External ventricular drain infections are independent of drain duration: an argument against elective revision


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Object. The authors explored the relationship among the duration of external ventricular drainage, revision of external ventricular drains (EVDs), and cerebrospinal fluid (CSF) infection to shed light on the practice of electively revising these drains.

Methods. In a retrospective study of 199 patients with 269 EVDs in the intensive care unit at a major trauma center in Australasia, the authors found 21 CSF infections. Acinetobacter accounted for 10 (48%) of these infections. Whereas the duration of drainage was not an independent predictor of infection, multiple insertions of EVDs was a significant risk factor. Second and third EVDs in previously uninfected patients were more likely to become infected than first EVDs. An EVD infection was initially identified a mean of 5.5 ± 0.7 days postinsertion (standard error of the mean); these data—that is, the number of days—were normally distributed.

Conclusions. This pattern of infection is best explained by EVD-associated CSF infections being acquired by the introduction of bacteria on insertion of the drain rather than by subsequent retrograde colonization. Elective EVD revision would be expected to increase infection rates in light of these results, and thus the practice has been abandoned by the authors’ institution.

KEY WORDS • ventriculostomy • Acinetobacter • meningitis • ventriculitis • external external ventricular drain

EXTERNAL ventricular drains are a vital component of emergency neurosurgical practice. They represent the mainstay in the emergency treatment of hydrocephalus, and after being connected to an external transducer they allow measurement of intracranial pressure. The Brain Trauma Foundation guidelines for the management of severe head injury6 indicate this device as the most accurate, reliable, and cost-effective intracranial pressure monitor. Drainage of CSF reduces intracranial volume and thus is one of the therapeutic tools available for the treatment of intracranial hypertension.

The most common complication of external ventricular drainage is that of CSF infection.16 Mayhall and coworkers20 found a strong relationship between the amount of time an EVD remained in situ and the risk of drain-associated infection. They recommended elective revision of an EVD on Day 5 postinsertion to reduce this risk. Conversely, authors of other larger studies have shown that the amount of time an EVD resides in a patient has no effect on the risk of infection.10,34 Furthermore, data from a randomized controlled trial37 revealed no difference in the infection rate between one group of patients undergoing elective EVD revision every 5 days and another group with EVDs left unchanged unless clinically indicated. Despite this evidence, elective revision of EVDs with the aim of preventing CSF infection remains a common practice.

Here we describe a retrospective study of nosocomial EVD-associated CSF infections. We evaluate the roles of the amount of time a catheter remained inserted and multiple catheter insertion as predictors of infection together with the timing of infection relative to insertion. We also discuss the practice of electively revising EVDs in light of our findings.

Clinical Material and Methods

Patient Population

The Alfred Hospital is a 340-bed teaching hospital and one of two Level I trauma centers in Victoria, Australia. Patients who had undergone placement of EVDs as part of
their treatment between October 2002 and May 2004 were identified retrospectively from the database of the ICU. Data were collected from the ICU and Alfred Hospital Infection Control and Hospital Epidemiology Unit databases (Powerchart, version 8.1, Cerner Corporation) and from patient records. For each patient we recorded age; sex; GCS score at presentation; underlying diagnosis; and the presence or absence of an open skull fracture, diabetes mellitus, and bacteremia within 14 days of EVD insertion. The outcome measure of death prior to discharge was also recorded.

Insertion of EVDs

External ventricular drains (TraumaCath ventricular catheter, Integra Neurosciences) were inserted using an aseptic technique usually via a frontal twist drill craniotomy; when placement occurred in the operating room, drains were inserted via a frontal bur hole or the craniotomy that had been made to treat the underlying condition. The EVDs were tunneled under the skin for approximately 5 cm and connected to a Becker external drainage and monitoring system (Medtronic, Inc.). Prophylactic antibiotics were not routinely prescribed. We recorded the experience level of the surgeon placing the drain, site of insertion, number of the EVD (that is, the first, second, third, fourth, or fifth drain placed in the patient), and amount of time the EVD remained in place.

Cerebrospinal Fluid Infection

Cerebrospinal fluid specimens were collected thrice weekly for microbiological examination and at other times as clinically indicated. Infection was defined using criteria modified from those of the Centers for Disease Control and Prevention. A culture of commensal organisms without affecting the composition of the CSF, evidence of meningism or sepsis, or the perceived need for antibiotic therapy was indicative of colonization of the EVD rather than a true infection. The duration of time from EVD insertion to the development of infection, and the infecting organism were recorded.

Statistical Analysis

Data were entered into Microsoft Excel (Microsoft Corporation) and analyzed using SPSS (version 11.0, SPSS, Inc.), and SAS software (version 8.2, SAS Institute, Inc.). Univariate analysis was performed using chi-square tests for equal proportion and Student t-tests, and the results were validated using a Wilcoxon rank-sum test and logistic regression. Multivariate logistic regression models were developed using a stepwise selection procedure and validated using a backwards elimination procedure. Results are presented as ORs (95% CIs), with a two-sided probability value of 0.05 indicating statistical significance.

Results

Two hundred patients were retrospectively identified as having undergone insertion of an EVD while in the ICU. One patient was transferred to another hospital before the EVD was removed and therefore was excluded from the study, leaving 199 patients. These patients had a mean age of 41 years (range 15–87 years) and 64% were male. Seventy-four percent had traumatic brain injuries, 19% of which were open skull fractures. Most of the remaining patients presented with spontaneous subarachnoid or intraventricular hemorrhage. No one in the study had a primary diagnosis of intracranial or spinal sepsis, or recorded bacteremia within 14 days of admission. The presenting consciousness level varied across the full range, but the median GCS score was 6. There were 269 EVDs, with each patient having between one and five drains (mean 1.35 drains). External drainage was continued for a mean of 8.2 days (range 0–49 days). Each EVD remained in place for a mean of 6.2 days (range 0–19 days).

Incidence of Infection

Twenty-one patients (10.6%) had nosocomial EVD-associated CSF infections. Another five patients had CSF cultures positive for infection but no other evidence of infection and were considered to have colonized EVDs. Diabetes mellitus, presenting GCS score, patient age, and the presence of an open fracture were not significant risk factors for infection.

The total duration of external drainage was twice as long in infected patients as in uninfected patients (14.9 days compared with 7.4 days, p < 0.0001), and infected patients had received significantly more EVDs than the uninfected patients (2.2 compared with 1.2, p < 0.0001). An underlying diagnosis of trauma (52% compared with 77%, p = 0.02) and male sex (38% compared with 67%, p = 0.01) were less common in infected than in uninfected patients (Table 1). A multivariate logistic regression model identified the number of EVDs and sex as the only statistically significant predictors. Each additional EVD increased the risk of infection fourfold (OR 4.6, 95% CI 2.3–9.1, p < 0.0001; Table 1), whereas female patients were three times more likely to be infected than male patients (OR 3.4, 95% CI 1.2–9.7, p = 0.02).

Multiple EVDs

Patients identified as having infected EVDs often underwent drain revision to facilitate treatment of the infection. Those with resistant infection sometimes received EVDs to allow the administration of intrathecal antibiotics. Other drains were revised electively or for blockage. To establish whether the association between multiple EVD insertion and infection was one of cause or effect, an analysis of infection in individual EVDs was conducted. For the purpose of this analysis, 16 drains that had been placed in previously infected patients were excluded, leaving 253 previously

<p>| TABLE 1 |</p>
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<th>Results of logistic regression analysis of risk factors for nosocomial EVD-associated CSF infection*</th>
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<tr>
<td><strong>Factor</strong></td>
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<tr>
<td>no. of drainage days</td>
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<tr>
<td>no. of EVDs</td>
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<tr>
<td>presence of trauma (%)</td>
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<td>male sex (%)</td>
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* NS = not significant.
uninfected EVDs. There was only one previously uninfected fourth EVD, which was grouped with the five uninfected third EVDs. The EVD number (first, second, and so forth) had a significant effect (p = 0.007) on the infection rate, with subsequent drains more likely to become infected than first EVDs (Table 2). Thus, multiple EVD insertion seems to be causatively associated with an increased infection rate.

Insertion of EVDs

Two hundred six EVDs were placed by trainees and 47 by consultants. One hundred thirteen drains were placed while the patient was in the emergency department, 67 while in the ICU, 70 while in the operating room, and three while on the neurosurgical ward. There was no significant difference in either the skill level of the person who had inserted the drain or the place where the insertion had been performed in comparing infected with uninfected EVDs. The amount of time each EVD had remained in place was not a significant risk factor for infection.

Timing of Infection

Most EVD-associated infections were identified while the subject drain was in place. In four patients infection was identified by lumbar puncture between 1 and 3 days after removing the drain associated with that infection and before any additional EVDs were inserted. A CSF infection first became evident a mean of 5.5 days postinsertion; the number of days were normally distributed around this mean.

An EVD was removed not only in response to infection but also electively, because of blockage, and when no longer required. Thus, the number of EVDs at risk of infection decreased with each day postinsertion. To facilitate calculating the daily incidence of infection, we considered infections identified on lumbar puncture as occurring on the last day that the EVD had remained in place. No correlation was found between the day postinsertion and the daily incidence of infection. The mean daily incidence of infection up to and including Day 5 (1.20%) was not significantly different from that after 5 days (1.12%).

Overall Outcome

Overall, 27% of the patients in this study died prior to discharge. Neither nosocomial EVD-associated CSF infection nor multiple EVD insertion was associated with an excess mortality rate. A low consciousness level on presentation and older patient age were both highly significant risk factors for death. Patients with trauma had a significantly better outcome than those with other pathophysiologies, and the duration of drainage was significantly lower in patients who died (Table 3).

Microbiological Factors

Acinetobacter was the most common infecting organism and was cultured from 10 of 21 infected patients. The incidence of other infecting organisms is shown in Table 4. The collected data were examined for any differences between patients who acquired Acinetobacter CSF infections and other infected patients. Acinetobacter infections occurred significantly earlier after EVD insertion than other infections (3.8 compared with 7 days, p < 0.05). No other significant differences were identified—in particular, no difference in the insertion site or the number of the EVD.

Two cultures of streptococcus and one each of diphtheroids, coagulase-negative staphylococcus, and corynebacterium were not associated with any other features of central nervous system infection and were regarded as representing EVD colonization.

Discussion

Infection Rate

Among this series of 199 patients with EVDs, 21 had an EVD-associated CSF infection. We found 34 previous studies in the literature, which included 467 infections in 6787 patients. Among this series of 199 patients with EVDs, 21 had an EVD-associated CSF infection. We found 34 previous studies in the literature, which included 467 infections in 6787 patients. These numbers represent an overall infection rate of 6.9%, which lies within the published range from 0, reported by four separate groups, to 22%. The mean rate of 10.6% (95% CI 6.4–14.8%) in the present study is slightly above average but well within the reported range.

In a review of this literature, Lozier et al. considered the variability in the definition of infection a major factor in the wide variation of quoted infection rates among the studies. For example, Lundberg reported that none of 105 patients had clinically significant CSF infections, although 13 had positive CSF cultures. In contrast, Mayhall and coauthors reported an infection rate of 11%, although only 11 of 172 patients in that study had positive CSF cultures. We have endeavored to use the best available definition of EVD-associated CSF infection; however, our parameters allow a higher proportion of patients with positive CSF cultures than those used in some previous studies. This factor may help to explain the relatively high infection rate in the current study.

Microbiological Factors

Among 467 cases of EVD-associated CSF infection in

### TABLE 2

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<th>Likelihood of EVD-associated infection, according to the drain placed</th>
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<td>Factor</td>
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<tr>
<td>no. of EVDs</td>
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<tr>
<td>previously uninfected EVDs</td>
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<td>no. of new infections</td>
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* p = 0.007.

### TABLE 3

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<th>Predictors of death prior to discharge</th>
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<td>Factor</td>
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<td>presence of trauma (%)</td>
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<td>GCS score</td>
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<td>age (yrs)</td>
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the literature, microbiological data are supplied for 288,1,13–15, 19,20,24–27,31–34,36–39 The most common infecting organism is coagulase-negative staphylococcus, accounting for 47% of cases. *Staphylococcus aureus* (14%) and *Klebsiella* (6.6%) are the next most common, with *Acinetobacter* (5.6%) representing the fourth most common infecting organism. Data in the present study are unusual in that *Acinetobacter* accounted for almost half of the infections. This aerobic gram-negative coccobacillus is a normal skin commensal, like many of the other common organisms causing EVD-associated CSF infection. *Acinetobacter* was endemic in the ICU at The Alfred Hospital at the time of the study. An outbreak of 25 cases of nosocomial meningitis with *Acinetobacter* occurring in a neurosurgical ICU has been reported.20

**Timing of the Incidence of Infection**

The normal distribution of the number of days postinsertion on which infection first occurred in the present study is remarkably similar to that in the much larger series reported on by Holloway et al.20 and as reanalyzed by Lozier et al.16 Authors of two other studies found that all infections occurred between 2 and 11 days after insertion.12,21 If only the first 5 or 6 days of such a distribution are examined, a strong relationship between the duration of drainage and the infection rate is revealed.22 Such a relationship was found by Paramore and Turner.23 In their study, however, no infections occurred after Day 6 postinsertion, and thus an alternative explanation for the timing of the incidence of infection in that series is, as in the present study, a normal distribution around a mean of approximately 5 days. Instead of indicating that infection is related to the duration of drainage, this finding suggests that infections are inoculated at the time of EVD insertion with a normally distributed incubation period around a mean of approximately 5 days.

In contrast, a series of 100 patients with long-tunnel EVDs had four infections, all of which occurred after 16 days of drainage.14 Data from several other series have shown the majority of infections to occur after Day 10 postinsertion.17,26,27 Although Winfield and colleagues series of 205 patients revealed the majority of infections to occur between Days 2 and 11 after insertion, there was a late peak of infection around Day 20. The present study includes too few EVDs remaining in situ for this amount of time to identify such a late peak of infection.

**Duration EVDs Remain Inserted**

Data in this study has demonstrated no evidence of a relationship between the amount of time that an EVD remains in situ and the risk of EVD-associated CSF infection. Results of a multivariate analysis showed that the total duration of drainage was not a significant independent risk factor for infection. Similarly, the amount of time each EVD remained inserted was also not a significant risk factor for infection. Furthermore, we found no significant relationship between the day postinsertion and the daily incidence of infection. Finally, the timing of the incidence of infection as discussed previously is not consistent with a relationship between the duration of drainage and infection risk.

As discussed in a recent review,16 previous authors are fairly evenly split between those who find an effect of drainage duration on EVD-associated CSF infection14,17,19–21, 24,26,27,29–38 and those who find none.4,9,10,15,23,25,31–34,36,39 Data from the two largest series in the literature, both by Sundbärg and colleagues33,34 and with 1586 patients between them, revealed prolonged drainage not to be a risk factor for infection. The clear association between the duration of drainage and the infection rate shown by Mayhall et al.20 represents a stark contrast.

**Multiple EVDs**

Our data reveal a clear effect of multiple EVDs on the infection rate. Sundbärg et al.14 found 60% of infections to occur after an EVD revision. Rebuck and colleagues35 found multiple EVDs to be a significant risk factor for infection. In the only randomized controlled trial in the field, Wong et al.37 found a higher infection rate in a group with multiple EVDs compared with that in another group with just one EVD, although this difference did not reach significance. In three other studies, however, the authors found multiple EVDs not to be a significant risk factor for infection.10,19,39

**A Unifying Hypothesis**

An EVD-associated CSF infection may be acquired at the time of EVD insertion through the inoculation of skin organisms into the previously sterile intracranial compartment. Further retrograde colonization risks result from: 1) the continuing externalization of the CSF space, which is opened from time to time for CSF sampling; and 2) the creation of a potential route of entry of cutaneous organisms around the outside of the EVD. Whereas the first risk is independent of the duration of drainage and increased by multiple EVD insertions, the second is dependent on drainage duration and has an uncertain relationship with multiple EVD insertions. Differences in the relative magnitude of each risk may explain the differences among series. In the present study the inoculation effect was preeminent. A weak retrograde colonization effect may explain the late infections seen by Khanna et al.14 and Winfield et al.,46 and a stronger effect may explain the strong association between drainage duration and infection rate reported by Mayhall and colleagues.20

**Elective Revision of EVDs**

The practice of electively revising EVDs at or around 5 days after insertion to prevent EVD-associated CSF infection was proposed by Mayhall and colleagues.20 Indeed, it is only when the retrograde colonization risk predominates that this approach has merit. Elective EVD revision increas-
es the patient’s exposure to an inoculation risk, but there is doubt about whether the retrograde colonization risk can be modified by elective revision; can placing a new EVD reset the clock for retrograde colonization of the CSF space along the externalized CSF column or around the outside of the EVD? Although this theoretical argument has appeal, the evidence, such as it is, does not support it. The randomized controlled trial conducted by Wong and colleagues demonstrated no benefit from elective EVD revision at Day 5, and although not statistically significant, infections were more common in the group with elective EVD revision. An analysis of the Traumatic Coma Data Bank revealed a higher infection rate in centers implementing a policy of elective EVD revision (16.8%) than in centers that did not (7.8%), a difference that closely approached significance (p = 0.054).

Conclusions
In analyzing this literature, two groups have found no evidence to support the practice of prophylactic EVD revision. Whereas Lozier et al. concluded that it remained a treatment option, the Infection in Neurosurgery Working Party of the British Society for Antimicrobial Chemotherapy recommended against the practice. Data in the current study have shown that multiple EVD insertion is causatively associated with an increased infection rate. This finding strongly suggests that elective revision of EVDs may actually increase the risk of EVD-associated CSF infection. Our institution has abandoned the practice in light of these results.

Acknowledgment
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