

# Measurement of Cerebrospinal Fluid Output through External Ventricular Drainage in One Hundred Infants and Children: Correlation with Cerebrospinal Fluid Production

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## Key Words

Cerebrospinal fluid production · Cerebrospinal fluid shunt · External ventricular drainage · Hydrocephalus · Shunt infection

## Abstract

**Objective:** Cerebrospinal fluid (CSF) production rates influence shunt design and the care of children with hydrocephalus. Measurement of hourly CSF output through external ventricular drainage (EVD) reflects the CSF production. In the present study, hourly CSF outputs in children with hydrocephalus were measured while they were treated with EVD and correlated with the age, sex and body weight of the patients as well as other clinical parameters. **Methods:** One hundred children with hydrocephalus due to various causes had EVD treatment. Twenty-six had EVD on two or three separate occasions; thus, the CSF output measurements were observed and analyzed on the basis of 130 EVDs. The most common reason for EVD treatment was shunt infection (n = 75). The duration of EVDs ranged from 25 to 774 h (mean 269 h). The height of the drip chamber from

the mid-head position ranged from 0 to 23 cm (mean 9.8 cm). The hourly CSF output was analyzed according to the patient's age, sex and body weight as well as the presence of CSF infection. **Results:** The hourly CSF output rapidly increases during the first year of life. By the second year, it reaches 64% of the hourly CSF output of 15-year-old children. The mean hourly output ranged from 0.1 to 26.5 ml/h (mean 8.1 ml/h), with the standard deviation ranging from 0.4 to 10.8 ml/h (mean 5.2 ml/h). A regression analysis indicated that the age and body weight appeared to correlate with the hourly CSF output. Using the natural logarithm of age, body weight and sex, these predictors accounted for 50.9% of the variability in hourly CSF output. The regression equation is as follows: hourly CSF output = 2.78 – 2.23(male = 0, female = 1) + 0.97 log(age in years) + 2.26 log(body weight in kg). R sd = 3.36, R<sup>2</sup> = 0.509. The type of infecting organism and the height of EVD did not influence the overall CSF output. **Conclusion:** The hourly CSF output fluctuates, but the CSF output increases logarithmically with age and body weight. The gender also influences the CSF output, with males having a greater output than females. The data produced by the present study will help us to understand CSF production rates in developing children. They will also help us in the care of children receiving EVD treatment, as well as in selecting and designing shunt systems.

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## Introduction

External ventricular drainage (EVD) is frequently used in the temporary management of hydrocephalus. The periods of EVD provide an opportunity to assess intracranial conditions such as intracranial pressure and cerebrospinal fluid (CSF) production. There are several reports in the literature concerning CSF production in children with hydrocephalus [1–4]. The production rates of CSF in humans were previously calculated by Pappenheimer's perfusion methods [5], which are quite invasive and have not been practiced in humans in modern times. By this method, the CSF production rates are considered to be 0.3–0.4 ml/min, which translates into an hourly production rate of approximately 20 ml. The CSF production rate is usually unchanged in hydrocephalic children, and it is relatively independent of pressure [2, 6]. EVD provides a measurement of CSF outflow under controlled conditions. Drake et al. [7] studied the CSF flow dynamics through EVD and found that the CSF output through EVD increased logarithmically with an increase in age and body weight. Also, they noted that the height of EVD and the type of infecting bacteria had a significant effect on CSF output. We conducted a retrospective study of the CSF output through EVD in a much larger number of pediatric patients with hydrocephalus. The purpose of this retrospective study was to correlate the CSF output with multiple clinical factors, particularly focusing upon the patients' age, sex and body weight.

## Patients and Methods

A review was undertaken of 100 children (61 males, 39 females) younger than 16 years of age who were treated with EVD at the Children's Memorial Hospital over a 2-year period. Patients who had intraventricular injection of antibiotics or ventricular irrigation for severe ventriculitis were excluded. Also, patients with multiple EVDs for loculated ventricles were excluded. Seventy-four patients had 1 episode of EVD, 22 had 2 episodes of EVD and 4 had 3 episodes of EVD. This produced a total of 130 episodes of EVD (81 males, 49 females) to study. Each period of EVD was considered as an independent measurement for data analysis.

The age of the patients at the time of EVD treatment ranged from 0.02 to 15.7 years, with a mean age of 4.6 years. The body weight of the patients at the time of EVD treatment ranged from 2.5 to 69 kg, with a mean body weight of 16.6 kg.

One hundred and six EVDs had a preexistent CSF diversion shunt and 24 had no shunt prior to EVD placement. The conditions requiring preexistent shunts were myelomeningocele in 32, congenital hydrocephalus in 31, intraventricular hemorrhage hydrocephalus in 25, postmeningitic hydrocephalus in 10, hydrocephalus due to brain tumor in 5 and posttraumatic hydrocephalus in 3. Of the 24 patients who did not have preexistent shunts, the causes of hydro-

cephalus were brain tumor in 11, subarachnoid hemorrhage in 3, intraventricular hemorrhage in 2, meningitis in 2, congenital hydrocephalus in 2 and other causes in 4.

The reasons for EVD treatment were shunt infection in 75, shunt malfunction in 19, congenital or acquired hydrocephalus in 15, brain tumor surgery in 12 and other causes in 9. There were 67 gram-positive and 8 gram-negative organisms. The common organisms were *Staphylococcus epidermis* in 33 patients, *Staphylococcus aureus* in 15 and other *Staphylococcus* species in 10.

All EVDs were placed newly or by the insertion of a new ventricular catheter following the removal of the preexisting shunt system. The patients who had distal shunt externalization with a shunt valve in place were excluded. The EVD system consisted of a ventricular catheter connected to the flow chamber and a drainage bag (The Becker External Draining System II, PS Medical, Goleta, Calif., USA). The flow chamber was placed at a specified height above the external auditory meatus. The height of the drip chamber was usually set at 10 cm, but ranged from 0 to 23 cm at the discretion of the attending neurosurgeon (average height 9.8 cm). These patients were confined to the bed, except for brief periods when the collecting tube was occluded or when older patients were permitted to use the bathroom. The CSF in the collecting system was sampled daily for cell counts, protein and glucose content and bacteriological studies. The patency of the system was determined frequently by examining the drainage chamber. The volume of the CSF drainage was recorded every hour in the hospital chart by nursing personnel from the beginning to the end of the EVD (phase 1). The hourly CSF loss was replaced intravenously with the same volume of normal saline in all patients. The duration of EVD ranged from 2 to 33 days, with a mean average of 8.1 days (269.7 h). We analyzed the standard deviation of the hourly output through the EVD as an indicator of fluctuation.

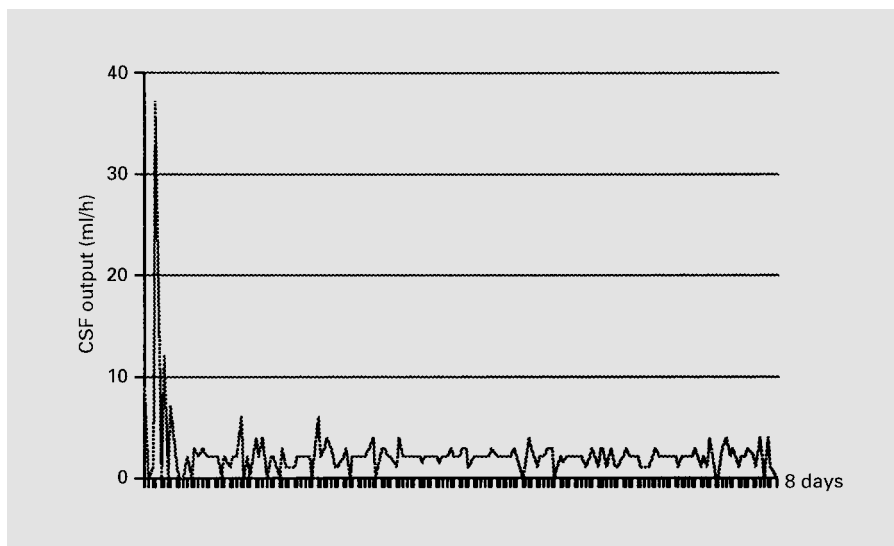
In order to obtain stable drainage of the CSF, in 117 periods of EVDs, the CSF output of the last 3 days was analyzed in patients who had EVD treatment over 6 days or longer (phase 2). Measurement and analysis of the last 3 days of EVD, when the CSF output is stabilized and infection, if present, is under control, provides more accurate information regarding hourly CSF output through EVD. In this group (49 males, 38 females), the age ranged from 0.02 to 15.7 years (mean average 4.7 years) and the body weight ranged from 2.5 to 69 kg (mean average 17.1 kg). The height of the dripping point in the drip chamber ranged from 0 to 20 cm (mean average 10 cm).

The effect of individual variables of EVD outputs was tested with either simple or multiple regression analysis. Those variables with no significant effect on the model were excluded.

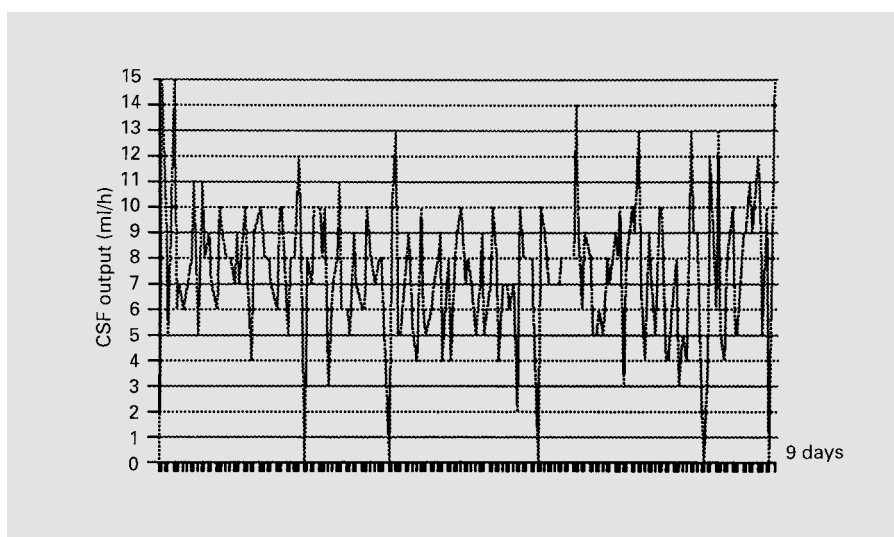
## Results

The CSF output was steady in most patients throughout observation of EVD. However, in some cases, two different patterns of CSF output through EVD were noted. One pattern showed a greater volume of output initially (during the first few days), followed by a gradual decrease to a steady state (fig. 1). The other was a random pattern of CSF output throughout EVD (fig. 2). These graphic patterns did not correlate with other parameters such as age, body weight, height of the drip chamber and shunt infection.

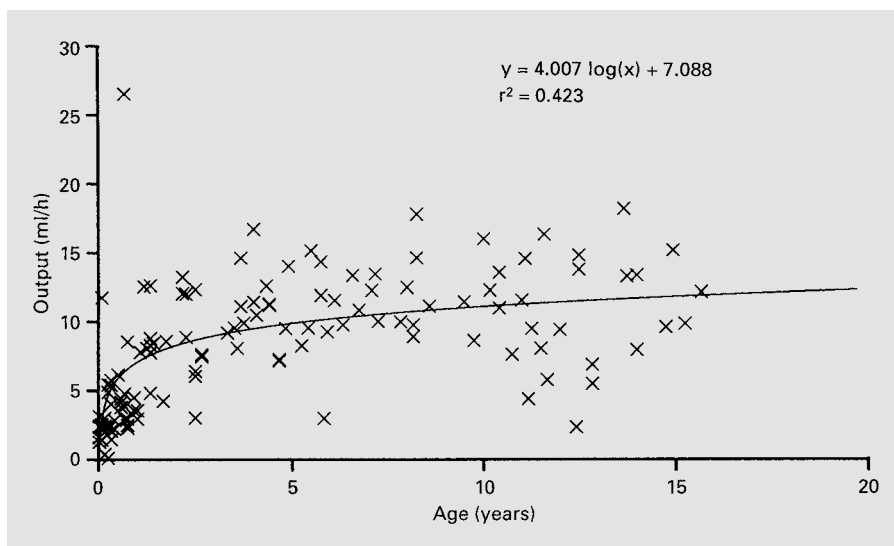
**Fig. 1.** CSF output rate for a 4-month-old male (body weight 5.9 kg) with posthemorrhagic hydrocephalus and shunt infection. With the drip chamber at a height of 10 cm, the overall hourly output for 8 days of observation was 2.29 ml. Note that there was a steady CSF output except for the first day.



**Fig. 2.** CSF output rate for a 30-month-old male with a body weight of 9.7 kg with congenital hydrocephalus. With the drip chamber at a height of 10 cm, the overall hourly output was 7.63 ml. A random pattern of CSF output was noted during the 9 days of observation.



**Fig. 3.** Average hourly CSF output (observed and fitted) for each patient (n = 130) over the entire EVD period (phase 1) as a function of age.



*Phase 1*

The average hourly output for all patients was 8.1 ml/h and ranged from 0.1 to 26.5 ml/h. Standard deviation of the hourly output was used as an indication of fluctuation. The fluctuation of hourly CSF output ranged from 0.4 to 10.8 ml, with a mean average of 5.2 ml/h and a median average of 5.0 ml/h. The increase with age follows a logarithmic profile with a correlation coefficient of 0.423 (fig. 3). During the first year of life, the increase is rapid.

**Table 1.** Overall hourly CSF output (phase 1)

Predictor	Coefficient	SE	t ratio	p
<i>Variables entered in multivariate regression</i>				
Constant	5.385	2.287	2.35	0.020
ln (age)	1.0058	0.3908	2.57	0.011
ln (BW)	2.24.91	0.8014	2.81	0.006
Sex	-2.2361	0.6402	-3.49	0.001
Height	-0.03687	0.09627	-0.38	0.702
<i>Final multiple regression model</i>				
Constant	5.009	2.059	2.43	0.016
ln (age)	0.9745	0.3808	2.56	0.012
ln (BW)	2.2610	0.7981	2.83	0.005
Sex	-2.2345	0.6380	-3.50	0.001

Hourly CSF output = 2.78 - 2.23(male = 0, female = 1) + 0.97 ln(age in years) + 2.26 ln(body weight in kg). R sd = 3.36, R<sup>2</sup> = 0.509.

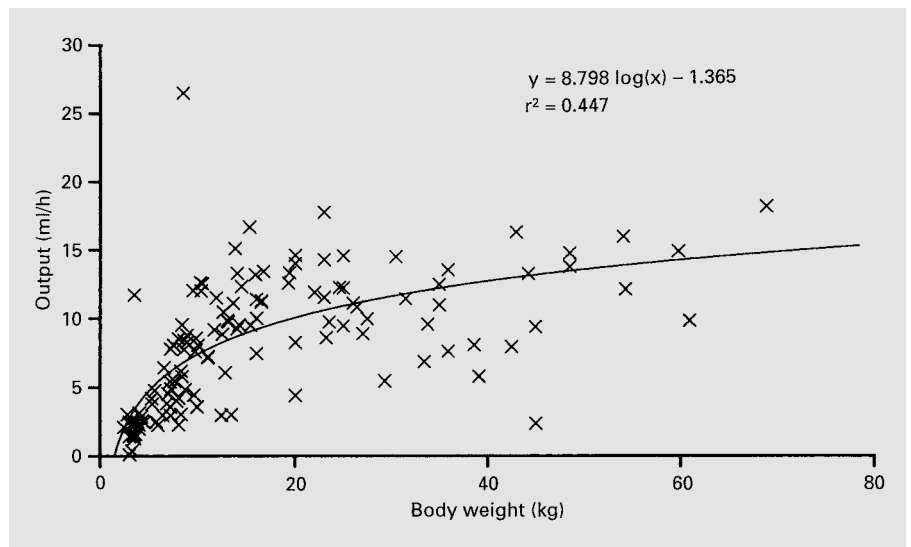
ln = Natural logarithm; BW = body weight.

The CSF outputs at 1 and 2 years of age reached 56 and 76%, respectively, of those at 15 years of age. Following the age of 1 year, the CSF output levels off. In older children, the values are higher, although quite variable. A similar relationship between body weight and CSF output was noted, because age and body weight are highly correlated (fig. 4). Regression analysis indicated that natural logarithm of age and natural logarithm of body weight correlate with CSF output. The equation for overall hourly output is shown in table 1.

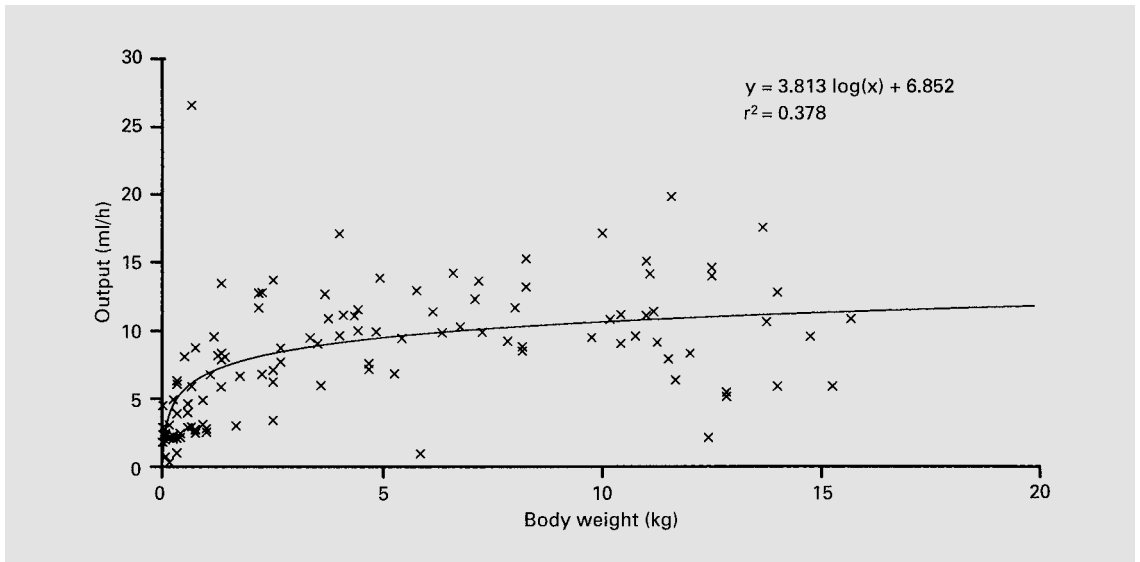
*Phase 2*

In this steady state of 117 EVD observations, a similar correlation was found as in the overall group. The hourly CSF output ranged from 0.4 to 26.6 ml/h, with a mean output of 7.9 ml/h. The fluctuation (standard deviation) of hourly CSF output ranged from 0.7 to 11.7 ml/h, with a mean average of 4.8 ml/h and a median average of 4.6 ml/h. They showed no statistical difference from the values in phase 1. The CSF output increased logarithmically with the increase in age and body weight (fig. 5, 6). The regression analysis indicated that natural logarithm of age, natural logarithm of body weight and sex correlated with the CSF output of the last 3 days of EVD in a steady state. The equation of the CSF output in the last 3 days of EVD is shown in table 2.

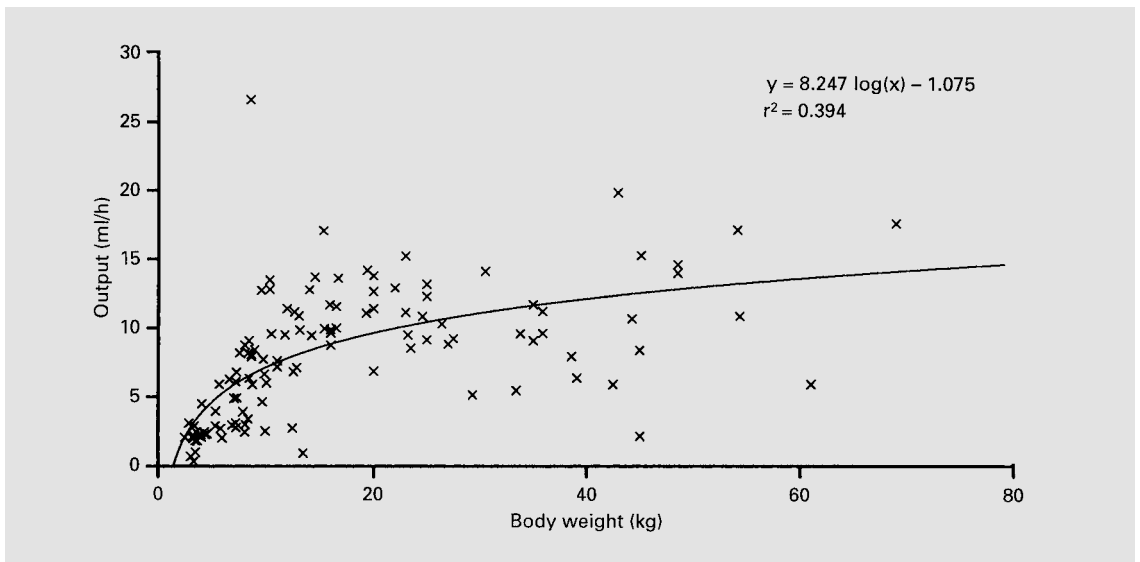
The height of the drip chamber, ranging from 0 to 20 cm from the mid-head level, remained constant in 78 episodes of EVD, whereas it was changed in 52. In 31 EVDs (60%) in which the height of the drip chamber was



**Fig. 4.** Average hourly CSF output (observed and fitted) for each patient (n = 130) over the entire EVD period (phase 1) as a function of body weight.



**Fig. 5.** Average hourly CSF output (observed and fitted) for each patient (n = 117) over the last 3 days of EVD (phase 2) as a function of age.



**Fig. 6.** Average hourly CSF output (observed and fitted) for each patient (n = 117) over the last 3 days of EVD (phase 2) as a function of body weight.

changed, the height change produced a negative effect upon CSF output, more than the individual standard deviation. However, the height of the drip chamber did not statistically influence the CSF output in either the phase 1 or phase 2 study ( $p = 0.702$  and  $0.802$ , respectively).

In phase 1, 112 patients had the shunt internalized and 18 did not require shunting following EVD treatment. Among 117 patients who had EVD for 6 days or longer, 103 had shunts and 14 did not have shunts after EVD. The mean hourly CSF output of patients of the shunted group was 8.0 ml/h (0.4–26.6 ml/h) and the mean hourly

**Table 2.** CSF output in the last 3 days of EVD (Phase 2)

Predictor	Coefficient	SE	t ratio	p
<i>Variable entered in multivariate regression</i>				
Constant	5.503	2.513	2.19	0.031
ln (age)	1.0249	0.4322	2.37	0.019
ln (BW)	1.9042	0.8906	2.14	0.035
Sex	-1.9835	0.7054	-2.81	0.006
Height	-0.02255	0.08974	-0.25	0.802
<i>Final multiple regression model</i>				
Constant	5.274	2.331	2.26	0.026
ln (age)	1.0122	0.4275	2.37	0.020
ln (BW)	1.9035	0.8869	2.15	0.034
Sex	-1.9735	0.7014	-2.81	0.006

Hourly CSF output = 3.30 - 1.97(male = 1, female = 0) + 1.01 ln(age in years) + 1.90 ln(body weight in kg). R sd = 3.55, R<sup>2</sup> = 0.447.

ln = Natural logarithm; BW = body weight.

output of those of the nonshunted group was 7.1 ml/h (0.7–17.6 ml/h). There was no statistical difference in hourly CSF output through EVD between these two groups ( $p = 0.479$ ). There was also no difference in the hourly CSF output between patients with CSF infection and those with no infection. Furthermore, there was no significant difference in hourly CSF output between gram-positive infection and gram-negative infection in our study.

## Discussion

An EVD provides an opportunity to understand the physiology of CSF production in humans. It has been extensively used in pediatric neurosurgical practice to control hydrocephalus in the presence of shunt infection or for the purpose of temporary intracranial pressure control. EVD allows drainage of the CSF when the intracranial pressure exceeds the pressure set by the height of the dripping chamber. The EVD drains the CSF, partly reflecting the volume of production minus absorption. However, during various physiological conditions such as crying, coughing [4] or REM sleep when the intracranial pressure increases [7, 9], the CSF drainage from EVD also increases. Therefore, the EVD output is not equal to the CSF production in the hydrocephalic children tested. However, it largely reflects the CSF production rates, particularly when the patient remains in a steady state in a

recumbent position, and EVD pressure is less than the pressure of the superior sagittal sinus [7].

The major site of CSF production is in the ventricles, particularly the choroid plexus. Roughly 80% of CSF production is from the choroid plexus in normal conditions [10]. There is free communication of fluid between the parenchymal extracellular space and the CSF space; thus, brain parenchyma is also a significant source of CSF production. It is generally agreed that the production of CSF remains normal in patients with hydrocephalus. CSF production in children with hydrocephalus has been reported to range from 15.0 to 24.5 ml/h [1–4]. No difference in CSF production between adults and older children has been shown by the perfusion method and both had a CSF production rate of 0.37 ml/min [6]. Similar CSF production rates were observed in children between 5 and 13 years of age [2]. However, in hydrocephalic children of much younger ages ranging from 1 month to 8 years, the CSF production rate decreases to 0.25 ml/min or 15 ml/h [4].

In vitro shunt flow rates have been measured by various methods using radioisotope or magnetic resonance imaging [11–13]. Hara et al. [14] measured the velocity of bubble flow generated by an extracorporeal high-frequency generator and electrolysis. In adult communicating hydrocephalus, the CSF flow ranged between 0.05 and 0.78 ml/min (3–43.8 ml/h). They noted a flow fluctuation over a 24-hour period, with an increase in the morning, especially between midnight and 6 a.m., which suggests a circadian rhythm [14]. On the other hand, data obtained from shunt flow measurements indicate that the shunt flow rates are influenced by several factors, particularly a patient's position and activities.

Drake et al. [7] conducted a similar study to ours. They observed CSF output through EVD in 25 patients and through an externalized peritoneal catheter with a shunt valve in place in 34 patients. These authors also found that the EVD output increased logarithmically with the age and weight of the patients, as our present study showed. The average 24-hour rate for all patients with the drip chamber at an average height of 3.9 cm was 6.33 ml/h, which is slightly less than our results (8.1 ml/h). This discrepancy may be due to our patients being slightly older (average 4.6 years) than theirs (average age 2.61 years), but in addition, they included patients who had the shunt externalized with a shunt valve in place, which would increase the resistance to the CSF outflow through external drains.

CSF outputs increase logarithmically with increase in age and body weight. The pattern of their increase is simi-

lar to the growth of head circumference during infancy and childhood [15]. The observation we made in our study strongly suggests that the CSF production increases proportionally with the growth of the brain. Perhaps maturation and increase of the choroid plexus together with brain growth account for the increased CSF production. The influence on CSF outflow of gender is of interest. Females showed lower output of CSF than males. The brain volume appears to influence CSF production. When one reviews the gender difference with respect to head circumference (greater in males) [15], the difference in brain volume is the likely explanation of our observation. A recent report indicated that lumbar CSF measured in adults showed a significantly lower CSF density in women than in men [16]. We are not certain whether the gender difference in CSF density influences the CSF outflow through EVD.

Drake et al. [7] monitored EVD CSF drainage continuously each second, using a computer monitoring system in 9 patients. These authors noted minute-to-minute variation in the CSF output and noted a periodic increase and decrease in the flow rate. In our present study, hourly fluctuations of the EVD output were noted frequently, with periods of increased output followed by a period of reduced output (average 5.0 ml/h). These fluctuations were primarily due to the children's activities. The average CSF output through EVD was constant from the beginning until the end, and there were no statistical differences between the phase 1 and phase 2 studies. The

increase or decrease in the height of drainage in individuals led to a significant decrease or increase in CSF output (greater than their standard deviation) in 60% of cases. However, with a constant height of the drip chamber, there were no statistical influences of the height upon the CSF output in the overall group. A larger prospective study would provide more accurate information on CSF output at different EVD pressures. In this study, we did not correlate the ventricular size with CSF output through EVD. Although it is our impression that the ventricular size at EVD does not influence CSF output, a prospective study would give us further information in this regard.

Severe ventriculitis due to gram-negative organisms depresses CSF production. Drake et al. [7] noted depressed CSF output due to ventriculitis, particularly with gram-negative or multiorganism infections. We did not, however, identify any difference in CSF output through EVD among 11 patients who had gram-negative ventriculitis. They did not show significance in the statistical data because patients with serious infection with decreased CSF production received intraventricular irrigation or installation of antibiotics and thus were excluded from study entry.

In conclusion, the data produced by the present study will help us to understand CSF production rates in the developing central nervous system of children. They also help us in the care of children who are receiving EVD treatment, as well as in selecting and designing shunt systems.

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