OBJECTIVE: The diagnosis and management of idiopathic normal-pressure hydrocephalus (INPH) remains unclear. Moreover, the value of supplementary tests to predict which patients would benefit from placement of a shunt has not been established. This report develops evidence-based guidelines for the use of supplementary tests as an aid in prognosis.

METHODS: MEDLINE searches from 1966 to the present were undertaken by use of the query NPH, normal-pressure hydrocephalus, lumbar drain, CSF [cerebrospinal fluid] tap test, and external CSF drainage in humans. This resulted in 242 articles. To provide a scientific, evidence-based review, we have chosen to restrict our analysis to clinically relevant studies usually consisting of large numbers of shunted NPH patients. Studies that did not specify INPH or secondary NPH were considered in a separate evidentiary table.

RESULTS: Evidence-based guidelines for use in supplementary tests have been developed. A positive response to a 40- to 50-ml tap test has a higher degree of certainty for a favorable response to shunt placement than can be obtained by clinical examination. However, the tap test cannot be used as an exclusionary test because of its low sensitivity (26–61%). Determination of the CSF outflow resistance via an infusion test carries a higher sensitivity (57–100%) compared with the tap test and a similar positive predictive value of 75 to 92%. Prolonged external lumbar drainage in excess of 300 ml is associated with high sensitivity (50–100%) and high positive predictive value (80–100%).

CONCLUSION: To date, a single standard for the prognostic evaluation of INPH patients is lacking. However, supplemental tests can increase predictive accuracy for prognosis to greater than 90%. Additional multicenter prospective randomized clinical trials are needed.

KEY WORDS: Assessment, CSF resistance, Idiopathic normal-pressure hydrocephalus, TAP test

RECOMMENDATIONS

Standard

There are insufficient data to support a clinical management standard for this topic.

Guidelines

Drainage of cerebrospinal fluid (CSF) via a lumbar tap can be of prognostic value if the response is significant. Lumbar puncture tap tests should withdraw 40 to 50 ml, because lesser volumes (25 ml or less) have low sensitivity. The prognostic value of this procedure for identifying patients who will benefit from shunt diversion of fluid increases as greater amounts of fluid are removed by external lumbar drainage (ELD). The highest sensitivity and specificity are associated with prolonged controlled lumbar drainage (500 ml/3 d). Measures of CSF outflow resistance (Ro) can increase the sensitivity for identifying patients who will benefit from shunting above that obtained with clinical assessment.

Options

In the recumbent position, opening CSF pressures ranging between 7 and 20 mm Hg...
have been reported in patients with suspected NPH. Expert opinion places the opening pressure range for INPH between 3 and 18 mm Hg (40–245 mm H_2O). The presence of B waves in recordings of intracranial pressure (ICP) has been identified in NPH patients but has limited prognostic value. Ro can be measured by either bolus or infusion. The threshold for an abnormal Ro varies on the basis of the method chosen. Both methods require access to CSF, usually via a lumbar route. For accurate lumbar puncture measures of resistance, a stenosis of the spinal canal or a functional aqueduct stenosis must be excluded. When combined with clinical evaluation, specificity and sensitivity for diagnosis of INPH and prediction of a positive shunt response are increased when measures of Ro are obtained.

**OVERVIEW**

The process of diagnosing and deciding whether or not to treat a patient with possible INPH is typically a multistage process. The initial phase consists of obtaining a clinical diagnosis on the basis of the history, neurological examination, and interpretation of routine computed tomographic (CT) and/or magnetic resonance imaging (MRI) scans. With regard to imaging studies, a review of the literature indicates that, beyond the confirmation that a communicating hydrocephalus is present, there is little supportive evidence that structural change on CT/MRI scans is effective in identifying patients who would do well with shunting. The early study by Petersen et al. (18) is an example. Here, the CT scans of 29 of 45 patients with a diagnosis of INPH were evaluated with regard to THE extent of ventricular dilation, cortical atrophy, and periventricular lucency. It was reported that these features did not correlate with a favorable response. These results were consistent with those of Takeuchi et al. (20), who studied patients with severe atrophy on CT scans and, after shunting, found that 48% (12 of 25) improved, providing supportive evidence that the degree of cortical atrophy does not correlate with potential benefit from shunting. Similarly, Vanneste et al. (22) classified patients into probable, possible, and improbable shunt responders on the basis of CT characteristics and achieved sensitivity values of 46% and specificity of 91% for the 17 patients in the probable shunt responder group. However, the positive predictive value (PPV) for this group was only 65%, and the PPV for the “possible shunt responder” group was only 24%. Thus, it is clear that the prognostic value of CT/MRI scans is limited and that other supplementary tests are necessary to increase the prognostic accuracy of identifying INPH responders to shunting. A more detailed review of CT/MRI scans is provided in a companion guideline article (see Part II).

It has been recommended that the clinical diagnosis of INPH be divided into probable, possible, and unlikely (see Part II). Older patients tend to have concomitant illnesses that may confound, mislead, or overlap the findings of INPH. Other patients may have minimal INPH-related symptoms or may have significant medical risk factors complicating possible surgical management. For these and other reasons, it is prudent to consider supplementary tests to help identify patients with INPH who will respond favorably with shunt placement. There is no expert consensus as to which test is optimal, and some clinicians opt for multiple supplemental tests to achieve a “preponderance of evidence” approach. In this article, we will review the scientific evidence supporting and/or discounting the following proposed INPH supplemental tests: radionuclide cisternogram, ICP monitoring, CSF tap test, ELD test, measurement of CSF Ro (or conductance), and measurement of CSF aqueductal flow velocity.

Depending on the results of one or more of these tests, it is hoped that the decision to proceed to a shunt will be made with greater certainty or be abandoned (or delayed) because of exclusionary evidence. For patients then being considered for a shunt, the third stage of assessing the risk/benefit of surgical management begins (see Part IV).

Although somewhat semantic, there is a practical issue as to whether the above tests are diagnostic or prognostic (or neither). In principle, a diagnostic test should be based on some relationship to the pathophysiology. Although the inception of many of these tests began with this concept (such as the radionuclide cisternogram), clinical investigations have in each case dampened the diagnostic usefulness. The finding of “normal” patients with “positive” tests and INPH patients with “negative” test results illustrates our incomplete understanding of the pathophysiology of INPH. Furthermore, the so-called “diagnostic” accuracy of each of the above tests has been based on shunt response rate. For multiple reasons (see Parts II and V), this outcome-based approach is error-prone with respect to either the diagnostic or prognostic usefulness of the test.

We have taken the approach that the diagnosis of INPH is made solely on clinical symptoms in combination with interpretation of routine CT/MRI scans and not the response to shunt placement. Thus, a correct diagnosis of INPH can be associated with an unfavorable response to shunting. In this case, the INPH symptoms may have progressed to a stage at which the patient is refractory to treatment. The terms shunt-responsive INPH (SRINPH) and shunt-nonresponsive INPH are useful in clarifying the distinction between diagnosis and prognosis. Observed in this light, the sensitivity and specificity of the supplemental tests can be evaluated with respect to their ability to identify SRINPH.

Aside from the response to these supplemental tests, there are many other factors that may influence whether or not a patient improves with shunting (see Part V). Furthermore, its value as a diagnostic or prognostic test will depend on the study design from which the evidence is drawn. Retrospective studies can be subject to rather significant biases, including poorly or narrowly defined patient selection, incomplete data sets, and/or skewed or inconsistent follow-up. Few supplemental INPH tests have been studied prospectively in a manner that allows us to determine the positive and negative predictive rates. Therefore, it is unknown how valuable many of these supplemental tests would be when patient inclusion is
based strictly on the proposed probable, possible, and unlikely categories. Nevertheless, a limited group of studies have been performed that provide some clarity to these issues and will be reviewed in this report.

**PROCESS**

MEDLINE searches from 1966 to the present were undertaken by use of the query NPH, normal-pressure hydrocephalus, lumbar drain, CSF tap test, and external CSF drainage in humans. This resulted in 242 articles. To provide a scientific, evidence-based review, we have chosen to restrict our analysis to clinically relevant studies usually consisting of large numbers of shunted NPH patients. Studies that did not specify INPH or secondary NPH were considered in a separate evidentiary table.

**SCIENTIFIC FOUNDATION**

There were no randomized prospective clinical trials conducted in patients with suspected INPH, and as a result, there are no standards for this topic. A considerable portion of the publications reviewed combine both INPH and secondary NPH, making it difficult to identify specific responses for any given supplemental test in the patient with INPH. Each study was analyzed with regard to retrospective versus prospective, patient selection criteria, study design, outcome criteria, and estimated positive and negative predictive rates. In some cases, information for a complete analysis was not available.

**Predictive Value of Radionuclide Cisternography**

**Background**

Before computed tomography, radionuclide cisternography was an easier and better-tolerated procedure for diagnosing hydrocephalus compared with pneumoencephalography. The procedure is typically performed by injecting an isotope (I-131-labeled serum albumin or indium In-111 pentetate) via a lumbar puncture, followed by intermittent two-dimensional gamma imaging over the course of 24 to 48 hours. Two “abnormal” isotope distribution and time course patterns were noted in hydrocephalic patients: 1) ventricular reflux and 2) delayed ascent and prolonged activity of the isotope over the cerebral convexities. Although radionuclide cisternography was initially a mainstay of the diagnostic protocol for NPH, most INPH experts currently believe that evidence-based support for its use in INPH does not support its continued use on a routine basis. However, given its long and extensive previous clinical history, and in the absence of experience in using other supplemental tests, cisternography is still commonly ordered by clinicians worldwide.

**Evidence-based Support**

Only one clinical study meeting the inclusion criteria for this Guidelines article exists. Vanneste et al. (21) studied 76 patients retrospectively and considered the question as to the usefulness of cisternography in selecting patients for shunting. The predictive value of a scale based on combined clinical and CT criteria was established first, followed by an assessment of the predictive value of cisternography. Predictions based on cisternograms were identical to those of the clinical/CT scale in 43%, better in 24%, and worse in 33%. These authors concluded that cisternography does not improve the diagnostic accuracy of combined clinical and CT criteria in patients with presumed normal-pressure hydrocephalus.

**Complications**

Although complication rates have not been reported, the radionuclide cisternogram is generally considered to carry virtually no risk for the evaluation of INPH.

**Summary**

Based on the one Class III study, cisternography does not improve the diagnostic accuracy of identifying SRINPH and therefore is not included as an option.

**Predictive Value of ICP Monitoring**

**Background**

There are several aspects to the measurement of ICP with regard to INPH. Historically, the term “normal-pressure” hydrocephalus was based on the observation that the lumbar puncture opening pressures were not elevated in these patients (1, 11). However, what ICP threshold is considered “elevated” has not been determined analytically, and many question the validity of the designation “normal pressure.” The average opening pressures in the cited INPH studies range from 8.8 ± 1.3 mm Hg (20) to 14.62 ± 1.5 mm Hg (15). Although most might consider 8.8 mm Hg as “normal,” there is less agreement that ICPs greater than 15 mm Hg are “normal.” Low ICPs are also not specific and therefore not diagnostic for INPH. Many secondary NPH patients present with low or “normal” ICPs, although the finding of a baseline elevated ICP raises the suspicion of secondary NPH. In summary, there is limited evidence regarding the lower and upper limits of opening pressure in idiopathic NPH. For this reason, a consensus of European and United States experts, combined with the results of limited published works, placed the expected range of INPH opening pressure between 60 and 240 mm H2O, or 4.4 to 17.6 mm Hg.

In addition to measuring the baseline opening pressure, many have been interested in possible relationships between continuous ICP recording variables and outcome for NPH. Most have sought a correlation between the number of B waves recorded (overnight during sleep) and outcome (19). It has been proposed that the increased frequency in B waves is indicative of lowered compliance and/or may play an important role in the pathophysiology of the ventriculomegaly and neuronal dysfunction. A common criticism of these studies has been the lack of normal aged-matched control data. Eide and Fremming (8) reported that the lumbar puncture opening pressure...
pressure has no correlation with the frequency of overnight B waves in hydrocephalic patients.

**Evidence-based Support**

The possible relationship of baseline ICP (opening pressure) and outcome for INPH has not been studied. On the basis of expert opinion, we have selected an upper limit of 240 mm H₂O (17.6 mm Hg) as acceptable for analysis as an INPH patient. In some cases, the results of supplemental testing will suggest that secondary NPH, rather than INPH, is present. For example, the measurement of the pressure of the CSF via a lumbar tap (or other method) is strongly recommended for determining whether the ICP is within the range expected for INPH (60–240 mm H₂O). Pressures greater than 240 mm H₂O might suggest secondary NPH.

There are no data available documenting the value of continuous monitoring of ICP in INPH patients that meet the requirements of this Guidelines article. Several investigators have studied NPH patients in general without independent INPH analysis. Raftopoulos et al. (19) studied 43 NPH patients, but the number of INPH patients was not specified. These authors concluded that it is not important to detect the frequency of B waves or A waves but rather their amplitude and duration. They further concluded that waves that predict positive outcomes after shunting are the great symmetrical waves and intermediate waves that they described. However, no data for INPH patients were reported, and it is not certain that the occurrence of these waves can be generalized to INPH. With regard to the entire patient group, by use of these criteria, 20 (83%) of 24 shunted patients improved. Williams et al. (25) studied 86 possible NPH patients with continuous pressure recordings and prolonged CSF drainage. Both A and B waves poorly predicted which patients responded to shunt surgery.

**Complications**

Complications related to measuring opening pressure in suspected INPH patients via lumbar puncture have not been reported. Complications related to continuous pressure monitoring have also not been reported; however, this procedure is often performed in conjunction with ELD (see below).

**Summary**

The measurement of ICP should be considered during the diagnostic/prognostic phase of INPH. An elevated ICP should prompt a reassessment to rule out a secondary cause of NPH. Class III evidence does not currently support continuous ICP monitoring to determine the frequency of B or A waves.

**Predictive Value of CSF Removal via High-volume “Tap Test”**

**Background**

In the classic description of NPH by Adams et al. (1) and Hakim and Adams (11), three hydrocephalic patients were presented, two posttraumatic and one diagnosed as having INPH. In each patient, a spinal tap was performed, and a volume of CSF on the order of 15 ml was removed, with improvement noted in all three patients. This reference is actually the first report documenting a CSF tap performed for the purpose of diagnosing and later shunting a patient with INPH. Since this early reference, many clinicians have used lumbar punctures and CSF removal of relatively small volume as an aid in identifying potential shunt responders in cases of both INPH and secondary NPH. This test, which is commonly referred to as the “tap test,” has evolved in that now most clinicians who use it tend to remove much larger volumes of CSF (40–50 ml). This is reviewed in greater detail in this report.

Although simple in concept, there are nuances to the interpretation of the test. What constitutes a “significant” improvement has not been formalized. Most experts agree that an objective improvement in gait, either by a quantitative method or by blinded videotape review, is preferable. The usefulness of before-and-after neuropsychiatric testing has not been validated for this test or even surgical treatment of INPH (see Part V), and the degree of improvement in any variable also lacks validation. Moreover, INPH patients have normal daily fluctuations in symptoms, and that motivation can transiently improve performance. Therefore, the analysis of reported studies must take these factors into account.

**Evidence-based Support**

No study performed to date has definitively addressed the efficacy of this test for identifying SRINPH (Table 3.1). Malm et al. (15) studied 35 patients with INPH and found that CSF removal improved gait performance but could not predict the outcome from shunt surgery. However, in this study, lumbar CSF pressure was lowered to zero, which implied removal of different amounts of CSF in different patients, depending on the volume and elasticity of the system. Sensitivity and specificity could be calculated from the data presented. Twenty-two of 35 INPH patients improved (63%) with this special tap test, and 16 patients improved after shunting (73%). Of the 13 patients who did not improve with CSF removal, 10 improved after shunting and 3 did not improve. Thus, with regard to improvement after shunting, the sensitivity of CSF removal in this case equaled 62%, and specificity equaled 33%.

Other studies have been weakened because of other methodological considerations. Wikkelsø et al. (24) studied 27 patients with NPH (INPH and secondary). The relationship of improvement of walking pattern after CSF removal in all 27 patients was expressed as a correlation (r = 0.96, P < 0.001). However, the number of INPH patients was small, and the sensitivity and specificity of the CSF tap test were not reported.

A 40-ml tap test by Walchenbach et al. (23) was performed in 49 NPH patients (43 INPH) from three institutions. Only those who improved were shunted. The authors reported a 26% sensitivity and a specificity of 100%. The PPV of a positive
tap test in this study equaled 100%, and the predictive value of a negative tap test was 32%. Haan and Thomeer (10) studied 32 patients with presumed INPH, and of these, 10 patients improved after a single lumbar puncture (volume not specified), and 9 were shunted. All 9 patients improved after shunt. A total of 22 patients who did not improve after the tap test were included in a subsequent ELD study.

Kahlon et al. (12) studied 68 patients with suspected NPH, 51 of whom had INPH. Only patients with either a positive CSF tap test or a high CSF Ro were shunted (see Discussion below). Most patients improved with surgery, and only 42% were selected as a result of a positive tap test. The PPV was high for the tap test (94%), but 22 patients (58%) with improvement after shunt operation would have been missed if this test had been used alone. The number of INPH patients who improved with tap test is not specified, and as a result, sensitivity, specificity, and PPV for INPH could not be calculated.

Complications

Malm et al. (15) reported that 2 of 36 patients developed headaches after a CSF tap test of 40 to 50 ml. Both Kahlon et al. (12) and Wikkelsø et al. (24) reported no complications related to the tap test.

Summary

The 40- to 50-ml CSF tap test has not undergone a rigorous prospective clinical evaluation to date. On the basis of a single Class II study using a somewhat different methodology (Malm et al. [15], lowering pressure to zero), the test had only a 62% sensitivity and 33% specificity. A multicenter Class II study did report a 100% positive predictive rate (23). Given these limited data, the CSF tap test may have good PPV for SRINPH (Table 3.2); however, specificity is low, suggesting that many patients who might benefit from shunting will be missed. The tap test therefore is listed as a Guideline for the prognostic evaluation of INPH, with the caveat that INPH candidates not be excluded on the basis of a negative tap test.

### Predictive Value of the ELD Test

**Background**

In view of the general experience that larger CSF volumes improved sensitivity with the CSF tap test, investigators speculated that continuous external CSF drainage might achieve a clinically useful diagnostic sensitivity (Table 3.3). This required the placement of a lumbar intrathecal catheter and controlled drainage while the patient was hospitalized. ELD was initially described by Haan and Thomeer (10) and consisted of draining 10 ml of CSF per hour for a period of 72 hours (total, 720 ml). There have been no studies assessing whether shorter or more prolonged drainage results in equivalent or better results.

As with the CSF tap test, there are important considerations with regard to the interpretation of what constitutes a “positive” result. In addition, prolonged external catheter drainage

---

**TABLE 3.1. Evidentiary table: Value of cerebrospinal fluid tap test for idiopathic normal-pressure hydrocephalus**

<table>
<thead>
<tr>
<th>Series (ref. no.)</th>
<th>INPH (n)</th>
<th>Description of study</th>
<th>Class</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malm et al., 1995 (15) Prospective</td>
<td>35</td>
<td>CSF tap test and outflow conductance was measured before shunting in 35 patients with INPH. After shunting, gait was improved in 72% of patients with clinical diagnosis alone; 16 of 26 shunted patients (61%) showed improvement with tap test. Gait was assessed 3 to 4 h after CSF tap test.</td>
<td>II</td>
<td>Neither the CSF tap test nor CSF conductance was considered predictive of shunt outcome.</td>
</tr>
<tr>
<td>Haan and Thomeer, 1988 (10) Retrospective</td>
<td>32</td>
<td>CSF tap test and ELD was used to predict shunt outcome in 32 patients with suspected INPH. Ten improved with a single tap and were not drained. The remaining 22 patients underwent ELD. Of 17 patients eligible for evaluation, ELD correctly predicted shunt outcome.</td>
<td>III</td>
<td>Temporary external drainage is a safe and effective means of predicting shunt outcome and enables patient selection in a poorly demarcated area of NPH.</td>
</tr>
<tr>
<td>Walchenbach et al., 2002 (23) Prospective</td>
<td>43</td>
<td>Patients with presumed NPH were prospectively studied. Of 49 NPH patients, 43 were INPH. Forty-eight patients were shunted; 73% showed improvement at 2 mo. Predictive value of ELD was 87% and of a negative ELD, 36%. Meningitis occurred in 2 patients without residual deficit.</td>
<td>II</td>
<td>In patients with positive ELD, shunting is justified. Shunting of patients with negative ELD should be considered in view of the high percentage of patients improving after a shunt despite a negative ELD.</td>
</tr>
</tbody>
</table>

a INPH, idiopathic normal-pressure hydrocephalus; CSF, cerebrospinal fluid; ELD, external lumbar drainage.
imposes increased risks of complications compared with the CSF tap test. Overdrainage complications can occur as a result of inadvertent catheter disconnections or changes in patient position, which may result in very large and rapid CSF loss. Patients with severe short-term memory dysfunction are at highest risk because of lowered patient compliance with remaining still in bed. Although subsequent studies have reported quite low complication rates (23, 25), this and other factors (such as morbidity and cost associated with hospitalization) demand consideration with regard to interpretation of the published results and the practical clinical use of the test.

**Evidence-based Support**

Several of the reported studies of ELD (Table 3.4) have used a two-step protocol, in which only “nonresponders” to the

<table>
<thead>
<tr>
<th>Series (ref. no.)</th>
<th>INPH/SNPH (n)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malm et al., 1995 (15)</td>
<td>35/0</td>
<td>62% (16/26)</td>
<td>33% (3/9)</td>
<td>73% (16/22)</td>
<td>23% (3/13)</td>
<td>54% (19/35)</td>
</tr>
<tr>
<td>Walchenbach et al., 2002 (23)</td>
<td>43/6</td>
<td>26% (9/35)</td>
<td>100% (12/12)</td>
<td>100% (9/9)</td>
<td>32% (12/38)</td>
<td>45% (21/47)</td>
</tr>
<tr>
<td>Haan and Thomeer, 1988 (10)</td>
<td>32/0</td>
<td>43% (9/21)</td>
<td>100% (5/5)</td>
<td>100% (9/9)</td>
<td>42% (5/12)</td>
<td>54% (14/26)</td>
</tr>
</tbody>
</table>

* INPH, idiopathic normal-pressure hydrocephalus; SNPH, secondary NPH; PPV, positive predictive value; NPV, negative predictive value.

<table>
<thead>
<tr>
<th>Series (ref. no.)</th>
<th>INPH/ SNPH (n)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haan and Thomeer, 1988 (10)</td>
<td>17/0</td>
<td>100% (12/12)</td>
<td>100% (5/5)</td>
<td>100% (12/12)</td>
<td>100% (5/5)</td>
<td>100% (17/17)</td>
</tr>
<tr>
<td>Williams et al., 1998 (25)</td>
<td>86 (mixed)</td>
<td>97% (31/32)</td>
<td>60% (9/15)</td>
<td>84% (31/37)</td>
<td>90% (9/10)</td>
<td>75% (40/47)</td>
</tr>
<tr>
<td>Walchenbach et al., 2002 (23)</td>
<td>43/6</td>
<td>50% (14/28)</td>
<td>80% (10/13)</td>
<td>80% (14/16)</td>
<td>36% (14/22)</td>
<td>58% (22/38)</td>
</tr>
</tbody>
</table>

* INPH, idiopathic normal-pressure hydrocephalus; SNPH, secondary NPH; PPV, positive predictive value; NPV, negative predictive value.

**Evidence-based Support**

Several of the reported studies of ELD (Table 3.4) have used a two-step protocol, in which only “nonresponders” to the

<table>
<thead>
<tr>
<th>Series (ref. no.)</th>
<th>Description of study</th>
<th>Class</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Takeuchi et al., 2000 (20) Retrospective</td>
<td>Patients with INPH accompanied by brain atrophy on CT (n = 25) were shunted. CSF outflow resistance (bolus) was 35.3 mm Hg/min in improved patients compared with 9.1 in unimproved patients. Pathological ICP pressure waves were observed in 8 of improved patients but none of unimproved patients.</td>
<td>III</td>
<td>Disturbance of CSF absorption is the most important factor in evaluation of the effectiveness of shunting. All patients with greater than 20 mm Hg/ml/min improved with shunting.</td>
</tr>
<tr>
<td>Peterson et al., 1985 (18) Retrospective</td>
<td>Retrospective review of 45 shunted patients with INPH. Patients were evaluated on the basis of initial symptoms, duration of symptoms, ADL status, CTs, CSF cisternograms, and EEGs; results of CSF and psychometric evaluations were reviewed when available.</td>
<td>III</td>
<td>Patients with symptoms for less than 2 yr were more likely to improve. CT played an important role in diagnosis and follow-up, but ventricular size or degree of atrophy did not correlate well with response.</td>
</tr>
</tbody>
</table>

* INPH, idiopathic normal-pressure hydrocephalus; CT, computed tomographic scan; CSF, cerebrospinal fluid; ICP, intracranial pressure; ADL, activities of daily living; EEG, electroencephalogram.
CSF tap test underwent the more prolonged drainage. A study by Haan and Thomeer (10) retrospectively analyzed the results of 32 INPH patients, all of whom underwent a CSF tap test first. Patients who did not improve after the tap test were included in an ELD study. Because patients improving from a tap test would more than likely improve with ELD, it is reasonable to suppose that the exclusion of these patients results in an underestimation of the prognostic value of ELD. One infection and one radiculopathy as a result of ELD were reported. Three additional patients were excluded because of shunt complications. Of the remaining 17 patients in the ELD study, 12 showed a good response to ELD and 5 did not. All 12 benefited from shunting. Five patients who did not improve with ELD did not improve after shunting. The sensitivity and specificity based on these data equaled 100%. Likewise, the PPV and negative predictive value (NPV) also equaled 100%. It was noted that complications of shunting in this series were seen in 50% of patients, and 23% of patients were left with permanent neurological deficit.

In the prospective study of ELD reported by Walchenbach et al. (23), 49 patients from three hospitals (43 with INPH) were studied. A total of 48 patients were shunted. A CSF tap test of 40 ml was performed in 47 of the 48 patients, and 9 were shunted because of marked improvement after tap. The 9 patients all improved after shunt. However, the predictive value of a negative tap test was very low and equaled 32% (Table 3.2). Patients who did not improve with a tap were given ELD in which 300 ml was removed over a 5-day period. Of the patient group not improving from the tap test, a total of 5 patients had to be excluded from the ELD study because of complications associated with ELD. Of 38 patients given ELD, 16 improved after drainage and 22 did not. Of the 16 who were improved after drainage, 14 improved after shunting, resulting in a sensitivity of 50% (14 of 28). Of the 22 patients who did not improve after drainage, 14 improved after shunt and 8 did not, resulting in a specificity of 80%. The PPV of ELD was 87%, and the NPV equaled 36%. The overall accuracy of ELD in this study equaled 62%.

In a study of ELD in 86 patients (INPH and secondary NPH), Williams et al. (25) reported a sensitivity of 97% and specificity of 60%. Although patients were combined, the PPV equaled 84%, and NPV was 90%. The false-negative rate equaled 3%. An external drainage rate of 10 ml/h for 3 days was used.

Complications
Walchenbach et al. (23) reported bacterial meningitis in 2 of 38 patients treated with ELD. Both patients recovered after antibiotic therapy. In the same study, lumbar drains had to be replaced in 5 of 38 patients after displacement of the drain. Haan and Thomeer (10), in a study of 22 patients treated with ELD, reported removal of drains in 4 patients, root irritation in 3, and infection in 2 patients.

Summary
The advantage of ELD is the increased sensitivity compared with the CSF tap test. These sensitivities are underestimated because those patients improving with tap test were excluded from ELD protocols in most studies. However, more patients who do not improve with a large-volume CSF tap test will show improvement with prolonged drainage and benefit from shunting. The PPV is high, ranging from 80 to 100%, and is associated with a weighted average of 85%. However, hospital admission is required. Reported complication rates with ELD are generally low but may be significant in terms of added morbidity.

Predictive Value of CSF Ro
Background
The Ro of CSF is considered to be the impedance of flow offered by the CSF absorption pathways. The reciprocal of resistance is conductance, and there is no general preference among investigators as to which term is used, because both impart similar information. Several methods can be used to measure the resistance. In the Katzman test (Katzman and Hussey [13]), a pump introduces mock CSF fluid or saline at a known rate through a needle placed in the lumbar subarachnoid space. The Ro, as defined by the Katzman infusion test, is the difference in the final steady-state pressure reached and the initial pressure divided by the infused flow rate. In contradistinction, the bolus method for estimating Ro involves injecting a known volume, usually 4 ml, into the lumbar subarachnoid space at a rate of 1 ml/s. The advantage of the bolus method is that it also provides a measure of the brain compliance, as defined by the pressure-volume index (16). A third method is based on an earlier mathematical model (16) and calculates both the resistance and compliance during the ascending pressure curve in response to a known infusion rate (6). Unlike the Katzman infusion test, it is not necessary to reach a steady-state pressure when using this method. Other less often used techniques include the constant-pressure method (15) and the ventriculocisternal method (3). For unknown reasons, Ro values determined by the infusion method (Katzman) are higher than those of the bolus technique, and it is important to distinguish between the reported thresholds for each method when the values are used for predicting SRINPH.

Regardless of the methodology used to estimate Ro, it is well known that Ro naturally increases with age in otherwise healthy individuals (5); this is a potentially important confounding variable that has not been adequately addressed in clinical studies.

Evidence-based Support
Two studies of Ro with regard to INPH exist that meet our Guidelines inclusion criteria. Malm et al. (15) prospectively evaluated the predictive value of CSF Ro in 35 INPH patients by use of a modification of the constant-pressure technique (9). The conductance of the INPH group was low (equivalent to a high Ro) and measured 9.1 ± 1.4 mm3 kPa (Ro = 8.2 mm Hg/ ml/min). The authors reported that the conductance could not predict the outcome of gait or neuropsychological indices. The
corresponding sensitivity and specificity equaled 58 and 44%, respectively, on the basis of our calculations from the reported data. The number of patients available for calculation of the specificity and NPV were few (four of nine). Predictive values are listed in Table 3.5, and the overall accuracy of prediction equaled 54%. Gait was improved in 25 (72%) of the 35 shunted patients.

Takeuchi et al. (20) used the bolus method for calculation of Ro in 25 shunted INPH patients in a retrospective study. The authors classified these patients as atypical INPH because of the severe atrophy on CT scans. The Ro was calculated from a single 10- to 15-ml bolus injected into the lumbar subarachnoid space (infusion speed, 1 ml/s). It is important to note that the ICP measurements used for the calculation of Ro were obtained from a cranial epidural monitor. The average Ro for the shunted group with improved outcome equaled 35.3 mm Hg/ml/min. The average value of Ro for the shunted group with no improvement equaled 9.1 mm Hg/ml/min (P < 0.01). On the basis of this threshold, the calculated sensitivity and specificity equaled 100 and 92%, respectively. The overall accuracy based on the reported data equaled 96%. It is important to note that the Ro values were not used to select patients for shunting but rather were analyzed postoperatively to identify prognostic thresholds.

Several clinical studies addressing the clinical value of Ro did not segregate out INPH-specific results (Table 3.6). In the Dutch NPH study, Boon et al. (2) examined whether measurements of Ro predicted outcome after shunting for NPH patients. Data were presented for combined INPH and secondary NPH, although the authors reported that “most” of the patients had INPH. The CSF resistance was measured by the constant flow infusion. This was a four-center prospective study, and patients who fulfilled strict clinical criteria underwent shunt surgery irrespective of the Ro value. Values of Ro ranged from 6.3 to 42.3 mm Hg/ml/min, with an average of 17.3 mm Hg/ml/min. The Ro values were correlated with primary and secondary outcome measures by use of linear regression analysis. Retrospectively, the authors recommended 18 mm Hg/ml/min as the Ro threshold on the basis of optimal sensitivity, specificity, PPV, and NPV values. At 18 mm Hg/ml/min, sensitivity and specificity equaled 46 and 87%, respectively. The calculated overall accuracy equaled 67%. The PPV and NPV equaled 92 and 34%, respectively (Table 3.7).

Børgesen et al. (3) also studied the conductance in a series of 40 NPH patients, 20 of whom were classified as having INPH. The method used was the ventriculocisternal technique. In this prospective study, the patients satisfying clinical criteria received a shunt when the conductance was below 0.13 ml/min (Ro > 8.0 mm Hg/ml/min). The authors commented that this value may be too high, because no patient with a conductance greater than 0.075 (Ro < 13.3 mm Hg/ml/min) benefited from shunt placement. The PPV for this technique equaled 96% for the conductance threshold of 0.075. Sensitivity and specificity could not be calculated from the reported data (Table 3.7).

Kahlon et al. (12) studied 68 patients with suspected NPH, 51 of whom had INPH. Only patients with either a positive CSF tap test or a positive Katzman infusion test were shunted (Ro threshold, 14 mm Hg/ml/min). Most patients improved with surgery, and only 42% were selected as a result of a positive tap test. The PPV of the lumbar infusion test was 80%, and if used alone, the test would have missed only 6 of the patients (16%) who improved after surgery. As noted above, the PPV was higher for the tap test (94%), but 22 patients (58%) with improvement after shunt operation would have been missed if this test had been used alone.

Meier and Bartels (17) studied 200 patients with suspected NPH. These were classified as “early” or “late” NPH by use of compliance computed from an infusion test. Of this group, 107 were diagnosed as having NPH on the basis of resistance, and 102 were shunted. Improvement in symptoms was found in 65% of patients with early-stage NPH (29 of 45) and 50% with advanced-stage NPH (31 of 62). Five patients were excluded from analysis, but it was not specified as to which group. The calculated PPV equaled 56%.

**Complications**

Meier and Bartels (17) reported that 19% of 107 patients developed headaches after lumbar infusion studies and 2 patients developed meningismus without signs of inflammation in the CSF. Kahlon et al. (12) reported no complications related to infusion test.

**Summary**

The information available for assessing the usefulness of Ro in INPH is limited, and the two reports cited for INPH are the

---

**TABLE 3.5. Predictive value of cerebrospinal fluid outflow resistance in shunt-responsive idiopathic normal-pressure hydrocephalus**

<table>
<thead>
<tr>
<th>Series (ref. no.)</th>
<th>INPH/SNPH (n)</th>
<th>Ro threshold</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malm et al., 1995 (15)</td>
<td>35/0</td>
<td>14 mm Hg/ml/min</td>
<td>58% (15/26)</td>
<td>44% (4/9)</td>
<td>75% (15/20)</td>
<td>27% (4/15)</td>
<td>54% (19/35)</td>
</tr>
<tr>
<td>Takekuchi et al., 2000 (20)</td>
<td>25/0</td>
<td>13 mm Hg/ml/min</td>
<td>100% (12/12)</td>
<td>92% (12/13)</td>
<td>92% (12/13)</td>
<td>92% (12/13)</td>
<td>96% (24/25)</td>
</tr>
</tbody>
</table>

* INPH, idiopathic normal-pressure hydrocephalus; SNPH, secondary NPH; Ro, outflow resistance; PPV, positive predictive value; NPV, negative predictive value.
### TABLE 3.6. Evidentiary table: Studies of combined idiopathic and secondary normal-pressure hydrocephalus

<table>
<thead>
<tr>
<th>Series (ref. no.)</th>
<th>INPH (n)</th>
<th>Description</th>
<th>Class</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Williams et al., 1998 (25) Retrospective</td>
<td>86</td>
<td>NPH patients (% INPH not specified) underwent controlled lumbar drainage for 3 d at 10 ml/h. Based on outcome analysis of 47 patients who were shunted; sensitivity equaled 97%; specificity, 60%; PPV, 84%; NPV, 90%; and false-negative rate, 3%.</td>
<td>III</td>
<td>Clinical response to controlled drainage accurately predicted outcome after shunt surgery in patients with suspected NPH.</td>
</tr>
<tr>
<td>Boon et al., 1997 (2) Prospective</td>
<td>101</td>
<td>Patients with NPH symptoms (% INPH not specified) in four centers underwent shunting irrespective of CSF resistance values. Outcome was then compared with levels of Ro (infusion). PPV were 78, 81, and 80% for Ro of 10, 12, or 15 mm Hg/ml/min, 92% for Ro of 18 mm Hg/ml/min, and 100% for Ro of 24 mm Hg/ml/min. NPVs were 50% or less.</td>
<td>II</td>
<td>Measurement of Ro reliably predicts outcome if the limit for shunting is raised to 18 mm Hg/ml/min. At lower Ro values, the decision depends mainly on the extent to which CT and clinical findings are typical for NPH.</td>
</tr>
<tr>
<td>Vanneste et al., 1986 (24) Prospective</td>
<td>27</td>
<td>A tap test was performed on 27 patients (6 INPH), of which 24 were evaluable. Nineteen patients improved after shunt, and 5 were unchanged. Calculated sensitivity equaled 68%, and specificity was 100%. PPV equaled 100%. NPV equaled 45%. Accuracy equaled 75%.</td>
<td>II</td>
<td>The CSF tap test is suitable when complicated decisions are to be taken.</td>
</tr>
<tr>
<td>Vanneste et al., 1992 (21) Retrospective</td>
<td>76</td>
<td>The clinical usefulness of cisternography in selecting patients with presumed NPH for shunting was investigated in 76 patients. The predictive value of a scale based on combined clinical and CT criteria was first established, followed by an assessment of the predictive value of cisternography. Predictions based on cisternograms were identical to those of the clinical/CT scale in 43%, better in 24%, and worse in 33%.</td>
<td>III</td>
<td>Cisternography does not improve the diagnostic accuracy of combined clinical and CT criteria in patients with presumed NPH.</td>
</tr>
<tr>
<td>Vanneste et al., 1993 (22) Retrospective</td>
<td>112</td>
<td>The value of an ordinal global scale derived from combined clinical and CT data (clin/CT scale) to predict the clinical outcome in 112 patients shunted for presumed NPH was analyzed. A clin/CT scale was determined blind to the results of further ancillary tests and to the postsurgical outcome. In the subgroup of patients with presumed communicating NPH, the prevalence of shunt responsiveness was 29%; the best strategy was to shunt only patients with probable shunt-responsive NPH: the sensitivity was 54%; the specificity, 84%; and the predictive accuracy, 75%; with a limited number of ineffective shunts (11%) and missed improvements (13%).</td>
<td>III</td>
<td>The study illustrates the need to assess the pretest probability of NPH based on combined clinical and CT data, before establishing the clinical usefulness of an ancillary test.</td>
</tr>
<tr>
<td>Meier and Bartels, 2001 (17) Retrospective</td>
<td>107</td>
<td>Intrathecal infusion test was used to separate patients with atrophy and NPH. Further differentiation into early- and late-stage NPH was made using compliance. Diagnosis of NPH was made in 107 patients, and 105 were shunted. Improvement in symptoms among early-stage NPH (29/45) was found in 65% of patients, and 50% of advanced stage NPH (31/62) reported improvement.</td>
<td>III</td>
<td>Computer-aided infusion test allows a reliable differentiation between patients with NPH and those with cerebral atrophy. Calculated sensitivity equaled 57%.</td>
</tr>
<tr>
<td>Kahlon et al., 2002 (12) Prospective</td>
<td>68</td>
<td>Study used CSF tap test and infusion test to identify shunt-responsive NPH. Of 68 patients, 51 (75%) were INPH. Patients were shunted only when either tap test or infusion test was positive. Of 47 patients shunted, 96% reported subjective improvement. PPV was 80% for lumbar infusion test and 94% for tap test. False-negatives in operated group were 50% with tap and 16% for infusion.</td>
<td>II</td>
<td>Surgery can be based on positive tap test alone, but, if test is negative, surgery can be based on a positive infusion study.</td>
</tr>
<tr>
<td>Borgesen et al., 1979 (3) Prospective</td>
<td>20</td>
<td>40 patients with NPH (INPH, n = 20; SNPH, n = 20) were studied by monitored intraventricular pressure for 24 hours. B waves and conductance were measured by the infusion technique. No patient with conductance above 0.075 benefited with shunt. No correlation of B waves with conductance was observed.</td>
<td>II</td>
<td>Presence of B waves does not imply a low conductance (high resistance) to outflow of CSF.</td>
</tr>
<tr>
<td>Raftopoulos et al., 1992 (19) Prospective</td>
<td>43</td>
<td>43 NPH patients (idiopathic and secondary, percentages not specified) were studied using continuous ICP monitoring, and records were analyzed for presence of ICP waves and subdivided into classes of small symmetrical waves, great symmetrical waves, and intermediate waves, B waves, and plateau waves. Twenty-four patients were shunted on the basis of great symmetrical waves and intermediate waves. Of these 24 patients, 20 improved.</td>
<td>II</td>
<td>It is not important to detect frequency of B waves or A waves but, rather, their amplitude and duration. Waves that predict positive outcomes after shunt are great symmetrical waves and intermediate waves.</td>
</tr>
</tbody>
</table>

a INPH, idiopathic normal-pressure hydrocephalus; PPV, positive predictive value; NPV, negative predictive value; Ro, outflow resistance; CSF, cerebrospinal fluid; CT, computed tomographic; SNPH, secondary NPH.
largest series of data currently available. On the basis of these
data, it is clear that the results, methods, and thresholds are
center-specific and are subject to wide variation. For INPH,
the reported sensitivity ranges from 57 to 100%. The sole Class
II prospective study (15) found marginal sensitivity, specific-
ity, and PPV values. Although data are scant, the reported
accuracy of resistance measures may be higher than that of the
CSF tap test. Therefore, determination of CSF Ro may be
helpful in increasing prognostic accuracy for identifying
SRINPH when tap test results are negative.

Tables 3.5 and 3.7 document the predictive value in SRINPH and combined
shunt-responsive NPH, respectively.

Predictive Value of Aqueductal CSF Flow Velocity

Background

It has been proposed that NPH patients have a higher CSF
flow velocity through the cerebral aqueduct. This was first
noted by an exaggerated aqueductal flow void on axial MRI
scans, and subsequently, methodologies were developed to
estimate the actual maximum flow velocity at that site. For
example, Luetmer et al. (14) suggested that velocities greater
than 18 ml/min were predictive for good outcome after shunt-
ing. The pathophysiological basis of increased CSF flow void
velocity in INPH has not been established.

Evidence-based Support

In a retrospective study, Dixon et al. (7) retrospectively
reviewed the records of 49 INPH patients who underwent
quantitative aqueductal CSF flow and received shunts. Al-
though an 86% improvement rate was reported after shunting,
increased CSF flow through the aqueduct was not signifi-
cantly associated with improvement or the magnitude of im-
provement in gait, cognition, or incontinence. Interestingly, 36
patients underwent high-volume lumbar puncture preopera-
tively, of whom 5 had no response. The aqueductal CSF flow
rates of these 5 patients were significantly higher than those of
the patients who improved after lumbar puncture. In contrast,
Bradley et al. (4) reported in a retrospective study of 18 pa-
tients with suspected NPH that there was no statistically
significant relationship between aqueductal flow void score
and responsiveness to shunting. These investigators concen-
trated on CSF stroke volume and reported that CSF stroke
volume greater than 42 ml and response to shunting were
statistically significant (P < 0.05). However, the numbers of
patients were small, and further study is necessary.

Complications

No known complications related to MRI of INPH have been
reported.

Summary

On the basis of current evidence, neither MRI CSF flow void
sign nor quantitative CSF flow velocity seems to have signif-
cant diagnostic value. However, CSF stroke volume may
potentially have greater prognostic value than aqueductal
flow void. The prognostic role of MRI for shunt-responsive
INPH requires further study.

SUMMARY OF RECOMMENDATIONS FOR
INPH DIAGNOSIS AND USE OF
SUPPLEMENTAL PROGNOSTIC INPH TESTS
FOR IDENTIFYING SHUNT-
RESPONSIVE PATIENTS

On the basis of the above evidence-based review of the
literature, there are no standards from which definitive rec-
ommendations can be made. In the formulation of these rec-
ommendations, the prognostic power of each study was taken
into consideration with respect to patient selection. For ex-
ample, the Dutch NPH study (2) gave us valuable information
with regard to the value of CSF Ro measurement in highly
selected patients (those most likely designated as probable
INPH as described in Part III). However, for the clinician
pondering how to best proceed with the evaluation of a pa-
tient in whom the clinical diagnosis is less certain (“possible”
or “unlikely” INPH), the role of Ro in these patients is not
clear. Differences in patient inclusion criteria are but one of
many possible reasons why the PPV of these tests varies

<table>
<thead>
<tr>
<th>Series (ref. no.)</th>
<th>INPH/SNPH (n)</th>
<th>Ro threshold (mm Hg/ml/min)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boon et al., 1997 (2)</td>
<td>101 (mixed)</td>
<td>&gt;18</td>
<td>46%</td>
<td>87%</td>
<td>92%</td>
<td>34%</td>
<td>67%</td>
</tr>
<tr>
<td>Børgesen et al., 1979 (3)</td>
<td>20/40</td>
<td>&gt;8</td>
<td></td>
<td></td>
<td>96%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kahlon et al., 2002 (12)</td>
<td>51/68</td>
<td>&gt;14</td>
<td></td>
<td></td>
<td>80%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meier and Bartels, 2001 (17)</td>
<td>102 (mixed)</td>
<td>&gt;13</td>
<td></td>
<td></td>
<td>56%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*INPH, idiopathic normal-pressure hydrocephalus; SNPH, secondary NPH; Ro, outflow resistance; PPV, positive predictive value; NPV, negative predictive value.

Data reported for combined INPH and SNPH. Individual group data not reported."
greatly across studies. None of the studies have addressed the value of these tests for patients with lower diagnostic certainties, and therefore, only expert opinion can be offered with respect to the evaluation of these patients. Taking all of these factors together, a recommended procedure for identifying shunt-responsive patients with INPH is shown in Figure 3.1.

**Identifying Shunt-responsive Patients**

**Step 1: Clinical Evaluation**

On the basis of the history, neurological examination, and basic neuroimaging (CT and/or MRI scans), the patient is categorized as probable, possible, or unlikely INPH (see Part II). Without further supplemental testing, the degree of certainty for improvement after shunt placement for probable and possible INPH ranges from as high as 61% to less than 50% (20–22). The probability of improvement for an unlikely INPH designation is presumably less; therefore, only in extraordinary cases would these patients be considered for further evaluation. In an otherwise healthy patient in whom the clinical diagnosis seems highly probable, it might not be unreasonable to proceed directly to treatment (the placement of a shunt) without supplemental tests, keeping in mind the 50 to 61% degree of certainty.

**Step 2: Supplemental Testing**

To avoid complications and improve the certainty of a positive shunt response beyond 50 to 61%, all probable and possible INPH patients should be considered for supplemental testing. One or more of the following three tests is recommended: CSF tap test, Ro determination, and/or ELD. The choice of which one to use can be based on many factors, including desired prognostic value, personal experience, and equipment/personnel availability.

**Step 3: Tap Test**

Given its ease, it is reasonable to proceed initially with a CSF tap test. A positive response to a 40- to 50-ml tap test has a higher degree of certainty for a favorable response to shunt placement than what can be obtained by clinical examination (10, 15, 23). However, the tap test cannot be used as an exclusionary test because of its low sensitivity (26–61%) for identifying SRINPH. If a negative tap test occurs, a subsequent supplemental test should be performed. If the opening pressure exceeds 18 mm Hg, an expanded diagnostic work-up for secondary causes of NPH should be initiated (such as obtaining a contrast MRI study to rule out a chronic meningitis).

**Step 4: Resistance Testing**

Determination of the CSF Ro via an infusion test carries a higher sensitivity (57–100%) compared with the tap test but a similar PPV of 75 to 92% (15, 20). Like the tap test, it can be performed in an outpatient setting but re-
quires ICP recording equipment and may take more than 30 minutes to complete. Heretofore, the prognostic value of this test has been validated in probable INPH patients; therefore, its sensitivity and PPV for possible and unlikely INPH may be lower.

**Step 5: External Lumbar Drainage**

Prolonged ELD in excess of 300 ml is associated with high sensitivity (50–100%) and high PPV (80–100%) (10, 23). It is a most effective test for identifying SRINPH but requires hospital admission and carries a higher complication rate than CSF tap or resistance studies. Of the three recommended supplemental tests, the prognostic value of the ELD is most likely retained even with possible and unlikely INPH clinical designations.

**KEY ISSUES FOR FUTURE INVESTIGATION**

To date, a single standard for the prognostic evaluation of INPH patients is lacking. To obtain these data, a multicenter study should be designed that 1) includes both probable and possible INPH patients; 2) administers multiple supplemental tests to each candidate irrespective of clinical diagnosis; 3) randomizes CSF volume removal; 4) shunts every patient with acceptable surgical risks, irrespective of supplemental testing results; and 5) uses good end points with high interobserver reliability.

Such a study should have clear and concise statistical analysis of the predictive power of these tests, which include sensitivity, specificity, PPV, and NPV, and the accuracy for each test as well as in combination. The inherent difficulty in proceeding with these types of studies is that all patients, regardless of supplemental test outcome, should be shunted for assessing the accuracy of these techniques. It is also possible that a combination of positive supplemental tests might improve sensitivity and PPV for certain patient groups, such as the evaluation of possible INPH patients. These studies should detail complications of the procedures. For all NPH studies, data for INPH and secondary NPH should be analyzed separately if broader inclusion criteria are chosen. Future studies should also proceed in developing less invasive methods for use by clinicians. Finally, it is important to implement more detailed pathophysiological studies of INPH to shed further light on the mechanisms leading to clinical symptoms.

**REFERENCES**