Cerebrospinal fluid shunt infections

A review of 35 infections in 32 patients

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The authors have reviewed the clinical manifestations and therapy of hydrocephalus shunt infections in 32 patients with a total of 35 shunt infections. First infections usually developed within 2 months following surgery. At the time of diagnosis, 89% of patients were febrile. Fever and cough as a symptom complex characterized the initial clinical presentation in six of 19 episodes of infection complicating ventriculoatrial (VA) shunts, as compared with none of 21 episodes in which infection complicated ventriculoperitoneal (VP) shunts. Seven of 21 infectious episodes occurring in patients with VP shunts in situ were associated with significant abdominal pain and tenderness. These patients usually had no other clinical features to suggest shunt infection. Both of these symptom complexes often led to delays in diagnosis and treatment. Causative organisms included Staphylococcus epidermidis in 21, Staphylococcus aureus in seven, Gram-negative aerobic bacilli in seven, diphtheroids in five, Streptococcus species in four, and anaerobes in three. Five infections were polymicrobial in nature. Positive blood cultures were seen in 13 of 17 infectious episodes complicating VA shunts, as compared with only three of 13 other infections. When the shunt was completely removed, with or without replacement, all 13 patients were cured. When intravenous antibiotics were administered in conjunction with incomplete shunt removal, only eight of 15 courses resulted in cure. Intraventricular antibiotics were administered in four patients and all were cured. Therapy of shunt infections with parenteral antibiotics and incomplete shunt removal is associated with an unacceptably high failure rate.

KEY WORDS • ventriculoperitoneal shunt • ventriculoatrial shunt • hydrocephalus • ventriculitis • shunt infection • cerebrospinal fluid

Infections of cerebrospinal fluid (CSF) shunts in patients with hydrocephalus are associated with significant mortality and morbidity. Despite this, a standardized therapeutic approach cannot be agreed upon. Several authors have suggested that shunt removal plus intravenously administered antibiotics is necessary for cure, while others have suggested that complete removal is not always necessary, especially when intraventricular antibiotic administration is employed in conjunction with intravenous therapy. In a large series of 84 shunt infections, Schoenbaum, et al., found that shunt removal plus antibiotic therapy resulted in cure in 28 of 30 infections, compared with only 17 of 54 infections when the entire apparatus was not removed. Wald and McLaurin reported cures in 13 of 14 patients not having complete shunt removal when intravenous and intraventricular antibiotics were given.

In order to evaluate our own experience, we reviewed the records of 32 patients with CSF shunt infections admitted to the St. Boniface General Hospital and the Health Sciences Centre between January, 1975, and May, 1981. Data on the clinical manifestations, microbiology, and treatment outcome are reported.

Clinical Material and Methods

Medical records were reviewed for all patients admitted with a primary or secondary diagnosis on discharge of CSF infection. Patients were included if their clinical symptoms were compatible with shunt infection and an organism was isolated from blood or CSF. The 32 patients (20 males and 12 females) had 35 separate
infections. Eight patients relapsed following what was considered an initial cure; therefore, a total of 43 clinical episodes could be characterized. Since these episodes were separated by an intervening symptom-free period, we chose to evaluate the clinical manifestations and therapy of these relapses as if they represented separate infections. Microbiological testing was carried out in the clinical laboratories of the St. Boniface General Hospital and the Health Sciences Centre, using standard techniques. Cerebrospinal fluid was not cultured anaerobically unless the clinical picture or Gram stain suggested that anaerobic bacteria were possible pathogens.

Treatment regimens were highly individualized but could be grouped in the following manner: Group I, episodes for which total shunt removal was performed and intravenous antibiotics administered (13 episodes); Group II, episodes for which shunt revision was performed (most often involving simple replacement of the distal catheter) and intravenous antibiotics administered (15 episodes); and Group III, episodes treated with intraventricular antibiotic administration with or without shunt removal (four episodes). For other episodes patients received intravenous antibiotics alone (two episodes), no therapy (one episode), or antibiotics for less than 48 hours before dying and were therefore considered unevaluable (two episodes). The other six episodes were considered to have an inadequate follow-up period to allow evaluation of therapeutic efficacy. Therefore, of the 43 clinical presentations, 34 treatment courses were followed for a minimum of 3 months after discontinuation of antibiotic therapy, and were included in the analysis.

Patients were considered cured if they remained afebrile and had no symptoms or signs of infection or shunt dysfunction for a 3-month period while they were not receiving antibiotics. If performed, CSF and blood cultures were negative in these patients.

**Results**

The 32 patients developed a total of 35 shunt infections. At the time infection developed, ventriculoatrial (VA) shunts were in place in 15 patients and ventriculoperitoneal (VP) shunts in 17. Three patients had shunts of other types (two ventriculocisternal and one lumboperitoneal), and three patients had more than one type of shunt. The patients ranged in age from 2 months to 70 years (median 14 years). Fourteen of the 32 patients were over the age of 20 years. The interval between surgery and diagnosis of infection was less than 4 months in 23 infections, 4 to 12 months in four infections, and longer than 1 year in eight infections (Fig. 1). Two of the four infections occurring after 2 years were secondary to scalp pressure sores.

The clinical manifestations of VA shunt infection contrasted with those of VP shunt infections. Fever and cough were prominent features of the clinical presentation of six of 19 episodes associated with VA shunts. Abdominal pain and tenderness characterized the initial clinical presentation in seven of 21 episodes associated with infections complicating VP shunts. Both symptom complexes often led physicians to disregard the possibility of shunt infection and to consider other diagnostic possibilities, since only one patient with either of these symptom complexes in these groups also had signs of inflammation along the course of the shunt or symptoms and signs of meningitis at the time of presentation. Fever was present in 34 of the 43 total episodes (79%), and was the only clinical finding in six episodes. Local signs of inflammation around the shunt reservoir or along the course of the tubing were present in 11 of the 43 episodes. Illness compatible with meningitis characterized 15 of the 43 clinical presentations. In three of these patients, there was also evidence of shunt inflammation or dysfunction. One patient presented with the distal end of the peritoneal catheter protruding through the anus. In one patient the initial clinical manifestations were not adequately documented.

Cerebrospinal fluid was aspirated and cultured in 36 instances, resulting in 34 positive specimens. Both patients with sterile cultures had *Staphylococcus aureus* infections of VA shunts. Neither had CSF pleocytosis, and both were cured with removal of the distal end of the shunt and administration of intravenous antibiotics. In nine episodes, the diagnosis of shunt infection was based on persistent bacteremia alone since CSF was not cultured. Blood cultures were performed in 17 patients with VA shunts and were positive in 13, in contrast to only three of 13 patients with VP or ventriculocisternal shunts (p < 0.01). *Staphylococcus epidermidis*, the commonest isolate, was cultured in 21 episodes. There were seven isolates each of *Staphylococcus aureus* and Gram-negative bacilli. *Corynebacterium* species were isolated five times, and *Streptococcus* species on four occasions. Three anaerobic microorganisms were isolated from two patients; both patients had VP shunts in place. There was a single isolate of *Candida* species, and on five other occasions the infections were polymicrobial in nature. In one patient in whom the distal end of the VP shunt perforated the bowel wall, two species of *Enterobacter*, two strains of *Klebsiella pneumoniae*, two *Corynebacterium* species (diphtheroids), and a...
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FIG. 2. Glucose and protein values and leukocyte count determined from cerebrospinal fluid sampled from the shunt reservoir at the time of diagnosis.

Single species of *Candida* and *Bacteroides* were recovered from the shunt reservoir. This patient therefore accounted for a large number of the Gram-negative aerobic enteric isolates.

Cell counts and protein and glucose determinations in CSF samples are shown in Fig. 2. Unlike other pyogenic bacterial infections involving the meninges, there was only a modest inflammatory reaction. Leukocyte counts were less than 100 cells/cu mm in 11 of 19 samples, with a median cell count of 76 cells/cu mm. Glucose levels were less than 50 mg/dl in only two of 11 instances, with a median of 63 mg/dl. Protein values ranged from 20 to 1004 mg/dl, with the median protein level being 56 mg/dl. On the other hand, in only one patient in whom the cell count and protein and glucose levels were determined were all within normal limits. We were unable to correlate the changes in cell count and protein or glucose values with the type of infecting organism or with the mode of clinical presentation.

The results of therapy are illustrated in Fig. 3. A wide variety of antibiotics were administered, the choice of which was usually based on the antibiotic sensitivity results. Usually a bactericidal antibiotic was chosen, and when possible combinations of agents were used to take advantage of possible synergistic or additive antibacterial activity. Therapeutic efficacy was evaluable in 34 clinical courses. Cure was achieved in all 13 patients whose therapy included removal of the entire shunt apparatus. Of these, six patients were no longer shunt-dependent and therefore did not require replacement. In five patients, shunt replacement was delayed for 2 to 5 days, and in two, hardware was reinserted at the time of the initial shunt removal.

Only eight of 15 patients were cured when the shunt was revised without removal of all components, despite concomitant systemic antibiotic administration (*p* < 0.05 compared with complete shunt removal). In seven of these patients, oral antibiotics were given to extend antibiotic therapy beyond 4 weeks, and only three patients in this subgroup were cured. In two patients, no surgery was performed. One of these was cured with intravenous antibiotic therapy followed by prolonged oral administration. The other patient relapsed despite a similar regimen. All but one patient suffering relapse did so within 6 weeks with discontinuation of antibiotics (range 2 to 16 weeks, median 5 weeks).

Direct instillation of antibiotics into the ventricle via the shunt reservoir was carried out in four patients, two of whom underwent complete shunt removal. In all four cases cure was achieved. Three patients died, two within 48 hours of diagnosis. Neither patient had surgical intervention. The first patient, a 2-month old girl, developed *Escherichia coli* ventriculitis and died within hours. The second was an 81-year-old man who developed symptoms compatible with meningitis 6 days following insertion of a VP shunt. Aspiration of the shunt reservoir grew *Streptococcus pyogenes*. Gram-negative bacilli were seen on Gram stain, but were not isolated. The third patient who died was a 55-year-old man who had a VA shunt inserted following subarachnoid hemorrhage. Because of his clinical condition, his attending physician decided to withhold active therapy and he therefore received no antibiotics.

**Discussion**

In this series, infections occurred in an older population than has been documented in other reports. This likely reflects the aging of the patient population that is maintaining functional shunts, as well as the increasing number of procedures being performed in adults. Infections were temporally closely related to surgery, lending support to the theory that bacteria most often enter the shunt system during the shunting pro-
procedure itself. At our institutions, prophylactic antibiotics were not routinely administered and unfortunately it was not possible to determine the incidence of infection since the exact number of shunt insertions and revisions was not available. Most studies, however, have suggested that the incidence of infection complicating shunt surgery ranges from 2.7% to 22%. These rates are in excess of those that might be expected following clean surgery. This high incidence may relate to the presence of a foreign body, and may be influenced by the occasional development of infection complicating local skin necrosis over the shunt apparatus or transmural migration of bowel organisms to colonize the distal end of VP shunts. Whether inoculation of the distal end of VA shunts during bacteremia is important or whether transmural migration of organisms to infect the distal end of VP shunts occurs has not been determined.

Prophylactic antibiotics have offered some benefit in uncontrolled series, but the advantage versus no prophylaxis is not statistically significant. It is unclear whether it is necessary for antibiotics to be administered in CSF levels that are bactericidal for the usual causative organisms or whether adequate tissue levels at the operative site are all that are required. In the former case, many antimicrobials currently available, in particular first- and second-generation cephalosporins, would not achieve adequate CSF levels. If, however, adequate tissue levels are all that are required, then the cephalosporins would seem ideally suited because of their range of activity against those isolates most frequently recovered from infected shunts. Early studies indicate that impregnation of Silastic elastomers with antimicrobial agents resulted in continued antibacterial activity, and it was suggested that impregnation of CSF shunting devices might provide means by which infection would be prevented. To our knowledge, this approach has not yet been applied to human studies. Even in centers where the incidence of infection is very low, the devastating consequence of infection once established in these prosthetic devices would seem to warrant consideration of antibiotic prophylaxis.

Initial presentations of shunt infection with symptoms suggestive of lower respiratory infection occurred in six of 19 episodes. This manner of presentation has not been emphasized in prior studies. The diagnosis of shunt infection, confirmed by microbiological examination of shunt reservoir aspirates or suggested by the presence of continued bacteremia, was often made when the chest x-ray film and sputum examination were negative, and often followed delays relating to the administration of short courses of antibiotics for suspected respiratory infection. The cause of these symptoms remains unclear, although the possibility of multiple small pulmonary emboli originating from the catheter tip is perhaps most likely. One patient had pulmonary embolization, confirmed on lung scanning, in the absence of any evidence for peripheral deep-vein thrombophlebitis. However, lung scans were infrequently performed in this patient population. When the initial patient contact was with a physician unfamiliar with complications of VP shunts, patients presenting with abdominal pain may have had inappropriate or delayed therapeutic intervention. Our observations are similar to those of Hubschmann and Countee, who reported seven patients with VP shunts presenting with abdominal pain without central nervous system symptomatology. The primary clinical diagnosis in all their patients was not that of an infectious complication of the shunting procedure. In all patients, acute appendicitis was considered in the differential diagnosis and in three patients laparotomy was performed.

It is apparent from our review that although treatment regimens were not standardized, an unacceptably high failure rate resulted from lack of surgical intervention, and from only partial revision plus intravenous antibiotic therapy. On the other hand, cure was achieved in all patients in whom the entire shunt apparatus was removed. Delayed shunt replacement was undertaken in six patients, and in six others who were no longer shunt-dependent replacement was not necessary. When a decision was made to remove the infected shunt, the decision to delay replacement of the shunt or to replace it immediately was usually based on clinical assessment of the patient rather than upon the results of microbiological studies. Those patients with symptoms or signs of intracranial pressure (ICP) usually had their shunts replaced immediately. External drainage was performed in only one patient. If there was no evidence of increased ICP, the decision was usually made to delay replacement of the shunt for as long as possible. In 12 of 16 patients in whom the shunt was removed, delayed replacement was considered feasible. In six of these patients, the need for another shunting procedure was reexamined and it was thought that there were no longer indications for shunting. In six other patients symptoms and signs of increased ICP developed between 2 and 5 days after the removal of the shunt, and the shunts were subsequently replaced. It has been suggested that immediate replacement may be possible when organisms of low virulence, for example S. epidermidis or Corynebacterium sp., are involved. There is, however, little information to support this approach.

In two patients who had infected nonfunctioning VA shunts the distal tubing was left in situ. In one of these patients, blood cultures were performed prior to the institution of antibiotic therapy, and were positive for S. epidermidis. In the second patient, infection was discovered at the time of surgery. Blood cultures were not performed before antibiotic therapy was started. In both of these patients, retained nonfunctioning shunt parts did not seem to interfere with the efficacy of the intravenous antibiotics.

Because of small numbers, analysis did not yield
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enough information to compare shunt removal with intraventricular antibiotic therapy alone. Wald and McLaurin\textsuperscript{14} indicated that intraventricular antibiotic administration on a once-daily basis usually led to antimicrobial levels in the CSF much in excess of the minimum bactericidal concentration of most commonly occurring organisms. In their study, 13 of 14 children were cured without requiring surgical intervention after receiving methicillin, nafcillin, ampicillin, gentamicin, or cephalothin, alone or in combination, intraventricularly as well as intravenously. Unfortunately no side-by-side comparison with other modes of therapy was made. Since the CSF penetration of most antibiotics is proportional to the degree of meningeal inflammation, the meager inflammatory response demonstrated by our patients would suggest that adequate CSF levels might be infrequently achieved with intravenous antibiotic administration alone.

When infection is associated with shunt dysfunction, the best mode of therapy appears to be complete shunt removal rather than revision. In two patients with VA shunt infections with negative reservoir cultures and lacking CSF pleocytosis, replacement of the distal end of the shunt was curative. This may represent a subset of patients in whom incomplete removal is possible, perhaps because only the venous end of the shunt has been colonized by transient bacteremia. However, further studies of this particular group of patients are needed. When the shunt is functional or when for technical reasons replacement of the shunt system is difficult, a lesser initial success rate might be accepted. In such patients, intraventricular antibiotics should be administered when possible. However, if emphasis is placed solely on the intraventricular administration of antibiotics and inadequate antibiotic dosages are given by the intravenous route, external infection around the shunt might lead to persistence of infection.\textsuperscript{8} In our experience, seven patients with peri-shunt infection were treated with shunt revision only. In four other cases, the infection was eradicated with concurrent use of intraventricular and intravenous antibiotics, and cure rates in this group were not different from those in patients without external shunt infection; thus, the coexistence of peri-shunt infection does not seem to constitute an added risk factor.

The determination of CSF antibiotic concentrations and bactericidal levels as an index of therapeutic efficacy is of undetermined value. However, it would seem reasonable to maintain a bactericidal level in the CSF at least eight times that required to kill the organism. Analysis of our data does not permit conclusions regarding which specific antibiotics would be most effective, as the therapeutic courses were so variable. Some general comments can be made, however. One should select an antibiotic with bactericidal activity, such as a semisynthetic penicillin or vancomycin, despite the fact that the former group of drugs may be becoming less useful as the incidence of resistance increases in S. epidermidis. No controlled data exist on the efficacy of combination antibiotic regimens, such as aminoglycoside plus semisynthetic penicillin or aminoglycoside plus vancomycin, in treating CSF shunt infections. The potential efficacy of combination agents, especially when given intraventricularly, deserves further study. Last, the addition of rifampin to conventional antistaphylococcal antibiotics has been shown to increase the serum bactericidal and CSF bactericidal levels in cases of endocarditis and cerebral shunt infection caused by S. epidermidis.\textsuperscript{1} Although a multicenter study is underway to assess rifampin combinations in S. epidermidis prosthetic valve endocarditis, to our knowledge no similar work has been directed against shunt infection.

The approach to management of CSF shunt infections requires consideration of a large number of variables. Such factors as the clinical status of the patient, the virulence and antimicrobial sensitivity of the infecting organism, the functional status of the shunt, and the accessibility of the shunt reservoir to repeated needle aspiration necessitate an individualized approach to each patient. Because of this need to individualize therapy, it is unlikely that large prospective studies will be done to comparatively evaluate the various treatment modalities outlined above. Given this limitation, our and other retrospective studies may provide some useful guidelines for therapy. It is hoped that application of these principles by neurosurgeons in cooperation with microbiologists and infectious disease consultants can improve the standard of care in patients with infections of CSF shunting devices.

References

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