Test for Patency of Ventriculovascular Shunt for Hydrocephalus with Radioactive Iodinated Serum Albumin

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Although the presence of a "pump" often makes it easy to determine if a ventriculovascular shunt is functioning, there are occasions when there is some doubt as to its function. Tests of the patency of the valve system in vivo have therefore been undertaken, using radioactive iodinated serum albumin (RISA). Bell injected RISA into the ventricular system in 30 adults, and followed the passage of the radioactive material in the tubing of ventriculoperitoneal shunts, using a Geiger counter. The abstract of Schlesinger et al. deals with much the same type of study, but details have not yet appeared. Atkinson and Foltz (p. 165) have also used RISA in testing patency of the shunt: "... the levels in blood are very helpful if a sudden surge of isotope activity can be picked up to indicate functioning of the shunt." This method appeared to depend on the time of sampling and the rate of flow in the shunt, and was apparently considered secondary to the determination of clearance of the isotope in ventricular fluid over a period of 24 hours. Migliore et al. have used a technic similar to that described in the present investigation, injecting 50-200 μc. of RISA into the lateral ventricle, and sampling radioactivity of blood and radioactivity of residual cerebrospinal fluid. Specific technical details were not given in this brief clinical note.

Methods

Ten hydrocephalic children, aged 1 to 18 months, have been studied before and after ventriculojugular shunting procedures. The diagnosis was made clinically on the basis of progressive enlargement of the head, and verified by diagnostic air study, study of passage of dye from ventricle to lumbar subarachnoid space, and by absence of subdural collections. Either before or a few days after the air study, the child was prepared with 2 drops of Lugol's iodine-potassium iodide solution, given orally to protect the thyroid gland against pickup of radioactive iodine. RISA was instilled into one lateral ventricle several hours after administration of the Lugol's solution. The total dose of RISA was 4 to 7 μc., calculated as 4 μc. per pound body weight. Blood samples were taken at ⅓, 1, 2 and 24 hours after injection of RISA, using tubes containing anticoagulants. After centrifugation, the serum was collected, and the counting was done with a deep-well scintillator on 1 cc. of serum. Each infant acted as its own control, with pre- and postoperative surveys. When the procedure was repeated 2 days to 2 weeks after operation, the only variation was collection of a sample of blood just before instillation of the RISA to permit evaluation of the background activity as a residue of the earlier injection. Early in the investigation, surface counts with flat-field (nonfocussed) and focussed collimation were made over the cerebral hemispheres, heart, liver, and thigh in a few babies. With the doses of RISA used, there was insufficient evidence of increased radioactivity over these areas to permit substitution of these pools of blood for the peripheral blood samples. Direct body counts therefore were abandoned.

A major concern was the possibility of allergic responses to repeated use of radioactive iodinated serum albumin, especially since microbiologists use animal serum albumin as a basic allergen to produce antibodies. Search of the literature failed to reveal previous studies directed at this point, although Crispell et al. mentioned specifically no adverse reactions with multiple doses of RISA in study of plasma volume.

† The well counter was Picker's model 8804A, using a sodium iodide crystal, 2" thick and 2" in diameter, activated by thallium. Corrections were made for background radioactivity and for physical decay of the isotope.

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* Preliminary results indicating the usefulness of the present technic were presented to the Chicago Neurological Society on May 3, 1960. A short abstract appeared in the Society Transactions in the Archives of Neurology in 1961.
Antihuman serum albumin antibodies were produced in rabbits using 3 weekly injections of antigen, consisting of human serum albumin to which had been added a few mg. of RISA and Freund's adjuvant. The anti-human serum albumin antibody was then used as a control in the complement fixation test as described by Boyden.\textsuperscript{3} The antigen was adsorbed on red blood cells of the sheep treated with tannic acid, then used with known antibodies and compared with unknown sera, which might contain antibodies.

In 3 patients, serum was collected prior to carrying out the second RISA study, usually 2 to 3 weeks after the first injection of RISA. In none of these sera were antibodies found, using concentrations of antiserum of up to 1:10. There was no evidence in the clinical course of these patients to indicate any antibody-antigen reaction.

**Results**

Fig. 1 shows typical graphs from a hydrocephalic baby (D.E.). The lowermost curve shows the slow pickup of radioactivity from the ventricular system found in an untreated hydrocephalic baby. The most rapid rate of uptake is in the first hour, with a slowly rising slope of the curve of radioactivity (ordinate) plotted against time (abscissa). The uppermost curve was made 7 days after insertion of a Heyer-Paudenz shunt: it shows a striking increase in uptake of radioactivity in the serum, amounting to 3000 units (corrected counts) in a half hour, and 5000 units in 1 hour. After several weeks, the valve was inoperative clinically, and the system was revised at the cardiac end. Fourteen days later, the fontanelle was depressed and the shunt appeared to be working. The isotope study was repeated (middle curve). Although the transfer of radioactivity into the blood stream was lower than the rate in the first postoperative series, it was still distinctly higher than before operation. The implication was that the shunt was working, although at a level below optimum. The shunt was still effective clinically when the child was seen 1 and 9 months later.

Even when circumstances do not permit pre- and postoperative studies, a single curve (Fig. 2) may be of considerable value in determining if a shunting system is effective. This child (T.R.) was seen in our clinic because of doubt if the shunt put in at another hospital was effective. The fontanelle had closed, and clinical data (size of head, irritability, etc.) were equivocal. The RISA study indicated the presence of a nonfunctioning shunt.

The child (G.O.) whose studies are graphed in Fig. 3 had the first shunt put in at age 1 month. About 2.5 months later, the fontanelle became full again, the child became irritable, and appetite declined. Two weeks later, the RISA study (lowest curve) indicated a nonfunctioning tube. Operation revealed that the tube had become too short to function well. A new one was put in place.
to reestablish the shunt. The fontanelle became soft, and the RISA test was repeated (upper curve). The abrupt rise in radioactivity within a half hour may be seen, indicating functioning of the shunt.

The usefulness of the RISA study with the low doses of this investigation has not been as marked with the Holter-Spitz valve as with the Heyer-Pudenz system. The reasons are not clear. The rate of flow through the Holter-Spitz valve has been shown by Forest\(^5\) to be dependent on ventricular pressure, and it may be that the rise in radioactivity after ventricular injection has not been as marked because of lowered intraventricular pressure. As Migliore et al.\(^7\) have pointed out, with higher doses of RISA, the rise in radioactivity can be sufficient to permit evaluation of patency, provided there is manual pumping of the valve. The Heyer-Pudenz valves of the current series did not have pumps.

**Discussion**

In this study, only blood levels of radioactivity were studied, in the hope of making as few incursions into the ventricular system as possible. Studies by van Wart et al.\(^10\) indicated little pickup from the ventricular systems of animals in 1 hour, but even without a shunt a significant exchange from cerebrospinal fluid to blood did appear in 2 hours. The maximum pickup was 45 per cent in 16 to 20 hours. Atkinson and Foltz\(^1\) believed that the RISA levels in blood after ventricular injection were, in general, too low for use in evaluation of patency of shunt.

Besides being concerned over protein sensitization, we have also been interested in safety from the standpoint of radioactivity. The amounts of RISA used have been small, and the thyroid was protected with Lugol’s solution. Bell\(^5\) expressed no concern over the use of 100 \(\mu\)c., and Migliore et al.\(^7\) used 50–100 \(\mu\)c. We believe adequate counts can be obtained with total doses of 4–7 \(\mu\)c. in infants. It is difficult to determine the total body radiation under these circumstances, for if the shunt is functioning, the radiation is rapidly dispersed into the general circulation. Scar et al.\(^3\) have shown that only 30 per cent of the original radioactivity is left in the blood 3 days after injection of RISA. By the 14th day, there is an equilibrium between all serum and extravascular albumin, including that tied to \(^{131}\)I. Crispell et al.\(^4\) have felt that repeated doses of 12 \(\mu\)c. in adults (for blood-volume studies) did not exceed the accepted safe level of radiation.

In those children with nonfunctioning ventriculo-atrial shunts, the concentration of radioactivity in the ventricular system obviously will be greater, at first, than in those with functioning shunts, but eventually the material finds its way into the blood stream and is dissipated. Thickness of cerebral mantle, volume of ventricular fluid, and site of spinal-fluid block are all of importance in this regard.

The curves shown (Figs. 1 and 3) for functioning valves differ markedly from the curve drawn by van Wart et al.\(^10\) in experiments with dogs. After injection of 25 \(\mu\)c. of \(^{131}\)I into the cisterna magna, there was little uptake in the blood in the first hour, although significant levels appeared in 2 hours. The curves of the babies of this series show rapid appearance of radioactivity in the blood when there is a functioning ventriculo-atrial shunt; conversely, there is a delay in appearance of large amounts of radioactivity in the blood after ventricular injection of
RISA if the shunt is not working. The utility of this test appears evident.

Disadvantages of the RISA test for patency are also apparent. If the fontanelle is closed, injection must be made through the same opening through which passes the tubing of the shunt. Whether possible puncture of the tubing is a hazard of importance remains to be seen. Repeated sampling of blood may be tedious or difficult in small children.

Determination of the functioning of a shunt without operation is, nevertheless, worth while, especially if there is doubt of the significance of partial collapse of the pump. Other techniques of testing patency of the shunt need exploration: we are currently investigating the use of fluorescein by injection into the ventricle and observing fluorescence in blood samples, fingernails, and conjunctivae. Large doses of this chemical may produce convulsions when injected into the ventricles, so careful assay of quantities used is necessary.

In this series of 10 cases, there have been 2 instances of episodes of short-lasting hyperpyrexia, with 1 sterile meningitis of short duration. Since giving up the use of multiple-dose containers of RISA, no further reactions of this sort have been seen.

Summary

1. Radioactive iodinated serum albumin (RISA) may be used to test the functional patency of ventriculo-atrial shunts in hydrocephalic individuals.

2. A technic is described for estimating radioactivity in blood samples before and after intraventricular instillation of RISA in doses of ½ µc. per pound of body weight.

3. Functioning Heyer-Pudenz-valve shunts permit a rapid surge of radioactivity to appear in peripheral blood within a half hour after intraventricular injection. The amount usually is doubled by the end of an hour. The rate of appearance of radioactivity with the Holter-Spitz system is more variable, but is accelerated by pumping the valve.

4. Three children were tested for antibodies to RISA using complement fixation studies with rabbit sera. No evidence of antibody-antigen reaction was found.

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References


