

## BROOKHAVEN NATIONAL LABORATORY

## MEMORANDUM

DATE: July 13, 1956

The Medical Research Center  
Brookhaven National Laboratory  
Upton, L. I., New York

TO: Committee for the Use of  
Isotopes in Humans  
FROM: L. I. Gidez, Ph.D.  
H. A. Eder, M. D.  
SUBJECT: Study of fat metabolism  
in hospitalized patients  
Proj. H-43

Request is made for the authorization for the use of glycerol  $\alpha$ - $C^{14}$  in selected hospitalized patients.

In conjunction with research on fat metabolism, both in normal subjects and in individuals with nephrosis, and hyperlipemia, studies on the incorporation of various lipid precursors into the different serum lipoproteins have been initiated. Thus far we have carried out studies using  $P^{32}$  as a precursor of phospholipid and alanine  $l$ - $C^{14}$  as a precursor for lipoprotein protein. Other investigators have labelled plasma lipids by administering  $C^{14}$  acetate, cholesterol, and fatty acids.

It is proposed to administer glycerol  $\alpha$ - $C^{14}$  by mouth and make suitable collections of expired air and blood. The studies on the rate of elimination of the  $C^{14}$  in the  $CO_2$  of the air will provide important data for exact determination of radiation in humans to whom glycerol is administered. No such data ~~was~~ at present available. Studies on the incorporation of the glycerol into the triglycerides and phosphatides of the various lipoproteins will be carried out.

It is proposed to use patient Ward 304, as a subject for these studies. He is 46 years old and has diabetes mellitus with marked hyperlipemia. He has peripheral arterial disease and an abnormal ballistocardiograph but no symptoms of coronary artery disease. He is an ideal subject for this study since his plasma contains 1200 mg. per 100 ml. of phosphatide and 6000 mg. per 100 ml. of triglyceride. This will permit the isolation of adequate amounts of these substances. Because of the high incidence of coronary artery disease in patients with hyperlipemia statistically it may be anticipated that this patient has a shortened life expectation.

The  $C^{14}$  has a  $T/2$  of ca. 5,000 years. On decay it yields  $N^{14} + \beta$  ( $E_{max}$  .155 MEV.)

REPOSITORY Records Holding Area Bldg. 494  
COLLECTION Protocols - Clinical  
BOX No. 4  
FOLDER Human Protocols 1950-1963  
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While there are no data on the metabolic fate of glycerol in humans, Gidez and Karnovsky have studied its metabolic fate in rats in considerable detail. Approximately 40% is oxidized to CO<sub>2</sub> in 6 hours and about 80% in 24 hours. During the initial hours after administration about 12% is in liver glycogen and about 4% in blood glucose. About 6% of the total radioactivity is found in various tissue lipides at 6 hours; liver has the most (5%) with small amounts in kidney and ~~hair~~ brain.

The remaining distribution at 6 hours is as follows:

muscle . . . . .	8%
urine and feces. . . . .	4%
skin and hair. . . . .	3%
carcass lipids . . . . .	2%
water soluble material from carcass. . . . .	12%
protein and other water soluble material from liver, kidney, and intestine . . . . .	20%

Proposed dose:

It is proposed to administer 3  $\mu$ c/Kg. (The patient weighs 80 Kg.)

The estimated radiation is as follows:

First day: D = .0082 rep

For the subsequent calculations we shall estimate that (1) 80% of the administered dose has a T/2 of 1 day and is distributed uniformly, (2) 15% has a T/2 of 12 days and is distributed in 2% of the tissue and (3) 5% has a T/2 of 180 days and is distributed in 1% of the tissues.

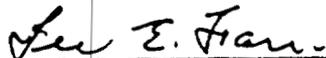
T <sub>∞</sub>	d <sub>1</sub> = .0095
	d <sub>2</sub> = .1040
	d <sub>3</sub> = <u>1.0650</u>
	D = 1.1785 rep

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First week:

The total dose for the first week is estimated by assuming that all of  $d_1$  is contributed, 33% of  $d_2$  is contributed and 3% of  $d_3$  is contributed. The dose for the first week is then 0.07 rep.

It is requested, therefore, that permission be given to administer the isotope glycerol  $\alpha\text{-Cl}_4$  to selected individuals in tracer amounts which in no case will exceed 0.3 rep/wk.



L. E. Farr, M. D.



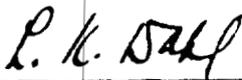
E. E. Stickley, Ph. D.



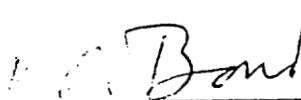
J. S. Robertson, M. D.



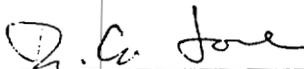
E. P. Cronkite, M. D.



L. K. Dahl, M. D.



V. P. Bond, M. D.



R. A. Love, M. D.

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