

BROOKHAVEN NATIONAL LABORATORY

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MEMORANDUM

DATE: May 10, 1954

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 COLLECTION Protocols - Clinical
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 FOLDER HUMAN PROTOCOLS 1950-1963

TO: BNL Committee for the Use of Isotopes
 in Humans
 FROM: C. G. Lewallen, M. D.
 SUBJECT: Project H-36 - Use of I¹³¹ HSA In
 Relatively Large Dosage In Donor-
 Recipient Human Experiment

This constitutes a request for authorization to use I¹³¹ HSA in relatively large dosage in donor-recipient human experiment.

I. In human studies with intravenous I¹³¹ HSA it has been consistently observed that the rate of deiodination as judged by urinary excretion rate has been more closely proportional to the plasma concentration (specific activity) than to the concentration of I¹³¹ HSA in any other compartment samples. This suggests that the iodoalbumin is deiodinated in plasma or in some compartment very rapidly equilibrated with plasma. One objection to this hypothesis is the possible presence of components in the injected iodoalbumin of heavily iodinated molecules with denaturation of greater or lesser degree, rendering them liable to more rapid deiodination.

The purpose of the proposed experiment is to clarify whether the initial rapid rate of deiodination is related to the high plasma level or to the presence of more easily deiodinated components.

It is proposed to inject a relatively large dose of I¹³¹ HSA into patient #1 (the donor) and follow the urine and plasma levels for a sufficient period (8 days) to demonstrate that deiodination is proceeding at a constant fractional rate - at this point the remaining iodoalbumin is demonstrably uniform as far as deiodination rate is concerned, and sufficient time has elapsed for degradation of the more easily deiodinated components. It is proposed at this time (8th day) to withdraw 400 cc. of blood from the donor and to inject 200 cc. of her labeled plasma into patient #2 (the recipient) and subsequently to follow urinary excretion rate and plasma levels in the recipient until a constant fractional deiodination rate has been reached. In the recipient the quantity of tag in the intravascular and extra vascular compartments will be known either by direct sampling or by difference, such that the rate of deiodination (urinary excretion of iodide I¹³¹) can be determined as being a fractional rate of either one or the other, or both. If it is related only to the quantity in plasma, it would be strong presumptive evidence that plasma is the site of deiodination.

II. From repeated I¹³¹ HSA studies in the past year it is clear that sufficient I¹³¹ HSA would have to be given to the donor such that the 200 cc. of plasma removed on day 8 would provide a minimum of 48 μ c for the recipient. The recipient dose of 48 μ c is the minimum which would allow quantitation of urine and plasma levels for 9 days. The 400 cc. of blood to be removed from the donor is considered the maximum

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which her cardio vascular status would safely allow.

From previous studies it is clear that:

- A. Mixing of the intra and extra vascular compartments of the injected I131 HSA would require about 5 days in the donor.
- B. A constant exponential rate of urinary excretion would occur at about the same time.
- C. Constant exponential rate of excretion could be established by measurements no earlier than the eighth day.
- D. The plasma level of tag at day 5 would be about 10% of dose per liter of plasma, decaying with a biological half of time of 16 days to about 9% per liter on day 8, and extrapolating to a level of 12.5% per liter at 0 time.

III. Calculations of Required Dose.

Plasma level (donor) at 8th day (day of withdrawal) = 9% per liter
 = 1000 x .09 = 90 µc per liter per mc. injected by
 dilution only or 45 µc per liter per mc. injected by
 dilution and decay. 200 cc. plasma would therefore
 contain .2 x 45 = 9 µc per mc. injected.

$$\frac{48 \mu\text{c}}{9 \mu\text{c}/\text{mc}} \text{ (minimum dose for recipient)} = 5.3 \text{ mc.} = \text{minimum feasible dose for injection into donor.}$$

IV. Radiation Dosage Calculation to Donor.

It is assumed here that the rep to bone marrow are essentially equal to the Beta and Gamma rep to the blood.

$$D_{\beta} = 88 \bar{E}_{\beta} T_c \qquad \text{Effective } T-1/2 = \frac{16 \times 8}{16 + 8} = 5.3 \text{ days}$$

$$= 88 \times .2 \times T-1/2 \text{ effective} \times c$$

$$= 88 \times .2 \times 5.3 \times c$$

$$= 93.3 c$$

c = 12.5% per liter of plasma = .125% dose per liter of plasma

Per mc administered (1000 µc) c = 125 µc per liter of plasma

$$= .125 \mu\text{c}/\text{cc plasma}$$

$$= .075 \mu\text{c}/\text{gm of blood}$$

assuming an hematocrit of 40%.

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$$D\beta \text{ (per mc administered)} = 93.3 \times .075 = 7.00 \text{ rep/mc}$$

$$D\beta + D\gamma \text{ (per mc administered)} = 1.8 D\beta \text{ (Marianelli)}$$

$$= 1.8 \times 7 = 12.6 \text{ Rep per mc}$$

$$D\beta + D\gamma \text{ (for 5.3 mc)} = 5.3 \times 12.6 = 66.8 \text{ rep.}$$

V. Only the donor need be given special consideration as far as radiation exposure is concerned, inasmuch as the recipient dose does not exceed permitted exposure. The proposed donor () is an elderly female with histologically proven carcinoma of the thyroid glands with metastases to the skull and with a large tumor mass in the neck. She has received therapeutic I¹³¹ in dosages of 247 mc and 176 mc. on 9/13/51 and 4/1/52, respectively, and has limited life expectancy from the standpoint of advanced age (80), hypertensive and arteriosclerotic heart disease with cardiac enlargement and angina pectoris, and thyroid cancer with cranial metastases. Her hematological status at present is normal.

Several years' experience with the above method of calculation of radiation dosage to the blood at this hospital and at Memorial Hospital has demonstrated that no serious hematological complications are seen until the calculated blood dosage exceeds 500 Rep. We would expect the donor to tolerate the specified 5.3 mc. dose with no radiation sickness or hemetological complications.

Accordingly, we request permission to perform the study outlined above, administering an intravenous dose of 5.3 mc. of I¹³¹ HSA to the above-named patient.

Approved: On condition that the donor receive a whole blood transfusion equivalent to volume lost at the time blood is withdrawn.

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