Cisternal Brain Scanning with Positron Emitting Isotopes*

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Radioactive isotopes have been administered intrathecally and intraventricularly for many diagnostic purposes since the report in 1953 of the myelographic technique by Bauer and Yuhl. In 1957, Bell\(^5\) used a Geiger-Müller tube and intraventricular injections of radioiodinated albumin to plot the flow of fluid along the cerebrospinal axis, and to demonstrate the patency of ventriculoperitoneal shunts. In 1960, Benda and Brownell,\(^6\) and in 1961, Dupont, et al.,\(^12\) scanned \(^{198}\)Au deposits in the basal cisterns of dogs; Rieselbach, et al.,\(^13\) used this same nuclide in the following year for clinical cisternography. De Chiro, et al.,\(^4,12\) expanded the technique to include methods for demonstrating intraventricular tumors, aqueductal blocks, cerebrospinal fluid rhinorrhea, and spontaneous ventriculostomies and introduced \(^{99m}\)Tc pertechnetate for cerebrospinal fluid studies.

During the past 8 years, we have had experience with intrathecal injections of two positron-emitters, \(^{74}\)As and \(^{68}\)Ga. Our results are presented here to emphasize the value of cisternal scanning in children, the safety of \(^{68}\)Ga as a scanning agent and to note the unusual observations with \(^{74}\)As as compared with those described previously after intrathecal injections of other materials (gold, iodinated albumin, pertechnetate).

Materials and Method

Our supply of \(^{74}\)As sodium arsenate was obtained from Abbott Laboratories and later from the Radiochemical Centre, Amersham, England. It was administered intrathecally through a 20-gauge needle in the lumbar region with a dosage of 75 \(\mu\)c in infants and 750 \(\mu\)c in adults. The pH lay within the physiological range and was not adjusted. The \(^{68}\)Ga was eluted from a germanium-gallium generator which was procured from the New England Nuclear Corp., Boston, Mass. EDTA (ethylene diamine tetra-acetic acid) was neutralized and used at a strength of 0.005M to remove \(^{68}\)Ga from the generator.\(^15\) The pH of the gallium chelate was 9.8 and hence unsuitable for intrathecal injections. It was therefore adjusted to pH 7.0 with HCl. The final pH was checked carefully with a meter and not by paper as suggested by Yano and Anger.\(^15\)

The dosages of gallium were 500 \(\mu\)c for children and 2 \(\mu\)c for adults. Because of the very short half-life of 68 min, these gave low total body radiations of 15–50 millirad.

All scans were carried out with the Sweet-Brownell positron scanner.\(^14\) The coincidence count (and not the unbalance) records were used. Poor definition of the cisterns was found with the use of the regular scanning heads because of the large aperture size (1 ⅓ in. diameter). Accordingly, extra shielding in the form of lead inserts with apertures of ¼ to 1 in. were used for all children and some adults. The usual scanning speed of the instrument was doubled so that each study was completed in 16 min. Alternate lateral and anteroposterior views were obtained.

A small vial containing 20–25% of the injected dose of \(^{74}\)As or 2.5% of that of \(^{68}\)Ga was scanned with the patient in order to quantitate the amount of isotope arriving intracranially.

Results

Radioarsenic. A significant amount of isotope rose quickly to the cisterns of the posterior fossa within the 16 min of the scan initiated immediately after injection. In infants, this was found without dilution or barbotage. On the later view, a triangular isotopic

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deposit was found (Fig. 1A) and appeared to occupy the cerebellar and pontine cisterns. Within an hour the isotope passed cephalad to lie in the position of the interpeduncular, chiasmatic, and quadrigeminal cisterns at the base of the hemisphere (Fig. 1C). The material in the spine disappeared during the same time and could be readily picked up in the bladder. A known amount of isotope was scanned with the patient as a standard; it was found with this that 20 to 25% of the injected dose passed intracranially. Later scans showed that radioarsenic appeared to be fixed in the basal cisterns for long periods whose half-time was about 24 hours. This retention is shown in the 24-hour scan in Fig. 1D and also in Fig. 2. For comparison, scans obtained following the lumbar subarachnoid injection of iodinated albumin are shown in Fig. 3. These show a definite passage over the surfaces of the hemispheres and an accumulation as a cap-like deposit near the superior sagittal sinus after 24 hours. This pattern was not found on any of our arsenic scans.

The anteroposterior scans were useful in showing that the ventricular system was entered only in the presence of a functioning shunt for hydrocephalus and in a few other instances (as in low-pressure hydroce-
Cisternal Brain Scanning

The common lack of filling was proven by sampling ventricular fluid for well-counting. Only \( \frac{1}{3} \) of the injection dose was found within the ventricle and was low enough to reflect, at least in part, a re-entry from blood.

In adults, the cisternal patterns were similar to those found in the pediatric age group. However, a relatively large dosage of 750 µc was required. With smaller amounts, the appearance of the isotope in the cisterns was delayed and it was difficult to differentiate normal and abnormal patterns. Barbotage was required. Two adult cisternal scans are shown in Fig. 4; Scan A shows the cisternal deposit using the regular brain scanning technique and Scan B was obtained with added lead inserts in the scanning heads and gives a much better depiction of the cisterns.

**Radiogallium.** Normal scans are shown in Fig. 5. This material rose quickly to the cranium; as with arsenic, an initial low cisternal pattern and a later high cisternal pattern were found. Due to the short half-life, the isotope disappeared rapidly and useful scans could not be obtained after 2\( \frac{1}{2} \) to 3 hours. Because of this rapid loss (shown in Scan C of Fig. 5), we could not ascertain whether gallium resembled albumin in passing over the brain surface. However, it appeared to be held much less firmly in the cisterns than arsenic. Standards were scanned with the patient and it was found that only about 7% of the injected dose reached the cranium, a much smaller amount than that found with arsenic.

**Cisternal Blockade.** A delayed (or absent) ascent to the posterior fossa or incomplete filling of the basal cisterns was found with communicating hydrocephalus. These changes are illustrated in Fig. 6, which reproduces the scan of an adult with advanced hydrocephalus and high-degree intracranial hypertension following a subarachnoid hemorrhage. Only a very small amount of iso-

Fig. 2. Normal 24-hour scan following an intrathecal injection of 75 µc "As. Note the retention in the upper cisterns.

Fig. 3. Normal depictions following an intrathecal injection of 100µc radio-iodinated human serum albumin to show a different scanning pattern from that noted in Figs. 1 and 2 (with "As). Scan A shows the spread to the cisterns at the end of 2 hours, and Scan B shows clearing of the cisterns at 24-hours with residual isotope over the brain surface near the superior sagittal sinus.
Isotope passed intracranially even after the removal of ventricular fluid to lower intracranial pressure to a normal range. This patient was scanned repeatedly over a 2 hour period and the scanning image did not change. Gallium was used in this instance; with arsenic, a delayed spread to the posterior fossa could be picked up on the following day in similar cases.

A second pattern for restricted flow is shown in Fig. 7, in the scans of a child with a proven glioma of the optic chiasm. This tumor had spread extensively into the basal cisterns and had, as noted in both pictures, limited the flow of radioactive material to the posterior fossa. In the first scan (to the left), an early rise to the cerebellar cisterns is seen. The next scan was obtained 1 hour later and shows a retention of isotope at the same site instead of the normal passage through the tentorial notch to the upper cisterns.

Aseptic Meningitis. One such complication was found with $^{74}$As from a group of 28 patients scanned with this material. In this instance the temperature rose to 102°F a few hours after the injection. This was accompanied by a pleocytosis of 1500 white cells in the spinal fluid and by a rise in protein content to 282 mg%. All cultures were negative. This response was particularly puzzling in view of the fact that the same vial of isotope had been used previously for other infants. Since these and other vials were noted to contain small amounts of particulate matter, the possibility of mechanical irritation from foreign matter was considered. Isotope from this same vial was then administered through a Millipore filter with a pore size of 0.22 μ (Millipore Corp., Bedford, Mass.)

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Fig. 4. Normal adult cisternal scans following an intrathecal injection of $^{74}$As. Scan A was obtained with the regular scanning head and shows poor definition of the cisterns. Scan B was obtained at about the same time but with an added lead insert and shows a much clearer cisternal outline. A dosage of 750μc was required in the adult because of the relatively long spinal segment.

Fig. 5. Normal scans in an infant following an intrathecal injection of 500μc $^{68}$Ga. Note the almost immediate rise to the basal cisterns, as with $^{74}$As. This material disappeared rapidly because of short half-life and useful scans were not obtained after 2½-3 hours. Scan A = 10 min, Scan B = 30 min, Scan C = 2 hours. Standard = 2.5% injected dose.
Cisternal Brain Scanning

into the subarachnoid space of a monkey. There was no reaction to this filtered material and clinical studies were then resumed using filtered material from this same vial.

Discussion

We have found this method to be of value in complementing air studies in the investigation of hydrocephalic children and it is now used routinely for this group. It has been helpful, for example, in evaluating arrest. The method has also been used for adults when cisternal blockade or occult hydrocephalus has been suspected. The results in both groups will be presented in detail elsewhere.

Two safety factors seem pertinent, one relating to total body radiation and the other to aseptic meningitis. Since $^{68}$Ga has a short half-life of 68 minutes, it is rapidly excreted. Total body radiation with the pediatric dosage is only 14 millirad, which is of particular importance in this age group. This radionuclide is therefore now used exclusively because of the safety factor; however, it should be noted that $^{74}$As is otherwise preferable because of the opportunity, with its usage, of depicting delays in cranial spread which may last for periods of 24 hours or more. Aseptic meningitis is a known complication with cisternal scanning. A possible harmful effect from protein has been suggested with injections of radioiodinated albumin. Our material did not contain protein and we feel, as noted above, that

Fig. 6. Abnormal scan showing cisternal blockade following subarachnoid hemorrhage. This patient received 1000μc $^{68}$Ga via the lumbar route after a ventricular tap was performed to relieve intracranial hypertension. Scans were repeated several times and showed essentially no intracranial spread.

Fig. 7. Cisternal blockade in an infant with posterior spread of a glioma of the optic chiasm. Five hundred μc of $^{68}$Ga were given via the lumbar route. In the first scan (Scan A) an early rise to the cerebellar cisterns is found. Later scans, including Scan B, showed that the isotope remained in the posterior fossa and did not pass upward. Note the difference between this pattern and that shown in Fig. 6 where the material failed to enter the posterior fossa.
some reactions may be due to contamination from foreign colloidal matter. We now use a filter in the preparation of material for all injections. The careful regulation of pH is similarly mandatory and untoward effects may be found with gallium without this precaution.

This technique affords the opportunity of studying the flow of materials within and from the subarachnoid compartment. The most notable finding is the rapid passage of materials to the basal cisterns in infants. This flow is so rapid that barbotage is not required. The delayed flow in adults is such that barbotage and a relatively high dosage are necessary. The adult dosage approximates that used for regular brain scanning whereas the pediatric dosage is considerably smaller. The delay in passage to the cranium in adults appears to represent only a prolonged transit time over the long spinal segment and we have occasionally used as much as 4mc of gallium in order to adequately evaluate the presence or absence of cisternal blockade.

The depictions with inorganic arsenic differ from those found with GA-EDTA in that: (a) a much larger amount of radioactive arsenic reached the cranium and (b) the fixation in the basal cisterns appeared to be more marked with arsenic. Since arsenic was given in the inorganic form it seems likely that it was retained because of binding to sulfhydryl or other groups; gallium was chelated and hence, unavailable for local tissue binding.

Summary

We have described a technique of cisternal brain scanning with positron-emitting 74As and 68Ga. We strongly preferred 68Ga because of the radiation safety factor. In children the basal cisterns were shown very quickly following injections of small amounts of either material and without the use of barbotage. The initial isotopic deposits were in the cisterns of the posterior fossa. Maximal activity occurred about 1 hour after passage of the radioactive material through the tentorial notch. The 74As pattern was unlike that described previously in that there was prolonged retention in the basal cisterns.

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References

1. Abbassion, K., and McQueen, J. D. The evaluation of hydrocephalic states with cisternal brain scanning techniques. (In preparation.)