CISTERNOGRAPHY WITH ^{169}Yb-DTPA

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Although the cerebrospinal fluid (CSF) is probably formed in many regions of the subarachnoid space, the bulk of CSF is produced in the choroid plexuses of the third and lateral ventricles (*1*). The normal direction of flow is from the ventricular system into the subarachnoid spaces surrounding the brain stem, spinal cord, and brain, finally concentrating in the parasagittal area. For radionuclide cisternography the radiopharmaceutical is usually introduced into the lumbar intrathecal region and from this point the activity can be followed from the spinal canal to the parasagittal regions where it is absorbed.

On the basis of the relatively constant flow pattern of cerebrospinal fluid, radionuclide cisternography reflects:

1. The movement of spinal fluid through the subarachnoid space.
2. Absorption of spinal fluid from the cerebrospinal spaces into the vascular and extravascular spaces (*2–6*), and
3. Entry and exit of spinal fluid into or from the ventricular system under pathologic circumstances.

In the past 12 months we have performed 125 cisternograms using ^{169}Yb-Ca-diethylenetriaminepentaacetic acid (DTPA) as the radiopharmaceutical at the Johns Hopkins Medical Institutions. This report summarizes our experience with the use of this radiopharmaceutical for cisternography.

METHODS

In the majority of cases, the radiopharmaceutical was injected into the lumbar intrathecal space. Radionuclide images of the brain were routinely performed in the anterior, posterior, and both lateral positions. When indicated, vertex views were obtained as well as other views such as the spinal region or abdomen when dictated by the specific requirements of the patient. Routinely examinations were performed at 2, 6, and 24 hr, and when the early images failed to show normal movement to the parasagittal region, delayed studies at 48–96 hr were also obtained. Table 1 summarizes the clinical categories that we studied using ^{169}Yb-DTPA.

The diagnosis of these cases as normal, normal pressure hydrocephalus, cerebral atrophy, shunts, etc., was established in all cases by clinical history, radiological studies, surgery, or postmortem examination.

RESULTS

Figure 1 shows a normal cisternogram performed at 2, 6, and 24 hr after the lumbar intrathecal injection of ^{169}Yb-DTPA. At 2 hr after injection (Fig. 1A) the radiopharmaceutical has migrated into the infratentorial cisterns and entered the Sylvian fissures. The tentorial limit of the posterior fossa is well illustrated in the posterior view. By 6 hr (Fig. 1B) the activity has flowed through the Sylvian fissures and is seen over and between the cerebral hemispheres. Activity is still present in the cisterns beneath the tentorium at this time but is decreased in concentration compared with the 2-hr study. Twenty-four hours after injection (Fig. 1C) the radiopharmaceutical is predominantly over the cerebral hemispheres and is concentrated in the parasagittal region. There is little activity remaining in the posterior fossa.

Table 2 summarizes the average distribution of

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TABLE 1. RESULTS OF 125 CISTERNOGRAMS

Diagnosis	No. of cases
Normal	31
"Normal pressure" hydrocephalus	25
Cerebral atrophy with hydrocephalus	26
Surgical shunts	18
Partial obstruction to CSF flow	10
Total obstruction to CSF flow	2
CSF leaks	5
Unsatisfactory	8

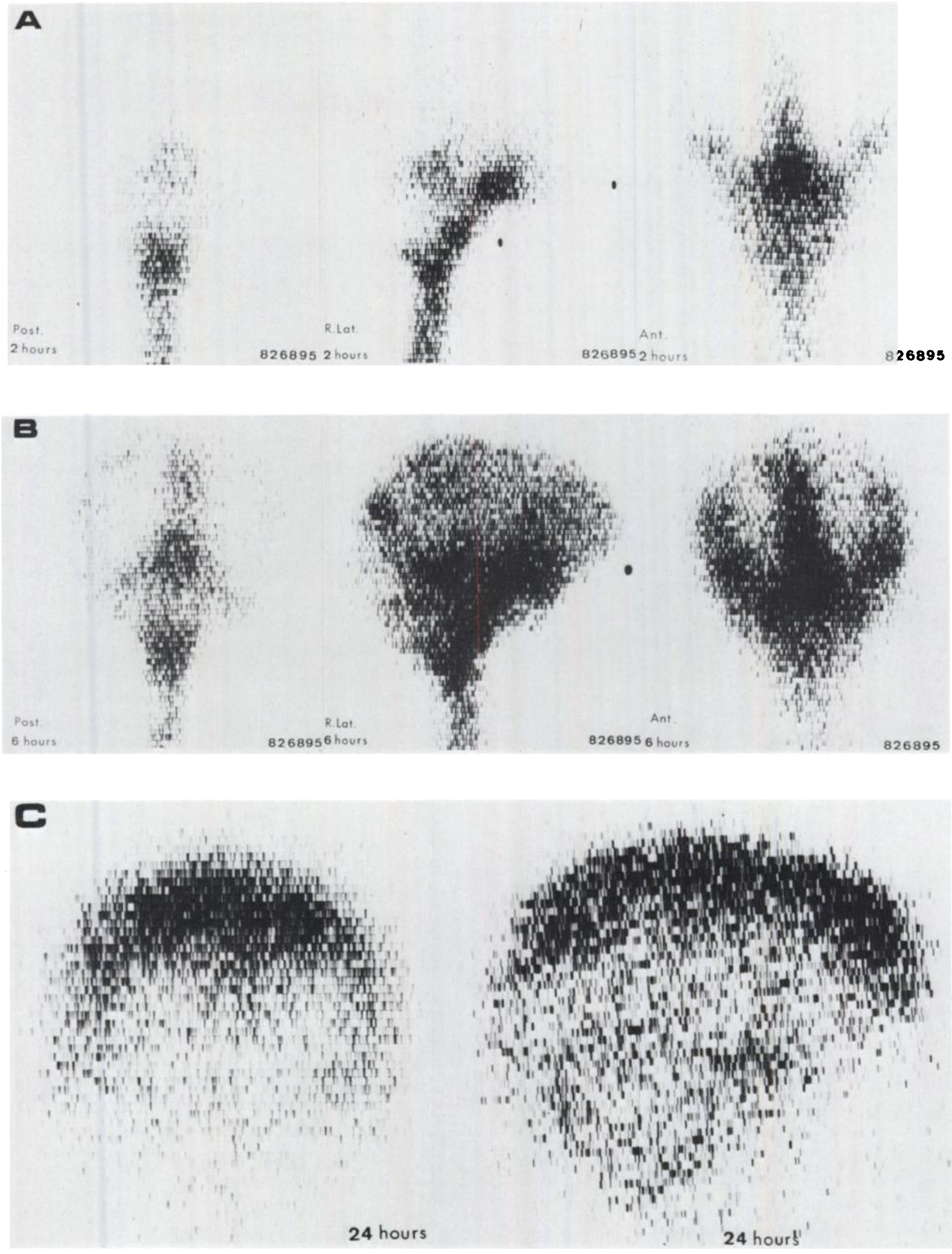

FIG. 1. A shows normal cisternograms 2 hr after lumber intrathecal injection of 1 mCi ^{169}Yb-DTPA. Radionuclide has migrated to basal cisterns and entered Sylvian fissures. B shows normal cisternogram 6 hr after lumbar intrathecal injection. Radioactivity is seen over and between cerebral hemispheres. C shows normal cisternogram 24 hr after lumbar intrathecal injection. Radioactivity is predominately over hemispheres and concentrated in parasagittal region.

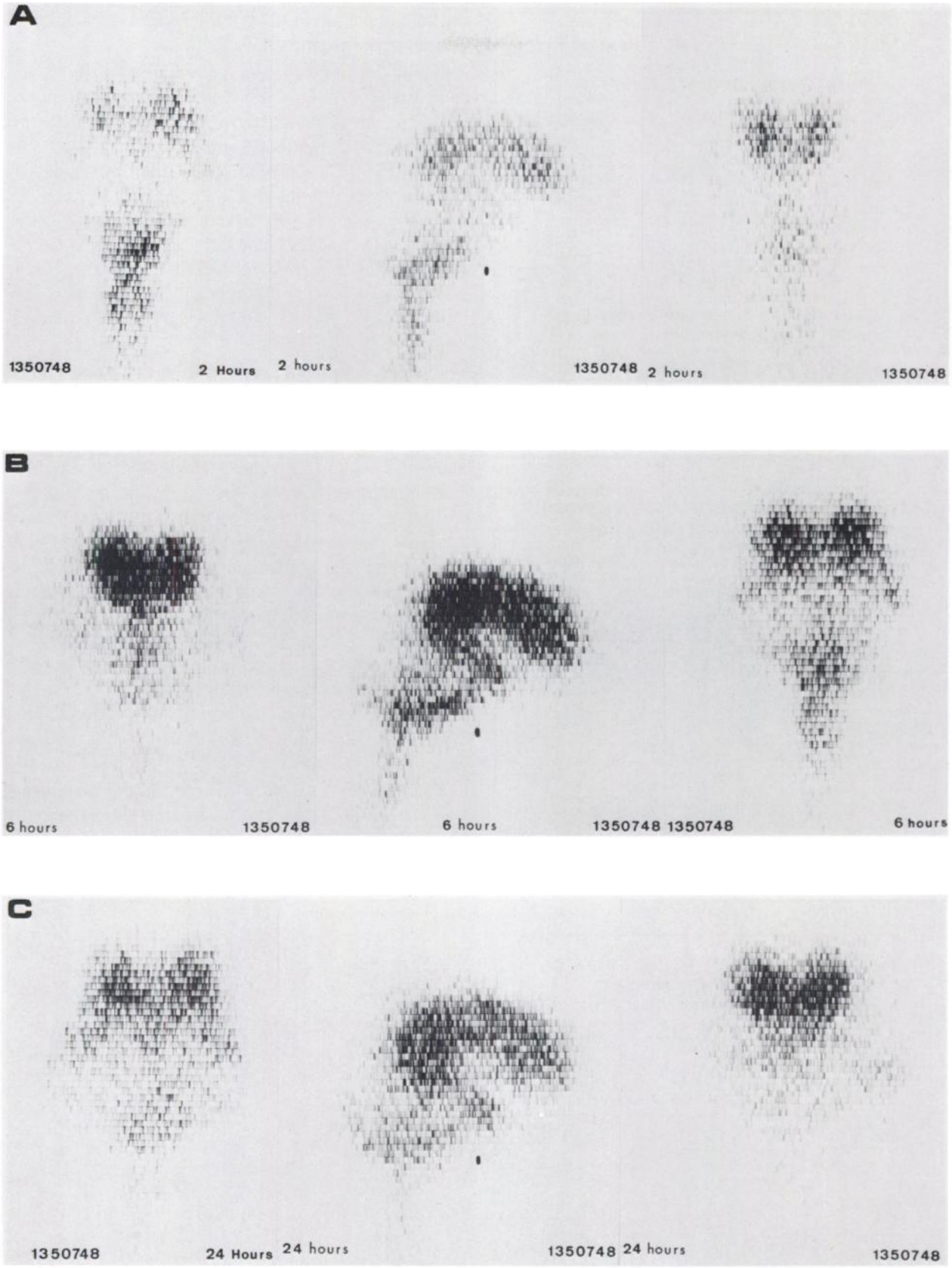

FIG. 2. A shows normal pressure hydrocephalus 2 hr after lumbar intrathecal injection of 1 mCi ^{169}Yb-DTPA. Radionuclide is in basal cisterns and lateral ventricles. B shows normal pressure hydrocephalus 6 hr after injection. Stasis of radionuclide occurs in basal cisterns and lateral ventricles. C shows normal pressure hydrocephalus 24 hr after injection when activity has migrated into Sylvian fissures. Failure of migration of radionuclide over cerebral convexities is clear.

TABLE 2. DISTRIBUTION OF ^{169}Yb-DTPA IN NORMAL PATIENTS (INTRATHECAL LUMBAR INJECTION)

	Time after intrathecal injection					
	2 hr		6 hr		24 hr	
	Mean	Range	Mean	Range	Mean	Range
Basal cisterns	+	+	+	—to+	—	—
Sylvian cisterns	+	+	+	+	—or+	—to+
Ventricles	—	—	—	—	—	—
Convexities	—	—to ½	⅔	⅓ to+	+	+
Parasagittal	—	—	—	—to sl	+	sl to+

+ indicates significant concentration of radioactivity.
— indicates little to no activity.
sl indicates slight activity; the numerical fractions indicate the distance over the cerebral hemispheres between the sylvian fissures and the superior sagittal sinus.

TABLE 3. DISTRIBUTION OF ^{169}Yb-DTPA IN CASES OF NORMAL PRESSURE HYDROCEPHALUS (INTRATHECAL LUMBAR INJECTION)

	Time after intrathecal injection					
	2 hr		6 hr		24 hr	
	Mean	Range	Mean	Range	Mean	Range
Basal cisterns	+	+	+	+	mod	—to+
Sylvian cisterns	sl	—to+	+	—to+	+	—to+
Ventricles	+	+	+	+	+	+
Convexities	—	—	—	—to ½	½	—to+
Parasagittal	—	—	—	—	—	—to sl

+ indicates significant concentration of radioactivity.
— indicates little to no activity.
sl indicates slight activity.
mod indicates moderate activity.
The numerical fractions indicate the distance over the cerebral hemispheres between the sylvian fissures and the parasagittal sinus.

TABLE 4. DISTRIBUTION OF ^{169}Yb-DTPA IN CASES OF CEREBRAL ATROPHY (INTRATHECAL LUMBAR INJECTION)

	Time after intrathecal injection					
	2 hr		6 hr		24 hr	
	Mean	Range	Mean	Range	Mean	Range
Basal cisterns	+	+	+	+	+	—to sl
Sylvian cisterns	—	—to sl	+	+	—	+
Ventricles	—	—to ocnl	—	—to ocnl	—	—
Convexities	—	—	sl	—to ½	+	+
Parasagittal	—	—	—	—	sl	—to +

+ indicates significant concentration of radioactivity.
— indicates little to no activity.
sl indicates slight activity.
ocnl indicates occasional.
The numerical fractions indicate the distance over the cerebral hemispheres between the sylvian fissures and the parasagittal sinus.

the radionuclide in 31 normal patients for each period of the examination.

Figure 2 is an example of normal pressure hydrocephalus. Two hours after intrathecal lumbar injection (Fig. 2A) radioactivity has migrated into the basal cisterns and lateral ventricles. At 6 hr after injection (Fig. 2B) there has been little movement of the radiopharmaceutical. By 24 hr (Fig. 2C) activity has migrated into the Sylvian fissures and slightly over the convexities. The region with the greatest concentration of activity is still the lateral ventricles. Table 3 summarizes the average distribution of activity in 25 patients with normal pressure hydrocephalus.

Figure 3 illustrates the cisternogram seen in a patient with primary cerebral atrophy. Two hours after intrathecal lumbar injection (Fig. 3A) the radiopharmaceutical has migrated into the basal cisterns and slightly into the Sylvian fissures. The nuclide images appear very similar to the normal cisternogram at the same interval. In Fig. 3B the images are quite similar to a normal cisternogram performed 6 hr after injection although these images were made 24 hr after injection of the radiopharmaceutical, demonstrating marked delay in movement. At 48 hr after injection (Fig. 3C) the activity is concentrated over the hemispheres and in the parasagittal region. Again, scintigrams are typical of those performed in a normal patient 24 hr after injection. Table 4 summarizes the distribution of activity in 26 patients with primary atrophy.

Figure 4 is an example of a partial obstruction to flow of injected radiopharmaceutical over the right hemisphere following head trauma in a patient with a suspected spinal fluid leak. This cisternographic pattern indicates that although a localized area of

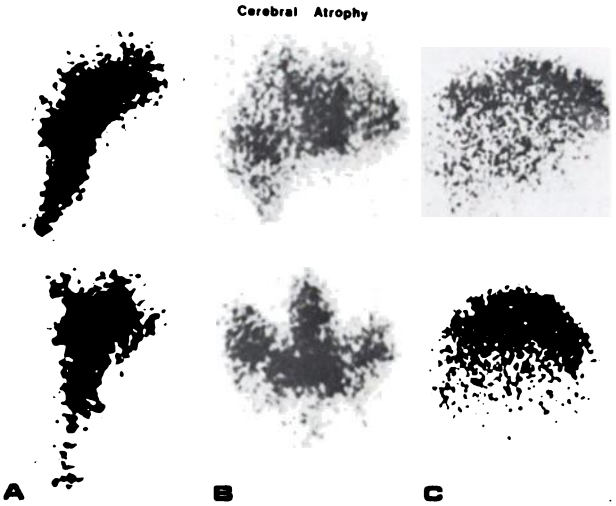

FIG. 3. Cerebral atrophy. Movement of radionuclide appears normal except for time required: A—2 hr after injection, B—24 hr, and C—48 hr.

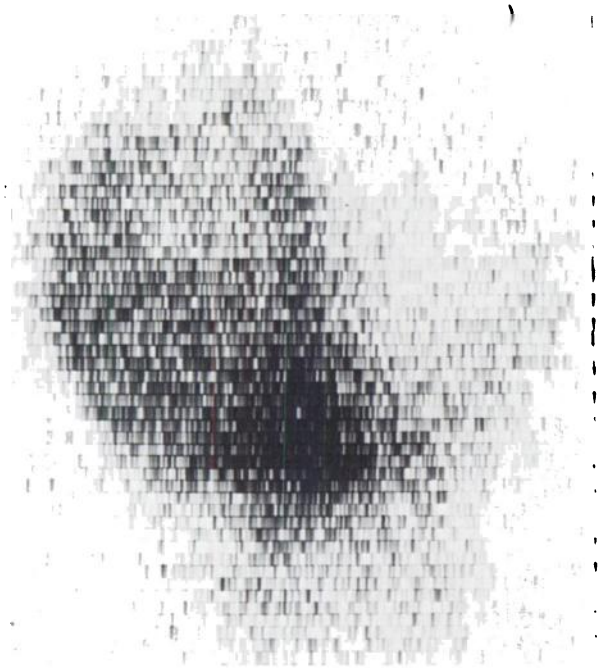

FIG. 4. Partial obstructive arachnoiditis over left cerebral hemisphere. Absorption of CSF appears adequate since radionuclide does not enter lateral ventricles.

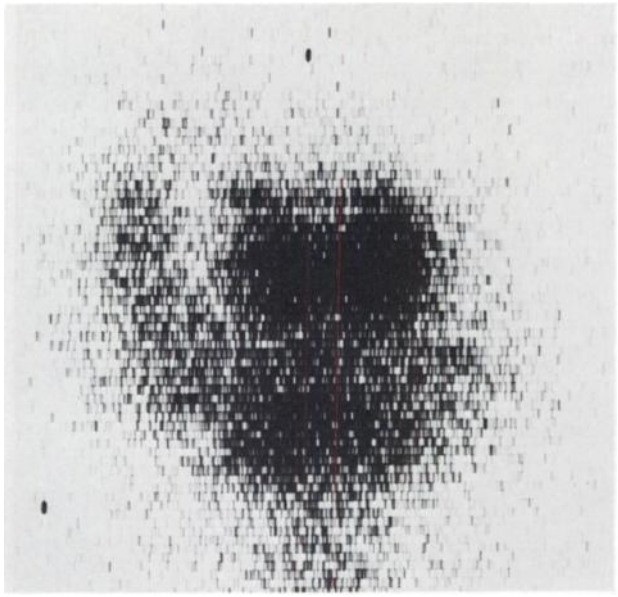

FIG. 5. Partial obstructive arachnoiditis over left cerebral hemisphere. Radioactivity has entered lateral ventricles indicating inadequate absorption of CSF.

adhesive arachnoiditis is present, absorption of CSF is still adequate since there is no entry of radioactivity into the lateral ventricles. By contrast Fig. 5 is an example of a partial obstruction to flow due to an adhesive arachnoiditis with entry of the radionuclide into the lateral ventricles. In this case which was due to subarachnoid hemorrhage, absorption of CSF is altered and ventricular dilation is present. The patient's symptoms were alleviated by a ventriculoatrial shunt. In Fig. 6 there is complete obstruction to flow at the level of the tentorial notch in a patient with Paget's disease of bone. The obstruction is probably due to basal arachnoid thickening.

Figure 7 illustrates the rapid excretion of ^{169}Yb-DTPA from the vascular pool in a patient with a functioning ventriculoatrial shunt. The radiopharmaceutical was introduced into the lumbar intrathecal space, migrated to the lateral ventricles, and then migrated into the shunt. The activity was extracted from the blood by glomerular filtration and can be seen in the kidneys, urinary bladder, and catheter.

Figure 8 shows a CSF leak through the cribiform plate and obstruction to flow over the right hemispheres. At 7 hr after lumbar intrathecal injection, activity has migrated anteriorly into the nasopharyngeal area (lateral view), and a localized area of activity has accumulated in the nose.

DISCUSSION

The characteristics of a good cisternographic radiopharmaceutical are high photon yield for images of good resolution, adequate effective half-life for extended studies beyond 24 hr, acceptable radiation

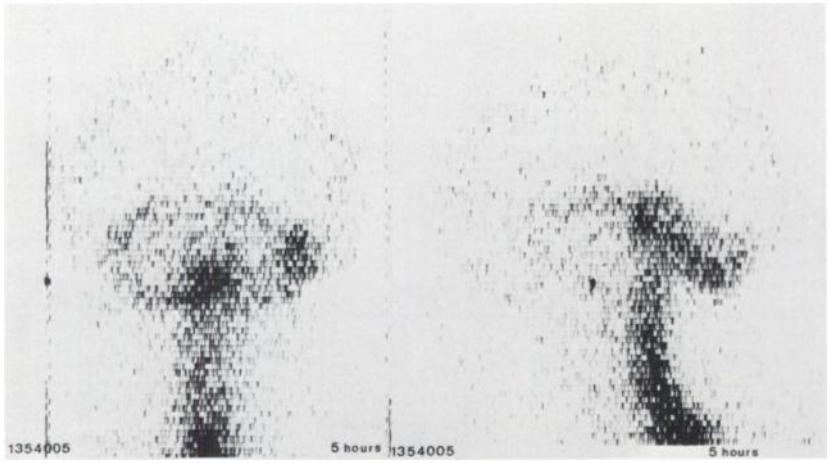

FIG. 6. Complete obstruction of CSF flow at level of tentorium in patient with Paget's disease.

dose, biological safety, photon yield of an appropriate gamma for available instrumentation, and acceptable availability and cost. Certain of the biological, chemical, and physical properties make ^{169}Yb-DTPA a desirable radiopharmaceutical. Experimental studies have shown that the effective half-life of ^{169}Yb-DTPA in the subarachnoid space is 10–12 hr. Although the molecular weight of ^{169}Yb-DTPA is 600, it demonstrates generally the same pattern of movement in the CSF as albumin and appears to be resorbed from the CSF space in the parasagittal region (arachnoid granulations). Once ^{169}Yb-DTPA has entered the vascular pool, it rapidly equilibrates with the extracellular fluid space and is then excreted in the urine. With normal renal function, 60–70% of an intravenous dose appears in the urine in the first 2 hr and 99% of the injected dose is excreted in the urine in 24 hr (*7,8*). In patients with normal glomerular function the radiation dose compares favorably with the most common radiopharmaceutical used for CSF imaging, ^{131}I-IHSA (*9*). The yield of 63×10^9 useful photons/rad whole-body dose characterizes ^{169}Yb-DTPA as a high photon-yield radionuclide with a long shelf-life ($T_{1/2} = 32$ days). We would caution against the use of this radiopharmaceutical in patients with reduced glomerular function.

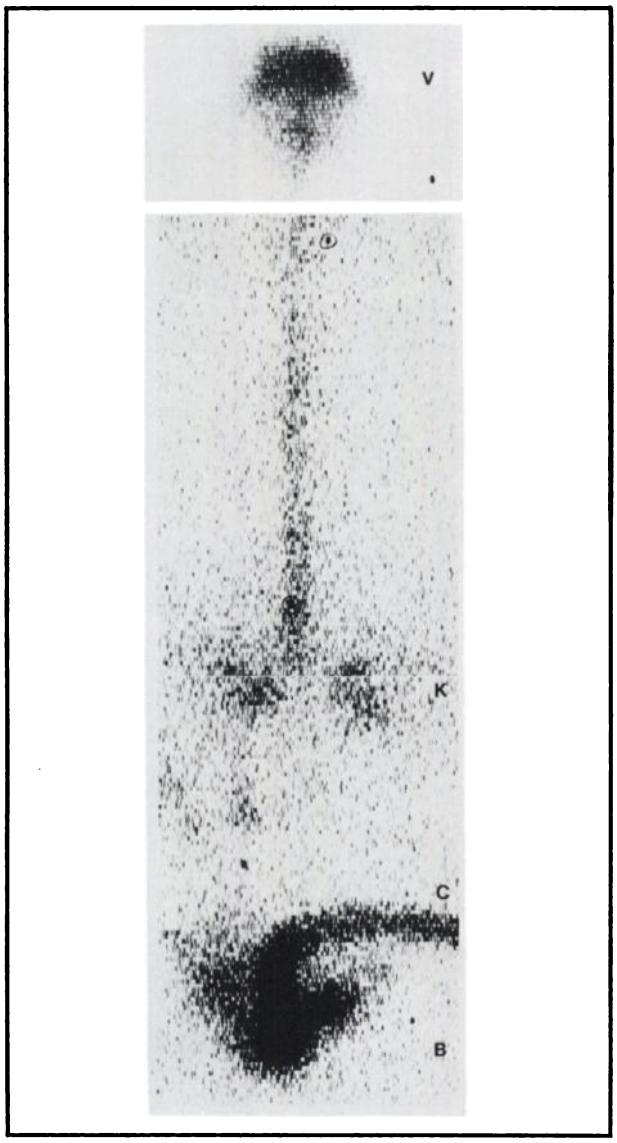

FIG. 7. Ventriculo-atrial shunt. After lumbar intrathecal injection of 1 mCi of ^{169}Yb-DTPA, radiopharmaceutical migrated to lateral ventricles, gained access to blood by shunt, and is rapidly excreted in kidneys. V—lateral ventricles, K—kidneys, C—urinary catheter, and B—urinary bladder.

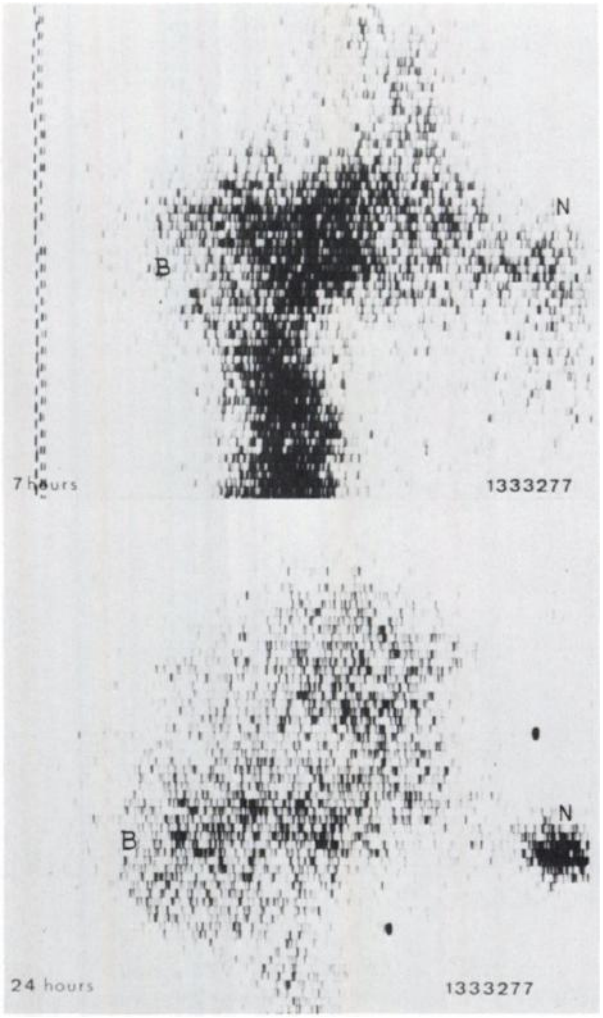

FIG. 8. Cerebrospinal fluid leak. Migration of the radionuclide into the nasopharynx and nose (N).

^{169}Yb-DTPA is administered in doses of 1 mCi for an adult patient, and this photon yield is adequate for images of high resolution. In comparing these studies with those obtained with ^{131}I-IHSA the major difference appears to be better resolution of anatomical detail, particularly in delayed studies (48–96 hr). In those patients with obstruction to normal CSF flow, delayed studies are very valuable (*10*). This is particularly true in differentiating hydrocephalus due to abnormal absorption of spinal fluid (normal pres-

sure hydrocephalus) and hydrocephalus due to primary brain atrophy from patients with normal flow patterns seen with radionuclide cisternography. Thus it is desirable that the effective half-life of the radiopharmaceutical be adequate for studies in excess of 24 hr, i.e., 48–72 hr. The 32-day physical half-life of ^{169}Yb insures adequate photons for extended studies, yet the biological half-life (12 hr) is short enough to provide adequate safety regarding radiation dose.

For imaging, the 177- and 198-keV gamma emission are detected. Their fractional abundance is relatively high (0.6 photon/disintegration) and excellent images can be obtained using a 160–220-keV window. Only a small fraction (10%) of the gamma emissions is above 198 keV, thus allowing imaging on both camera and rectilinear scan devices.

Ytterbium complexes with diethylenetriaminepentaacetic acid to form a stable compound. Three of the five bonds of the DTPA chelate are taken up by the ytterbium; the remaining two are taken up by the calcium which is added to prevent calcium depletion of the cerebrospinal fluid. The preparation of ^{169}Yb-DTPA for cisternography is described in another publication (*9*).

The bond between ^{169}Yb and DTPA is very stable and therefore provides a good shelf-life. Equally important, the long shelf-life permits thorough testing for sterility and pyrogenicity. As we have shown, there was no tissue reaction found in experiments with laboratory animals (*9*). Ytterbium-169-DTPA has many advantages for cisternography (*11*). Of prime importance is the fact that it can be furnished ready for use, thus obviating any necessity for local preparation. This radiopharmaceutical has been used in our laboratory in over 125 patients, and no adverse patient reactions have been observed. The radionuclide images are of excellent quality, and extended studies up to 108 hr after injection have been performed.

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