Infected Ventriculoatrial Shunts
A Method of Treatment

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Bacterial colonization of the tubing and valve is an important complication of ventriculovenous shunting procedures for hydrocephalus. The incidence of shunt infection is reported in the range of 15 to 20%, and the resulting syndrome may take the form of acute sepsis or indolent bacteremia most often caused by coagulase negative staphylococci.4,7,9,11,13

Although occasional success has been reported in treating these infections without removal of the valve and catheter,8 use of antibiotics alone almost invariably fails to sterilize the colonized foreign body. The resulting obligatory extraction of a functioning right-sided ventriculoatrial shunt, with replacement at another site several days or weeks later, subjects the patient to increased risk of morbidity from active hydrocephalus, ventriculitis, and multiple surgical procedures.

We have successfully treated six hydrocephalic children by total removal of infected valve and catheters and immediate replacement in the same site with a sterile shunt including a Rickham reservoir.12 To prevent reinfection the surgical procedure was followed by systemic and intraventricular antibiotic coverage, the latter route in order to percolate the valve directly with high concentrations of drugs. All six patients had had persistent bacteremia without ventriculitis.

Method

Bacteriological Identification. For serial cultures, specimens of venous blood or ventricular fluid drawn by aseptic technique were dispersed in 0.5 ml aliquots into several tubes of triple soy broth and incubated at 37° C aerobically. A pour plate from 0.5 ml of the broth inoculum was also incubated aerobically, and a thioglycollate tube was set up for anaerobic culture. All specimens were examined daily for 14 days, and the broth tubes were subcultured on days 1, 7, and 14.

Staphylococcal species were identified by colonial and microscopic characteristics and by the slide method of coagulase testing using human serum. In this paper the coagulase negative staphylococcus is referred to by the species name Staphylococcus epidermidis according to the seventh edition of Bergey's Manual.1

Antibiotic sensitivity was determined with commercially prepared discs, penicillin in a concentration of 10 mg per ml and methicillin 5 mg per ml.

Surgical Procedure. Each patient originally had had a right-sided Holter valve ventriculoatrial shunt placed for the treatment of hydrocephalus. When serial blood cultures gave evidence of shunt colonization, the entire apparatus was removed and immediately replaced with a new one. The right internal jugular vein was used, and placement of the distal tubing in the right atrium was determined by electrocardiography. Postoperative skull and chest films also demonstrated proximal and distal catheter positions. In five of the six patients a Rickham reservoir was included with the ventricular catheter.

Antibiotic Regimen. Intravenous sodium methicillin (Staphcillin) alone or in combination with another appropriate antibiotic was given in a dose of 100 to 150 mg/kg per day for a 48-hour period preoperatively and for a 7-day period following shunt replacement; thereafter oxacillin (Prostaphlin) was given orally 50 to 100 mg/kg per day for an additional 7 days, to total 14 days postoperative therapy. Methicillin is a semisynthetic penicillin not degraded by penicillinase-producing (penicillin-resistant) organisms. Concurrent with systemic antibiotics, intraventricular methicillin in a dose of 3 mg/kg per day, not exceeding 90 mg per day, was injected once daily through the reservoir, diluted with 5 to 10 ml of ventricular fluid by barbotage. The initial dose was
given in the operating room, and subsequent injections were made daily for 14 days. At this time all antibiotics were discontinued and blood cultures drawn 48 hours and 96 hours later.

Case Reports
We have summarized our six cases of infected ventriculostriatal shunt in Table 1. Treatment of each case is described below.

Case 1. A boy born on June 16, 1961, had a lumbar myelomeningocele repaired at 3 days of age and a ventriculostriatal shunt placed at 5 weeks. From infancy he suffered multiple respiratory infections and failed to thrive. Three blood cultures grown in April, 1965, produced S. epidermidis, coagulase negative; there was no hepatosplomengal hypoglobulin 8.2 gm, and white cell count was 9,250 per cu mm. Ten days of intravenous penicillin and methicillin followed by long-term oral sulfafoxazole failed to eradicate the infection. Blood cultures in July, 1965, produced S. epidermidis, now resistant to penicillin; this was unsuccessfully treated with 2 weeks of intravenous chloramphenicol and methicillin, followed by 6 weeks of oral oxacillin. Ventricular fluid on December 9, 1965, was sterile with a total protein content of 31 mg%, glucose 48 mg%, and 9 white blood cells. The shunt was replaced (without a reservoir) on December 10; no thrombus was evident on the distal catheter, but S. epidermidis grew from the valve and tubing. Antibiotic coverages are noted in Table 1. During the course of treatment, daily cerebrospinal fluid specimens ranged in total protein levels from 24 to 36 mg% and glucose levels from 47 to 65 mg%.

Case 2. A boy born on December 3, 1963, had a lumbosacral myelomeningocele repaired at 15 days of age and a ventriculostriatal shunt placed at 7 weeks. On December 6, 1965, the shunt was functioning, but he was febrile. Three blood cultures grew coagulase-negative S. epidermidis, sensitive to penicillin and methicillin; hemoglobin was 9.7 gm, and white cell count was 14,300 per cu mm. Two weeks of intravenous and intraventricular methicillin failed to control the fever. Four ventricular fluid specimens during this therapy were sterile, with 0 to 13 white blood cells, protein of 20 to 69 mg%, and glucose 37 to 56 mg%. On January 7, 1966, the shunt was replaced by one with a Rickham reservoir, under antibiotic coverage. The removed shunt was cultured in four sections, all producing S. epidermidis, resistant to penicillin.

Case 3. A boy was born on October 19, 1961, and at 3 weeks of age had a shunt placed for obstruction of the third ventricle. On March 10, 1965, after a 2-year history of intermittent fever, he had blood cultures grown which showed coagulase negative S. epidermidis, moderately sensitive to penicillin. Hemoglobin was 6.7 gm, white cell count 9,100 per cu mm, and albuminuria 3+ with red and white blood cells in the urine sediment and sterile urine cultures. Blood cultures continued to be positive in spite of systemic antibiotics and revisions of the shunt. Ventricular fluid was sterile in June, 1965, protein was 8 mg%, and glucose, 45 mg%. On March 4, 1966, the shunt was completely replaced by one with a Rickham reservoir, under antibiotic coverage. The ventricular catheter cultured coagulase-negative S. epidermidis, resistant to penicillin. A postoperative left hemiparesis, due to difficult insertion of the new ventricular catheter, resolved slowly.

Case 4. A girl born on January 19, 1956, had a shunt placed for aqueduct stenosis 6 years later (January 26, 1962). Six blood cultures in February, 1965, grew coagulase-negative S. epidermidis, sensitive to penicillin and methicillin. There was a Grade 2 systolic murmur, no splenomegaly, a hemoglobin of 11.2 gm, and a white cell count of 7,400 per cu mm. Three courses of intravenous penicillin and methicillin in high doses failed to eradicate the infection. On January 28, 1966, the shunt was replaced by one with a Rickham reservoir, under antibiotic coverage. The organism was cultured from all sections of the old shunt. Two months later she developed a pneumococcal meningitis, from which she recovered with no evidence of shunt colonization. The reservoir was used for intraventricular penicillin treatment (15,000 units per day) of this meningitis.

Case 5. A boy born on August 9, 1961, had a lumbar myelomeningocele repaired at 5 days of age and a ventriculostriatal shunt
### TABLE 1  
*Treatment of infected ventriculoatrial shunts in six hydrocephalic children*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Interval, Shunt to Bacteremia</th>
<th>Shunt Level by X-ray</th>
<th>Cultures</th>
<th>Preop. Treatment*</th>
<th>Postop. Treatment*</th>
<th>Follow-Up</th>
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<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td>Systemic</td>
<td>Ventricular</td>
<td>Clinical</td>
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<td>Blood</td>
<td>CSF</td>
<td>Blood</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Shunt</td>
<td>Shunt</td>
<td>Cultures</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>I.V.: MTC &amp; CMC x2w Oral: OXA x6w</td>
<td>I.V.: MTC &amp; CMC x1w Oral: OXA x6w</td>
<td>MTC (20 mg/d) x10d</td>
</tr>
<tr>
<td>1</td>
<td>4 yrs</td>
<td>D-6</td>
<td>sterile</td>
<td>S. epidermidis (penicillin resistant)</td>
<td>S. epidermidis (PCN resistant)</td>
<td>I.V.: PCN 20 mil. u/d x2w Ventricular: MTC 30 mg/d x10d</td>
</tr>
<tr>
<td>2</td>
<td>2 yrs</td>
<td>D-6</td>
<td>sterile</td>
<td>S. epidermidis (penicillin sensitive)</td>
<td>S. epidermidis (PCN resistant)</td>
<td>I.V.: PCN 2 mil. u/d &amp; MCT x10d Oral: long-term PCN, SSX, CMC</td>
</tr>
<tr>
<td>3</td>
<td>3 yrs</td>
<td>D-6</td>
<td>sterile</td>
<td>S. epidermidis (penicillin resistant)</td>
<td>—</td>
<td>I.V.: 3 courses of PCN &amp; MCT x10d each Oral: PCN &amp; SSX between I.V. courses</td>
</tr>
<tr>
<td>4</td>
<td>3 yrs</td>
<td>D-6-7</td>
<td>sterile</td>
<td>S. epidermidis (penicillin resistant)</td>
<td>—</td>
<td>I.V.: PCN 2.4 mil. u/d x6w Oral: long-term PCN, SSX</td>
</tr>
<tr>
<td>5</td>
<td>4 yrs</td>
<td>D-6</td>
<td>sterile</td>
<td>S. epidermidis (penicillin sensitive)</td>
<td>—</td>
<td>I.V.: MTC &amp; PCN x2w</td>
</tr>
<tr>
<td>6</td>
<td>7 yrs</td>
<td>D-7</td>
<td>sterile</td>
<td>—</td>
<td>bacillus, unknown</td>
<td>I.M.: PCN 2.4 mil. u/d x6w Oral: long-term PCN, SSX</td>
</tr>
</tbody>
</table>

* MTC: Methicillin; CMC: Chloramphenicol; PCN: Penicillin; SSX: Sulfasoxazole; NTF: Nitrofurantoin; NAL: Nalidixic acid; OXA: Oxacillin; AMP: Ampicillin; x2w = for 2 weeks; mil. u/d = milliliters per day; x10d = for 10 days; mg/d = milligrams per day.
placed at 1 month. By August, 1964, he showed evidence of severe bilateral hydronephrosis and Proteus morgani urinary tract infection, but four blood cultures were sterile. A bilateral pyelo-ileal cutaneous conduit operation was performed on October 30, 1964, and pure cultures of coagulase-negative S. epidermidis were taken from each renal pelvis. One year later, 10 blood cultures produced S. epidermidis, sensitive to penicillin and methicillin; ventricular fluid was sterile. Because of continued bacteremia, the total shunt was replaced on February 19, 1966, with inclusion of a Rickham reservoir, under antibiotic coverage. S. epidermidis was cultured from the shunt that had been removed.

Case 6. A boy born on June 3, 1957, had a ventriculoatrial shunt placed for communicating hydrocephalus at age 5 months. By September, 1964, he was having recurrent bouts of fever, and the spleen was enlarged. Three blood cultures grew coagulase-negative S. epidermidis; spinal fluid was sterile. The staphylococcal bacteremia continued during 1965, and the shunt was replaced under antibiotic coverage on February 28, 1966. In this instance a bacillus of unidentified species was cultured from the infected valve.

Results

All six patients had persistent coagulase-negative Staphylococcus epidermidis bacteremia. This organism was cultured from the valve or catheter (or both) of five of the extracted shunts. The unidentified bacillus, cultured from the valve in Case 6, had never been present in blood culture and was presumably a contaminant.

Postoperatively, all patients have been free of clinical signs of shunt infection during the 5- to 9-month follow-up periods. Patient 4 developed an unrelated pneumococcal meningitis 2 months postoperatively, from which she recovered uneventfully. The six patients had sterile blood cultures at 2 and 4 days following cessation of postoperative antibiotics; four of these patients have had subsequent blood specimens drawn which have shown no growth.

The only postoperative complication was the left hemiparesis in Case 3. Although 65 mg of methicillin were instilled in the reservoir at operation, there were no seizures, pyrexia, or altered vital signs to suggest drug reaction. The hemiparesis was attributed to surgical manipulation of the ventricular catheter, and resolved slowly. No complications were definitely attributed to intraventricular methicillin. No clinical signs of cortical irritation occurred, and in those two patients whose ventricular fluid was tested during the course of therapy (Cases 1 and 2) no significant elevation of cell count or total protein occurred.

Discussion

Thromboembolic complications of ventriculovenous shunting have been well documented in recent years, and those associated with bacteremia include bacterial endocarditis, thrombus formation in the superior vena cava and right atrium, vegetations on the tricuspid valve, pulmonary emboli, and a proliferating glomerulonephritis. Chronic bacteremia may contribute to vascular occlusion and pulmonary hypertension as well as causing systemic illness, and may lead to abscess formation in major organs.

Associated with occasional wound infections, coagulase positive Staphylococcus aureus may invade the shunt system to cause acute ventriculitis or septicemia. Experience in recent years, however, has shown that organisms usually considered saprophytes may also colonize the shunt to cause an indolent bacteremia. In a series of 54 hydrocephalic patients reported by Schinke, et al., 11 had infected shunts: 2 died of S. aureus septicemia, and 9 survived with S. epidermidis bacteremia. Bruce, et al., reported 19 infections in a group of 300 patients with Holter valve shunts, and the 6 with scalp erosion over the valves had S. aureus septicemia. Organisms cultured from the other 13 included S. epidermidis, Serratia marcescens, E. coli, and Achromobacter.

If the criteria of fever and persistent bacteremia can be relied upon to indicate a colonization of the valve or catheter, our six patients had established shunt infections by S. epidermidis to 82 months following initial placement. All six had fever and anemia, but only two had persistent leukocytosis. Two had splenomegaly and transient
cardiac murmurs. Patient 3 had persistent albuminuria and hematuria with a normal pyelogram. This suggested the presence of proliferative glomerulonephritis as described by Black, but no renal biopsy was done. Ventricular fluid was sterile in the five patients tested.

Bacteremia persisted due to *S. epidermidis* is rare; only 5 of 338 cases of staphylococcal bacteremia reported by Smith, et al.,14 were caused by *S. epidermidis*. The presence of a foreign body, however, seems to enhance pathogenicity of organisms having low virulence. It is presumed that phagocytes cannot reach organisms within a shunt valve and catheter, so that the relative pathogenicity of noncoagulase-producing staphylococci is increased by this type of foreign body.

Nulsen and Becker10 have presented impressive evidence that the level of the distal catheter is a determining factor in shunt colonization. Of 17 bacteremic episodes in 82 patients, 14 involved those whose distal shunts were at the level of the seventh dorsal vertebra or below, as visualized on chest x-ray. These authors believe that a low catheter may traumatize the tricuspid valve and permit septic thrombus formation. In our present small series, however, only two patients had catheters below D-6 at the time of established bacteremia (Table 1).

Jasper and Merrill7 inferred a portal of entry in 10 of 34 cases by culturing identical species from the blood and from another site. The portal of entry was uncertain in our cases, although Case 5 proved to be harboring *S. epidermidis* in pure culture in both renal pelves 1 year prior to shunt infection. Three of the patients had myelomeningocele repairs, but these were performed several years before the shunt infection and could not be incriminated.

The technique of treatment was based on the hypothesis that a septic thrombus in the vascular system would not cause colonization of a freshly inserted sterile shunt if high levels of bactericidal drug were delivered to the site. This method permits immediate shunt replacement in a potentially infected area, thus eliminating the need for repeated ventricular taps or of subsequent shunt replacement in a less desirable site. Placement of a clean valve and tubing may allow sterilization by antibiotics which could not be achieved in a shunt system containing the debris of active bacterial colonization. An attempt to eradicate infection from a colonized shunt proved futile in the single case in which an antibiotic drug was percolated through a valve that had been left in place (Case 2).

Systemic therapy alone failed to eradicate infection in all six cases. Systemic antibiotics cross the meninges poorly in the absence of inflammation and do not reach the inside of a shunt. Callaghan, et al.14 assayed in vivo methicillin levels. With a systemic dose of 100 mg/kg per day, blood levels reached 10 mg/ml at 1 hour and were 0.5 mg/ml at 5 hours, but no drug was detectable in the cerebrospinal fluid at any time. When 3 mg were injected into the ventricle, the cerebral spinal fluid drug level was 11.2 mg/ml at 30 minutes, and still 3.4 mg/ml at 24 hours. Sensitive organisms are inhibited by 1 to 5 mg/ml in vitro.

The organism was resistant to penicillin in three of our cases. Since *S. epidermidis* can also develop resistance to methicillin,15 sensitivity testing with that drug is obligatory. The organisms cultured from the removed shunts were methicillin sensitive. Methicillin was chosen as the intraventricular drug of choice, even in those patients with penicillin-sensitive organisms, because of the diminished risk of drug reaction. Whereas penicillin is known to be irritating to cerebral cortex,16,17 our experience with methicillin and that reported by Callaghan4 indicate that it causes no apparent untoward reaction in the dosages used. The dose properly should be related to cerebrospinal fluid volume rather than body weight. However, there is no simple technique for measuring cerebrospinal fluid volume in vivo. The dose of 3 mg/kg per day produced no signs of cortical irritation in our six patients, although the ventricular systems ranged from slightly to moderately enlarged.

**Summary**

Infection was eradicated in six patients whose ventriculoatrial shunts were colonized with *S. epidermidis* by: 1) removal of the entire shunt followed by immediate replacement at the same site with a fresh one adapted to include a Rickham reservoir; and 2) systemic antibiotic coverage plus daily
intraventricular methicillin in doses of 3 mg/kg per day for 2 weeks postoperatively. This technique of drug administration was simple, and no untoward reactions occurred.

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References


