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Cerebrospinal Fluid Flow Dynamics in Children with External Ventricular Drains

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Fifty-five children had 64 external ventricular drains (EVDs) placed predominantly (95%) for cerebrospinal fluid (CSF) shunt infections. In 9 children, a computer monitoring system measured the CSF output each second continuously for up to 24 hours. The monitoring was repeated daily for up to 9 days. The state of arousal of the patients was recorded simultaneously. In all children, daily EVD outputs were related to age, sex, weight, method of establishing the EVD, height of the drip chamber, time since insertion, and type of infecting organism. Computer monitoring revealed wide fluctuations in flow rate, with peak rates frequently >20 ml/h and periods of flow arrest. These changes were usually associated with increased arousal, but also occurred with sleep. The mean EVD flow rate for all children was 6.3 ml/h. EVD output increased with age and weight. EVD output decreased with Gram-negative or multiple-organism infections and with elevation of the drip chamber. Resolution of the infection, sex of the patient, and method of establishing the EVD had no effect on output. These results predict that CSF production increases with brain growth in humans; that CSF production is depressed by Gram-negative and multiple-organism infections; that implanted CSF shunts with standard valves flow at equivalent rates to an EVD in the supine position; and that the CSF drainage requirements in this group are approximately equal to their EVD outputs. (*Neurosurgery* 28:242–250, 1991)

Key words: Cerebrospinal fluid production, Cerebrospinal fluid shunts, External hydrocephalus, Ventricular drainage

INTRODUCTION

External ventricular drainage is used most often in children as an interim measure in the treatment of cerebrospinal fluid (CSF) shunt infection (2, 10, 17, 23, 24). It is less frequently used in patients with head injuries and raised intracranial pressures who have an indwelling ventricular catheter that also serves as a pressure monitor (22). It is now rarely used in the treatment of intraventricular hemorrhage in premature infants or as a temporary CSF diversion method for hydrocephalus secondary to posterior fossa tumors.

Although it is a treatment familiar to all neurosurgeons, the very simple external ventricular drain (EVD) can provide very important information about CSF production and absorption, the in vivo performance of CSF shunts, the CSF drainage requirements of hydrocephalic patients, and design criteria for new CSF shunts. The measurement of the minute-to-minute dynamic changes in EVD flow required the development of a computer monitoring system on which the patient's activity level could also be recorded. The factors that affected the background, or steady-state EVD flow, on which the dynamic changes were superimposed required the analysis of the 24-hour EVD outputs of a large group of patients by means of a chart review.

METHODS

External ventricular drains were established by either the externalization of the distal portion of a CSF shunt system or by the removal of the shunt system and insertion of a new ventricular catheter. The ventricular CSF was collected in a closed sterile system, typically a drip chamber and collecting bag (Codman External Drainage System, Codman Corporation, Randolph, Massachusetts; or Cordis External Ventricular Drainage Set, Cordis Corporation, Miami, Florida). The drip chamber was placed at a specified height above the middle of the head. The patients were confined to bed, except for brief intervals at which time the collecting tube was occluded. The fluid in the collecting system was sampled daily for evidence of infection. The patency of the system was determined frequently by examining the drip chamber.

Computer monitoring system for dynamic external ventricular drain flow

To measure the dynamic changes in EVD flow, a computer monitoring system was developed (Fig. 1). The drip chamber and collecting bag were suspended from the weighing hook of a digital balance (Mettler PJ3000, Mettler Instrument Corporation, Hightstown, New Jersey). The balance was attached to a platform that could be raised and lowered so that the drip chamber was at the appropriate height. The balance was equipped with bidirectional interface and connected to an IBM-compatible computer (Compaq Deskpro 286, Compaq Computer Corporation, Houston, Texas) by means of an RS232 port.

The weight of the collecting system plus the accumulated CSF was measured every second to the nearest 0.01 g. A mean weight for each minute was determined. Flow rates were calculated from the difference in mean weights in consecutive minutes.

So that the relationship between level of arousal and flow rate could be determined, an interactive display on the computer system was developed. Arousal was graded from low to high in four categories: asleep, awake, crying, and nursing care. The medical staff could enter a change in functional status by simply pressing one of four corresponding function keys. The functional status was displayed and assumed to be unchanged unless a different status was entered.

The EVD flow data were displayed on the computer screen. In addition to the functional status, it included the weight of the CSF, the calculated flow rate for each minute, the weight and flow rates for the previous 15 minutes, and the hourly output for the previous 12 hours. This helped in determining whether the EVD was patent and also with recording the EVD output in the hospital chart. The program could be paused if the collecting system was manipulated and the reason for the pause recorded with the data. The data were stored on disk for subsequent analysis. Four patients from the Hôpital Enfants Malades in Paris and 5 from the Hospital for Sick Children in Toronto were monitored in this way.

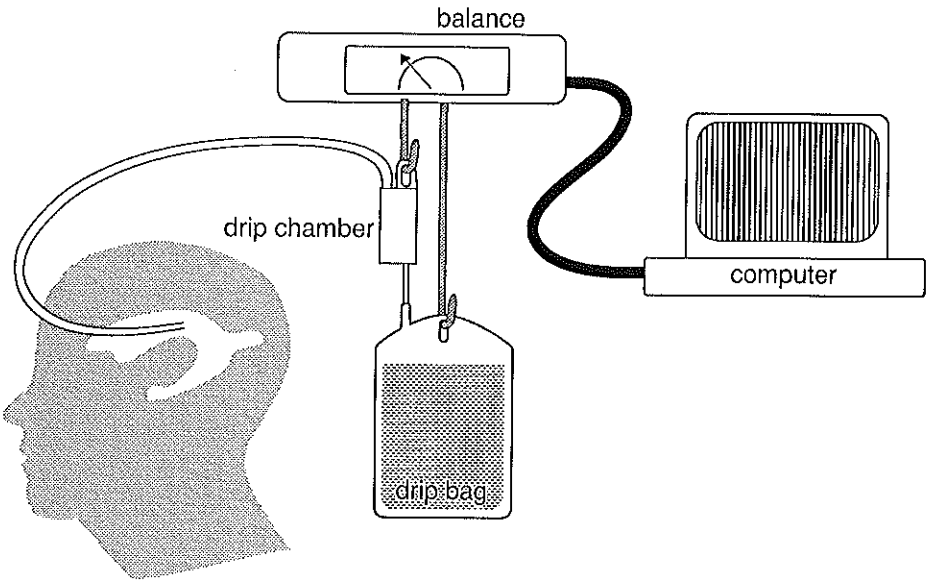

FIG. 1. Schematic of the computer monitoring system. The drip chamber and collecting bag are suspended from a balance that records the weight each second and transmits the data to the computer. An interactive display allows the entry of the patient's functional status as well as the display of the current flow rate and previous 12-hour outputs.

TABLE 1
Causes of Hydrocephalus

Cause	Number of Patients	Percentage
Myelomeningocele	19	34.5
Neoplasm	8	14.5
Intraventricular hemorrhage	7	12.7
Post-infection	5	9.1
Dandy-Walker malformation	4	7.3
Arachnoid cyst	2	3.6
Aqueduct stenosis	1	1.8
Posttraumatic	1	1.8
Vein of Galen aneurysm	1	1.8
Other causes	5	9.1
Unknown	2	3.6

Hospital record review of steady-state external ventricular drain flow

To determine which factors influenced EVD output in the steady state, we reviewed retrospectively the hospital records of all children who had either a shunt externalized or an external drain placed from 1984 to 1988 at the Hospital for Sick Children in Toronto. The records contained information on the output of the EVDs under fluid balance calculations as well as the height of the drip chamber. The amount of fluid drained was measured and recorded at variable intervals, usually every 8 hours and at least every 24 hours. The measured output was determined by estimating the volume in the collecting bag according to its scale, or by emptying the contents into a graduated cylinder when the bag was emptied or changed.

Because of the variability of the timing of the recorded outflows, 24-hour totals were used, as this was standard throughout. Measurements were considered unusable if the period of drainage was <24 hours, if the information was improperly recorded, or if the EVD was clamped, flushed, or thought to be nonfunctional. The 24-hour measurements in the 9 patients who underwent computer monitoring were included in the steady-state analysis.

Statistical analysis

The effect of individual variables on steady-state EVD output was tested with either linear regression or analysis of variance. The model of steady-state EVD output was constructed by multiple linear regression analysis. Those variables having no significant effect on the model were excluded.

TABLE 2
Infecting Organisms

	Number of Patients	Percentage
Gram-positive		
Staphylococcus epidermidis	36	40.9
Staphylococcus aureus	14	15.9
Enterococcus	5	5.7
Other streptococcal species	6	6.8
Gram-negative		
Escherichia coli	7	8.0
Klebsiella	5	5.7
Pseudomonas	1	1.1
Proteus	1	1.1
Morganella	1	1.1
Haemophilus influenzae	3	3.4
Fungi	4	4.5
Candida	4	4.5
No organism identified	5	5.7
Totals	88[a]	100

[a] Fifteen patients were infected with two or more organsims.

RESULTS

Nine patients underwent computer monitoring. Forty-six patients had undergone external drainage during the period from 1984 to 1988. Of this group, 5 patients had 2 periods of external drainage, and 2 had had 3 periods of drainage, all for recurring shunt infections. This produced a total of 64 periods of external drainage for study. Each period of drainage was treated as an independent measurement for data analysis.

The causes of the hydrocephalus for the entire group are shown in Table 1. Hydrocephalus in association with myelomeningocele was by far the most common cause at 34.5%. Sixty-one of the 64 periods of external drainage were for infected shunts. One EVD was placed after intraventricular rupture of an abscess before placing a ventriculoperitoneal (VP) shunt; one was placed after a failed attempt to place a

TABLE 3
External Ventricular Drainage

Parameter	Mean (±SE)	*N*	Median	Range
Age (yr)	4.51 (±0.7)	55	2.61	0.04–18.4
Sex				
Male	32			
Female	23			
Weight (kg)	15.4 (±1.8)	64	10.95	2.3–65.7
Duration of drainage	16.4 (±1.2)	62	13.5	4–44
Number of usable 24-h measurements per patient	11.2 (±0.9)	64	8.5	1–39
Height of drain (cm above center of head)	3.9 (±0.22)	637	5	−10–20
24-h output				
Total (ml)	152 (±4.2)	717	122	2–533
Per hour (ml)	6.33 (±0.173)	717	5.08	0.08–22.2

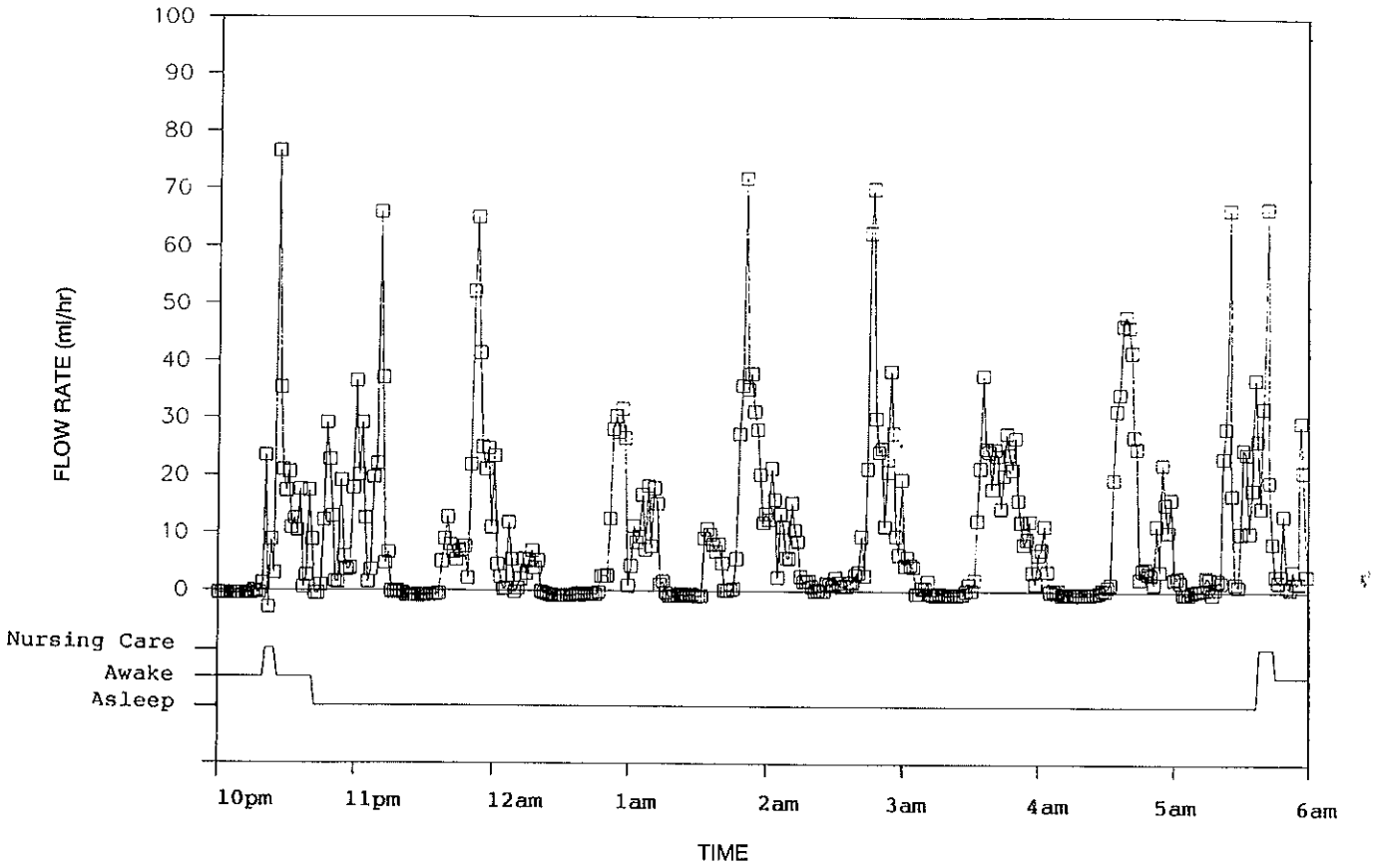

FIG. 2. Minute-to-minute variation in flow rate in a 1-year-old child with an EVD for abdominal wound dehiscence. The average flow rate for this 8-hour period is 10 ml/h. The height of the EVD is 10 cm. There are periodic increases in flow rate to approximately 70 ml/h. These occur during sleep and last approximately 20 minutes. They are followed by arrest of flow for an approximately equal time period.

VP shunt with subcutaneous emphysema; and one was placed for hydrocephalus associated with presumed tuberculous meningitis.

Table 2 shows the distribution of infecting organisms. The most common infecting organisms were Gram-positive. *Staphylococcus epidermidis* was the most frequent, accounting for 40.9% of the organisms identified. Fifteen patients were infected with more than one organism. The patients were treated with a variety of antibiotic regimens according to the identity and sensitivity of the infecting organisms.

Twenty-five patients had external ventricular drains. Thirty-four patients had the peritoneal end of the shunt externalized. One patient with bilateral VP shunts had both peritoneal catheters externalized. Two patients had one of two VP shunts externalized. In one patient, the method of establishing external drainage was not recorded.

The median age of the patients was 2.61 years and ranged from a few days to 18 years (Table 3). There were 32 boys and 23 girls. The median duration for the EVD to be in place was 13.5 days, with a minimum of 4 and a maximum of 44 days. The median number of usable 24-hour measurements per patient was 8.5. The average height of the EVD was 3.9

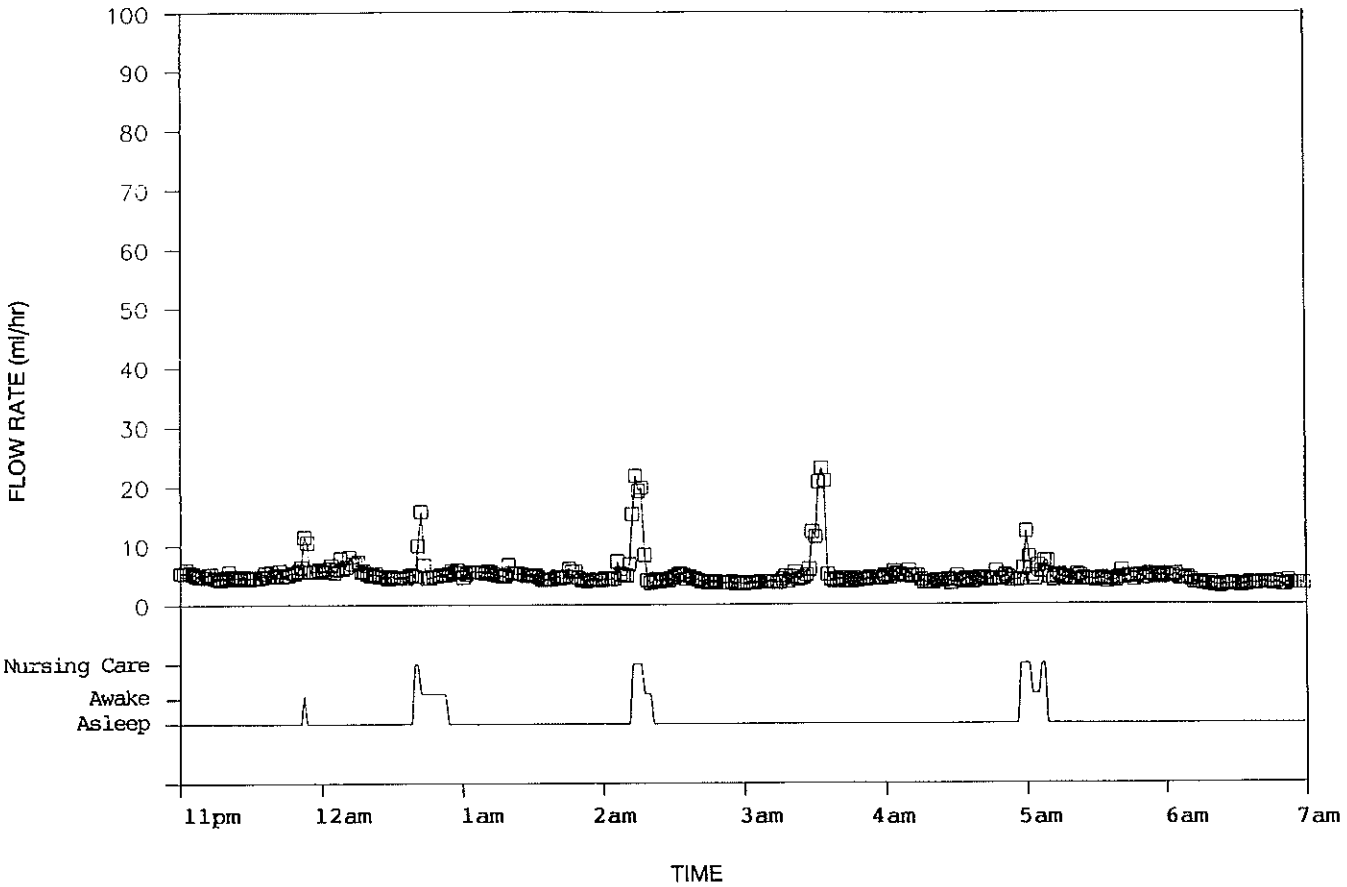

FIG. 3. Flow rate for a 3-week-old infant (born at 39 weeks of gestation) with hydrocephalus after intraventricular hemorrhage. The EVD is for failed VP shunt insertion (subcutaneous emphysema after subcutaneous tunneling). The average flow rate for the 8-hour period is 5.2 ml/h. The height of the EVD is 0 cm. Increases in flow rate are related to increased activity of the child.

cm, but ranged from −10 to 20 cm. The average 24-hour rate for all patients was 6.33 ml/h. The maximum flow rate in any 24-hour period for all patients was 22.2 ml/h.

Dynamic characteristics of external ventricular drain flow

The 9 children underwent an average of 5.7 days of computer monitoring (range, 2–9 days). The monitoring system worked well. The nursing staff found this a convenient way to evaluate EVD function and record EVD output. The requirement to record the functional status of the patient was not an undue burden. Care was taken that the balance was not disturbed and that the drip chamber and collecting system hung free. These patients were monitored closely by the medical personnel, but changes in functional status could have occurred and not have been recorded on the computer.

Examples of the minute-to-minute variation in flow rates obtained by computer monitoring for 3 patients are shown in Figures 2 to 4. In the first patient, a 1-year-old child with an EVD inserted for abdominal wound dehiscence, there was periodic variation in the flow rate while asleep. These variations occurred every 60 minutes, lasted approximately 20 minutes, and had peak values of 70 ml/h. The total amount of CSF vented during these episodes was approximately 10 ml. The period of increased flow was followed by a period of flow arrest. These variations may have occurred in association with rapid-eye-movement (REM) sleep, in which case the increased flow would be in response to vasodilatation, and the flow arrest would occur as CSF production accounted for the vented CSF. This pattern was not seen in the other 8 children.

In the other children, peak flow rates tended to occur in response to wakefulness, crying, or when they were being manipulated for nursing care, where the only increases in flow were associated with activity (Fig. 3). Sometimes the pattern was chaotic, with a child who was wakeful throughout the night (Fig. 4). The striking finding is the variability of the flow rate.

Effects on steady-state external ventricular drain flow

The relationship between age and average daily flow rates is shown in Figure 5. The increase with age follows a logarithmic profile with a correlation coefficient of 0.6755. The flow rates in children younger than 1 year of age are quite low (<4 ml/h). In older children, the values are higher, although quite variable. As age and weight are highly correlated, a similar type of profile occurred with weight versus flow rate, with a similar correlation coefficient (Fig. 6).

Other factors that might be expected to influence the steady-state flow rates include height of the EVD, type of infecting organism, time elapsed since insertion, type of EVD, and sex. By use of multiple regression analysis, a model was fitted to 24-hour flow data using these factors as well as age and weight. The results of the final model are shown in Table 4.

There was no significant effect related to time elapsed since

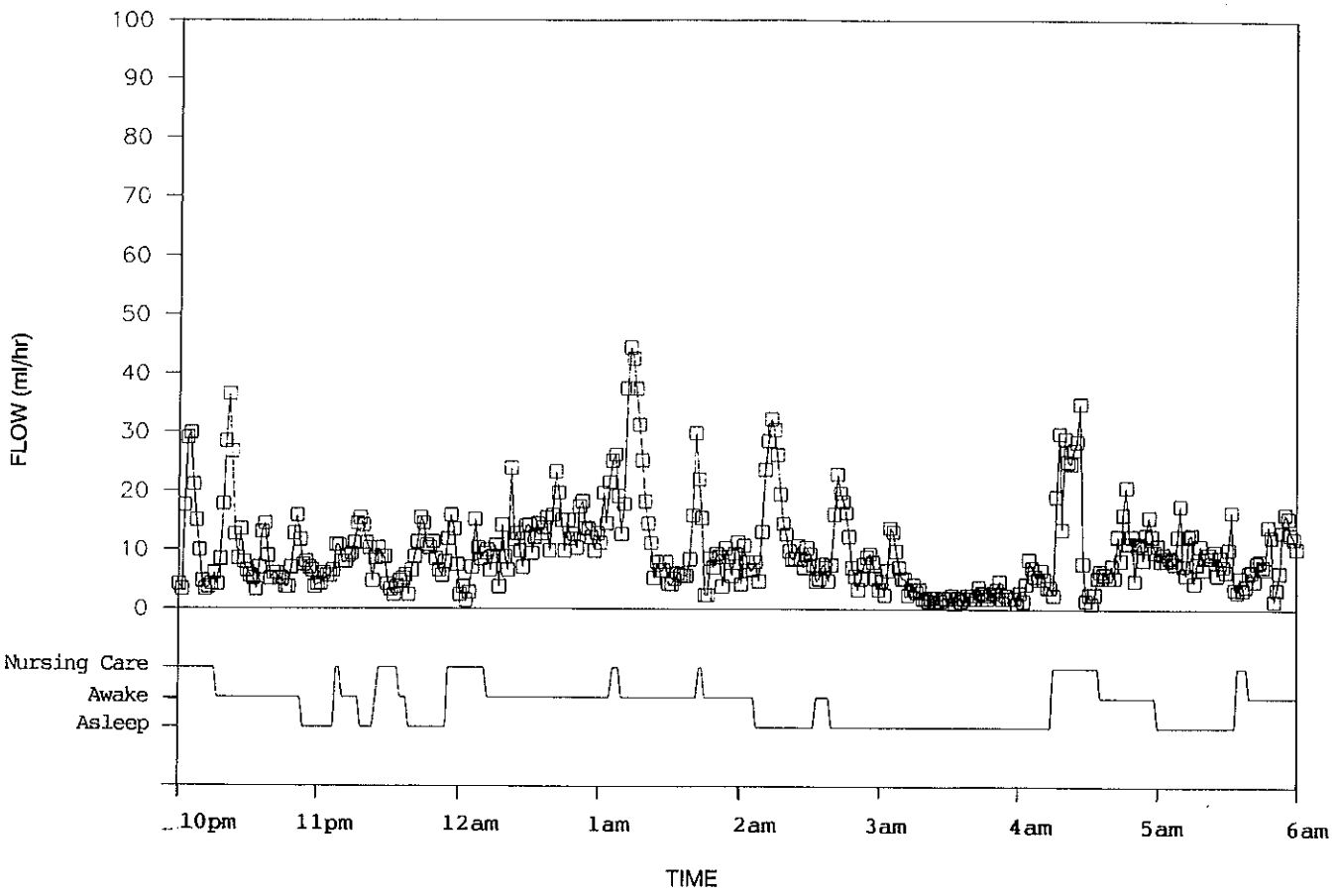

FIG. 4. Flow rate for a 2-year-old child with presumed tuberculous meningitis and secondary hydrocephalus. The average flow rate for the 8-hour period is 10.2 ml. The height of the EVD is 0 cm. The infant is awake, and the flow pattern, although partially related to activity, is chaotic.

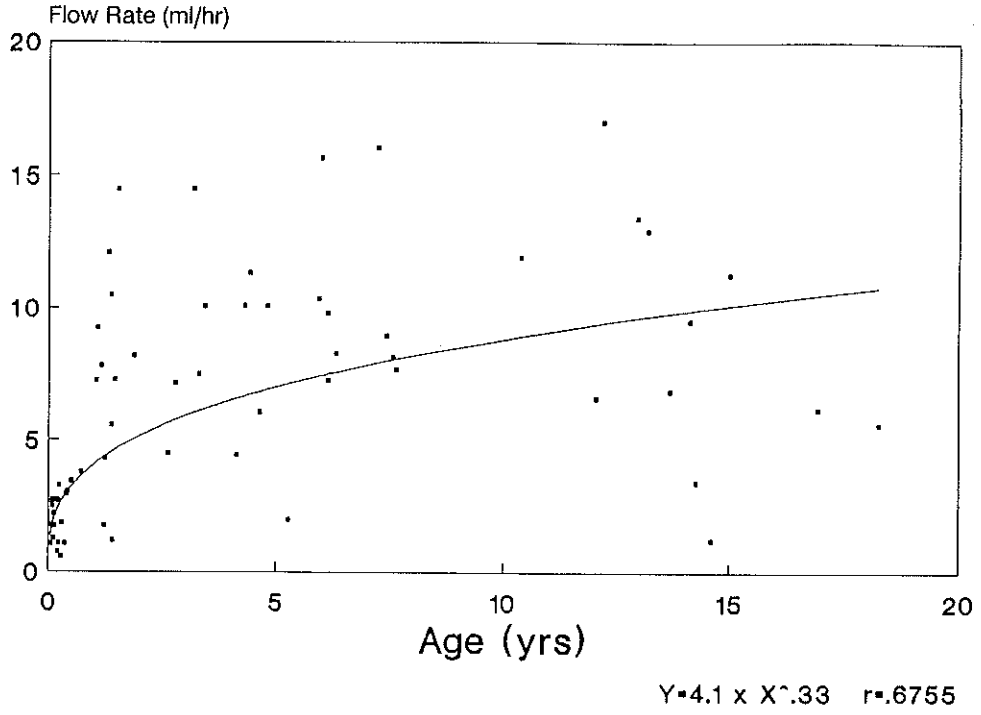

FIG. 5. Average EVD flow for each patient over the entire drainage period as a function of age.

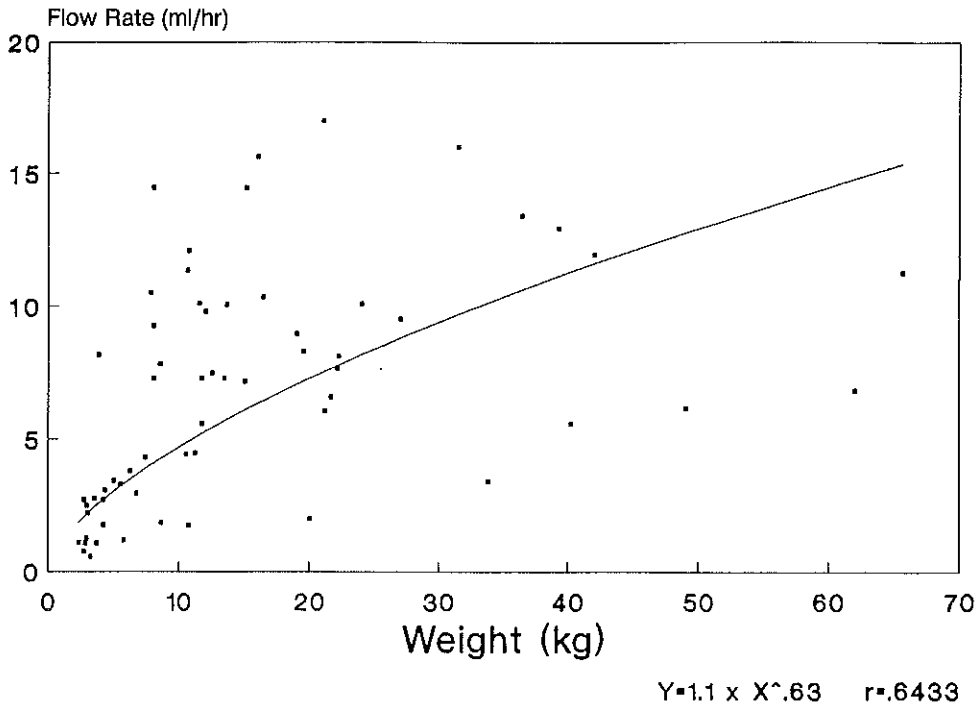

FIG. 6. Average EVD flow for each patient over the entire drainage period as a function of weight.

TABLE 4
Model Fitting Results for Flow[a]

Independent Variable	Coefficient	SE	*t*	*P*
Constant	−21.367137	16.862175	−1.2672	0.2056
(Weight)$^{1/2}$[b]	55.070696	8.641147	6.3731	<0.0001
(Age)$^{1/2}$[c]	2.000774	0.476235	4.2012	<0.0001
Weight*Age[d]	−0.001054	0.000111	−9.5222	<0.0001
Height	−4.666707	0.652308	−7.1541	<0.0001
Bacteria 1	−44.957683	8.666207	−5.1877	<0.0001
Bacteria 2	−82.120047	11.250994	−7.2989	<0.0001

[a] Milliliters per 24 hours.
[b] The square root of weight.
[c] The square root of age.
[d] The interaction between weight and age, which are highly correlated.

insertion, type of EVD, or sex. The height of the EVD had a significant negative effect on output. This same effect seen in the group as a whole was also seen in individual patients when the EVD level was altered during the drainage period, shown in 5 patients in Figure 7. Finally, the type of infecting bacteria had a significant effect. Flow rates were highest in patients with Gram-positive infections and lowest with Gram-negative and mixed infections (Fig. 8). There were no significant differences in age, weight, or height of the reservoir among patients with Gram-positive, Gram-negative, or mixed infections.

DISCUSSION

An EVD consists of a ventricular catheter, a connecting tube to a drip chamber, and a collecting bag. There may be an integral one-way valve or, if the shunt is externalized, a proximal shunt valve. The height of the drip chamber acts as a hydrostatic valve analogous to the opening pressure of standard shunt valves. The total opening pressure of the system is the sum of the height of the drip chamber plus any intervening valves. An EVD, like a standard shunt valve, has very little resistance to flow once open and, similarly, has a closing pressure at which it closes passively.

In this configuration, the EVD drains CSF at a rate equal to the CSF production minus the CSF absorption. If the total pressure of the EVD is less than the pressure in the superior sagittal sinus, then the EVD flow rate should equal the CSF production rate.

As an EVD has a proximal ventricular catheter and a hydrostatic valve, the main difference between the mechanics of an EVD and an implanted shunt lie with the distal end. The drip chamber is always at atmospheric pressure. Although measurement of the intraperitoneal pressure in infants with hydrocephalus has shown it to be near atmospheric pressure at rest, 0 to 50 mm H_2O (25), there are large increases in intra-abdominal pressure that accompany crying, coughing, and straining. These are associated with the corresponding increases in intracranial pressure occurring with the same events (25).

The absence of this distal increase in intraperitoneal pressure leads to venting of the CSF with these activities with an EVD. This was evident in those patients undergoing computer monitoring, in whom flow rates in excess of 20 ml/h were common and flow rates as high as 100 ml/h occurred for a few minutes with increased activity. Although one would expect venting to be less with an implanted shunt, in fact increased flow, as measured by radioisotope injection, has been reported with these activities (12).

Other differences between a patient with an EVD and a shunt include the constant recumbent position and initial CSF infection. The EVD flow in a patient lying quietly at rest would be expected to be the same as in a patient with a shunt of equal pressure characteristics. This level of activity, although proportionally much higher in infants, would still occupy approximately 25% of the time in adults.

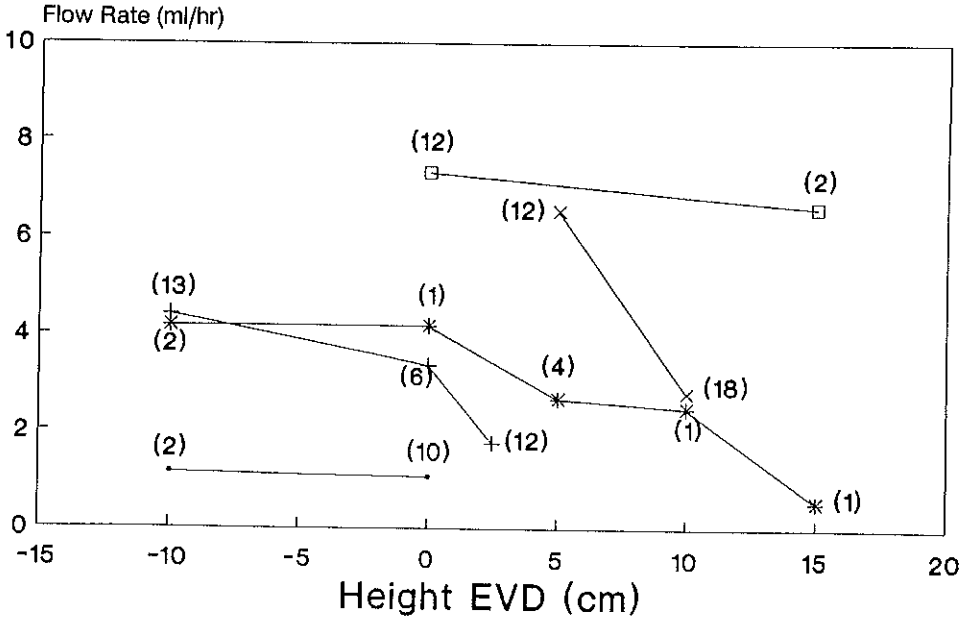

FIG. 7. Average 24-hour EVD flow as a function of the height of the drip chamber in 5 patients in whom the height was changed during the drainage period. The numbers in parentheses indicate the number of 24-hour measurements at that height.

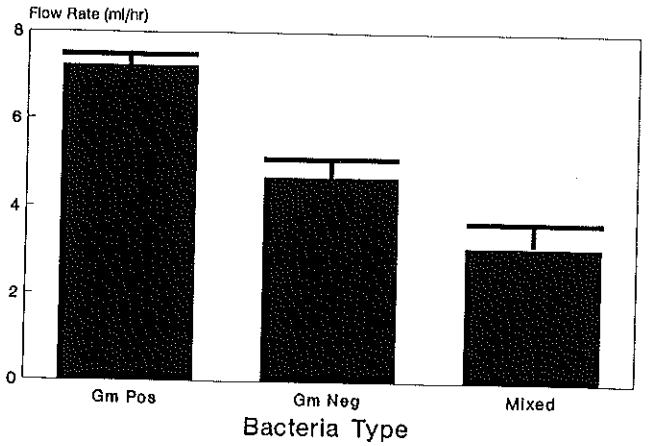

FIG. 8. Average EVD flow as a function of the type of infecting bacteria. The *bars* indicate standard error. The average EVD flow is significantly lower with Gram-negative or mixed infections ($P < 0.001$).

In 55 children (median age, 2.61 years), the average EVD flow rate observed with the drip chamber an average height of 3.9 cm was 6.33 ml/h. EVD flow increased logarithmically with increasing age and weight, being very low in infants. As some CSF absorption may have taken place with the EVD in place, no comments regarding the absolute EVD output and CSF production can be made. The relationship, however, between age and output indicates that CSF output is a function of age or, more probably, brain weight. This concept is also supported by animal studies in which CSF production was a function of size of the species studied: 0.02 ml/h in the mouse; 0.6 ml/h in rabbits; and 9.2 ml/h in the goat (9).

To date, there have been few studies on CSF production in man, and there has been no suggestion that CSF production in children is different from that in adults. A group of older children and adults undergoing CSF perfusion chemotherapy for central nervous system neoplasms had a CSF production rate of 0.37 ml/min (22.2 ml/h) (20). There was no obvious difference between children and adults in this study. Cutler an co-workers (8) studied 12 children aged 5 to 13 years also undergoing cerebrospinal fluid perfusion chemotherapy and found production rates of 0.35 ml/min (21 ml/h). Page et al. (19) studied 8 children, aged 1 month to 8 years, who had hydrocephalus and found a CSF production rate of 0.25 ml/min (15 ml/h).

CSF absorption, although impaired in hydrocephalus, remains pressure-dependent (13). One would expect absorption to increase and EVD flow to fall with increasing height of the drip chamber. This was observed both as an overall effect on the model (Table 4) and in individual patients (Fig. 7). Casey and Vries (5) also observed this negative effect of increasing height in EVD output. In fact, neurosurgeons make use of this effect when adjusting the height of the EVD to control output or by selecting a higher pressure valve to attempt to reduce the effects of overdrainage.

To our knowledge, the effect of infection on CSF production has not been studied in man. A decrease in CSF production in the presence of Gram-negative ventriculitis in infants undergoing external drainage, however, was reported as an "observation" by Breeze et al. (3). There is animal model evidence for the effects of infection on CSF production. Breeze et al. (3) produced *Escherichia coli* ventriculitis in the rabbit and noted a 50% reduction in CSF output in the infected animals. They speculated that this reduction was due to either a reduction of choroid plexus blood flow or to a reduction in ionic transport caused by enterotoxins. Similarly, Scheld et al. (21) found that the most pronounced reduction of CSF production in experimental meningitis in the rabbit occurred with *E. coli*. Cooper et al. (7) failed to find a reduction in CSF production in a model of *Streptococcus pneumoniae* meningitis in the dog.

Our data on the effects of infection on EVD flow support these experimental results and is the first evidence for this in man. Gram-negative infections had lower EVD flow rates. Mixed infections also produced lower rates. Although some of these included Gram-negative organisms, they may have also indicated a more severe infection. Perhaps the most interesting effect of an infection was the failure of the flow rates to increase with resolution of the infection. The average duration of the EVD in this study was 16.4 days, with a

maximum of 44 days. How long the flow levels would remain at this level is unknown, but Gram-negative infections may produce changes in the choroid plexus, such as destruction or scarring, which are long lasting.

The limited circumstances under which EVD flow is equivalent to shunt flow have been discussed. There was no change of EVD flow rate with time during the drainage period, and these children were in a state of equilibrium in terms of CSF drainage. One would therefore expect shunts implanted immediately after the EVD to perform the same, in the recumbent position, providing the opening pressure of the valve and the height of the drip chamber were the same. The average drip chamber height of 3.9 cm corresponds to a low pressure valve. The average EVD flow rate was 6.3 ml/h. This gives some indication of the probable shunt flow rates and CSF drainage requirements in this group of children, at least in the period immediately after external ventricular drainage.

In vivo shunt flow rates have been comparable to the values we measured with the EVD. Measurement by means of an implanted electrolysis unit showed a wide variation in flow rates, from 0.6 to 116 ml/h (11, 18). The average flow rate in 2 patients was approximately 15 ml/h. (11). Using magnetic resonance phase imaging in 5 adolescents and young adults, we found flow rates between 3 and 19 ml/h (14). Injection of radioisotope and use of an external detector, which must be calibrated for each type of reservoir (12), gave similar values over a wide range, from <1 to >20 ml/h (4, 6, 12, 15). With the computer monitoring system, we measured flow rates from 0 to >100 ml/h. The average flow over a 24-hour period had a mean of 6.33 ml/h, with a range of 0.08 to 22.2 ml/h.

The dynamic fluctuations in EVD flow rate were predominantly related to increased level of arousal. Similar fluctuations may occur in implanted shunts. The fluctuations that occurred during sleep in one child (Fig. 2) could certainly occur in implanted shunts. Hara et al. (11) also noted an increase in shunt flow at night, lasting several hours, and suggested the possibility of a circadian rhythm. The fluctuations in our patient occurred much more rapidly. The particular pattern we observed may be related to REM sleep. Hydrocephalic infants (1) have been found to have periodic increases in intracranial pressure, associated with increased intracerebral blood volume, occurring with REM sleep. These occurred approximately every hour and lasted about 20 minutes. Transient increases in intracerebral blood volume in a patient with an EVD occurring with REM sleep would be expected to produce the type of flow pattern shown in Figure 2.

Important differences between EVD flow and in vivo shunt flow occur with patients in the erect posture. We noted increased EVD flow with decreasing drip chamber height and, when the drip chamber was dropped well below head level, the EVD rapidly vented. An increase in shunt flow (3, 15) and remarkably high negative intracranial pressures have been measured in patients in the sitting position who have implanted shunts (16). One can surmise from these two observations that, in patients with standard valves and without antisiphon devices, there is similarly an initial venting in the erect posture, followed by an average CSF flow rate equal to the CSF production.

The data from EVD flow measurement can be used to predict the performance of currently implanted valves and new valve designs; however, the average rate and range of flow rates required to optimize the treatment of hydrocephalus are unknown. It is unlikely that these flow rates are the same for all causes of hydrocephalus or for all patients at every stage of development. Perhaps in the future, with improved knowledge of the pathogenesis of hydrocephalus and more sophisticated valve design, each patient will have a shunt tailored to his or her specific needs.

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COMMENTS

The authors suggest that their quantitative measurements of cerebrospinal fluid (CSF) flow in patients on external ventricular drainage should be useful to study the flow characteristics of various shunt systems. As they point out, regardless of valve characteristics, CSF flow rapidly increases as a result of siphoning when their drip chamber is lowered well below the head. If their technique is to be of value in testing shunt systems, they must study their patients when siphoning occurs. It is likely that the CSF drainage occurring as a result of positional siphoning is much larger than the regulated drainage that occurs as a result of shunt design. Indeed, a 24-hour summary of shunt flow under conditions in which siphoning is allowed to occur when the patients are awake would be very interesting. These data may indicate that the various flow characteristics of many of the available valves are of little quantitative importance compared to siphoned flow. I urge the authors to study their patients with shunts using their technique to look at the relative importance of this siphoning issue.

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This paper presents CSF flow data derived in two different ways in a group of 9 patients. "Dynamic" changes were documented by the use of a computer-aided collection system that sampled output every second. An interactive display registered the corresponding functional status of the patient. A remarkable fluctuation in flow rate, ranging from flow arrest to 70 ml/h, was measured. In a second group of 46 patients, the "steady state" flow rate was derived from a retrospective chart review. Decreasing flow rates were seen when the height of the ventricular drain was increased and with resolution of the infection. The flow rate increased with age and weight of the patient.

Because most of the external ventricular drains were placed for infection, the mean flow rates in this study will err on the low side. These data suggest that CSF diversion may not be necessary after a shunt infection, as the CSF flow decreases and remains decreased after resolution of the infection. However, patients were monitored for a mean of only 16 days, which may not adequately reflect the postinfection steady-state flow.

I anticipate that the applications of this technique and data are limited, but it is a substantial beginning in an effort to explore CSF flow variation, valve performance, and valve design. Perhaps this technique will shed light on the problem of slit ventricles or the small ventricle syndrome.

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