NEUROSURGERY 40:3 | MARCH 1997 | 497-502
DOI: 10.1097/0006123-199703000-00013

Clinical Studies

Frontal Brain and Leptomeningeal Biopsy Specimens Correlated with Cerebrospinal Fluid Outflow Resistance and B-wave Activity in Patients Suspected of Normal-pressure Hydrocephalus

Rachid Azeddine Bech, MD[1,*], Marianne Juhler, MD, PhD[1], Gunhild Waldemar, MD, PhD[1], Leif Klinken, MD, PhD[1], Flemming Gjerris, MD, PhD[1]

[1]University Clinics of Neurosurgery, University of Copenhagen, Copenhagen, Denmark

[2]Neurology, University of Copenhagen, Copenhagen, Denmark

[3]Rigshospitalet, and Institute of Neuropathology, University of Copenhagen, Copenhagen, Denmark

Abstract

OBJECTIVE

Normal-pressure hydrocephalus (NPH) is a potentially treatable syndrome with abnormal cerebrospinal fluid dynamics. Meningeal fibrosis and/or obliteration of the subarachnoid space has been suggested as the pathoanatomic basis. The purpose of the present study was to investigate whether meningeal fibrosis causes increased resistance to cerebrospinal fluid outflow(R_{out}) and/or increased B-wave activity and whether pathological changes in the brain parenchyma alter brain compliance, causing increased B-wave activity.

METHODS

The study involved a group of 38 consecutively studied patients with clinical and radiological evidence of idiopathic NPH, for whom a frontal brain biopsy was obtained. For 29 patients, hydrodynamic criteria of NPH were fulfilled and a ventriculoperitoneal shunt was performed.

RESULTS

Meningeal fibrosis was found in 12 of 25 biopsies containing arachnoid tissue, but no correlation with R_{out} or B-waves was found. Pathological parenchymal changes, most often Alzheimer's disease (10 cases) or vascular changes (10 cases), were found in 21 biopsies, but no correlation with B-waves or R_{out} was found.

CONCLUSION

The results suggest that leptomeningeal fibrosis is not the only pathoanatomic basis of increased R_{out} and/or B-wave activity in patients with NPH and that various degenerative changes in the parenchyma may be responsible for the altered cerebrospinal fluid dynamics characteristic of NPH.

Key words: Biopsy, Brain, Cerebrospinal fluid pressure, Hydrocephalus, Meninges, Normal pressure

*Reprint requests: Rachid Azeddine Bech, M.D., University Clinics of Neurosurgery, N2092, Rigshospitalet, Blegdamsvej 9, DK-2100, Copenhagen, Denmark.

Received: April 09, 1996
Accepted: October 14, 1996

Normal-pressure hydrocephalus (NPH), as described more than 3 decades ago by Hakim and Adams (22), is a potentially treatable syndrome with a clinical triad of progressive dementia, gait disturbance, and urinary incontinence. Ventricular dilation, with normal cerebrospinal fluid(CSF) pressure but altered CSF dynamics, is a prominent feature.

The underlying process appears to involve a partial obstruction of the CSF flow between the ventricular and subarachnoid spaces. It is usually assumed that the obstruction is caused by leptomeningeal fibrosis and/or obliteration of the subarachnoid space, resulting in increased resistance to CSF outflow(R_{out}) (6). The presence of B-waves during more than 50% of the monitoring period is another established indicator of altered CSF dynamics (19). Treatment is undertaken on the assumption that improvement or normalization of CSF dynamics is obtained by CSF drainage, thereby improving the brain function and clinical condition of the patient. However, only 25 to 80% of the patients selected for shunting do improve clinically (20) (30), even when strict hydrodynamic criteria are applied. The best outcomes are found with patients with conditions of known pathogenesis.

Interest has been focused on the differentiation between NPH and other common, non-shunt-responsive, types of adult-onset dementia with

similar clinical presentation, e.g., Alzheimer's disease (AD) and multiple-infarction dementia (21),(23). To date, very few studies, involving few patients, have described pathoanatomic findings in autopsies or brain biopsies of patients suspected of having NPH (8),(11),(12),(18).

The purpose of this study was to correlate brain biopsy findings with CSF dynamics in a consecutive group of patients suspected, based on radiological and clinical findings, of having NPH. The following hypotheses were tested: 1) that arachnoid fibrosis causes altered CSF dynamics, resulting in increased R_{out} and/or the presence of B-waves, and 2) that pathological changes in the brain parenchyma alter brain compliance and thus CSF dynamics, measured as the presence of B-waves and/or increased R_{out}.

PATIENTS AND METHODS

Patient selection

The present study included 38 patients (21 men and 17 women; mean age, 64 years; range, 44-77 years), for whom a frontal biopsy was obtained during the 2-year period of 1990 to 1992. All patients below the age of 80 years with clinical and radiological evidence of NPH were offered the opportunity to enter the study. Exclusion criteria were cerebral infarction, hemorrhage, tumors, and known neurological diseases such as parkinsonism and epilepsia. Furthermore, included patients had no history of significant head trauma, meningitis, or subarachnoid hemorrhage, all factors known to be associated with the development of NPH. The admitted patients were thus suspected to have idiopathic NPH. All patients (with their relatives) gave informed consent for participation in the study, which was approved by the Danish Central Ethical Committee (Protocol V.100.1500/90).

Study program

At admission, all patients underwent a clinical and neurological evaluation, a standard laboratory test battery for possible causes of metabolic dementia, and computed tomographic (CT) scanning. Gait was rated on a 5-degree scale (1, gait is normal; 2, gait is abnormal but walking is possible without support; 3, a cane is needed; 4, support from another person is needed; 5, the patient is bedridden), as was urinary incontinence (1, no incontinence; 2, rare incontinence; 3, occasional incontinence; 4, constant incontinence; 5, catheter required). The presence of dementia was evaluated according to DSM III-R criteria (14). The severity of dementia was assessed with the Mini-Mental State Examination (MMSE)(17) and the Global Deterioration Scale (GDS)(26). The diagnosis of NPH was based on the following currently accepted criteria(6) (20): the presence of at least two of the symptoms from the clinical triad, 2) significant ventricular enlargement on the CT scan (Evans ratio = 0.30) (16), and 3) hydrodynamic criteria (see below).

CSF perfusion study

The intracranial pressure was monitored for 24 hours by using an intraventricular catheter in the right frontal horn. The presence of B-waves was evaluated as percentage of appearance in the 24 hours. R_{out} was measured by a lumboventricular perfusion test (19) or a computerized infusion test (9); the correlation between the two tests is well established (7). Increased R_{out} (=10 mm Hg/ml/min) and normal or only slightly elevated intracranial pressure (<15 mm Hg) (2) were required for the final diagnosis of NPH. The indication for shunt surgery was a R_{out} of =10 mm Hg/ml per minute, with or without a B-wave activity (=50%) of the monitoring period.

Biopsy procedures and tissue analysis

Biopsy sampling, followed immediately by placement of a ventriculoperitoneal shunt, took place 1 to 4 weeks after the R_{out} measurement, through the burr-hole used for the R_{out} measurement. The biopsy (0.5-1 cm^3) was taken from the right superior frontal cortex and underlying white matter, with avoidance of the tissue affected by the earlier intracranial pressure monitoring and without electrocoagulation of the tissue before its excision. Biopsies were taken in a similar way from the patients for whom shunt surgery was not indicated.

Five-micrometer-thick slices of the formalin-fixed, paraffin-embedded, biopsy specimens were stained with hematoxylin and eosin, periodic acid-Schiff reagent, Red Congo stain, and according to the method of Van Gieson, the method of Klüver, and the method of Glees. Immunohistochemical staining was performed by using markers for glial fibrillary acidic protein (Dakopatt Catalog No. Z334; Copenhagen, Denmark), ubiquitin (Dakopatt Z458), tau (Dakopatt A024), and ß-amyloid(Dakopatt M872). Where appropriate, these stains were supplemented with Oil Red O, Sudan Black, Alcian Blue, methenamin, reticulin, or stained according to the method of Ziehl-Neelsen. In a few cases, immunohistochemical staining for cytomegalovirus (Dakopatt M757) or von Willebrand factor (Dakopatt A082) was performed. The biopsy specimens were then examined for the presence of arachnoid membrane, with or without meningeal fibrosis, and pathological changes in the cerebral parenchyma. When there were more than 10 neuritic plaques/mm^2 in the most affected areas of the biopsy, AD changes were said to be present. In all biopsies, the number of neurofibrillary tangles was relatively low.

Clinical outcome

Patients who had a shunt inserted were evaluated clinically by MMSE scoring and cerebral CT scanning 3 months after shunt insertion. Similar final follow-up examinations and GDS assessments were performed 9 months after shunt insertion for patients with shunts and 9 months after initial admission for patients without shunts.

A score of +1 point was assigned for each 1 degree of improvement in the scales for the four following variables: gait, incontinence, GDS assessment, and MMSE score (a change of 5 points in the MMSE score corresponded to a change of 1 degree). Similarly, a score of -1 point was assigned for each 1 degree of deterioration. A summation of the improvement/deterioration scores was performed and, according to the result, the patients were classified as having their conditions being worse (final score $\leq$ -2 points), showing no improvement (-1 point $\leq$ final score $\leq$ + 1 point), being slightly improved (final score = +2 points), or being considerably improved (final score = +3 points). An improvement/deterioration of at least 2 degrees in the ordinal scales was thus required to classify the clinical condition as being changed.

RESULTS

Clinical symptoms at admission

The presence of dementia, according to the DSM III-R criteria, was established for 24 patients (11 patients were admitted to the study before the neuropsychological test was included in the test battery, and the presence of dementia was uncertain for 3 patients). Of these, 16 patients(67%) presented the complete clinical triad. A GDS assessment was performed for 35 patients, and 86% of these presented Grade 4 or above on the GDS.

Correlation between R_{out} and arachnoid fibrosis

Arachnoid tissue was present in 25 biopsies; arachnoid fibrosis was present in 12 of these. Patients with normal R_{out} and those with increased R_{out} were evenly distributed when grouped according to the presence of arachnoid fibrosis in the biopsies, and no correlation was found(Table 1). If the analysis was restricted to cases fulfilling stricter hydrodynamic criteria (by redefining increased R_{out} as being =20 mm Hg/ml/min) or to the 15 biopsies without pathological changes in the parenchyma, no correlation could be found(Tables 1 and 2). Similarly, no correlation was found between arachnoid fibrosis and the presence of B-waves (Tables 3 and 4).

TABLE 1.

Arachnoid Fibrosis Correlated with Cerebrospinal Fluid Outflow Resistance = 10 mm Hg/ml/minute and Cerebrospinal Fluid Outflow Resistance = 20 mm Hg/ml/minute among Cases with Arachnoid Tissue in the Biopsy[a]

	R_{out} < 10 mm Hg/ml/min (n = 6)	R_{out} ≥ 10 mm Hg/ml/min (n = 19)	R_{out} < 20 mm Hg/ml/min (n = 19)	R_{out} ≥ 20 mm Hg/ml/min (n = 6)
−AF (n = 13)	3	10	10	3
+AF (n = 12)	3	9	9	3

[a] **Total, n = 25. R_{out}, resistance to cerebrospinal fluid outflow; AF, arachnoid fibrosis.**

TABLE 2.

Arachnoid Fibrosis Correlated with Cerebrospinal Fluid Outflow Resistance = 10 mm Hg/ml/minute and Cerebrospinal Fluid Outflow Resistance = 20 mm Hg/ml/minute among Cases without Parenchymal Changes in the Biopsy[a]

	R_{out} < 10 mm Hg/ml/min (n = 4)	R_{out} ≥ 10 mm Hg/ml/min (n = 11)	R_{out} < 20 mm Hg/ml/min (n = 12)	R_{out} ≥ 20 mm Hg/ml/min (n = 3)
−AF (n = 9)	2	7	7	2
+AF (n = 6)	2	4	5	1

[a] **Total, n = 15. R_{out}, resistance to cerebrospinal fluid outflow; AF, arachnoid fibrosis.**

TABLE 3.

Arachnoid Fibrosis Correlated with B-wave Activity among Cases with Arachnoid Tissue in the Biopsy[a]

	B-wave Activity < 50% (n = 16)	B-wave Activity ≥ 50% (n = 9)
−AF (n = 13)	11	2
+AF (n = 12)	5	7

[a] **Total, n = 25. AF, arachnoid fibrosis.**

TABLE 4.

Arachnoid Fibrosis Correlated with B-wave Activity among Cases without Parenchymal Changes in the Biopsy[a]

	B-wave Activity < 50% (n = 11)	B-wave Activity ≥ 50% (n = 4)
−AF (n = 9)	7	2
+AF (n = 6)	4	2

[a] **Total, n = 15. AF, arachnoid fibrosis.**

Pathological changes correlated with B-waves and R_{out}

Various pathological changes in the cerebral parenchyma were described in 21 of 38 biopsies (Table 5). Patients with pathological changes and those without pathological changes were distributed evenly, without any correlation, when grouped according to the presence of B-waves for more than or less than 50% of the monitoring period (Table 6). In analysis of only the 13 patients without arachnoid fibrosis, no correlation was found (Table 7). Similarly, no correlation was found between the absence/presence of pathological changes and normal/increased R_{out} when all of the patients were analyzed(Table 8). When the analysis was restricted to the subgroup without arachnoid fibrosis, using stricter hydrodynamic criteria (increased R_{out} = 20 mm Hg/ml/min), no correlation was found(Table 8).

TABLE 5.

Biopsy Diagnoses According to Pathological Changes in the Cerebral Parenchyma[a]

	No. of Cases
Normal (no significant pathological changes present)	17
Alzheimer disease	8
Arteriosclerosis	4
Subrecent ischemic encephalomalacia	4
Alzheimer disease and arteriosclerosis	1
Alzheimer disease and encephalitis	1
Encephalitis	1
Nonspecific cortical degeneration	1
Cerebral hemorrhage, sequelae	1

[a] **Total, n = 38.**

TABLE 6.

Presence of Parenchymal Changes in the Biopsy Correlated with B-wave Activity among All Cases[a]

	B-wave Activity < 50% (n = 22)	B-wave Activity ≥ 50% (n = 16)
−Pathology (n = 17)	11	6
+Pathology (n = 21)	11	10

[a] **Total, n = 38.**

TABLE 7.

Presence of Parenchymal Changes in the Biopsy Correlated with B-wave Activity among Cases without Arachnoid Fibrosis[a]

	B-wave Activity < 50% (n = 11)	B-wave Activity ≥ 50% (n = 2)
−Pathology (n = 9)	7	2
+Pathology (n = 4)	4	0

[a] **Total, n = 13.**

TABLE 8.

Pathological Changes in the Cerebral Parenchyma Correlated with Cerebrospinal Fluid Outflow Resistance = 10 mm Hg/ml/minute and Cerebrospinal Fluid Outflow Resistance = 20 mm Hg/ml/minute[a]

	All Biopsies (n = 38)		Biopsies without AF (n = 13)	
	R_{out} < 10 mm Hg/ml/min (n = 7)	R_{out} ≥ 10 mm Hg/ml/min (n = 31)	R_{out} < 20 mm Hg/ml/min (n = 10)	R_{out} ≥ 20 mm Hg/ml/min (n = 3)
−Pathology	4	13	7	2
+Pathology	3	18	3	1

[a] **R_{out}, resistance to cerebrospinal fluid outflow; AF, arachnoid fibrosis.**

Clinical outcome

Twenty-nine of the 38 patients originally admitted to this study fulfilled the hydrodynamic criteria of NPH and had a shunt insertion performed. Follow-up was performed for 32 patients. For 22 patients, the follow-up examination was a 9-month evaluation (17 patients with shunts and 5 without shunts); for 10 patients, it was a 3-month evaluation. The lack of follow-up for six patients was the result of shunt removal because of complications, death, or requests to be excluded from the study.

Overall, 33.3% (n = 9) of the patients with shunts showed improvement, 37.0% (n = 10) showed no improvement, and 29.6% (n = 8) showed deterioration of their conditions at the 3- or 9-month evaluation. Of the nine patients without shunts, three patients showed deterioration of their conditions and two showed no improvement; for four patients, no follow-up was performed.

DISCUSSION

To our knowledge, this is the first prospective study of a group of patients with NPH, for whom cerebral biopsies were obtained and correlated with the hydrodynamic findings. We think the patients in the present study are representative of patients with idiopathic NPH. The improvement rate for patients with shunts was 33%, which is in accordance with improvement rates for patients with idiopathic NPH, with shunts, in other studies(30),(31).

A defect in the CSF absorption pathways, presumably at the level of the arachnoid villi and/or the subarachnoid space, is generally thought to be involved in the pathogenesis of NPH. The resulting increased R_{out} is a well-established prognostic factor of shunt responsiveness (5),(6),(27),(28). On the basis of theoretical considerations and autopsy studies of patients with NPH, it has been suggested that the pathoanatomic factors involved are arachnoid fibrosis and/or obliteration of the subarachnoid space (1),(11),(13),(32). However, correlation of NPH with the retrospectively observed, pathological meningeal changes seen in the autopsies of patients with NPH is subject to certain errors, as follows: 1) insertion of a shunt may itself have provoked a meningeal reaction, 2) other diseases affecting the meninges may have presented after the diagnosis of NPH, and, 3) depending on the length of the period from the onset of NPH to the time of the autopsy, the meninges may have changed radically.

The present prospective study, which was free from the aforementioned sources of errors, was primarily undertaken to test the hypothesis that, in patients with idiopathic NPH, the increased R_{out} is the result of arachnoid fibrosis obliterating the subarachnoid space. Arachnoid fibrosis was found in 12 of 25 biopsies containing arachnoid tissue, but no correlation between normal/increased R_{out} and the presence/absence of arachnoid fibrosis was found. Even when stricter hydrodynamic criteria were used (redefining increased R_{out} as =20 mm Hg/ml/min) and the analysis was restricted to the 15 patients without pathological changes in the parenchyma (to exclude this as a cause of abnormal CSF dynamics), no correlation was found between arachnoid fibrosis and R_{out}. Similarly, no correlation was found between the presence of arachnoid fibrosis and the presence of B-waves for less than or more than 50% of the monitoring period.

The second hypothesis of this study, i.e., that a correlation exists between the presence of pathological changes in the cerebral parenchyma and the presence of B-waves and/or an increased R_{out}, was not supported either. No correlation was found with either, even when the analysis was restricted to the biopsies without arachnoid fibrosis, to exclude this as a potential cause of abnormal CSF dynamics. Furthermore, no correlation was found with R_{out} when stricter hydrodynamic criteria (increased R_{out} = 20 mm Hg/ml/min) were used.

Pathological parenchymal changes were found in 21 of 38 biopsies. The changes were various and in a few cases concomitant, in the same biopsy. Most common were AD changes (10 cases), arteriosclerotic changes (5 cases), and changes resulting from ischemia, denoted subrecent encephalomalacia (4 cases).

Reports based on autopsy studies of patients with clinically and radiologically diagnosed NPH are very few, with few patients, and correlations with CSF dynamics (when measured) were not attempted. The reports implied different pathogeneses by describing the following observations, singly or concomitantly, for patients with NPH. 1) Akai et al.(1) reported, in four of seven cases, diminution and hyalinization of arachnoid granulations and obliteration of the lateral lacunae, which they found sufficiently extensive to suggest a block of CSF absorption. Furthermore, mild to moderate focal arachnoid fibrosis, with partial obliteration of the subarachnoid space, was observed in all seven cases. Similar findings were reported in some cases in other autopsy studies, with more limited groups of one to five patients 11 13 32. 2) Degenerative findings associated with microinfarctions in the periventricular and deep white matter were the most significant findings by Akai et al. (1), but these findings were also reported and related to hypertensive cerebrovascular disease in previous studies (3),(13),(15),(24),(32). 3) Neuritic plaques and neurofibrillary tangles have been reported in a few of the autopsy cases (1),(3),(4),(13),(15)

These heterogeneous neuropathological findings are in accordance with the biopsy findings in our study. However, most of the patients in other studies, as opposed to the patients in our study, were patients with NPH of known pathogenesis. Therefore, other degenerative findings were even less likely to exist, compared with our study.

The diagnostic accuracy of a single frontal biopsy, with regard to general degenerative cerebral disorders, can be discussed. Neuritic plaques are rarely, if ever, seen in the frontal cortex in normal autopsy cases, whereas they are virtually invariably seen in the frontal lobes of patients with AD(10),(25). Consequently, a frontal biopsy without AD changes cannot with certainty exclude the possibility of AD, whereas a biopsy with AD

changes allows a definite diagnosis of AD, although concomitant disorders cannot be ruled out.

Regarding the presence of arachnoid fibrosis in the biopsy, it was reasoned that leptomeningeal fibrosis sufficiently extensive to cause increased R_{out} would be present at the site of the frontal biopsy. Therefore, the occurrence of arachnoid fibrosis in the biopsies is assumed to reflect the actual number of patients with generalized leptomeningeal fibrosis. However, even in autopsy studies, as argued by Di Rocco et al.(13), there is substantial difficulty in determining whether a finding of mild to moderate arachnoid fibrosis with partial obliteration of the subarachnoid space is significant enough to interfere with CSF outflow. The general assumption that NPH is the result of defective CSF absorption through the arachnoid villi has even been called a myth(29).

In conclusion, we found no evidence of meningeal fibrosis being the causative factor of increased R_{out} in a prospectively studied group of patients with idiopathic NPH, which was diagnosed according to well-defined criteria. In more than one-half of the biopsies, various degenerative changes (most often AD changes) in the cerebral parenchyma were present. However, no correlations between the presence of pathological changes in the parenchyma and B-wave activity or R_{out} were found. The results suggest that leptomeningeal fibrosis is not the sole pathoanatomic basis of increased R_{out} and that several degenerative changes in the parenchyma may be responsible for the altered CSF dynamics that are characteristic of NPH. To elucidate the role of various degenerative parenchymal changes and the role of arachnoid fibrosis in the pathogenetic mechanisms of NPH, additional prospective biopsy and autopsy studies with more patients are needed.

REFERENCES

1.Akai K, Uchigasaki S, Tanaka U, Komatsu A Normal pressure hydrocephalus neuropathological study. Acta Pathol Jpn 37:97–110, 1987.

2.Albeck MJ, Børgesen SE, Gjerris F, Schmidt J, Sørensen PS The intracranial pressure and conductance to cerebrospinal outflow in healthy subjects. J Neurosurg 74:597–600, 1991.

3.Ball MJ Neurofibrillary tangles in the dementia of "normal pressure" hydrocephalus. Can J Neurol Sci 3:227–235, 1976.

4.Ball MJ, Vis CL Relationship of granulovacuolar degeneration in hippocampal neurones to aging and to dementia in normal pressure hydrocephalics. J Gerontol 33:815–824, 1978.

5.Børgesen SE Conductance to outflow of CSF in normal pressure hydrocephalus. Acta Neurochir (Wien) 71:1–45, 1984.

6.Børgesen SE, Gjerris F The predictive value of conductance to outflow of CSF in normal pressure hydrocephalus. Brain 105:65–86, 1982.

7.Børgesen SE, Albeck MJ, Gjerris F, Czosnyka M, Laniewski P Computerized infusion test compared to steady pressure constant infusion test in measurement of resistance to CSF out flow. Acta Neurochir (Wien) 119:12–16, 1992.

8.Brusa G, Piccardo A, Pizio N, Gambibi C Anatomopathological study of dementia syndrome linked with an abnormal cerebrospinal fluid flow. Pathologica 83:351–358, 1991.

9.Czosnyka M, Wollk-Laniewski D, Darwaj P Software for neurosurgery intensive care, in Hoff JT, Betz AL (eds): Intracranial Pressure VII. Berlin, Springer, 1989, pp 84–87.

10.Dekosky ST, Harbaugh RE, Schmitt FA, Bakay RAE, Chui HC, Knopman DS, Reeder TM, Shetter AG, Senter HJ, Markesbery WR Intraventricular Bethanecol Study Group: Cortical biopsy in Alzheimer's disease: Diagnostic accuracy and neurochemical, neuropathological, and cognitive correlations. Ann Neurol 32:625–635, 1992.

11.DeLand FH, James AE Jr, Ladd DJ, Konigsmark BW Normal pressure hydrocephalus: A histologic study. Am J Clin Pathol 58:58–63, 1972.

12.Del Bigio MR Neuropathological changes caused by hydrocephalus. Acta Neuropathol (Berl) 85:573–585, 1993.

13.Di Rocco C, Di Trapani G, Maria G, Bentivoglio M, Macchi G, Rossi GF Anatomo-clinical correlations in normotensive hydrocephalus: Report on three cases. J Neurol Sci 33:437–452, 1977.

14.DSM R III Diagnostic and Statistical Manual of Mental Disorders. Washington, American Psychiatric Association, 1987, ed 3.

15.Earnest MP, Fahn S, Karp JH, Rowland LP Normal pressure hydrocephalus and hypertensive cerebrovascular disease. Arch Neurol 31:262–266, 1974.

16.Evans WA An encephalographic ratio for estimating ventricular enlargement and cerebral atrophy. Arch Neurol 47:931–937, 1942.

17.Folstein MF, Folstein SE, McHugh PR Mini-mental state: A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 12:189–198, 1975.

18.Foncin JF, Redondo A, Le Beau J Le cortex cerebral des malades atteints d'hydrocephalie a pression normale: Etude ultrastructurale Acta Neuropathol (Berl) 34:353–357, 1976.

19.Gjerris F, Børgesen SE Current concepts of measurement of cerebrospinal fluid absorption and biomechanics of hydrocephalus. Adv Tech Stand Neurosurg 19:147–177, 1992.

20.Gjerris F, Børgesen SE, Schmidt J, Sørensen PS Resistance to cerebrospinal outflow in patients with normal pressure hydrocephalus, in Gjerris F, Børgesen SE, Sørensen PS (eds): Outflow of Cerebrospinal Fluid. Copenhagen, Munksgaard, 1989, pp 329–338.

21.Gustafson L Clinical classification of dementia conditions. Acta Neurol Scand Suppl 139:16–20, 1992.

22.Hakim S, Adams RD The special clinical problem of symptomatic hydrocephalus with normal cerebrospinal fluid pressure. J Neurol Sci 2:307–327, 1965.

23.Jack CR Jr, Mokri B, Laws ER Jr, Houser OW, Baker HL Jr, Petersen RC MR findings in normal-pressure hydrocephalus: Significance and comparison with other forms of dementia. J Comput Assist Tomogr 11:923–931, 1987.

24.Koto A, Rosenberg G, Zingesser LH, Horoupian D, Katzman R Syndrome of normal pressure hydrocephalus: Possible relation to hypertensive and arteriosclerotic vasculopathy. J Neurol Neurosurg Psychiatry 40:73–79, 1977.

25.Price JL, Davis PD, Morris JC, White DL The distribution of tangles, plaques and related immunohistochemical markers in healthy aging and Alzheimer's disease. Neurobiol Aging 12:295–312, 1991.

26.Reisberg B, Ferris SH, de Leon M, Crook T The global deterioration scale for assessment of primary degenerative dementia. Am J Psychiatry 139:1136–1139, 1982.

27.Rossi GF, Maira G, Anile C Intracranial pressure behaviour and its relation to the outcome of surgical CSF shunting in normotensive hydrocephalus. Neurol Res 9:183–187, 1987.

28.Sahuquillo J, Rubio E, Codina A, Molins A, Guitart JM, Poca MA, Chasampi A Reappraisal of the intracranial pressure and cerebrospinal fluid dynamics in patients with the so-called "pressure hydrocephalus" syndrome. Acta Neurochir (Wien) 112:50–61, 1991.

29.Vanneste J Three decades of normal pressure hydrocephalus: Are we wiser now? J Neurol Neurosurg Psychiatry 57:1021–1025, 1994.

30.Vanneste J, Augustijn P, Dirven C, Tan WF, Goedhart ZD Shunting normal pressure hydrocephalus: Do the benefits outweigh the risks? Neurology 42:54–59, 1992.

31.Vanneste J, Augustijn P, Tan WF, Dirven C Shunting normal pressure hydrocephalus: The predictive value of combined clinical and CT data. J Neurol Neurosurg Psychiatry 56:251–256, 1993.

32.Vessal K, Sperber EE, James AE Jr Chronic communicating hydrocephalus with normal CSF pressure: A cisternographic pathologic correlation. Ann Radiol (Paris) 17:785–793, 1974.

The authors performed brain biopsies, which suggested that there is no relation between arachnoid fibrosis and normal-pressure hydrocephalus (NPH). However, the arachnoid fibrosis seen in biopsies may not be the fibrosis that increases the resistance to cerebrospinal fluid (CSF) flow. Presumably, there is an increase in arachnoid trabeculations that closes the subarachnoid space. It is probably overly optimistic to think that arachnoid fibrosis is equivalent to increased resistance of CSF pathways.

Two other features of this report deserve attention. First, the rate of documented improvement was 33%, even with lumboventricular perfusion, when strict criteria were used. This is considerably lower than the rates in some recent series, but those series did not use strict criteria. Second, the findings of changes suggesting Alzheimer's disease in 8 of 38 patients and arteriosclerosis or ischemic changes in another 8 patients again raise the possibility that NPH is primarily a cerebral parenchymal disease, rather than a disorder of CSF absorption.

Peter McL. Black
Boston, Massachusetts

The authors studied a group of 38 patients suspected, based on clinical and imaging findings, of having NPH. Patients with ischemic or hemorrhagic infarction, tumor, subarachnoid hemorrhage, meningitis, or head trauma were all excluded, thus eliminating known causes of hydrocephalus. All of the patients had a frontal ventricular catheter placed and underwent intracranial pressure monitoring for a 24-hour period. The presence and frequency of B-waves, as well as CSF outflow resistance, after ventricular infusion or ventriculolumbar perfusion were noted. Twenty-nine of the 38 patients had increased CSF outflow resistance and significant B-wave frequency. They fulfilled the hydrodynamic criteria for NPH and so underwent CSF diversion. Of this group, one-third showed improvement, one-third remained the same, and one-third had progression of symptoms. These results are comparable to those obtained with the clinical criteria of dementia, ataxia, and incontinence in patients with large ventricles.

A frontal brain biopsy was performed at the time of CSF diversion, 1 month after the initial evaluation, and examined for the presence of arachnoid fibrosis and histopathological changes, which were correlated with B-wave activity, CSF outflow resistance, and the response to CSF diversion. No positive correlation was found with any of the parameters studied.

Because CSF diversion in this patient population has a number of significant risks, one would prefer to limit operative intervention to those patients who are very likely to benefit. Unfortunately, we do not seem to be much closer to this goal than we were 30 years ago, when NPH was first described. Although this study does not improve patient selection for CSF diversion or further define the pathophysiology of NPH, it provides valuable information on which to base future investigations.

J. Gordon McComb
Los Angeles, California