. epidermidis</em></td>
<td>1:16</td>
</tr>
</tbody>
</table>

* Samples were withdrawn 24 hours after an intrashunt antibiotic dose. See Table 3 for antibiotics delivered. CSF = cerebrospinal fluid.
† Lumbar cerebrospinal fluid tested.

TABLE 5
Details of adjunctive surgery with oral and intraventricular therapy of shunt infections

<table>
<thead>
<tr>
<th>Case No.</th>
<th>No Surgery</th>
<th>Shunt Externalized</th>
<th>Shunt Revisited</th>
<th>Retrieve Foreign Body</th>
<th>Remove Shunt</th>
<th>Duration of &quot;Cure&quot; (mos)</th>
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<tr>
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<td>—</td>
<td>—</td>
<td>—</td>
<td>X</td>
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<td>—</td>
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<td>—</td>
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<td>total cases</td>
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<td>4</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>10/11</td>
</tr>
</tbody>
</table>

* Died from other causes.

equal to a 1:8 dilution of CSF against their most significant organism. Case 8 had bactericidal titer that were consistently undetectable while receiving vancomycin, T/S, and rifampin. Higher titers were achieved with cephalosporins and rifampin, but that patient was a therapeutic failure. The second patient with bactericidal titers under 1:8 (Case 9) is currently considered to be cured 18 months after the infection was treated.

Eight patients required one or more surgical procedures on their CSF shunts during the course of therapy (Table 5). Four required temporary external drainage by externalization of the distal end of the shunt, because of intraperitoneal infection. Each of these patients had the peritoneal catheter replaced near the end of therapy. Two patients required revision, but not removal, of the shunt because of malfunction. Two patients had complete removal of their shunts with temporary external drainage before shunt placement. Both patients with free intraventricular catheters from previous shunts had surgery to remove the extra hardware. Both VJ shunts were converted to VP shunts. Of the three patients who were not operated on during the therapy, one was considered a treatment failure. In retrospect, some malfunction of his shunt was present throughout the treatment period.

At present, eight of the 11 patients have presumed cures of their CSF shunt infections for a period of 9 months or more, and one additional patient has been infection-free for 2 months. One patient with a meningomyelocele (Case 4) died with an acute Pseudomonas fluorescens subarachnoid meningitis unrelated to the CSF shunt, 1 month after his Staphylococcus epidermidis shunt infection was treated. Although there was no clinical evidence of shunt infection, CSF aspirated from the subcutaneous reservoir grew a slightly different S. epidermidis 24 hours before death. The acute subarachnoid meningitis did not involve the ventricles or the shunt and, at autopsy, there was no acute inflammation in the ventricles, although some chronic inflammatory changes were present. It is unclear whether this patient's shunt infection was cured or not.

Thirteen months after treatment for a Corynebacterium Group 3 infection, one patient (Case 7) developed a new infection with Corynebacterium Group ANF-1. During the period between the two infections, he had been admitted several times for shunt malfunction which involved aspiration and/or revision surgery.

One patient (Case 8) was considered a treatment failure. This patient relapsed with Staphylococcus epidermidis infection in a poorly functioning shunt 1 month after completing therapy with oral cephalaxin and intrashunt cephaapin therapy.

The only toxicity we have seen from this regimen is a case of apparent sulfa allergy manifested by fever, rash, lymphadenopathy, and mild neutropenia, which occurred near the end of 2 weeks' therapy with oral T/S, rifampin, and intrashunt vancomycin (Case 10). Blood cultures and viral studies were negative, and the reaction subsided during the 48 hours after antibiotics were discontinued. One additional patient had a rash of undetermined etiology for less than 24 hours on two occasions during therapy. One patient developed a Candida diaper rash. No patient had the onset of seizures after intrashunt vancomycin. One child (Case 6) was receiving phenobarbital for a preexisting seizure disorder, and developed seizures before and for 2 days after the initiation of intrashunt vancomycin. Vancomycin was continued, and the seizures stopped after the patient became afebrile. Case 7 was admitted with an increased frequency of preexisting myoclonic seizures, which improved with therapy. Case 10 was also admitted while suffering from seizures which resolved during therapy.

Discussion

At this medical center we have favored management strategies for CSF shunt infections which maintain the shunt hardware in place while treating the infection.
Treatment of shunt infections

with both systemic and intrashunt antibiotics.\textsuperscript{14,15,18} We have thought it necessary to deliver antibiotics directly into the CSF shunt by daily injections through a reservoir because of the poor penetration of most antibiotics into the CSF. In addition, the internal surfaces of the CSF shunt are relatively inaccessible to phagocytes, so we presume that bactericidal concentrations of antibiotics are required to eradicate organisms from shunt hardware. The presence of foreign material also makes phagocytosis less effective. Recently, Peters, et al.,\textsuperscript{19} have demonstrated that \textit{Staphylococcus} can actually degrade the polyethylene material of intravascular catheters and can form microscopic colonies embedded below the surface of the catheter. For these reasons it is not surprising that systemic antibiotic therapy alone is ineffective in eradicating CSF shunt infections.\textsuperscript{24}

Many patients with CSF shunt infections do, indeed, require some surgical procedure. The most important principle to be observed is that good shunt function must be maintained in order to effect a cure. To this end, early surgery to establish adequate shunt function is necessary. In retrospect, the one treatment failure in this series probably had inadequate shunt function. In patients with VP shunts who have malfunction of the distal intraperitoneal catheter or who have evidence of intraperitoneal infection or intraperitoneal fluid collections, the distal end of the shunt should be temporarily externalized and attached to an external drainage system until the intraperitoneal infection is cleared. During this time systemic and intrashunt therapy may proceed. The distal catheter is reinserted into the abdomen before the antibiotic therapy is discontinued. Intrashunt therapy with antibiotics requires a reservoir, and, if the infected shunt does not have one, surgery to place a reservoir is indicated.

Many patients who have infection of intravascular shunts have the additional complications of bacteremia, shunt nephritis, and possible right-sided endocarditis. Our policy has been to revise these shunts to VP shunts if possible.

We have continued to use a combination of intrashunt and oral systemic therapy because of successes in several patients with difficult infections in whom previous attempts to eradicate the infection had failed. In addition, we have been concurrently acquiring experience with the use of vancomycin, rifampin, and T/S combination therapy for methicillin-resistant \textit{Staphylococcus aureus} infections that had become a hospital epidemic centering around the burn and trauma unit of the University of Cincinnati Hospital.\textsuperscript{13,17} Methicillin resistance in \textit{Staphylococcus epidermidis} is common, and cephalosporins are often ineffective against these organisms.\textsuperscript{2,11}

Vancomycin has long been recognized as an effective antistaphylococcal agent.\textsuperscript{23} Systemically administered vancomycin does not penetrate into the CSF, at least in meninges without inflammation.\textsuperscript{5} In addition to the cases reported here, intrashunt vancomycin has been used in the therapy of CSF shunt infections by Visconti and Peter\textsuperscript{27} and Ryan, \textit{et al.}\textsuperscript{22} The two patients from those reports received intraventricular vancomycin in a dose of 20 mg/day. In our early patients we cautiously administered the drug at doses of 1 or 2 mg/day, but the remainder of our patients received 10 to 20 mg/day, intraventricularly, with no apparent side effects. Gombert, \textit{et al.},\textsuperscript{8} treated three patients with vancomycin and rifampin systemically, along with removal of the CSF shunt. Intrashunt injections were not used. Two Ommaya reservoir infections have been treated with intrashunt vancomycin.\textsuperscript{4,26}

Rifampin is an extremely effective antistaphylococcal agent, but \textit{Staphylococcus} frequently develop resistance to this agent when it is given alone.\textsuperscript{2} Seven previous patients with CSF shunt infections have been treated with combinations of antibiotics including oral rifampin.\textsuperscript{3,8,20,22} Rifampin penetrates CSF reasonably well and achieves concentrations which may be as high as 1000 times the MIC of \textit{Staphylococci}.\textsuperscript{5} Incidentally, rifampin is a potent inducer of hepatic enzymes and modifies hepatic metabolism and clearance of a number of drugs, including trimethoprim.\textsuperscript{9}

Both trimethoprim and sulfamethoxazole penetrate into CSF very well.\textsuperscript{1,21} Most \textit{Staphylococci} are susceptible \textit{in vitro}, although the drug combination has not been used extensively for staphylococcal infection. Synergism between rifampin and trimethoprim has been demonstrated by Kerry, \textit{et al.},\textsuperscript{12} although at very low concentrations of rifampin they demonstrated antagonism. In their studies, trimethoprim reduced the incidence of rifampin-resistant variant strains.

In our 11 patients, we have seen one clear case of sulfua allergy as a complication of antibiotic therapy. When we began using this therapy, trimethoprim was only available in combination with sulfamethoxazole. Of the two drugs in the combination, the sulfua component is most toxic, and requires monitoring of drug levels so that toxicity can be minimized. It is unclear whether sulfamethoxazole is a required component of our successful combination antibiotic therapy. If not, rifampin with trimethoprim may be effective and less toxic.

In the patient in our study with a short-term failure of therapy (Case 7), a number of factors may have been operative. First, the patient had been on chronic T/S therapy for recurrent urinary tract infections. His isolate of \textit{Staphylococcus epidermidis} was, in fact, resistant to T/S, and thus one of the initial agents he received was ineffective. Second, although \textit{in vitro} testing suggested the organism was susceptible to cephalosporins, it is becoming increasingly apparent that cephalosporin susceptibility testing with \textit{S. epidermidis} may not reflect therapeutic efficacy because of resistant subpopulations not detected by \textit{in vitro} tests.\textsuperscript{1} Finally, and probably most importantly, this child's shunt was not working well. Although hydrocephalus was reasonably controlled, the reservoir pumped sluggishly and injection of vancomycin was difficult. As a reflection of the inadequacy of this patient's antibiotic therapy, his CSF...
inhibitory and bactericidal titers were below the range we consider to be adequate.

In the series of 11 patients reported here, we have achieved long-term cures (more than 9 months) in eight, short-term cures in one, and have had one short-term treatment failure. One patient cannot be adequately evaluated since he died of unrelated causes 1 month after the completion of therapy for his shunt infection. Our cure rate is thus nine or 10 of 11 patients (82% or 91%).

Most of these shunt infections were caused by *Staphylococcus epidermidis* and most of the patients received intrashunt vancomycin plus oral T/S and rifampin. Surgical revision was required for most of the shunts because of malfunction or the presence of a foreign body. Three patients did not require surgery; two of these were cured. The third, in retrospect, had shunt malfunction which probably should have been corrected.

The advantages of an oral antibiotic regimen over an intravenous one are obvious, particularly in young children. We have not managed these children as outpatients, but that is an additional potential benefit of this type of therapy, with the child returning for daily intrashunt injections. Further modifications of this regimen might eliminate the sultamethoxazole component. The necessary duration of intrashunt vancomycin therapy is also unknown, and might be shortened to reduce the risks and inconvenience of daily intraventricular injections.

### References


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