

# Cerebrospinal fluid conductance and compliance of the craniospinal space in normal-pressure hydrocephalus

## A comparison between two methods for measuring conductance to outflow

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✓ Conductance to outflow of cerebrospinal fluid (CSF) has been measured by both a lumboventricular perfusion and a bolus injection method in 24 patients with normal-pressure hydrocephalus. One purpose was to investigate whether the less time-consuming technique of bolus injection gave results comparable to the results obtained by the lumboventricular perfusion technique. There was a poor correlation between the results obtained by the two measurements of conductance to outflow of CSF. It is concluded that the bolus-injection technique cannot substitute for the lumboventricular perfusion test. Compliance of the CSF space was measured by the bolus injection. The presence of B-waves, recorded from long-term intraventricular pressure monitoring, could be correlated to the sum of conductance to outflow and compliance. The correlation offers a possible explanation of the nature of B-waves.

**KEY WORDS** • conductance to outflow • compliance • intracranial pressures • B-waves • normal-pressure hydrocephalus • cerebrospinal fluid dynamics

**N**ORMAL-PRESSURE hydrocephalus (NPH) is supposed to be the result of an increased resistance to absorption of cerebrospinal fluid (CSF) across the arachnoid villi. Therefore, patients with this disease have been treated by implanting a shunt between the ventricular system and blood. Sometimes disappointing results have been obtained in patients selected on the basis of clinical and laboratory findings, such as hydrocephalus, progressive dementia, gait disturbances, isotope cisternography, and intracranial pressure (ICP) measurements. There is a need for a method by which patients who may benefit from a shunt can be selected. We have, therefore, measured conductance to outflow ( $C_{out}$ ) of CSF by a "steady-state" method<sup>8</sup> in patients who fulfilled the clinical criteria for hydrocephalus, and have selected the patients for shunting therapy on the basis of this measurement.

Our method for selection is based on a lumboventricular perfusion technique. We wanted to compare the results obtained with our method with those of the

less time-consuming technique of bolus injection described by Marmarou, *et al.*<sup>9</sup> Furthermore, the latter method allowed us to obtain an estimate of the compliance of the craniospinal space ( $C_{cbs}$ ).

The B-waves in the pressure recording are most probably the result of variations in cerebral vascular volume, and the greater frequency of these pressure variations in certain pathological states, such as NPH,<sup>2,4</sup> might indicate that the pressure response to changes in cerebral vascular volume is exaggerated. We have also examined whether the frequency of B-waves in these patients might be correlated to  $C_{out}$  and/or  $C_{cbs}$ .

### Clinical Material and Methods

#### *Patients and Procedure*

This series included 24 patients, all of whom had progressive dementia, gait disturbances, increased ventricular size on computerized tomography, and ab-

TABLE 1

*Data obtained from the bolus injection, lumboventricular perfusion,  
and 24-hour pressure recordings\**

Case No.	Age (yrs)	Etiology of Disease	C <sub>out</sub> (ml/min/mm Hg)		C <sub>css</sub>	Duration of B-waves†
			Perf. Test	Bolus Inject.		
1	65	meningitis	.149	.136	.536	10
2	61	unknown	.116	.130	.469	5
3	71	unknown	.094	.123	.650	5
4	54	SAH	.074	.078	.530	20
5	49	unknown	.062	.073	.317	40
6	56	meningitis	.062	.012	.459	50
7	71	SAH	.043	.091	.403	30
8	58	unknown	.073	.209	.295	40
9	68	unknown	.132	.181	.479	10
10	39	unknown	.058	.105	.695	10
11	59	unknown	.177	.226	.580	5
12	47	SAH	.033	.008	.650	20
13	62	unknown	.098	.188	.580	20
14	60	encephalitis	.511	.241	.470	0
15	47	SAH	.019	.028	.340	75
16	71	unknown	.083	.221	.403	50
17	56	unknown	.108	.409	.788	10
18	69	unknown	.060	.177	.461	30
19	59	SAH	.123	.236	.921	0
20	71	SAH	.038	.061	.510	15
21	62	SAH	.052	.076	.540	25
22	53	trauma	.048	.035	.412	40
23	54	SAH	.123	.175	.980	5
24	59	SAH	.036	.034	.339	55

\*SAH = subarachnoid hemorrhage; C<sub>out</sub> = conductance to cerebrospinal fluid (CSF) outflow; C<sub>css</sub> = compliance of craniospinal space.

†Total duration of B-waves as a percentage of total recording time.

normal isotope cisternography. Age and etiology of their disease are shown in Table 1.

Intraventricular pressure was measured via a catheter placed in the right lateral ventricle. The pressure was recorded continuously for 24 hours on a servo recorder\* and the pressure tracing was examined afterward. The mean resting intraventricular pressure did not exceed 12 mm Hg in any patient. B-waves were defined as pressure fluctuations occurring once to twice per minute in periods lasting more than 10 minutes. The total duration of periods with B-waves was calculated as a percentage of the total recording time.

At the end of the 24-hour period the bolus-injection test<sup>9</sup> was performed. Intraventricular pressure was recorded on a servo recorder with a paper speed of 20 mm/min. During the steady state, 6 ml of Ringer's lactate solution was injected into the subarachnoid space through a lumbar cannula. The volume was injected by hand over a period of 2 to 4 seconds. The following intraventricular pressures were recorded: pre-injection pressure (P<sub>0</sub>), peak pressure after injection (P<sub>p</sub>), and the pressure 2 minutes after the end of the injection (P<sub>t</sub>) (Fig. 1). Subsequently the lumboventricular perfusion test for measurement of C<sub>out</sub> was performed.

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### Calculations

During the steady state, the rate of formation of CSF (V<sub>csf</sub>) equals the rate of absorption of CSF. The intraventricular pressure in the steady-state situation (P<sub>eq</sub>) is determined by sagittal sinus pressure (P<sub>v</sub>), V<sub>csf</sub>, and C<sub>out</sub> as expressed by the equation:

$$P_{eq} = P_v + V_{csf} \times \frac{1}{C_{out}} \quad (1)$$

Injection of a volume of fluid (dV) into the subarachnoid space causes an increase in intraventricular pressure (dP). If the fluid is injected during an infinitely short period of time, the ratio dV/dP is determined only by the compliance of the craniospinal space and therefore compliance (C<sub>css</sub>) is defined as follows:

$$C_{css} = \frac{dV}{dP} \quad (2)$$

\*Servo recorder manufactured by Philips Medico, Strandlodsvej 1, 2300 København S, Denmark.

Compliance depends on  $P_{eq}$  as expressed by the pressure-volume curve. That is,  $C_{css}$  decreases with increasing  $P_{eq}$  as expressed by the equation:

$$C_{css} = \frac{1}{K \times P_{eq}}, \quad (3)$$

where  $K$  is a constant, and describes the shape of the pressure-volume curve. Thus,

$$\frac{dP}{dt} = K \times P_{eq} \frac{dV}{dt}, \quad (4)$$

when  $dt$  approaches zero.

The pressure-volume curve is an exponential function, and consequently a straight line, when plotted in a semilogarithmic plot.<sup>8,10</sup> Friedenwald,<sup>6</sup> who described an analogous system in the eye, defined the rigidity of the system as the slope of this line. The slope  $\beta$  is described by

$$\beta = \frac{dV}{\log P_p - \log P_o}. \quad (5)$$

Marmarou, *et al.*,<sup>9</sup> termed this slope the pressure-volume index (PVI). The PVI is defined as the volume required to cause a tenfold increase in pressure level. The constant  $K$ , relating pressure to compliance, is thus defined as  $10^{\frac{1}{PVI}}$  or  $0.4343 \times PVI$ . The  $C_{css}$  is inversely related to the CSF pressure ( $P_o$ ) at which it is evaluated, and the degree to which it is inversely related is proportional to PVI, as

$$C_{css} = \frac{0.4343 \text{ PVI}}{P_o}. \quad (6)$$

When injection of the volume of fluid  $dV$  takes a finite period of time, the change in pressure  $dP$  is determined not only by  $C_{css}$ , but also by the increased rate of CSF absorption due to the increased ICP. The volume retained in the CSF space plus the volume absorbed must equal the volume injected. Thus, the following expression may be obtained by adding Equations 1 and 4:

$$dV = (P(t) - P_v) \times C_{out} + \frac{1}{K \times P_o} \times \frac{dP}{dt}. \quad (7)$$

A solution of this equation for calculation of  $C_{out}$  from the pressure decay following bolus injection has been suggested by several authors.<sup>6</sup> A solution suggested by Marmarou, *et al.*,<sup>9</sup> has the following form:

$$C_{out} = \frac{\text{PVI} \log \frac{P_t (P_p - P_o)}{P_p (P_t - P_o)}}{t \times P_o}, \quad (8)$$

where  $P_t$  is the pressure at time  $t$  after injection of the fluid.

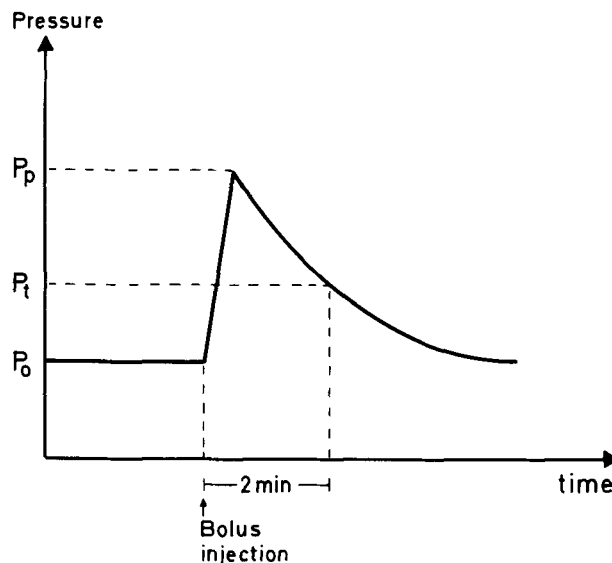


FIG. 1. Schematic drawing of the pressure rise and decay following bolus injection. Note the protracted pressure rise after injection. Peak pressure ( $P_p$ ), basis pressure ( $P_o$ ), and the pressure 2 minutes after injection ( $P_t$ ) are recorded for calculation of  $C_{css}$  and  $C_{out}$ .

Thus, with the bolus-injection technique  $C_{css}$  may be calculated from Equations 5 and 6, and  $C_{out}$  may be calculated from Equations 5 and 8. Also  $C_{out}$  may be calculated from the lumboventricular perfusion technique described by us,<sup>3</sup> and the results obtained with the two techniques may be compared.

## Results

The  $C_{out}$  values calculated from results obtained with the lumboventricular perfusion technique and the bolus-injection technique are shown in Table 1. The values obtained with the two techniques show a poor correlation ( $r = 0.477$ ). The  $C_{out}$  values obtained with the bolus-injection technique are as likely to be higher as lower than the  $C_{out}$  values obtained with the technique of lumboventricular perfusion.

The  $C_{css}$  was calculated according to Equations 5 and 6 from the results obtained with the bolus-injection technique. The results are also shown in Table 1. The  $C_{css}$  values did not correlate with the  $C_{out}$  values calculated with either of the two methods, and could not be correlated to age or etiology.

The total duration of periods with B-waves as percentage of total recording time (24 hours) is shown in Table 1. These percentages were plotted against  $C_{out}$  values obtained with the lumboventricular perfusion test and  $C_{css}$  obtained with the bolus-injection technique. The best power fits showed correlation coefficients of 0.42 and 0.51, respectively. When  $C_{out}$  and  $C_{css}$  values for each patient were simply added, the plot of  $C_{out} + C_{css}$  versus duration of B waves could be fitted by an exponential curve with a correlation coefficient of 0.84 (Fig. 2).

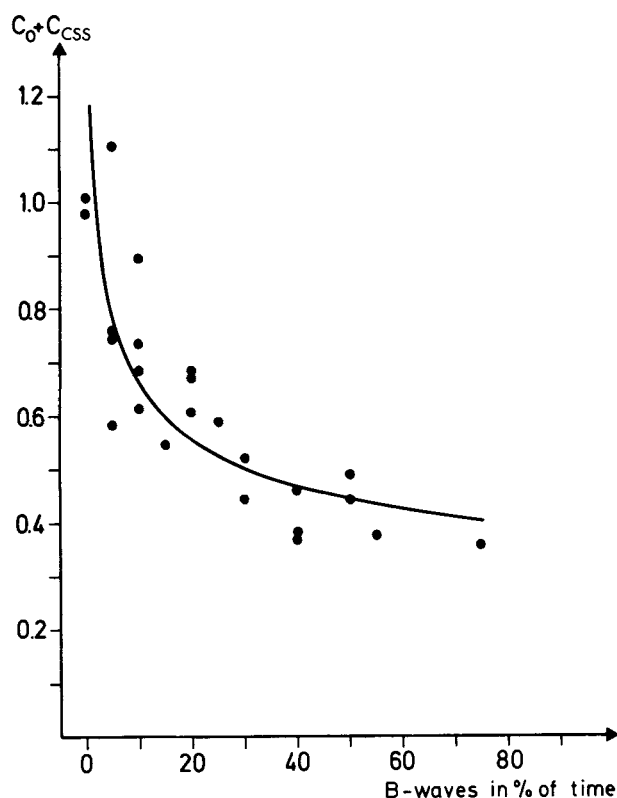


FIG. 2. Plot of  $C_{out} + C_{css}$  against the presence of B waves. The heavy line indicates the curve calculated as the best power curve fit. Correlation coefficient of the points is 0.84.

### Discussion

There were two purposes of this study. One was to compare two methods for measuring  $C_{out}$ , and the other was to evaluate whether the duration of periods with B-waves could be correlated on either  $C_{out}$  or  $C_{css}$ .

The  $C_{out}$  obtained by lumboventricular perfusion is not influenced by compliance of the craniospinal space, and  $C_{css}$  cannot be calculated from this test.<sup>3</sup> If a volume of fluid (a bolus) is rapidly injected into the CSF space,  $C_{css}$  may be calculated from the pressure rise. The shape of the subsequent pressure decay depends on both  $C_{out}$  and  $C_{css}$ . Several suggestions have been made to describe the pressure decay in order to be able to calculate  $C_{out}$ .<sup>5</sup> Marmarou, *et al.*,<sup>9</sup> tested in normal cats a hypothetical solution for the dependent variable pressure decay using the previously calculated  $C_{css}$ . They found their solution valid in their experimental situation. In the present study we have used their method for calculating  $C_{out}$  from the pressure changes following lumbar bolus injection. It is apparent from Table 1 that the  $C_{out}$  values obtained with this method show a poor agreement with the values obtained with the lumboven-

tricular perfusion technique. By covariance analysis the correlation coefficient was as low as 0.47.

It is difficult to point to factors that may lead to systematic errors in determining  $C_{out}$  by the lumboventricular perfusion technique, because of its simple design. In contrast, we may point to factors that may lead to errors in calculation of  $C_{out}$  by the bolus-injection technique. With the bolus-injection technique the calculation of PVI, and thus  $C_{css}$ , assumes that the fluid is infused so rapidly that an increased absorption of CSF during the infusion does not affect the pressure. In our hands the infusion of 6 ml of fluid lasted between 2 and 4 seconds. During this period of time the absorption of CSF is increased, and the pressure rise is not determined only by the compliance of the craniospinal space. Furthermore, in the present study the rise in intraventricular pressure following the lumbar bolus injection was delayed (Fig. 1). The pressure rise typically lasted 10 to 20 seconds. Consequently, the pressure increase does not depend only on  $C_{css}$ , but also on the amount of fluid absorbed during the infusion and the following pressure rise. Our method of using the bolus-injection technique may therefore not do justice to the technique described by Marmarou, *et al.*<sup>9</sup> However, we must conclude that the two techniques gave such different results that the less time-consuming bolus-injection technique cannot substitute for the lumboventricular perfusion technique, which we have hitherto used.

The second purpose of this study was to evaluate whether the total duration of periods with B-waves could be related to  $C_{out}$  and/or  $C_{css}$ . We assume that B-waves are the result of changes in cerebral vascular volume. Oscillations in blood flow to different organs with a frequency of 1 to 5/min are well known and are probably due to changes in vascular resistance, the so-called Traube-Hering waves. Synchronous variations in blood flow in different muscle groups with a frequency of 1/min were observed by Hildebrandt and Golenhofen.<sup>7</sup> Oscillatory changes of the intraocular volume at constant intraocular pressure were shown by Thorburn.<sup>11</sup> Ocular pressure recordings show waves of a similar pattern and frequency as B-waves.<sup>1</sup>

The increased incidence of B-waves in certain pathological states, such as normal-pressure hydrocephalus, might indicate either that the volume changes are exaggerated, or that the pressure response to volume changes is exaggerated. The pressure response to volume change lasting a finite period of time depends both on  $C_{out}$  and  $C_{css}$  (Equation 7). We have examined the relationship between the presence of B-waves and  $C_{out}$  obtained with the lumboventricular perfusion technique. These two variables are inversely related with a correlation coefficient of 0.42. Although the  $C_{css}$  values obtained with the bolus-injection technique in this study may be too low, as discussed above, we have also examined the relationship between the sum of  $C_{out} + C_{css}$  and the duration of periods with B-waves. By simply adding

$C_{out}$  and  $C_{csf}$  these two variables are weighted equally, which may not be justified, as the variation in  $C_{out}$  was larger than the variation in  $C_{csf}$ . It is, however, worth noting that the sum  $C_{out} + C_{csf}$  is inversely related to the presence of B-waves, with a correlation coefficient of 0.84, and that the plot may be fitted by an exponential curve (Fig. 2). This relationship suggests that an increase in presence of B-waves reflects an exaggerated response to volume changes. The B-waves present an on-off phenomenon that cannot be explained by the relationship, but the combination of a low  $C_{csf}$  and a low  $C_{out}$  may be a necessary factor in the origination of B-waves.

This means that, in patients with a very low compliance, only a small reduction in conductance to outflow of CSF will result in pressure elevations following increases in vascular volume. It explains why B-waves can be present in patients with only slightly reduced  $C_{out}$ .<sup>2</sup> It also indicates that the presence of B waves in the pressure recording in patients with NPH is not in itself of value in predicting the results of shunting therapy.

The small number of patients in the present study does not allow conclusions on the influence of age and etiology on the measured  $C_{csf}$ . There is, however, no trend toward low compliance with increasing age or known etiology.

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