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Radioactive Iodinated Human Serum Albumin as Tracer Agent for Diagnosing and Localizing Intracranial Lesions.* (18720)

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(Introduced by R. L. Varco.)

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Various isotopes have been used to diagnose and localize intracranial lesions by the isotope-encephalometric technic described by Moore (2-4). So far, diiodofluorescein has given the most satisfactory results and therefore gained the widest acceptance. However, at this clinic radioactive-iodinated-human-serum albumin has been used and appears to be as satisfactory, if not superior, to diiodofluorescein(1). The iodination of human serum albumin (RIHSA‡) is carried out with elemental iodine in an essentially neutral buffer. One cc of RIHSA contains 5 mg of human

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3. Moore, G. E., Peyton, W. T., French, L. A., and Walker, W. W., *J. Neurosurg.*, 1948, v5, 392.

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‡ Obtained from the Abbott Laboratories, North Chicago, Ill.

serum albumin with a salt concentration of approximately 2 mg(6). Metabolic studies in both animals and humans have shown that RIHSA given intravenously remains in the blood stream for a long period of time. It is apparently gradually metabolised by the body and free iodine liberated. Although most of the radioactive iodine is excreted through the urine, about 5% of it is taken up by the thyroid gland by the end of 24 hours(5). A small amount of RIHSA, which is not readily metabolized, diffuses out into the tissue and into lymphatics unchanged. About 1-2% of the tagged albumin can be obtained from the thoracic duct by the end of one hour. The liver, however, apparently does not participate in the excretion of RIHSA. It has been shown in experimental animals that only a negligible amount of RIHSA can be recovered in the bile(5). Kidneys are the main organs that are responsible for the excretion of I^{131}. At the end of the first day, the total urinary excretion reaches about 15% to 20% of the total amount given. The blood as well as the tissue level gradually falls and eventually all the injected RIHSA is metabolized and I^{131} excreted by the kidneys.

The uptake of I^{131} by the thyroid raises the question of whether or not it is safe to use RIHSA as a tracer agent to diagnose intracranial lesions. However, it is possible to prevent the deposition of I^{131} in the thyroid. It has been shown that stable iodine administered to patients as Lugol's solution for a week starting at least 24 hours previous to the administration of RIHSA will block the uptake of I^{131} by the thyroid and thereby eliminate the danger of excess irradiation.

At this clinic, the present regime requires intravenous administration of from 400 to 500 μc of RIHSA to the patient who has been given 10 drops of Lugol's solution, 3 times daily at least 24 hours prior to the test. An interval of not less than 30 minutes should elapse before the head is monitored. However, when time is available the initial counting should be done 24 hours later in order to get a more significant differential "uptake" between the tumor and normal brain. It is important, for the purpose of obtaining counts during the optimal time when ratio between the tissue concentration and blood concentration is the greatest, that the patient is counted daily for 2 to 3 days. A focus of high uptake obtained by the initial counting after injection should persist through the second and third or even fourth days. In fact, our experience has been that the differential uptake between the site of the lesion and the symmetrical contralateral area, should increase on the second and third day. Table I illustrates this point. Ten cases have been subjected to this technic up to date. We were able to localize tumors in 5 cases, subdural hematoma in one case, and rule out tumors in 2 cases which subsequently had both negative air studies and angiograms. The remaining two patients were still undergoing study.

TABLE I. D.M. ♂ 25 U.H. #829584. 460 μc RIHSA Given I.V.

		c/m	%D
First survey—1 hr after administration			
R_3		1857	L
L_3	Lateral frontal	2005	7%
L_5		2823	L
R_5	Midtemporal	2532	10%
R_6		1641	L
L_6	Temporo-parietal	1686	2.5%
L_7	Parasagittal	1798	0
R_7	(earline)	1801	0
R_9		1656	L
L_9	Post-temporal	1712	3%
L_{10}		1867	L
R_{10}	Post-parietal	1843	1%
Second survey—24 hr later			
R_3		1978	L
L_3	Lateral frontal	2163	8%
L_5		2154	L*
R_5	Midtemporal	1934	10%
R_6		1593	L*
L_6	Temporo-parietal	1931	17%
L_7	Parasagittal	1974	L*
R_7	(earline)	1749	11%
R_9		1499	L*
L_9	Post-temporal	1796	16%
L_{10}		1872	L
R_{10}	Post-parietal	1811	3.5%

On the first day, only one position showed a differential uptake of 10%. On the second day, the positions over the tumor all showed a significant increase of differential uptake.

* Site of tumor—craniotomy—extensive left temporal astrocytoma.

5. Storrasli, J. P., Krieger, H., Friedell, H. L., and Holden, W. D., *Surg., Gyn., and Obst.*, 1950, v91, 458.

6. Tabern, D. L., personal communication.

Admittedly, it is too early to predict what a role RIHSA will play in the diagnosis and localization of intracranial lesions. However, advantages are many: (a) It is much less expensive than diiodofluorescein (DIF*), (b) 400-500 μc will give about the same counting rate as 1 mc of DIF, (c) RIHSA stays in the tissue longer and therefore permits repeated counting, and (d) an increase in differential uptake by the focus on the 2nd and 3rd days survey will serve to confirm the presence of a lesion demonstrated in the initial counting.

The only disadvantage of this method is the uptake by the thyroid gland of I^{131} split off RIHSA. Although stable iodine serves to block this uptake, experience is too limited to say anything definite as to the amount of radiation the thyroid gland might receive as a result of RIHSA administration. However, with the adoption of scintillation type counters, it is possible that the counting rate will be increased to such an extent that the dosage of RIHSA can be greatly reduced to a much safer level.

It is our feeling that RIHSA and DIF may act in a more or less identical manner in the body. When DIF is administered, it may combine physically with the serum albumin of the patient. In other words, DIF is merely used as a reagent to tag the serum albumin of the patient. This hypothesis is being investigated.

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Diminished Adrenal Cortical Function in Diabetes as Shown in Eosinophil Response to Stress of Surgery. (18721)

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The relationship between the adrenal glands and the pancreas in diabetes mellitus has been the subject of investigation for many years. Recently several observations have been made which suggest, if anything, a reduction of adrenal cortical function in diabetes. Miller and Mason(1) measured the 17-ketosteroids in the urine of 64 adult diabetic patients and found that 88% of the values were below the average normal, while 27% fell below the minimal normal value. They were unable to correlate the excretion of 17-ketosteroids with either the age of the patient or the severity of the diabetes. No mention was made of a possible relationship to the duration of the disease. These investigators concluded that diabetes often has an effect on the adrenal glands which results in a lowered excretion of 17-ketosteroids which is not related to the degree of impairment of carbohydrate metabolism. This finding of reduced 17-ketosteroid excretion in diabetes has been reported by several other workers(2-4). Forbes *et al.*(3) postulated that the decrease was due to the accompanying secondary malnutrition rather than the diabetes *per se*.

The 11-17 oxysteroid excretion in diabetes has also been measured(5,6). Although none of the series is large enough to be statistically significant, the results seem to confirm the trend toward lowered adrenal cortical function in diabetes. The mean value for five diabetics as measured by Talbot was 0.058 mg/sq.m of body surface per day as compared to a mean value of 0.132 mg/sq.m of body surface per day for normals. Three of his 5 patients

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5. McArthur, J. W., Personal communication.

6. Talbot, N. B., Personal communication.