DIAGNOSIS OF NORMAL-PRESSURE HYDROCEPHALUS BY RISA CISTERNOGRAPHY

David H. Patten and D. Frank Benson

Boston Veterans Administration Hospital, Boston, Massachusetts

In the past few years there have been a number of reports (*1–3*) outlining the dynamics of cerebrospinal-fluid (CSF) circulation by scanning after intrathecal injection of radioactive isotopes. This technique has been used successfully to investigate hydrocephalus (*2,4,5*). We would like to present our preliminary experience with intrathecal isotope sequential scanning in the diagnosis of "normal-pressure hydrocephalus."

NORMAL-PRESSURE HYDROCEPHALUS

The term "normal-pressure hydrocephalus" (also called "occult hydrocephalus") has been used in the past few years (*6,7*) to define a specific diagnostic entity. For further definition of this entity, a short review of spinal-fluid circulation is necessary. Most spinal fluid is formed in the choroid plexuses of the ventricles, flows out to enter the subarachnoid space at the base of the brain and eventually flows over the cortex to be absorbed in the sagittal area (Fig. 1). Obstructive hydrocephalus is most frequently produced by a block within the ventricular system whereas communicating hydrocephalus is most often ventricular enlargement secondary to cerebral atrophy. Normal-pressure hydrocephalus results from an obstruction in the cortical subarachnoid space preventing flow of CSF to the sagittal area for absorption (see Fig. 1) but without increase of the CSF pressure. Thus it is both an obstructive and a communicating hydrocephalus.

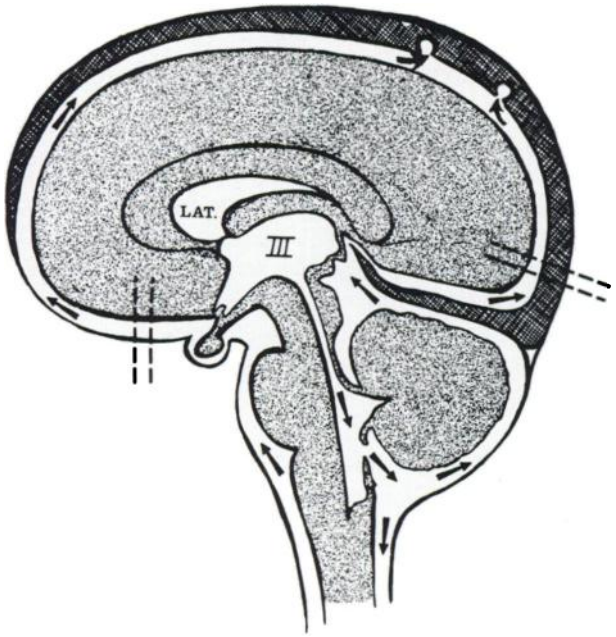

FIG. 1. Outline drawing showing pathway of normal spinal fluid circulation. Dotted lines symbolize subarachnoid obstruction which blocks normal outflow passage.

Most cases of normal-pressure hydrocephalus result from subarachnoid fibrosis secondary to blood or infection in the meninges. Recently a similar hydrocephalus has been reported in cases with elongated basilar artery (*8*). Occasionally no specific etiology can be found to explain the syndrome (*6*).

Clinically the major findings are dementia with a distinct disturbance of recent memory and a striking motor disturbance. The dementia is characterized by apathy, irritability, incontinence and a severe disorientation. The motor defect is not one of paralysis but rather uncertainty and awkwardness in movement, particularly in initiating movement resulting in marked impairment of motility. In severity the syndrome ranges from a comparatively mild Korsakoff's syndrome with awkwardness to the full picture of akinetic mutism. Spinal-fluid examination demonstrates nothing remarkable. The pressure may be abnormally low or moderately elevated but, as the name implies, it is most often in the range of normal. The cell and chemical studies of the CSF do not reveal pertinent abnormalities.

The differential diagnosis includes all varieties of obstructive and communicating hydrocephalus and most types of acquired dementia. The importance of

Received Sept. 25, 1967; revision accepted Jan. 22, 1968.

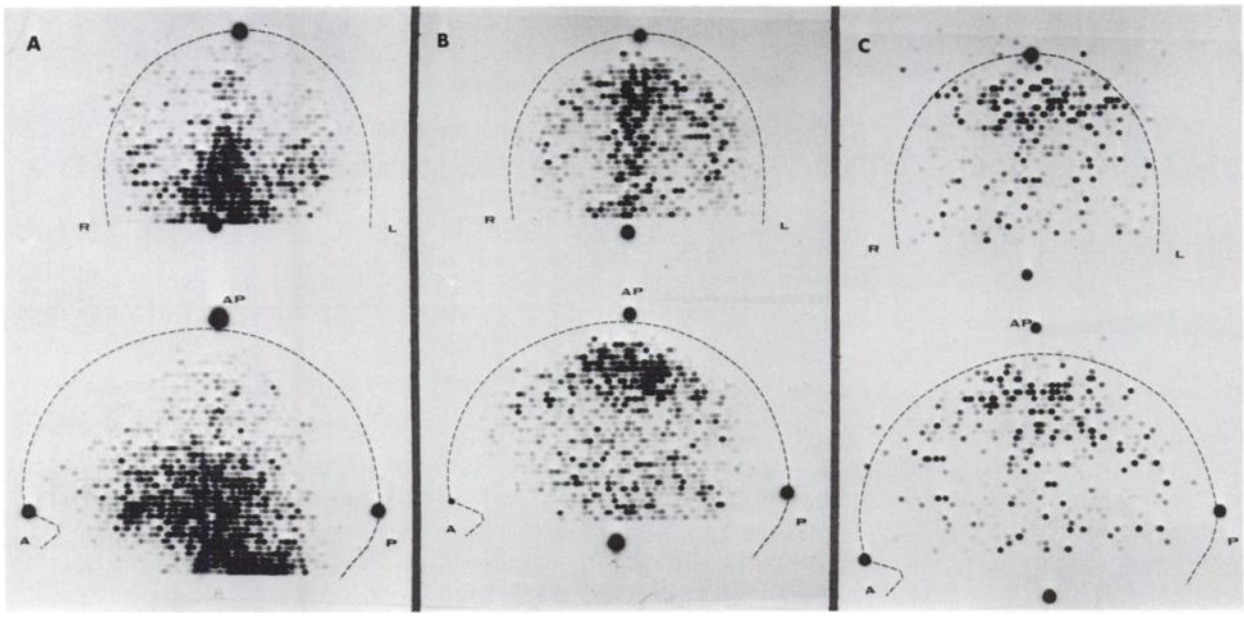

FIG. 2. Intrathecal RISA scan demonstrating normal CSF circulation. A was made at 3 hr, B at 24 hr and C at 48 hr after injection.

correct diagnosis is emphasized by the effectiveness of ventriculo-venous shunting making this entity one of the rare forms of dementia that can be treated successfully.

Several diagnostic tests have been suggested to confirm the diagnosis. The EEG has proved inadequate because it demonstrates only diffuse slow-wave activity and therefore is not specific for this disorder. McHugh (*9*) has recently demonstrated the value of the lateral projection of the carotid arteriogram for this diagnosis. In advanced cases the anterior cerebral artery will have an increased circumferential sweep (bowing) around the anterior corpus callosum, but this is not seen in milder cases and does not aid in differentiation from other varieties of obstructive hydrocephalus. At present the pneumoencephalogram is the most reliable diagnostic tool for this entity. When gas is introduced from below, the ventricles fill and show marked enlargement, greater than that seen in other varieties of communicating hydrocephalus. There is a striking absence of gas over the cortical surface, and absorption of ventricular gas is abnormally slow. Thus a 24-hr radiograph will show an excessive gas residual. This combination of findings allows a confident diagnosis of normal-pressure hydrocephalus from air studies.

Unfortunately the pneumoencephalogram has significant disadvantages. The morbidity following air study is distinctly greater in this entity (*6,7,10*), and this test is not consistently diagnostic. If inadequate quantities of gas are used (we routinely use over 100 cc when this condition is suspected), the radiologist will be unable to make a positive diagnosis of normal-pressure hydrocephalus. In this situation a second air study must be contemplated to confirm the diagnosis before advising surgical treatment.

Because of the shortcomings of the available diagnostic tests, we desired a simpler and safer procedure and believe that the intrathecal isotope study provides such a diagnostic test.

RISA CISTERNOGRAPHY IN NORMAL-PRESSURE HYDROCEPHALUS

The technique of performing the radioisotope CSF flow study is relatively simple in all of its aspects. ^{131}I tagged human serum albumin (RISA) is injected intrathecally in the lumbar region, and serial scans similar to the conventional brain scan are made at 3-, 24- and 48-hr intervals after the injection.

^{131}I RISA of high specific activity (over 500 μc/ml) in a 1% solution* is used to keep the amount of albumin to a minimum, usually less than 5–6 mg for the procedure. Reports of aseptic meningitis following intrathecal injection of serum albumin (*11, 12*) have involved larger amounts of albumin, and DiChiro (*13*) has shown the safety of using the low protein RISA in his many studies.

A dose of 100 μc consisting of 0.2–0.6 ml is added to 3–4 ml of spinal fluid at the time of injection and flushed in and out to assure adequate mixing. Subsequent posture does not affect the rate of distribution in the subarachnoid space (*14*).

* Available from Abbott Laboratories.

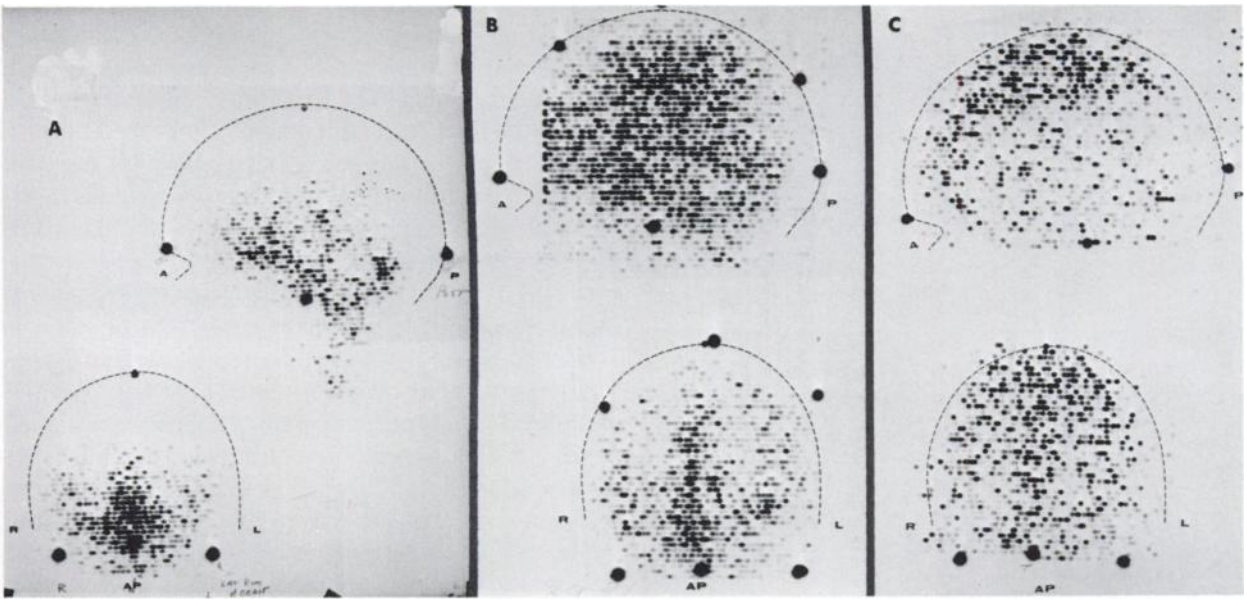

FIG. 3. Intrathecal RISA scan in patient with Alzheimer's Disease. A was made at 3 hr, B at 24 hr and C at 48 hr after injection.

Our current practice is to do AP and lateral scans of the head at intervals of 3, 24 and 48 hr after injection using a 3-in. Picker Magnascanner. The patient's head is positioned to get as true AP and lateral scans as possible. In the AP position the line between the lateral angle of the eye and the external auditory meatus is perpendicular to the plane of the bed. Accordingly, the lateral position requires the sagittal plane of the head to be parallel to the bed. The same views are repeated at each interval marking the inion and glabella or nasion as well as the vertex of the skull.

Normally the RISA appears in the subarachnoid spaces of the head in approximately 1 hr and shows in the cisterns and Sylvian fissures at 3 hr. By 24 hr the majority of the activity is well circulated over the hemispheres and into the sagittal area with little residual in the cisterns (Fig. 2). Any ventricular concentration would be abnormal and usually indicates some variety of hydrocephalus.

In normal-pressure hydrocephalus the RISA does not circulate over the hemispheres and fails to appear in the sagittal area (Fig. 4). There may be a delay in other forms of communicating hydrocephalus (e.g. —Alzheimer's Degeneration) but within 48 hr these show adequate sagittal activity despite the high ventricular concentration (Fig. 3). When there is little or no activity seen over the cortical surfaces at 48 hr, a 72-hr scan may be done to further document the obstruction to CSF flow.

If little or no radioactivity is shown in the sagittal area after 48 and 72 hr, a diagnosis of normal-pressure hydrocephalus is proposed. In addition to the lack of sagittal activity, the large dilated ventricles usually contain a high concentration of RISA which persists through the series of scans but is best outlined at 24 hr. The ventricular RISA pattern may persist in other types of communicating hydrocephalus, but these also show concentration along the Sylvian fissures in the AP view and perhaps where CSF is pooled over the widened sulci as well as in the sagittal area.

Two technical problems are encountered with this procedure. If the injection is made in the epidural space, the appearance of the RISA is delayed, and there will be a lower counting rate. However, at 24 hr the pattern resembles that of a subarachnoid injection. The second problem concerns the management of demented patients. Immobility of the head during the scan is important and is sometimes difficult to maintain with the flexicast pillow alone; therefore further restraint and occasionally sedation may be necessary. Maintaining position is particularly important because the 3–6-cm segment of the scan between the level of the ventricles and the vertex is critical to the diagnosis.

RESULTS

To date we have performed 22 intrathecal RISA studies for diagnostic purposes. With the exception of one patient (a normal control) each scan was done to investigate the possibility of normal-pressure hydrocephalus as a cause of neurological symptoms. The group includes one undiagnosed patient, six patients ultimately diagnosed as Alzheimer's or senile dementia, two cases of post traumatic encephalopathy, three of arteriosclerotic dementia, two postinfectious encephalopathy, two postsurgical enceph-

TABLE 1. SUMMARY OF INTRATHECAL RISA STUDIES

Diagnosis	No. of patients	Scan results
Alzheimer's dis.	6	6 negative
Subarachnoid hem.	6	4 positive—2 question
Arteriosclerotic dis.	3	3 negative
Trauma	2	2 negative
Infectious	2	1 positive*—1 negative
Post surgical	2	1 positive*—1 negative
Obstructive hydrocephalus	1	1 negative
Undiagnosed	1	1 negative
Normal	1	1 negative
	24*	16 negative 2 question 4 positive

* These two patients considered under two headings.

alopathy, one obstructive hydrocephalus and six cases with known history of subarachnoid hemorrhage. Two patients are considered under two of the above headings (Table 1).

The results were positive (enlarged ventricles and no sagittal activity in 48 hr) in four of the 22 studies, and each of these four had a history of subarachnoid hemorrhage. In addition two were considered questionably positive, and these also were from the subarachnoid hemorrhage group. The remainder of the cases were considered negative as far as the criteria for normal-pressure hydrocephalus were concerned. Eleven studies clearly showed ventricular concentration suggesting hydrocephalus, while another eight were doubtful. Three cases (including the normal control) did not show any suggestion of ventricular filling. The Alzheimer patients all revealed distinct sagittal concentration of RISA at 24 hr despite ventricular enlargement as demonstrated by scan (Fig. 3) and pneumoencephalogram.

Of the four patients who had both the clinical and scan criteria for normal pressure hydrocephalus only one has received surgical treatment (a ventriculoatrial shunt). This patient changed from a state of akinetic mutism preoperatively to an essentially normal mental status within hours of recovery from the anesthesia. He went on to full self-care and ambulation. Another patient from this group is still being evaluated for surgery, one was denied surgery on the basis of a pre-existing serious psychosis and the last patient is clinically improving without surgery. Of the two questionably positive results one patient is still being evaluated and the other has been turned down for surgical shunt because of a widespread carcinoma of the base of the tongue.

There have been no untoward effects from this scan procedure. One evaluation had to be repeated because the first lumbar injection was epidural rather than intrathecal providing insufficient radioactivity for an adequate interpretation. The CSF taken at the time of the second procedure showed no change. Another patient had a lumbar puncture 2 weeks after the scan procedure and again no reactive alteration was demonstrated.

This series is admittedly too small for firm conclusions, but does offer considerable promise. We

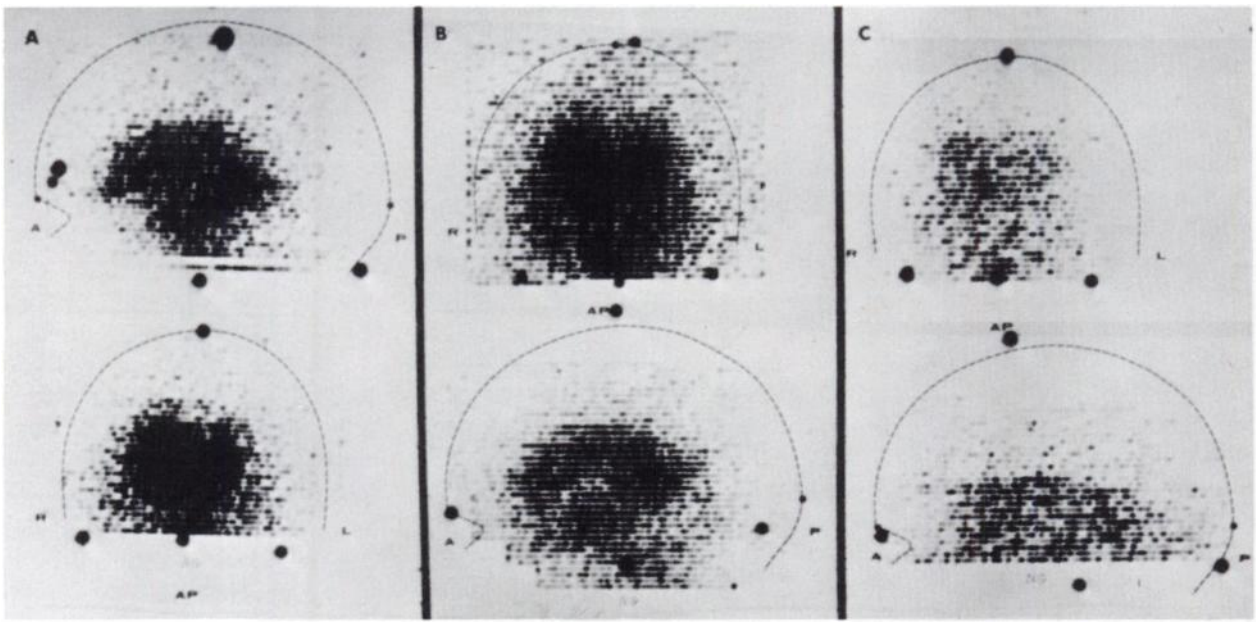

FIG. 4. Intrathecal RISA scan in patient with normal pressure hydrocephalus. A was made at 3 hr, B at 24 hr and C at 48 hr.

feel that the intrathecal radioisotope scan provides a safe, simple and inexpensive test which provides valuable diagnostic information in patients suspected of having normal-pressure hydrocephalus. Although this diagnosis is not common, the fact that a relatively simple surgical treatment is available for a severe dementia enhances the value of this technique.

SUMMARY

This study describes the use of intrathecal RISA scanning for demonstrating "normal-pressure hydrocephalus" a condition exhibiting obstruction of flow through the cortical subarachnoid space preventing normal CSF absorption. The technique is simple, with introduction of RISA by spinal tap followed by sequential scanning over the next 2 or 3 days. A positive diagnosis is made by demonstrating enlarged ventricles and lack of radioactivity in the sagittal region. Because "normal-pressure hydrocephalus" can be treated successfully by ventriculovenous shunting, this technique offers considerable value.

ACKNOWLEDGMENT

This study was supported in part by Grant No. NB-06209 from the National Institute of Neurological Diseases and Blindness to Boston University School of Medicine.

REFERENCES

1. DiChiro, G.: Movement of the cerebrospinal fluid in human beings. *Nature* **204**:290, 1964.

2. DiChiro, G., Reams, P. M. and Matthews, W. B.: RISA—ventriculography and RISA—cisternography. *Neurology* **14**:185, 1964.

3. Sweet, W. H., Brownell, G. L., School, J. A., Bowsher, D. R., Benda, P. and Stickley, E. E.: The formation, flow and absorption of cerebrospinal fluid: newer concepts based on studies with isotopes. *Res. Nervous Mental Disease* **34**:101, 1964.

4. Bell, R. L.: Isotope transfer test for diagnosis of ventriculo-subarachnoid block. *J. Neurosurg.* **14**:674, 1957.

5. Atkinson, J. R. and Folz, E. L.: Intraventricular "RISA" as a diagnostic aid in pre- and post-operative hydrocephalus. *J. Neurosurg.* **19**:159, 1962.

6. Adams, R. L., Fisher, C. M., Hakim, S., Ojemenn, R. G. and Sweet, W. H.: Symptomatic occult hydrocephalus with "normal" cerebrospinal fluid pressure. *New Engl. J. Med.* **273**:117, 1965.

7. Hakim, S. and Adams, R.: The special clinical problem of symptomatic hydrocephalus with normal cerebrospinal fluid pressure. *J. Neurol. Sci.* **2**:307, 1965.

8. Brieg, A., Ekbom, K., Grietz, T. and Kogelberg, E.: Hydrocephalus due to elongated basilar artery. *Lancet* **1**:874, 1967.

9. McHugh, P. R.: Hydrocephalic dementia. *Bull. N.Y. Acad. Med.* **42**:907, 1966.

10. Folz, E. L. and Ward, A. A.: Communicating hydrocephalus from subarachnoid bleeding. *J. Neurosurg.* **13**:546, 1956.

11. Detmer, D. E. and Blacker, H. M.: A case of aseptic meningitis secondary to intrathecal injection of I^{131} human serum albumin. *Neurology* **15**:642, 1965.

12. Nicol, C. F.: A second case of aseptic meningitis following isotope cisternography using I^{131} human serum albumin. *Neurology* **17**:199, 1967.

13. DiChiro, G.: Specific activity of radio-iodinated human serum albumin for intrathecal injection. A correction. *Neurology* **15**:950, 1965.

14. DiChiro, G.: Observations on the circulation of cerebrospinal fluid. *Acta Radiol.* (Diag), **5**:988, 1966.