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Conductance to Outflow of CSF in Normal Pressure Hydrocephalus

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Summary

Normal pressure hydrocephalus (NPH) is defined as a combination of dementia, gait disturbances and/or urinary incontinence, hydrocephalus, and a normal intracranial mean pressure. The clinical effect of CSF shunting in patients with this syndrome is sometimes striking, but generally only 50–60% of the shunted patients benefit from the treatment. It is assumed that the condition is caused by reduced conductance to outflow of CSF (C_{out}). A clinically usable method for the measurement of C_{out} has been developed. C_{out} has been measured in 80 patients with NPH. The results of clinical examination, computed tomography (CT), long-term intracranial pressure recording, isotope cisternography (ICG), and C_{out} have been compared to the clinical results of shunting 3 and 12 months after operation. Among the preoperative investigations C_{out} proved to have the best diagnostic specifity and sensitivity. Thus, selection of patients for shunting on the basis of C_{out} should lead to a satisfyingly high success rate.

The different methods for measurement of C_{out} are discussed, and a theory on the pathophysiology of NPH is proposed. A clinical investigational programme, based on the results from clinical examination, CT, pressure recording, and measurements of C_{out} is suggested.

Keywords: Normal pressure hydrocephalus; conductance to CSF outflow; results from shunting; pressure recording; computed tomography; isotope cisternography.

Introduction

The syndrome consisting of hydrocephalus in adults, dementia, gait disturbances, and a normal intracranial pressure has become a generally accepted clinical entity. The report of Adams *et al.*[1] of good clinical results following shunting of CSF led to increasing attention to this group of patients, where the dementia could

possibly be reversed or stopped in its progression. Occult hydrocephalus, aquired hydrocephalus, adult hydrocephalus, symptomatic hydrocephalus, normotensive hydrocephalus, and low pressure hydrocephalus are some of the terms used to describe the syndrome. However, normal pressure hydrocephalus (NPH) seems to be the most widely accepted term.

The encouraging initial results of treatment have, however, not been satisfactorily confirmed in reports with adequate numbers of patients. In Table 1 the results of treatment in a larger series of

Table 1. *Summary of Results of Studies in Larger Series of Patients with Normal Pressure Hydrocephalus*

Study	Year	Patients treated	Patients improved (%)	Complications (%)
Salmon [69]	1972	80	42	19
Wood *et al.* [87]	1974	55	60	44
Stein and Langfitt [77]	1974	43	67	10
Laws and Mokri [50]	1976	56	50	37
Greenberg *et al.* [23]	1977	73	45	40
Hughes *et al.* [43]	1980	62	47	35
Total		369	52	31

patients are summarized. The average improvement rate has been 52%, which, with a complication rate varying between 10 and 44% (average 31%), seems to be unacceptably low.

A number of diagnostic investigations and preoperative tests have been proposed for a more precise selection of patients for shunting therapy. In the reports cited in Table 1, the use of computerized tomography (CT), isotope cisternography (ICG), intracranial pressure monitoring, and infusion tests, have not essentially improved the results, and it has not been possible to point out a single, preoperative test with a satisfyingly high predictive value.

The natural course of NPH is, in fact, not known. In the relevant literature, all patients suspected of impairment of CSF resorption have been treated by CSF shunting. Doubtless, a progression may

be observed in some patients, stated both by a history of progressing dementia and gait disturbances, and by the severe clinical condition some patients develop, before admission to hospital. But whether the symptoms continue to progress in all patients or are arrested at different stages in different patients is not known. Some patients may have had symptoms of dementia and gait disturbancies for more than two years, and still improve after shunting[12]. This indicates that even long-standing neuronal dysfunction may be reversible, and that progression in the disease may be very slow, if present at all.

The fact that the clinical symptoms associated with NPH may be relieved by shunting CSF past its normal resorption sites indicates that the resorption of CSF does not occur under normal conditions in patients with NPH. A shunt has two modes of action:

1. Diversion of CSF with all its components. No detailed biochemical screening of CSF in patients has, so far, been reported, and no noxious components have been identified.

2. Modification of the intracranial pressure by the preset opening pressure and flow characteristics of the shunt.

It is obvious that the resorptive capacity for CSF plays a role in establishing and maintaining the CSF pressure. The purpose of diverting CSF by a shunt is to compensate for a too low resorptive capacity, and a clinical effect can only be expected in cases where the symptoms are due to a decreased resorptive capacity. The resorptive capacity can be measured as conductance to outflow of CSF (C_{out})—the reciprocal of resistance to outflow. C_{out} can be measured by different perfusion techniques. Børgesen has developed a clinically usable lumboventricular perfusion[13].

On the basis of these considerations and on the lumbo-ventricular perfusion a prospective study including measurements of C_{out} and intraventricular pressure, CT, and ICG was planned in patients with NPH. The purpose of the study was two fold:

First, to investigate the correlation between C_{out} and the clinical effect of shunting in patients with NPH. If a low preoperative C_{out} is significantly correlated with a clinical effect of shunting CSF, it can be concluded that a decreased resorptive capacity is the main factor in the production of symptoms in NPH. In addition, a preoperative measurement of C_{out} may provide a better selection of patients for shunting therapy.

Second, to compare the results of other preoperative investigations and clinical findings to the values of C_{out}. Such a comparison may demonstrate which findings in the clinical

examination, and long-term pressure monitoring indicate a decreased resorptive capacity.

In the following, the clinical material from 80 patients with NPH, who participated in the study, will be presented. The methods of the investigations will be explained and discussed. The clinical results will be presented and discussed. Thereafter, the results will be compared to C_{out} values. The preoperative findings in the CT, ICG, and in pressure monitoring will be compared with the clinical results and to values of C_{out}. In the conclusion, the general results and their clinical utility will be discussed. A hypothesis for the pathogenesis and pathophysiology of NPH will be proposed.

Definitions

Normal pressure hydrocephalus: The combination of progressive dementia, gait disturbances, and/or urinary incontinence, hydrocephalus and a normal intracranial pressure.

Progressive dementia: A dementia that is evident to observers and prevents social function which was previously normal.

Gait disturbances: A history of difficulty in walking, and at least signs of difficulty in turning around or walking blindfold.

Urinary incontinence: Urgency or incontinence at least once a week.

Hydrocephalus: Evan's ratio above 0.30 in the CT.

Normal intracranial pressure: Mean, resting intraventricular pressure not exceeding 12 mm Hg and no plateau waves during 24 hours of continuous recording.

Clinical Material

80 patients were included in the study. They were selected among adult patients admitted consecutively to the Department of Neurosurgery, Rigshospitalet, Copenhagen, for investigation of symptomatic hydrocephalus, in the years 1977–1980. Only patients fulfilling the above-mentioned definition of NPH were included. Further criteria for inclusion were: a length of history of more than three months, and no signs of cerebral infarction or tumour in the CT.

Two patients were included in spite of an Evan's ratio in the CT = 0.30. The reason for this was that the patients were included on the basis of pneumoencephalography, where the Evan's ratios were 0.33 and 0.35 respectively, performed before the CT[16] (patients no. 4 and 27, Table 5). One patient underwent all the preoperative investigations, but refused to be operated on, and was thus excluded from the rest of the study (patient no. 27 in Børgesen *et al.*[14].)

The age of the patiens varied between 21 and 73 years, mean 64.6 years. 51 patients were male; 29 female. This data is listed in Table 5, together with the aetiology and other clinical data. In Table 2 the number of patients in the different aetiological groups can be seen. The miscellaneous group is comprised of patients

Table 2. *Number of Patients with Different Aetiologies of NPH.* Note, that half of the patients had no known aetiology

Subarachnoid haemorrhage	16
Trauma	10
Meningitis	8
Miscellaneous	6
Unknown aetiology	40
Total	80

with an earlier intracranial operation (patients no. 8 and 19 in Table 5) and patients with cerebral apoplexy without infarction in the CT or permanent neurological deficits (patients no. 54, 63, 71, and 75 in Table 5). As seen in Table 2, half of the patients had a known (or supposedly known) aetiology of NPH, while the other half had no known aetiology.

None of the patients were able to work, either in their previous job or in another, easier job. None of the patients were able to do normal house-work without help.

Differences in the mode of selection presents one of the main difficulties in comparing reports in the literature of patients treated for what, in a diffuse term may be called "symptomatic hydrocephalus".

The patients in the present material were, as given above, selected on clinical premises supplied with the criteria of a hydrocephalus and a normal intracranial pressure. However, some of the patients were referred from other clinics, where they had been selected for further investigation on the basis of clinical signs *and* signs in PEG interpreted as indication of defective CSF resorption (see Børgesen *et al.*[16]).

Thus, the 34 patients in whom PEG had been performed, were selected from an unknown number of patients, where clinical and radiological signs may have been sufficient for inclusion in the present study. This limitation in parts of the present material at least, restricts the conclusions which may be made on the findings in PEG. This, and the finding that periventricular hypodensity was not seen in patients, in whom PEG had been performed, will be discussed later in the chapter on CT in NPH. Otherwise, the patients in whom PEG had been performed did not differ from the rest of the material.

Methods

The study was prospective. Besides the clinical examination and grading, the pretreatment investigations included CT, ICG, long-term intracranial pressure monitoring, and lumboventricular perfusion. After shunting, the patients were seen at 3 and 12 months follow-up, when the clinical examination and CT were repeated, and the shunt, if necessary, tested.

a) Clinical Examination. Dementia was examined by testing and by interview with the patient and with the patient's family. Testing of the patient included "100-7" test, remembering and restructuring a 4-cipher number, and repetition of a 10 word text. The dementia was categorized as mild, when deficits could be shown only by testing and the interview revealed difficulties in daily activities such as reading, watching television, participating in social activities etc.; moderate, when there was a partial memory deficit, slowed mentation and obvious difficulties with daily affairs; and severe, when the patient was disorientated, lacking short-time memory, unable to attend to himself, or in a worse condition.

Gait disturbances were recorded as mild when the patient walked with small steps and had difficulties in turning around and in walking blindfold; moderate, when the gait was unstable, legs wide apart, with small steps; and severe when the patient was unable to walk, or only with support.

Urinary incontinence was noted according to the definition. Possible *spasticity, tremor* or *ataxia* was noted.

The patients were assigned to one of the following functional grades, modified after Stein and Langfitt[77]:

0: no neurological deficit, able to work,
I: minimal deficit, able to function independently at home,
II: some supervision required at home,
III: custodial care required in spite of considerable independent function,
IV: no practical capacity for independent function,
V: vegetative; bedridden, no spontaneous activity, no verbal contact.

b) Computed tomography (CT) was performed in all patients. The size of the ventricles was calculated as the Evan's ratio, and the widths of the largest cortical sulci high in the frontal or parietal region were measured. The presence of periventricular hypodensity was judged visually. CT was repeated at 3 and 12 months follow-up, when the same measurements were made.

c) Isotope cisternography (ICG) was performed in 55 of the patients. The ICG scans were examined for ventricular activity and the distribution of the isotope 6, 24, and 48 hours following injection. For further details, see Børgesen *et al.*[17].

d) Intracranial pressure was recorded continuously for 24 hours via an intraventricular catheter. The records were examined for the mean intraventricular pressure level, amplitude of pulse-pressure waves, and the presence and amplitude of B waves. For definitions of pressure waves and further details, see Børgesen *et al.*[14].

e) The conductance to outflow of CSF was measured by a lumboventricular perfusion test, following the pressure monitoring.

Measurement of Conductance to Outflow of CSF

The resorptive capacity for CSF can be evaluated by several methods. Most of these allow quantitative measurement of C_{out}, but some are too time-consuming for routine clinical use. In the following, five different methods will be described. They represent all so far described methods for the evaluation of the resorptive

capacity. Their theoretical presuppositions and possible sources of error will be discussed. The five methods are:

1. Constant rate lumbar infusion test.
2. Constant pressure lumbar infusion test.
3. Ventricular steady-state perfusion.
4. Lumboventricular steady-state perfusion.
5. Bolus injection method.

1. Constant rate lumbar infusion test. This method was described by Mortensen and Weed[59], and applied in humans by Katzman and Hussey[48]. Via a lumbar cannula, fluid is infused at a constant rate. The resulting increase in CSF pressure is monitored. The relation between infusion rate and pressure level obtained at a steady-state situation is an expression of the resorptive capacity for CSF. Katzman and Hussey[48] found that at an infusion rate of 0.76 ml/min. the pressure level in normals gradually increased to a constant level of about 14 mm Hg. As only one set of values for the infusion rate and pressure is known, the C_{out} cannot be calculated by this method (see below).

2. The constant pressure lumbar infusion test was first described by Davson *et al.*[24], and modified by Ekstedt[27]. The infusion via a lumbar cannula is kept constant at a constant pressure level by means of a servo-controlled infusion pump. By increasing the infusion rate stepwise, several values of infusion rates can be obtained at different constant pressure levels, and C_{out} can be calculated (see below).

3. Ventricular steady-state perfusion with a radioactive tracer added to the perfusate was described by Pappenheimer *et al.*[62]. Infusion is done via a catheter placed in the ventricles. Unabsorbed fluid flows out via a catheter placed *e.g.* in the cisterna magna or in the lumbar subarachnoid space. By elevating the height of the outflow catheter tip the CSF pressure can be increased. From the dilution of the radioactive tracer and the absorbed volume at different constant pressure levels the formation rate of CSF, the CSF volume, and C_{out} can be calculated.

4. Lumboventricular steady-state perfusion was developed by Børgesen *et al.*[12]. The principle of this method is that, at a constant infusion rate via a lumbar cannula, constant intraventricular pressure, and constant outflow rate via an intraventricular catheter, the absorbed volume can be calculated from:

$$V_{abs} = V_{in} + V_f - V_{out} \quad (1)$$

where V_{abs} is the absorbed volume, V_{in} the infused volume per minute, and V_{out} the non-absorbed volume collected from the outflow catheter. V_{abs} is calculated at several (4–5) different pressure levels, and plotted against pressure (P) in an absorption/pressure regression line. The regression coefficient of this line can be expressed as:

$$C_{out} = \frac{d\,V_{abs}}{d\,P}\,\text{ml/min/mmHg} \qquad (2)$$

C_{out} is thus the reciprocal to the resistance to the outflow of CSF. The different pressure levels are obtained by elevating the tip of the outflow catheter, infusion rate can be kept between 0.5 and 4.0 ml/minute. The surplus fluid is collected from the outflow catheter in two periods of 5 minutes. The two samples are compared and must be equal to secure a stable outflow rate (for further details see Børgesen *et al.*[12]).

5. Bolus injection method. Rapid intrathecal injection of a small volume (a bolus) results in a sudden rise in pressure followed by a decline in pressure. The pressure increase depends on the compliance of the craniospinal space (C_{CSS}). Subsequent the fall in pressure depends on both C_{CSS} and C_{out}. From the pressure changes and the injected volume C_{CSS} and C_{out} can be computed from the formulae proposed by Marmarou *et al.*[54]. They found good agreement between C_{out} measured by bolus injection and by infusion test in cats. Sullivan *et al.*[79] compared C_{out} measured by bolus injection and by infusion tests in both cats and man, and found, that the bolus injection method underestimates the C_{out}, but that the C_{out} measured by the two methods agreed.

Børgesen *et al.*[15] found no correlation between C_{out} measured by the bolus injection method and by lumboventricular perfusion in one and the same patient. It was concluded that the bolus injection method cannot substitute lumboventricular perfusion for measurements of C_{out}.

The reason why the theoretically correct measurement of C_{out} by bolus injection does not correlate with C_{out} measured by lumboventricular perfusion in humans is probably technical[15]. The pressure increase following injection of the bolus depends not only on C_{CSS} as there is often a delay in pressure rise of 10–20 seconds, during which time part of the injected bolus will be absorbed. To this is added the 2–4 seconds used for the injection. Thus an

indeterminable part of the bolus does not contribute to the pressure rise, rendering the calculation of C_{CSS} invalid. As C_{CSS} is used for calculation of C_{out}, also this parameter is affected.

Theoretical Considerations and Sources of Error

The calculation of C_{out} from any of the above-mentioned methods has three presuppositions:

1. The production rate of CSF remains constant during the test, irrespective of the increase in intracranial pressure.
2. The rate of absorption of CSF is a rectilinear function of the intraventricular pressure.
3. The CSF volume and the cerebral blood volume (CBV) remains constant during the sampling of unabsorbed fluid.

1: The production rate has been shown to be constant within the actual pressure range[22, 52, 68]. Martins *et al.*[56] found a 4% decline in the production rate in animals after 6 hours perfusion. In the calculation of C_{out} from the steady-state lumboventricular perfusion, the production rate is assumed to be constant at 0.4 ml/min. However, the actual value is unimportant as long as it does not change as a function of the intraventricular pressure. Furthermore, a supposed decline in CSF rate to 50% of normal (which seems unlikely) at IVP = 40 mm Hg will result in a reduction in C_{out} (calculated at an initial production rate of 0.4 ml/min) for example from 0.066 to 0.060 ml/min/mm Hg, an error of only 10%.

2: The absorption/pressure relationship has been shown to be rectilinear in several investigations[12, 13, 28, 74]. Lorenzo *et al.*[52] and Stevenaert *et al.*[78] used ventricular steady-state perfusion and found the absorption/pressure function to be rectilinear in 15 patients. In a total of 5 patients, they found, however, that the absorption rate declined abruptly at a certain pressure level. This discrepancy is probably due to calculation of the absorption/pressure function from too few (2–3) different pressure levels. A deviation in only one of the absorbed volumes will result in bending of the absorption/pressure curve.

As the absorption rate is presumably a rectilinear function of the pressure, it can be deducted that the drainage of CSF is a bulk flow phenomenon. Whether the absorption occurs through valves, as proposed by Welch and Friedman[85], or by vacuolar transcellular channels, as shown by Tripathi[83] is unimportant in this respect, as both mechanisms permit bulk flow of CSF[25].

3: The formula (1) from which the absorbed volume at a steady state pressure level is calculated may be modified by incorporating changes in the cerebral blood volume (dCBV/dt) during the measurement:

$$V_{abs} = V_{inf} + V_f - V_{out} + \frac{d\,CBV}{d\,t} \tag{3}$$

This modification implies that an increase in CBV will result in an increase in V_{abs} and thus an increase in the calculated C_{out} formula (2).

It is not readily apparent from the literature that changes in CBV indeed occur with sudden increases in intracranial pressure. The local increase in CBV observed by Risberg *et al.*[67] to occur during a plateau-wave of more than 30 mm Hg may well be the eliciting factor of the pressure increment and therefore only occurring in patients, where plateau-waves are present for some reason. However, even if there is an increase in CBV, Sklar *et al.*[73] have deducted that the influence on the calculated C_{out} is near to insignificant.

The design of the lumboventricular perfusion test is so, that gross changes in CSF volume, from for example increases in CBV during the measurement of V_{abs}, can be detected. The outflow of unabsorbed CSF (V_{out}) is sampled in two periods of five minutes and the two volumes are compared. Differences indicate changes in CSF volume during the measurement (in spite of the steady-state pressure level), and mean the actual measurement will have to be redone.

Beyond the possible changes in CBV it is difficult to imagine other causes for changes in the CSF volume, which will not result in disruption of the steady-state pressure level.

The constant pressure infusion test, the ventricular steady-state perfusion and the lumboventricular steady-state perfusion all lead to a quantitative measurement of the resorptive capacity for CSF. They are all based on the same principle: That at a given infusion rate and a given steady-state pressure the absorbed volume can be calculated. The advantages of lumboventricular steady-state perfusion are therefore of a practical nature. First of all, the lumboventricular perfusion is less time consuming than the other two methods: a test can be completed in less than two hours. In ventricular perfusion with an indicator Lorenzo *et al.*[52] states that 2–3 hours are required to obtain adequate mixing of indicator and

CSF, so that a single value for CSF absorption can be determined. This method will therefore be difficult to use in clinical practice. Ekstedt[27] gives an investigation duration of about three hours to obtain a sufficient number of determinations of absorbed volumes at steady-state pressure levels. Next, the technical equipment required for a lumboventricular perfusion is simple: together with standard pressure monitoring system and recorder, only an infusion pump and a weight are needed. The servocontroller for pressure-regulated infusion rate (as described by Ekstedt[27] for the constant rate infusion test), or the laboratory equipment required for measurement of indicator-concentration in the ventricular perfusion are avoided.

One technical cause of error is common to all tests where infusion is used: Leakage of CSF or infusate at the puncture site. In the constant rate lumbar infusion test the steady-state pressure level will in this case be too low, giving the impression of a normal absorption capacity for CSF. In the constant pressure infusion test and in the lumboventricular steady-state perfusion test leakage of CSF or infusate will lead to a too high value of the absorbed volume, and thus to a falsely high C_{out}. Therefore, the puncture of the dura with the lumbar cannula must be smooth and only performed once. Unexpected high values of C_{out} in patients with clinical indications of decreased C_{out} should therefore lead to repetition of the test not earlier than one week after the last dura perforation. If a leakage opens up during the test, after the first one or two determinations of absorbed volume, the absorption/pressure line will start to bend downwards. The regression coefficient will become low, and the calculation of C_{out} will be invalidated. Such a "late" leakage is thus easily detected both in the constant pressure infusion test and in the lumboventricular perfusion test.

Reproduceability and Comparability of Measurements of C_{out}

It is a condition for the use of a physiological parameter in clinical practice that the measurement of the parameter is reliable. However, the importance of this hardly justifies an investigation with repeated measurements of C_{out} in the same patient, for example two or three times several weeks apart. Accordingly, no serial measurements in patients with NPH have been reported. Sklar *et al.*[73] repeated the measurement of C_{out} in five patients with pseudotumour cerebri. C_{out} was found to be the same in

measurements months apart, independent of whether the patient was under medication or not.

In the present material the reproduceability of the measurement was tested in eight patients. In the same procedure C_{out} was measured twice with a short pause between. The measured C_{out} did not vary more than 5% in these measurements. This indication of good reliability is not a proof of this, as C_{out} of course may vary over longer periods of time. However, for the actual value the reproduceability seems to be acceptable.

Concerning the comparability of C_{out} measured by the different methods, no such comparisons have been reported—except in the report referred to above of Børgesen *et al.*[15] comparing the lumboventricular perfusion and bolus injection methods. The calculation of C_{out} from absorbed volumes at different pressure levels are basically the same in the infusion and perfusion methods. However, differences in the methods of obtaining the steady-state pressure levels may, as stated by Sklar *et al.*[73], result in variations in C_{out} measurements. This is explained by the possible influence from alterations in the CSF volume when the steady-state pressures are selected at random and not in a directional form, as for example in the lumboventricular perfusion test. This difference may be responsible for the small discrepancy in the "lower normal limit" of C_{out} given by Ekstedt[28] and Sklar *et al.*[72] (see below).

It is probably possible to design a CSF-space perfusion test in an even more simplified form than the lumboventricular steady-state perfusion. If the conductance of the infusion cannula is sufficiently high, the outflow catheter may be connected to the side of the infusion cannula. The test could then be performed via a single cannula inserted into the lumbar region. However, the flow along the spinal canal must be unhindered, so that the infusion pressure, which will be the same as the pressure measured in the outflow catheter, equals the intraventricular pressure. Therefore, the method would have to be compared with the lumboventricular perfusion test in a series of patients.

The Normal Range of C_{out} Selection for Shunting

The normal range of C_{out} is not exactly known. C_{out} has not been measured in humans without neurological disease. The 58 patients considered as normal in the report of Ekstedt[28] were nevertheless included for investigation on the suspicion of "altered CSF hydrodynamics". However, this material probably represents the

closest one can come to a normal group without investigating completely healthy persons. The lower normal limit in the material was found to be $C_{out} = 0.10$ ml/min/mm Hg. Sklar *et al.*[72] states that, based on infusion tests in different types of patients they have found, values of C_{out} less than 0.13 ml/min/mm Hg may be considered abnormal. The clinical material has not been presented.

It had already become clear in the first part of the present study[13] that even among patients selected as given above, there would be a considerable variation in the level of C_{out}. As it was unlikely that patients with C_{out} above the above cited values would show improvement in clinical symptoms after shunting, it was soon decided that only patients with C_{out} less than 0.120 ml/min/mm Hg were to be treated by CSF shunting. One patient, with $C_{out} = 0.128$ ml/min/mm Hg (patient no. 7 in Table 5) was shunted before this decision was made. Another patient (no. 19 in Table 5), who had had an operation for an acoustic neurinoma 8 years earlier, and who had been moderately demented, with gait disturbances and urinary incontinence for more than two years, had a $C_{out} = 0.118$ ml/min/mm Hg. With this borderline result it was decided not to shunt the patient.

Results

Evaluation of Results of Shunting

In order to avoid bias in the post-shunting evaluation of the patients, three precautions have been taken: First, all perfusion tests were performed by the same investigator (the author); second, all results from pressure recordings and C_{out} measurements were unknown to the clinical investigator at the follow-up examination; thirdly, all follow-up examinations were done by another investigator (F. Gjerris).

At the 3 months follow-up investigation the following were recorded:

1. Functional grade: This was, as in the pretreatment investigation, determined by interview with the patient and his family or the daily nursing staff.

2. The family's estimation of the result of the treatment was recorded as "excellent", "good", or "poor". If the family found the condition of the patient to be unchanged from that before shunting, the estimation was recorded as poor.

3. Degree of dementia: If it became apparent either by testing or by interview with the patient and his family, as given above, that the dementia had improved, this was recorded as such. All other cases were recorded as unimproved.

4. Gait disturbances were in the same way recorded as improved or unimproved.

5. Urinary incontinence was recorded as improved only when it had disappeared.

A CT was done at the 3 months follow-up. Evan's ratio and the width of the cortical sulci were measured, and both recorded as "normalized" when the Evan's ratio was less than 0.31 and the width of sulci less than 2.0 mm, "diminished": only when they were less than pretreatment size, or unchanged. These measurements were made by a neuroradiologist independent of the study and without knowledge of pretreatment parameters.

At the 12 months follow-up all the above examinations were repeated, including CT.

Shunt Operation. Testing of Shunt Function

All shunts used were of the Hakim medium-pressure type, fitted with a prechamber which made pressure measurements possible. CSF was shunted to the right atrium.

Normalization of the ventricular system was taken as a sign of a satisfactory function of the shunt. In cases where there was no clinical improvement, and Evan's ratio was unchanged or only slightly diminished in the CT, the shunt was tested by measuring the opening pressure of the shunt, and the intraventricular pressure was recorded via the prechamber of the shunt. If malfunction of the shunt was shown or suspected, the shunt system was changed.

Definition of Improvement Following Shunting

The evaluation of the clinical result of shunting is one of the crucial points in the present investigation. A patient was considered improved after shunting when there was either:

1. An improvement of one degree or more in the functional grade, or
2. an improvement in both dementia, gait disturbances and possible urinary incontinence *and* the family's estimation of the result was good or excellent, in spite of no improvement in the functional grade.

It may thus be stressed, that improvement for example in dementia alone, or in gait disturbances alone, was not sufficient for the result to be categorized as improved.

Some patients experienced only a short lasting (less than 3 months) clinical effect of the shunt. This result was recorded as "transient improvement" when the improvement was definitely observed by the patients family or by nursing staff to occur both in the dementia and gait disturbances and possible urinary incontinence.

The result of shunting was recorded as unimproved: when the clinical status remained unchanged or had become worse, or when there was only partial improvement, as for example, in dementia alone.

Clinical Results

In the following, the results of clinical examination and of shunting in 80 patients with NPH will be presented and discussed. In Table 3 the number of patients in the different groups of: dementia, gait disturbances, urinary incontinence and spasticity, categorized according to the definitions given above, are compared with the functional grades to which the patients were assigned. As

Table 3. *The Clinical Findings Compared with the Functional Grade*

	Total	Functional grade				
		I	II	III	IV	V
Dementia						
mild	4	3	1	0	0	0
moderate	28	8	15	5	0	0
severe	48	0	2	16	19	11
total	80	11	18	21	19	11
Gait disturb.						
mild + moder.	24	9	10	5	0	0
severe	55	1	8	16	19	11
Urinary incont.	52	2	5	15	19	11
Spasticity	41	0	5	12	13	11

Table 4. *The Aetiology Compared with the Clinical Findings*

	Aetiology	
	Unknown	Known
Dementia		
mild	3	1
moderate	14	14
severe	23	25
Gait disturb.		
mild + mod.	13	11
severe	26	29
Urinary incont.	24	28
Spasticity	17	24

may be expected, the severity of clinical signs correlates well with the functional grade. Severe dementia was only seen in patients assigned to grade II or worse; of the 55 patients with severe gait disturbances, 46 were in a functional grade III or worse.

The two groups of patients with a known or unknown aetiology are compared with the clinical status in Table 4. It is readily seen that there is no difference in the severity of the clinical signs between the two groups. It must be stressed that the

Table 5. *Clinical Data, C_{out} (ml/min/mm Hg), Evan's Ratio in CT3 and 12 Months* subarachnoid haemorrhage. "Norm.": Evans' ratio below 0.31. Paper no. I: Paper no. IV:

Pt.	No. in pr. paper			Sex and	Etiology	Funct. grade	C_{out}	Evans' ratio	ICG-group
No.	I	II	IV	age					
1	1	1	1	M 54	trauma	I	0.057	0.33	—
2	2	2	35	F 59	SAH	IV	0.040	0.45	—
3	3	3	36	M 66	mening.	IV	0.013	0.42	—
4	4	4	2	F 49	unknown	I	0.133	0.30	IV
5	5	5	3	M 62	unknown	III	0.045	0.34	—
6	6	6	4	M 60	trauma	II	0.060	0.36	—
7	7	7	5	M 47	unknown	I	0.128	0.43	—
8	8	8	37	M 48	tumour	II	0.055	0.37	—
9	9	9	6	M 65	unknown	III	0.070	0.34	—
10	10	10	7	M 60	SAH	III	0.071	0.32	—
11	11	11	8	M 56	unknown	I	0.058	0.32	—
12	12	12	9	M 21	congen.?	II	0.157	0.44	—
13	13	13	10	M 54	trauma	II	0.086	0.31	—
14	14	14	38	M 61	mening.	IV	0.044	0.42	—
15	15	15	11	M 60	unknown	IV	0.113	0.31	—
16		16	12	M 57	unknown	I	0.055	0.31	II
17		17	13	F 65	unknown	III	0.390	0.33	
18		18	14	M 53	unknown	I	0.410	0.34	II
19		19		F 67	tumour	II	0.118	0.33	
20		20	15	M 52	unknown	III	0.112	0.38	II
21		21	39	F 59	trauma	V	0.066	0.34	IV
22		22	16	M 56	unknown	II	0.025	0.40	IV
23		23	17	M 48	trauma	II	0.056	0.36	III
24		24	40	M 69	unknown	II	0.035	0.35	IV
25		25	41	M 69	mening.	V	0.032	0.34	—
26		26	18	F 50	unknown	I	0.066	0.35	III
27		28	19	M 66	mening.	II	0.098	0.30	II
28		29	20	F 54	unknown	I	0.051	0.31	II
29		30	21	M 44	trauma	I	0.098	0.31	III
30		31	22	M 63	unknown	IV	0.026	0.35	III
31		32	42	M 73	unknown	III	0.024	0.36	III
32	33	1	43	F 65	mening.	IV	0.149	0.45	I
33	34	2	44	F 61	unknown	II	0.116	0.41	III
34	35	3	23	M 71	unknown	III	0.094	0.32	II
35	36	4	45	M 53	SAH	III	0.074	0.35	IV
36	37	5	24	F 49	unknown	IV	0.062	0.41	IV
37	38	6	46	M 57	mening.	V	0.062	0.34	IV

After Operation. Isotope cisternography-groups are also shown. SAH: Børgesen *et al.*[13]. Paper no. II: Børgesen *et al.*[14]. Paper no. III: Børgesen *et al.*[15]. Børgesen *et al.*[16]

3 months follow-up			12 months follow-up			Comments
Funct. grade	Clin. result	Evans' ratio	Funct. grade	Clin. result	Evans' ratio	
I	+	norm.				suicide 4 months postop.
III	+	0.35	II	+	0.35	
II	+	norm.	I	+	norm.	
no shunt						perfusion repeated
III	+	norm.	IV	trans.	norm.	worse 12 months postop.
I	+	0.31	I	+	0.31	
I	—	0.43	I	—	0.43	shunt tested
0	+	norm.	0	+	norm.	
III	+	norm.	IV	trans.	norm.	worse 12 months postop.
III	+	0.32				shunt revised, died 7 months postop.
0	+	norm.				died 8 months postop.
noshunt						aetiology uncertain
II	—	norm.	II	—	norm.	
I	+	norm.	I	+	norm.	SAH before mening.
IV	—	norm.	IV	—	norm.	
0	+	norm.	0	+	norm.	
no shunt						
no shunt						
no shunt						see text
III	—	norm.				died 12 months postop.
III	+	norm.	III	+	norm.	
I	+	0.33	I	+	0.33	
I	+	norm.	I	+	norm.	
I	+	0.35	I	+	0.35	shunt tested
V	trans.	—				died 2 months postop. CT not obtained
0	+	norm.	0	+	norm.	
II	—	norm.	II	—	norm.	
0	+	norm.	0	+	norm.	
I	—	norm.	I	—	norm.	
IV	trans.	norm.	IV	—	norm.	
II	+	0.32				died 6 months postop.
no shunt						
II	—	0.35	II	—	0.35	
III	—	norm.	III	—	norm.	
0	+	norm.	0	+	norm.	
III	+	norm.	IV	trans.	norm.	worse 12 months postop.
V	—	—				died 3 months postop., CT not obtained

Table 5 (continued)

Pt. No.	No. in pr. paper IV			Sex and age	Etiology	Funct. grade	C_{out}	Evans' ratio	ICG-group
38	39	7	47	F 71	SAH	IV	0.043	0.34	IV
39	40	8	48	F 58	unknown	II	0.073	0.33	II
40		9	25	F 68	unknown	IV	0.132	0.32	II
41		10	26	M 39	unknown	II	0.058	0.39	II
42		11	49	M 59	unknown	III	0.177	0.33	I
43		12	50	F 47	SAH	III	0.033	0.41	IV
44		13	27	M 62	unknown	III	0.098	0.45	III
45		14	28	F 60	unknown	IV	0.511	0.47	IV
46		15	51	F 47	SAH	III	0.019	0.36	—
47		16	52	M 71	unknown	I	0.083	0.37	IV
48		17	29	M 58	apoplexy	II	0.108	0.33	II
49		18	30	M 69	unknown	III	0.061	0.33	III
50		19	53	F 59	SAH	V	0.125	0.37	III
51		20	54	F 52	SAH	IV	0.038	0.36	III
52		21	31	M 62	SAH	III	0.052	0.35	III
53		22	55	F 53	trauma	V	0.048	0.36	—
54		23	56	M 54	apoplexy	V	0.125	0.35	II
55		24	57	F 59	SAH	III	0.036	0.35	II
56		32		F 67	unknown	IV	0.071	0.33	II
57		58		M 37	SAH	III	0.030	0.42	—
58		33		M 73	SAH	V	0.156	0.42	IV
59		59		M 56	trauma	II	0.009	0.54	IV
60		60		M 65	unknown	IV	0.091	0.41	III
61		61		F 67	unknown	IV	0.035	0.45	—
62		62		M 39	unknown	II	0.059	0.36	IV
63		63		M 67	apoplexy	IV	0.032	0.34	IV
64		64		M 64	unknown	IV	0.024	0.36	IV
65		65		F 55	mening.	V	0.028	0.36	—
66		34		M 49	SAH	III	0.061	0.33	IV
67		66		M 64	trauma	V	0.070	0.43	III
68				M 65	trauma	III	0.034	0.37	IV
69				F 31	unknown	III	0.320	0.32	IV
70				M 55	unknown	II	0.052	0.43	IV
71				F 56	apoplexy	III	0.057	0.36	IV
72				F 23	SAH	II	0.121	0.45	II
73				M 61	unknown	I	0.120	0.39	II
74				M 60	unknown	III	0.057	0.35	III
75				M 42	apoplexy	II	0.048	0.40	III
76				M 45	SAH	V	0.055	0.41	—
77				F 58	SAH	IV	0.022	0.36	IV
78				M 70	unknown	IV	0.146	0.37	II
79				M 60	SAH	V	0.040	0.35	—
80				F 62	unknown	IV	0.084	0.34	—

3 months follow-up			12 months follow-up			Comments
Funct. grade	Clin. result	Evans' ratio	Funct. grade	Clin. result	Evans' ratio	
III	+	0.34	III	+	0.34	shunt revised
I	+	norm.	I	+	norm.	
no shunt						
0	+	norm.	0	+	norm.	
no shunt						
I	+	norm.	I	+	norm.	
III	—	0.45	III	—	0.45	shunt tested
no shunt						perfusion repeated
I	+	norm.	I	+	norm.	
I	—	0.37	I	—	0.37	shunt tested and changed
II	—	norm.	II	—	norm.	aetiology uncertain
II	+	norm.	II	+	norm.	
no shunt						
II	+	norm.	II	+	norm.	
III	trans.	0.35	III	—	norm.	aetiology uncertain shunt test. + chang.
II	+	norm.	I	+	norm.	
no shunt						aetiology uncertain
I	+	norm.	I	+	norm.	
IV	—	0.31	IV	—	0.31	shunt tested
II	+	norm.	II	+	norm.	
no shunt						
I	+	0.37	I	+	norm.	shunt revised
IV	—	0.33	IV	—	0.33	
II	+	norm.	II	+	norm.	
0	+	0.36	0	+	0.36	shunt tested
IV	trans.	norm.	IV	—	norm.	aetiology uncertain
II	+	norm.	II	+	norm.	
II	+	norm.	II	+	norm.	
II	+	norm.	II	+	norm.	
III	+	norm.	I	+	norm.	
I	+	norm.	I	+	norm.	
no shunt						
I	+	0.43	I	+	0.36	shunt revised
II	+	norm.	II	+	norm.	
no shunt						
no shunt						
II	+	norm.	II	+	norm.	
I	+	norm.	I	+	norm.	
0	+	norm.	0	+	norm.	
I	+	0.33	I	+	0.33	
no shunt						
III	+	norm.				died 8 months postop.
IV	—	0.34	IV	—	0.36	shunt revised

patients without a known aetiology were in the same clinical status as those with a known aetiology such as subarachnoidal haemorrhage, meningitis, or trauma. A possible difference in the results of treatment between the two groups cannot be attributed to differences in the pretreatment clinical status.

Of the 80 patients included in the study, only 64 were shunted. These were selected as mentioned above on the basis of the results of the lumboventricular perfusion for the measurement of C_{out} (C_{out} less than 0.120 ml/min/mm Hg).

Sixty-three of the shunted patients were seen 3 months after operation; one patient died from a pulmonary embolus 2 months after operation.

Fifty-six patients were seen at a follow-up examination 12 months after the operation. The remaining 7 patients died between 3 and 12 months after the operation. Thus, 8 patients in all died in the observation period.

Causes of death were:

Pt. no. 1: suicide 4 months after operation.

Pt. no. 10: cerebral infarction 7 months after operation.

Pt. no. 11: cerebral infarction 8 months after operation.

Pt. no. 20: pulmonary cancer 12 months after operation.

Pt. no. 25: pulmonary embolus 2 months after operation.

Pt. no. 31: cerebral infarction 6 months after operation.

Pt. no. 37: deterioration into vegetative state due to NPH, 3 months after operation.

Pt. no. 79: pneumonia (and NPH) 8 months after operation.

None of the non-shunted patients died within the observation period of the study. The seemingly high mortality rate of 10% (12.5% of shunted patients) must be considered mainly as a result of the severity of the diseases which had led to their NPH, rather than as a result of the age of the patients themselves; the mean age of the patients who died being not more than 56.5 years. There is however, no trend in the causes of death in the patients.

In Table 5 clinical data: age, sex, aetiology, functional grade, before, 3 and 12 months after shunting, and results of shunting are shown. The numbers with which the patients appear in the reports of Børgesen *et al.*[13–16] are also shown.

Some of the discrepancies between the data given in Table 5 and in the above-mentioned reports, need explanation. Concerning the age of the patients, some of the differences are due to the time elapsed between the investigation and the time of data-compiling for publication, and some are due to miscalculations, the ages are corrected in Table 5 to the time of pretreatment investigation. One patient (no. 4) had, after the first lumboventricular perfusion a C_{out} = 0.262 ml/min/mm Hg. On suspicion of a technical error the test was repeated at a later date, where the C_{out} was found to be = 0.133 ml/min/mm Hg, the value given in Table 5. In some cases the aetiology was determined by questioning and thus sometimes uncertain. These cases are commented by "aetiology uncertain" in Table 5.

Results 3 Months After Operation

Of the 64 shunted patients, 41 improved one or more functional grades. Nine patients in all improved to grade 0, *i.e.*, became able to work; 14 patients improved to grade 1 (able to function

independently at home); 12 patients improved to grade II (some supervision required at home). Thus a total of 35 patients did not need institutional care. As mentioned above, all patients who improved in functional grade also improved in their degree of dementia, gait disturbances, and possible urinary incontinence, and the estimation given by the relatives of the result of shunting was in all cases good or excellent.

Among the 23 patients who did not improve in functional grade, 4 patients (No. 1, 5, 9, and 10) were considered improved in dementia, gait disturbances and urinary incontinence at the 3 months follow-up examination, where also the relatives estimated the result of treatment as good or excellent. These patients were, in the report of Børgesen and Gjerris[12], recorded as improved according to the definitions given above for improvement. However, the improvement seen at the 3 months follow-up was not a lasting one: patients no. 5 and 9 had deteriorated again 12 months after operation, and patients no. 1 and 10 had died before the 12 months follow-up examination.

A further 4 patients were described by relatives or nursing staff as having experienced a short-lasting (1 to 2 months) improvement in dementia, gait disturbances and urinary incontinence, and were according the the criteria for improvement, recorded as „transient improvement" at the 3 months follow-up examination. One of these, patient no. 25, died of pulmonary embolus 2 months after operation. In patient no. 53, the CT showed an unchanged ventricular size. The shunt was tested and subsequently changed, but the patient did not improve further. In 3 patients: no. 5, 30, and 63, the size of the ventricular system was normalized in the control CT.

The phenomenon of transient improvement has been reported to occur in some of the patients in the few other series with long-term observation, *i.e.*, one year or more, after shunting[1, 3, 69, 77]. It is not possible to explain why an obvious improvement in the clinical status, occurring after CSF shunting, can be followed by a deterioration after a while, in spite of a seemingly satisfactory function of the shunt.

In the present material 11 patients had only mild or moderate dementia, moderate gait disturbances and an unknown aetiology of NPH. Such patients present, in most reports of results of treatment of NPH, the group where the results are most unpredictable. Seven out of these 11 patients were shunted, 3 improved from functional grade I to 0; 2 from grade II to I, and 2 were unimproved. These

results emphasize that, also in this group of patients, shunting may be rewarding in some of the cases.

On the other hand, 14 patients had a known aetiology, short history, severe dementia and gait disturbances, and urinary incontinence. Of these, 12 improved one or more functional grades, some of them dramatically from grade V to grade II (patients no. 53 and 65) or even grade 0 (patient no. 76). One patient had a transient improvement (but died 2 months after operation), and only one patient was unimproved.

To summarize, the results 3 months after shunting, 41 patients (64%) had improved in functional grade, 4 had improved only in the degree of dementia, gait disturbances and urinary incontinence, and 4 patients had only a short-lasting improvement. Thus 49 patients (76%) experienced some sort of improvement.

Results 12 Months After Shunting

Of the 64 shunted patients, 56 were seen at the 12 months follow-up examination. The remaining 8 patients were dead (see above). Five patients had improved one functional grade further as compared with the results at the 3 months follow-up, 48 patients were unchanged in their functional grades compared with the 3 months follow-up. Three patients had deteriorated again: no. 5 and 9 as mentioned above, and No. 36. No explanations for these deteriorations were found, the shunts were functioning and the ventricular systems had normalized.

A total of 37 patients remained improved in their functional grade one year after operation (58% of the shunted patients). In Table 6 the improvement in functional grades is compared with the results in the groups of patients with or without a known aetiology. Of the 31 patients without a known aetiology only 13 patients were improved one year after shunting, while 24 of the 33 patients with a known aetiology were improved. The trend towards better results in patients with a known aetiology is significant (Chi-square test, $p < 0.01$).

The overall success rate is, especially in view of the relatively strict criteria for post-operative improvement employed in the study, comparable to that described in the literature (Table 1). Stein and Langfitt[77], who used functional grading in the evaluation of treatment results, found that 24% of patients with NPH without a known aetiology improved after shunting, while as many as 80% of those with a known aetiology, improved.

Table 6. *Improvement in Functional Grade Compared with the Aetiology.* The difference between improvement in patients with known and with unknown aetiology is significant (Chi-square-test, p = 0.01)

Aetiology	Improved	Unimproved
Known	24 (72%)	9
Unknown	13 (42%)	18

In the present material 40 patients were neuropsychologically examined before and 12 months after shunting (A. M. Thomsen *et al.*, to be published). The testing of the degree of dementia showed that only 14 patients had improved significantly in dementia, 21 patients were unchanged, and 5 had become worse. The discrepancy between the improvement in functional grade in 58% of the patients and in dementia, as tested by the neuropsychologists in 35% of the patients, is probably due to the well-known difficulties in the psychological testing of dementia with the relatively narrow testing methods. However, clinical dementia tests and functional grading are based on a variety of different information, among which the functional capability in daily activities is the most important.

Clinical Value of Shunting

It is beyond doubt, that in some patients all symptoms of NPH may disappear after CSF shunting. This is apparent from the present study as well as from the literature. Most often, however, the symptoms are only partly alleviated. Evaluation of clinical results of shunting therefore, necessitates grading of the clinical condition before and after treatment. In the present study, assessment of the functional grade has been employed. In comparison with evaluation methods in the literature, this mode of evaluation is relatively strict[77]. The functional grade describes only which kind of help or care the patient needs, and thus which functions in daily activity the patient may be able to undertake. A more precise evaluation of the clinical condition, *e.g.*, by using rating scales on degree of dementia and gait disturbances and results of neuropsychological examination, may reveal more detailed information on the results of shunting. It is, however, difficult to imagine an improvement in functional grade, as

described in the present study, without improvement in the rating scales on dementia, gait and neuropsychological examination. Evaluation by functional grade therefore serves the purpose of the present study, which is to demonstrate a possible correlation between impaired capacity for CSF resorption and clinical improvement after shunting.

Only 8 patients in the present series improved to a degree that rendered them able to work one year after treatment. In the remaining patients the observed improvement was, in spite of a regression in the symptoms, not complete. This raises the question whether CSF shunting in patients with NPH may be considered worthwhile. The importance of the question is emphasized by the high complication rate associated with shunting therapy. Partial improvement in dementia and in gait disturbancy, which results in a reduction in the patient's need for help or care cannot, neither from an ethical nor from an economical point of view, be discarded as an unsatisfactory result, especially if the mode of selection of patients for shunting excludes patients where shunting is futile.

Complications

As mentioned above, the rate of complications in the treatment of patients by CSF shunting is high, and the rate in the present study did not differ essentially from those reported in the literature (see Table 1). Twelve patients had shunt related complications: shunt infection in 4, subdural haematomas in 4, and shunt revisions because of malfunction in 4. The shunt-related complication rate was thus 19%.

Two patients developed non-purulent meningitis in relation to pressure monitoring and lumboventricular perfusion. The symptoms disappeared in both patients after antibiotic medication. A few of the patients complained of headache and nausea during the lumboventricular perfusion, when the intraventricular pressure level was elevated above 30 mm Hg, but otherwise no adverse reactions were observed during the tests.

Results Compated to C_{out}

In the series of 80 patients with NPH[12], C_{out} varied between 0.009 and 0.511 ml/min/mm Hg. This variation seems surprisingly high in a group of patients selected uniformly on a basis of strict clinical and investigational criteria. In order to detect which clinical

findings indicate low C_{out}—and thus a possible clinical effect of CSF shunting, C_{out} was compared to the pretreatment clinical findings. No correlation could be found between C_{out} and length of history, age, sex, and possible aetiology. The trend of a high C_{out} in patients with a longer history was not significant when tested by a contingency table analysis. Testing by trend in proportions, as described by Armitage [3], confirmed the lack of a significant correlation. Likewise, the findings in clinical examination were not correlated to C_{out}, and thus no single clinical factor was found to indicate a low C_{out}. The combination of a short history (less than 6 months), known aetiology, severe dementia and gait disturbances, and urinary incontinence, was, however, only seen in patients with C_{out} below 0.067 ml/min/mm Hg. No other combinations could be significantly related to a low C_{out}.

In the present series, 67 patients were tested neuropsychologically (A. M. Thomsen *et al.*, to be published). The test results were classified into degrees of dementia and compared with clinical findings and C_{out}. The degree of dementia could only be significantly related to C_{out}: The lower the C_{out}, the more demented the patient was found to be.

In 64 patients the C_{out} was below 0.120 ml/min/mm Hg, and these patients were accordingly shunted. In the report of Børgesen and Gjerris [12], C_{out} was compared to the "effect of shunting", defined as improvement after 3 months in either functional grade, *or* in dementia, gait and in the opinion of relatives, even when this improvement was transitory only. By this mode of evaluation it was found, that 49 out of the 51 patients with C_{out} below 0.080 ml/min/mm Hg improved, a success rate of 96%. Thirteen patients had a C_{out} between 0.080 and 0.120 ml/min/mm Hg; in none of these were any clinical effects of shunting observed. The correlation between C_{out} below 0.080 ml/min/mm Hg and the effects of shunting is statistically highly significant (Fisher's exact test, $p = 0.001$). The reason for using this mode of evaluation was the wish to demonstrate even a slight clinical improvement in patients whith low values of C_{out}, in order to show a possible causal correlation between this parameter and the symptoms and signs in NPH.

However, with a success rate of 58% of all shunted patients one year after shunting, the above evaluation may be considered to be too optimistic. In Table 7 C_{out} is compared with the results of shunting, evaluated by functional grade 12 months after shunting. Patients who died before the 12 months follow-up are not included.

Table 7. *Improvement in Functional Grade One Year After Operation Compared with C_{out} Below and Above 0.080 ml/min/mm Hg.* The correlation between low C_{out} and improvement after shunting is significant. (Fisher's exact text, $p < 0.001$)

	Improved	Unimproved
$C_{out} \leqq 0.080$	37	7
$C_{out} > 0.080$	0	12

Here, Fisher's exact test shows also a highly significant correlation between C_{out} below 0.080 ml/min/mm Hg and improvement ($p < 0.001$).

The diagnostic specifity and sensitivity can be calculated from the figures in Table 7[84].

$$\text{Specifity:} \quad \frac{\text{true positive}}{\text{true pos.} + \text{false pos.}} = \frac{37}{37+7} = 0.84$$

$$\text{Sensitivity:} \quad \frac{\text{true negative}}{\text{true neg.} + \text{false neg.}} = \frac{12}{12+0} = 1.0$$

The high diagnostic sensitivity may be related to the type of shunt used, as a too high opening pressure or too low conductance may preclude clinical effects in patients with only moderately decreased C_{out}. The Hakim "medium-pressure" shunt has an opening pressure between 6 and 8 mm Hg and the conductance is 0.468 ml/min/mm Hg. The pressure range is within the upper normal for intracranial pressure in the present patients. It is therefore unlikely, that another shunt, with lower opening pressure or higher conductance would alter the results. Furthermore, the normalization of the size of the ventricular systems, found in most of the shunted patients, improved or unimproved, confirms the assumption that the drainage obtained by the shunt was sufficient.

The highly significant correlation between low C_{out} and improvement after shunting, and the good diagnostic sensitivity strongly supports the assumption that patients with C_{out} above 0.120 ml/min/mm Hg cannot be expected to improve after shunting.

Neuropsychological examination, repeated 12 months after shunting in 40 patients of the present series (A. M. Thomsen *et al.*,

to be published) showed, that an improvement in the degree of dementia was seen in 14 out of 24 patients with C_{out} below 0.080 ml/min/mm Hg, and that none of the patients with C_{out} above this value could be shown to have improved after shunting. It was not possible to point out a singular finding in the psychological examination that was significantly associated with improvement after shunting.

Recently, two reports on a smaller series of patients with hydrocephalus have confirmed these results. Costabile *et al.*[21] found that only patients with C_{out} below 0.081 ml/min/mm Hg, 11 out of 20 patients, improved after shunting. Tans and Poortvliet[82] found, among 20 patients, 13 with a C_{out} below 0.076 ml/min/mm Hg. Twelve of these improved after shunting, while 6 out of the 7 patients with C_{out} above this value were diagnosed as having "arrested hydrocephalus".

Constant rate lumbar infusion as described by Katzman and Hussey[48] for the assessment of CSF-resorptive capacity has been used for the evaluation of patients with hydrocephalus with somewhat different results. Wolinsky *et al.*[86] found only 6 abnormal infusion tests among 20 patients suspected of NPH. None of these 6 improved after shunting, while 2 with normal infusion tests improved after shunting. Stein and Langfitt[77] found 20 abnormal infusion tests in patients with idiopathic hydrocephalus and none of these improved in functional grade after shunting. Belloni *et al.*[6] found no evident relationship between infusion tests and the outcome of shunting in 12 patients with symptomatic hydrocephalus. Symon and Hinzpeter[81] found only 5 abnormal results among 20 infusion tests in patients with NPH. Of these 5 only 2 of the patients improved after shunting. Sprung *et al.*[76] found the predictive value of infusion tests equal to that of isotope cisternography, with improvement in 15 out of the 21 shunted patients, in whom improvement was expected. Philippon *et al.*[64] found that infusion tests predicted improvement in 78% out of 37 shunted patients, but as there were 3 false positives and 2 false negatives, they do not advise against shunting in the presence of a normal infusion test. Lamas and Lobato[49] report the best correlation of 88% between an abnormal infusion test and the result in 23 patients. However, those who responded also had increased intracranial pressure level and plateau-waves.

The failure of the constant rate infusion test to demonstrate clinically important impairment in the resorptive capacity for CSF may be explained by several factors. It is not possible to calculate

C_{out} by this method, as only one set of values for absorption and pressure level is obtained. It is thus difficult to quantify the result of the infusion test, which is especially important when "borderline" pressure increases are elicited by the infusion. Determination of C_{out} from the resting pressure, rate of pressure increase and infusion rate is not possible as the rate in pressure rise is influenced by both the compliance of the craniospinal space (Børgesen *et al.*[15]) and probably also by changes in the CBV.

Intracranial Pressure in NPH

It seems reasonable to assume, that in patients whose symptoms disappear after a shunt-mediated pressure regulation, a periodical or permanent increase in the intracranial pressure will be found in a pre-operative pressure recording.

This assumption has been confirmed in nearly all studies reported in the literature: only patients with some sort of abnormalities in the pressure record will improve after shunting. However, the finding of such abnormalities does not guarantee a clinical improvement after shunting.

The pressure profile in patients with hydrocephalus presents as a continuum, extending from a normal mean pressure level without abnormal pressure fluctuations over a normal mean pressure combined with periodical 1–2 per minute waves (B-waves), to an increased mean pressure level with plateau-waves (A-waves) and possible permanent B-wave activity. Obviously, the term "normal pressure hydrocephalus" should not cover all these pressure conditions, but should be reserved for patients with symptomatic hydrocephalus and normal intracranial pressure level (*e.g.*, below 12 mm Hg).

It is readily understandable, that the increase in mean pressure in patients with high pressure hydrocephalus is caused by reduced C_{out}. That the combination of hydrocephalus, normal mean pressure level and possible B-waves may also be caused by low C_{out} seems less obvious. Consequently, Børgesen *et al.*[14] investigated the correlation between the pressure records and C_{out} in patients with NPH according to the present definition. Two important conclusions can be drawn from this investigation:

1. *C_{out} could not be correlated to the mean intraventricular pressure level.* From the relationship between the mean pressure, CSF formation rate and C_{out}, it can be calculated that C_{out} must be lower than 0.03 ml/min/mm Hg to be able to produce a mean pressure level above 12 mm Hg, when the production rate is

0.4 ml/min. Among 40 patients, only 4 had a C_{out} below this value. The small influence of C_{out} variations on the pressure level in the range above 0.03 explains the lack of correlation.

2. *B-waves were observed significantly more frequently in patients with a low C_{out}.* However, B-waves were also observed in patients with C_{out} above 0.08, and the frequency with which B-waves appeared in the pressure records differed greatly, also between patients with very low C_{out}. This implies that B-waves are not only the result of impaired CSF outflow, but that other factors must be involved in the formation of these pressure fluctuations.

Børgesen *et al.*[15] have shown that one other factor may be the compliance of the craniospinal space (C_{CSS}). C_{CSS} was measured in 24 patients with NPH by the bolus injection method. There was no correlation between C_{CSS} and C_{out}. In agreement with this, Sklar *et al.*[72] found no relationship between the compliance and C_{out} in 32 patients with hydrocephalus or "pseudotumour cerebri". It was shown, that the compliance decreased with increasing ventricular size. A decrease in either C_{out} or C_{CSS} or both will add to the pressure response to volume loads of the craniospinal space. When the sum of C_{CSS} and C_{out}—equally weighted—was compared with the presence of B-waves, an exponential correlation was found[15]. The increased presence of B-waves in patients with NPH may thus be a result of a decrease in the complementary function $C_{out} + C_{CSS}$. This role of C_{css} explains why some patients with low C_{out} present with permanent B-wave activity, while other patients with low C_{out} have less prominent B-wave activity. The eliciting factor of the B-waves is only poorly understood. Changes in vascular tonus probably create the volume loads of the CSF space, but the on-off picture of the B-waves remains unexplained.

In patients with dementia, hydrocephalus, gait disturbances and/or urinary incontinence, and a normal mean intracranial pressure, the presence of B-waves seems to be obligatory for a favourable clinical effect of shunting. Crockard *et al.*[22] concluded that B-waves present for 2 hours in the day indicate that the patient may benefit from shunting. Pickard *et al.*[65] found that only patients with B-waves improved after shunting. In agreement with this, Børgesen and Gjerris[12] found that the presence of B-waves in more than 50% of a 24-hour recording was invariably associated with the effect of shunting. In patients with B-waves in less than 5% of the recording time, there was no clinical effect of shunting. In patients with B-waves in 5–50% of the recording time the effect of shunting was not predictable.

These tendencies are affirmed in Table 8, where the clinical results one year after shunting are compared with the presence of B-waves in the pressure records. Fourteen patients had B-waves in more than 50% of the recording time. Eight of these improved in functional grade (57%), 29 out of the 44 shunted patients with B-waves in 5–50% of the recording time were improved—66%. No

Table 8. *Presence of B-waves Compared to Results from Shunting.* The difference between improvement in patients with B-waves in less than 5% of recording time and in more than 5% of recording time is significant (Fisher's exact text, $p < 0.001$)

B-waves in per cent of record. time	Improved	Unimproved	No shunt	Dead
< 5%	0	5	9	1
5–50%	29	10	7	5
>50%	8	4	0	2

patients with B-waves in less than 5% of the recording time improved after shunting. If B-waves in more than 5% of the recording time is taken as an indication for shunting therapy, the diagnostic specifity of B-waves is 0.72, while the diagnostic sensitivity is 1.0 in the present study.

Contradictory to the clinical results at the 3 months follow-up, where B-waves only in more than 50% of the recording time were strongly correlated to effect of shunting, there was no such difference between the results in patients with B-waves in 5–50% an more than 50% of recording time one year after shunting. This may be related to the severe clinical condition of patients with nearly constant B-wave activity, but also to the mode of evaluation at the 3 months follow-up, where 3 of the patients with B-waves in more than 50% of recording time were improved in dementia and gait, but not in functional grade. These 3 were found to have deteriorated one year after the operation.

Chawla *et al.*[18], Symon and Dorsch[80], Belloni[6], Hartmann and Alberti[41], Jeffrey and Wood[46], and Lamas and Lobato[49] all found that patients presenting with dementia, gait disturbances, hydrocephalus and increased mean pressure level with plateau

waves will probably improve after shunting. Such patients cannot, however, be classified as having NPH according to the present definition, and high pressure hydrocephalus seems to be a more correct term.

Computed Tomography in NPH

CT has substituted pneumoencephalography in the investigation of patients suspected of NPH. The features of interest in CT are:

1. size of cortical sulci,
2. hypodensity in the periventricular tissue, and
3. ventricular size.

1. In pneumoencephalography, the absence of air in the fronto-parietal cortical sulci in patients with NPH, has been interpreted as a sign of obstructive hydrocephalus [53], from which it has been deducted that large cortical sulci in the CT indicate that the hydrocephalus is of atrophic origin. Thus, Gawler *et al.* [31] and Harbert *et al.* [40] suggested that cortical atrophy in patients with dementia and hydrocephalus have primary cerebral atrophy, rendering shunting futile. This assumption was supported by Gunasakera and Richardson [78] and by Crockard *et al.* [22] who found that no patients with dementia, hydrocephalus, and large cortical sulci improved after shunting. In contrast to these reports, Jacobs and Kinkel [45] found no relationship between presence or absence of cortical sulci and the clinical response to shunting. This observation was further supported by Laws and Mokri [50], Greenberg *et al.* [34] and le May and Hochberg [51], who found that, while there was a correlation between small cortical sulci in the CT and improvement after shunting, improvement could also be seen in patients with large cortical sulci.

Comparison of C_{out} and the findings in CT was done by Børgesen *et al.* [16] and Børgesen and Gjerris [12]. The apparent trend towards correlation between small cortical sulci and low C_{out} was not found to be significant when tested by a contingency table analysis, while a Fisher's test on the correlation between sulci smaller than 1.9 mm and C_{out} below 0.075 ml/min/mm Hg was significant ($p < 0.01$). In accordance with this, there was a significant correlation between the occurrence of small cortical sulci in the CT and the effect of shunting [12]. More interesting was, however, the association of cortical sulci larger than 5.0 mm and a C_{out} below 0.08 in 13 patients [16], and the favourable effect of shunting in 15 of the 27 patients with large cortical sulci [12].

In Table 9 the width of cortical sulci is compared with the clinical results 12 months after operation, evaluated by the functional grade. The number of patients who died or who were not shunted are also shown. It is apparent, that most patients with small (or absent) cortical sulci improved after shunting. The correlation is statistically significant (Fisher's exact test, $p < 0.01$).

Table 9. *Width of Cortical Sulci Compared with the Results One Year After Shunting.* The correlation between sulci smaller than 1.9 mm and the improvement after shunting is significant (Fisher's exact test, $p < 0.001$). Note that 7 patients with large cortical sulci had improved in functional grade one year after shunting

Width of cortical sulci (mm)	Improved	Unimproved	No shunt	Dead
< 1.9	15	1	3	1
1.9–5.0	15	4	7	1
> 5.0	7	14	6	6

Three patients with small sulci had a C_{out} above 0.120 ml/min/mm Hg, and were not shunted. It is also apparent that improvement may be seen in patients with normal or even dilated cortical sulci. However, of the 15 patients with dilated cortical sulci, who in the report of Børgesen and Gjerris[12], were found to have experienced some sort of improvement 3 months after shunting, only 7 maintained the improvement one year after shunting. Although it may be emphasized that the finding of large cortical sulci in the CT does not preclude the patients improvement after shunting, the chances of improvement are rather small. It can be concluded that the decision to shunt cannot be made on the size of the cortical sulci in the CT alone.

2. Increased water content in the periventricular tissues was demonstrated in experimental hydrocephalus by Clark and Milhorat[19] and by Milhorat *et al.*[58]. Granholm[33] and Pasquini *et al.*[63] described periventricular hypodensity in the CT in patients with hydrocephalus and increased intracranial pressure. In agreement with this, Mosely and Radu[60] found that periventricular hypodensity was common in patients with symptoms of raised intracranial pressure and papilloedema. They

also observed, in agreement with Hopkins *et al.*[42] and Asada *et al.*[4], that periventricular hypodensity may be present in hydrocephalic patients with a normal intracranial pressure. This is confirmed by the observation of periventricular hypodensity in 16 patients with NPH in the report of Børgesen and Gjerris[12]. All these patients had a mean intraventricular pressure below 12 mm Hg and no plateau waves, and all had a C_{out} below 0.080 ml/min/mm Hg. The periventricular hypodensity disappeared after shunting. One of the patients died before the 12 months follow-up. The remaining 15 were all improved in functional grade one year after shunting, indicating, that this finding predicts a good result of shunting.

3. The size of the ventricles has no relation to the level of C_{out} in patients with NPH, graphically demonstrated by Børgesen *et al.*[16]. In accordance with this, the size of the ventricles does not predict the outcome of shunting, whether evaluated 3 or 12 months after shunting.

In 34 patients in the series of Børgesen *et al.*[16] PEG was performed at the admission to the department, and only patients with signs in the PEG believed to indicate impaired CSF resorption (hydrocephalus and absence of air in the parietal sulci) were admitted. Either small, normal or even dilated cortical sulci were seen in the CT in all these patients[16]. This suggests also, that patients with visible, airfilled cortical sulci may have fulfilled the inclusion criteria of the present investigation. Thus, the only conclusion to be made is that absence of air does not indicate either absent cortical sulci or decreased C_{out}. Another observation that separates the patients with and without PEG is that periventricular hypodensity was only seen in patients where PEG had not been performed. This difference is probably due to differences in clinical conditions: patients with a short history and severe symptoms were readmitted without PEG. Today, most patients suspected of NPH probably have a CT performed, and the difference is thus of less practical relevance.

One would assume, that clinical improvement after shunting in a patient with NPH was associated with a decrease in ventricular size. This was the case in most of the shunted patients in the present study, and a diminished or normalized ventricular system was taken as an indication of sufficient function of the shunt. It was interesting to observe, however, that the ventricular systems were unchanged in 6 patients recorded as improved after 3 months. Three of these still had improved at the 12-months follow-up,

where the Evan's ratio was the same as that in the pre-operative CT, as shown in Table V. The same observation was made by Shenkin *et al.*[71] in post-operative PEG, by Black and Sweet[8], and Sprung and Schultz[76] in CT. This observation indicates, that the symptoms in NPH are not only related to ventricular enlargement.

Isotope Cisternography in NPH

In order to depict abnormalities in the CSF flow and absorption, a radioactive isotope can be introduced into the subarachnoid space. This method was first applied in patients with hydrocephalus and dementia by Bannister *et al.*[5] and Fleming *et al.*[30]. Since then, the investigation has been widely used. Isotope cisternography (ICG) has been found to be able to predict the outcome of shunting in 50–70% of patients with NPH[6, 32, 47, 57, 70, 81, 87].

The findings in ICG in patients with NPH were compared with C_{out} by Børgesen *et al.*[17]. Ventricular retention and absent parasagittal accumulation of the tracer 48 hours following injection, generally interpreted as signs of severe obstruction to CSF outflow, were significantly correlated to a low C_{out} (Chi-square test, $p < 0.01$). Both findings were, however, also observed in 11 of the 20 patients with C_{out} above 0.080 ml/min/mm Hg. Assymmetrical tracer distribution and pooling, often considered insignificant, were in agreement with this, seen in all ranges of C_{out}, but, more important, were the only findings in 6 patients with C_{out} below 0.080 ml/min/mm Hg.

In the present study 55 patients underwent ICG. Combinations of findings in ICG, assigned to four different groups as described by Børgesen *et al.*[17] are compared with C_{out} in Table 10. Group IV and III consist of findings indicating severe obstruction to CSF outflow, group II the less conspicuous, but still abnormal findings, and group I the normal ICG. Analysis by trend in proportions (Armitage[3]) shows a significant correlation between low C_{out} and findings indicating obstruction to CSF outflow. However, the correlation is in no way absolute ($p = 0.07$).

In Table 11 the findings in ICG are compared with the results of shunting, evaluated 12 months after shunting from the functional grade. Three patients in group I were not shunted, as their C_{out} was above 0.120 ml/min/mm Hg. When only the patients with findings categorized as groups IV or III were shunted, the diagnostic specifity of ICG in the present series was 0.68, and the diagnostic sensitivity 0.7 (see p. 37)—when the non-shunted patients are included as having been unimproved after shunting. The

Table 10. *Findings in ICG Compared with the C_{out}.* In 10 patients the findings indicated severe obstruction to CSF-outflow, while C_{out} was above 0.080 ml/min/mm Hg. In spite of this, the correlation is statistically significant Chi-square test, $p < 0.01$)

C_{out}	ICG-groups			
	IV	III	II	I
< 0.080	17	10	6	0
0.08–0.120	2	4	4	0
> 0.120	3	1	5	3

Table 11. *Comparison of ICG-Groups and Results One Year After Shunting.* The 3 patients in group I were not shunted. Chi-square test on the correlation between improvement and group III + IV shows no significant correlation ($p = 0.6$)

Results one year postop.	ICG-groups			
	IV	III	II	I
Improved	15	7	6	—
Unimproved	3	7	4	(3)

correlation between improvement and ICG findings of CSF outflow obstruction (groups III + IV) is not statistically significant ($p = 0.6$). The predictive value of ICG has not differed from that reported in the literature and, in agreement with Coblentz *et al.*[20], Jacobs *et al.*[45], Laws and Mokri[50], and Black[8], it may be considered to be unsatisfyingly low.

The flow of CSF as depicted by ICG is the net result of three factors: CSF production rate, condition of the CSF space, and C_{out} at the resorption sites. The comparison of ICG findings between different patients presumes constant and equal production rates and an equal effect of the "stirring-effect"—the pulsatile forces of brain and vessels that lead to the distribution of the CSF tracer. Finally, the size of the ventricles influences the wash-out time of the tracer: the larger the volume, the slower the wash-out of the tracer. Therefore, the distribution and flow of the CSF tracer is not only an expression of the degree of obstruction to CSF outflow, which may explain the low diagnostic sensitivity and specifity of ICG.

The Pathophysiology of NPH

Sufficient evidence is at hand to propose a hypothesis for the pathogenesis and pathophysiology of NPH.

It is known that increased content of cells or proteins in the CSF (*e.g.*, in subarachnoid haemorrhage, meningitis, and certain tumours) may lead to increased intracranial pressure. Børgesen *et al.*[11] found severe obstruction to CSF outflow in 2 patients with high concentrations of proteins in the CSF, and Gjerris *et al.*[32] showed very low values of C_{out} in patients with subarachnoid haemorrhage, meningitis, and hydrocephalus. It was shown by Davson[24] that C_{out} decreases and remains decreased when serum or erythrocytes are infused into the subarachnoid space. The mechanism behind this is probably the clogging of the CSF outflow pathways in the arachnoidal villi. Whether the CSF flows out via fluid valves, as suggested by Welch and Friedman[85], by pinocytosis in a continuous epithelium between CSF and blood in the arachnoidal villi[2], or via vacuolar, transcellular channels as described by Tripathi[83] is less important in this context, provided that none of the mechanisms contradict that the CSF flow is a pressure dependent bulk-flow phenomenon.

In some cases the defective CSF resorption system is not restored, and the intraventricular pressure remains elevated. The continuing increased tension on the ventricular walls leads to flattening of the ependyma[66]. The pressure in the subarachnoidal space over the cerebral cortex is also increased. The increased pressure leads to dilatation of the ventricles[39] and, probably by the same mechanism, also to widening of the cortical sulci. The ependymal attenuation leads to seeping of CSF into the periventricular tissues, as demonstrated in experimental hydrocephalus[56], in patients with increased intracranial pressure[33, 63] and in patients with normal intracranial pressure[16, 60]. The seeping of water through the ependyma has been described as an expression of a resorptive process, but, as shown by Børgesen *et al.*[16], the C_{out} is very low in patients with periventricular hypodensity in CT, indicating that this absorption is very slow.

The seemingly paradoxical decrease in pressure despite continuing impairment of CSF outflow has been explained by Bloch and Tallala[9], Hakim *et al.*[39], and Early and Fink[26], on the basis of the mathematical principle of the law of La Place. While the mean pressure thus may assume a normal level, it is shown, that pressure fluctuations occur in patients with decreased C_{out}. The rise in pulse-pressure amplitude and the increasing presence of B-waves

exert periodically increased tension on the ventricular walls (and the cortical surface). Bregnan and Wolinsky[10], showed that a pulsating stress may lead to hydrocephalus and to changes in the tissues surrounding the ventricles.

Several investigations have shown that the cerebral blood flow is decreased in patients with hydrocephalus and dementia[35, 36, 61] and that the flow increases when the CSF is shunted from the ventricles. Both the global and the focal reduction in the cerebral blood flow may participate in the pathogenesis of the neurological symptoms associated with NPH.

The exact anatomical localization of the neuronal dysfunction leading to the neurological symptoms is not yet possible. Granholm[33] suggested that dysfunction of the hippocampus, which forms part of the ventricle in the temporal region, may result in a defective short-time memory. Impairment of function of the paracentral long tract fibres may be responsible for the extrapyramidal motor disturbances: gait impairment, ataxia, tremor. Affection of the prefrontal miction centre may be responsible for the urinary incontinence. The dementia may be attributed to the general reduction in cerebral blood flow.

The mechanism by which CSF shunting relieves the symptoms in NPH may be twofold:

1. The shunt modifies the intraventricular pressure by its preset opening pressure and flow characteristics. The pressure modification may diminish the tension on the ventricular walls and the underlying cerebral tissue, so that the cerebral blood flow becomes sufficient, and so that neurones may resume their function. It is thus possible for the shunt to function satisfactorily also in patients where the ventricles have not returned to their normal size after shunting.

2. The shunt diverts CSF from the ventricles. CSF contains proteins and products from cerebral metabolism, and while it is unknown what influence such contamination of CSF may have on neuronal function, it is certainly possible that drainage of CSF is the main action of the shunt in the alleviation of neurological deficits.

From the knowledge obtained by CSF pressure monitoring and measurement of C_{out} it may, however, be concluded that the rationale behind CSF shunting is to divert CSF past its normal resorption sites at a sufficiently low opening pressure and a sufficiently high conductance, so that accumulation of CSF in the cerebro-spinal space is avoided.

Conclusion

NPH has in the present study been defined as a syndrome consisting of dementia, gait disturbances, and/or urinary incontinence, hydrocephalus, and a mean intracranial pressure not exceeding 12 mm Hg. Some of the patients presenting with this triad may succesfully be treated by CSF shunting. The purpose of the pre-operative investigations is to differentiate between those patients who will benefit from CSF shunting and those who will not.

Investigations in NPH

To establish the diagnosis of NPH, the size of the ventricles must be known. CT is the method of choice for this investigation. Besides information on other possible causes of dementia and on the size and shape of the ventricular system, information is also obtained on possible periventricular hypodensity and on the width of the cortical sulci. Of the findings in CT only periventricular hypodensity has been found to indicate clinically important impairment in CSF resorption. No findings in CT exclude possible impairment, and thus possible improvement after shunting.

Long-term monitoring of the intracranial pressure in patients with dementia and gait disturbances may reveal a normal intracranial pressure level and thus the diagnosis of normal pressure hydrocephalus is established. If the pressure level is increased, and plateau-waves are observed, high-pressure hydrocephalus is the correct term, and CSF shunting may be decided on. In cases of normal pressure level, abnormal pressure fluctuations must be observed if a clinical effect from CSF shunting is to be expected. In this study, the presence of B-waves in more than 5% of recording time, was found to be obligatory for a clinical effect of shunting. This observation is in accordance with the reports in the literature. Constant or nearly constant B-wave activity during pressure recording indicates severe obstruction to CSF resorption, and a decision to shunt can be made on this finding alone. The overall diagnostic specifity of B-waves observed in more than 5% of recording time was found to be 0.72 in the present study. Thus, the observation of B-waves in 5–50% of the recording time is not sufficient indication for shunting, and other investigations must be employed. In cases where no B-waves are observed in the pressure records, no effect from shunting can be expected, and further investigations are unnecessary.

ICG may be used to demonstrate obstruction to CSF outflow.

However, the diagnostic specifity of ICG was low in the present study: if only the patients with evidently abnormal findings in the ICG were shunted, the specifity was 0.68, and the sensitivity 0.7—that is, some patients who in fact improved after shunting, would not have been treated when selected on the basis of ICG. From these results ICG does not seem recommendable in the preoperative investigation of patients with NPH.

The resorptive capacity for CSF may be measured by lumboventricular perfusion, and expressed by conductance to outflow of CSF (C_{out}). The predictive value of C_{out} has, in the preoperative evaluation of patients with NPH, been shown to be good in the present study. The diagnostic specifity was 0.84 and the diagnostic sensitivity was 1.0, when $C_{out} = 0.080$ ml/min/mm Hg is chosen as the limit below which patients may be expected to improve after shunting. If the results of clinical investigation, CT, and long-term pressure monitoring have not revealed signs of severe impairment in CSF resorption, measurement of C_{out} may be used to select patients for CSF shunting. Technically the lumboventricular perfusion is easy to perform, and it is not too time-consuming for routine clinical use. It can, if it proves necessary, be suitable performed following of long-term pressure recording.

Treatment of NPH

The only known treatment of NPH is to divert CSF from the ventricles by means of an operative shunt insertion. The operation is technically simple, and while the complications are seldom fatal, the complication rate is rather high—19% in the present study, making unnecessary shunting undesirable.

In some patients the CSF shunting has a dramatic effect, and patients in a severe clinical condition may improve to a degree that they may be able to resume their premorbid occupation. Most often, however, the improvement is less pronounced. An improvement that makes the patient able to attend to himself or makes constant supervision superfluous, nevertheless makes shunting worthwhile, and an attempt to disclose a clinically important obstruction to CSF outflow in patients presenting with progressing dementia, may be recommended.

In the report of Børgesen and Gjerris[12] a flow chart for the practical management of patients suspected of NPH is proposed. The results of shunting, which this proposal was based upon, were the optimistic 3 months follow-up results including transiently

improved patients. But also when the results of shunting are compiled one year after shunting, the flow chart holds true: when applied to the patients in the present series, it will result in an acceptable success rate of 84%, by means of the fewest possible pre-operative investigations (the 8 patients who died have been withdrawn from this calculation). According to the flow chart, patients with a known aetiology for their hydrocephalus, severe dementia, severe gait disturbances, urinary incontinence and a short history can be shunted directly, as can patients with periventricular hypodensity in the CT, without further investigations. Patients, who do not fulfil these criteria should be investigated by long-term (24 hours) pressure recording. Patients with B-waves in more than 50% of recording time can be shunted, while patients with less than 5% B-waves should not be operated on. The remaining patients may be investigated by lumbo-ventricular perfusion for the measurement of C_{out}. Only patients witgh C_{out} below 0.080 ml/min/mm Hg should be shunted.

By using this method of selection of patients for shunting therapy, an acceptable success rate may be achieved by the means of least possible invasive investigations.

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