

MEMORANDUM

DATE: October 3, 1956

REPOSITORY Records Holding Area Bldg 494

TO: Committee for the Use of Isotopes in Humans

COLLECTION Protocols - Clinical

FROM: Nicola Di Ferrante, M.D.

BOX No. 4

SUBJECT: Study of the metabolism of acid mucopolysaccharides in patients with rheumatoid arthritis and in normal individuals. Project H-47

FOLDER Human Protocols 1950-1963

Request is made for the authorization for the use of S^{35} (as inorganic sulfate) in patients with rheumatoid arthritis and in patients hospitalized for other conditions.

I. Isotope

- A. Physical characteristics: S^{35} has a $T/2$ of 87.1 days. Its decay scheme is $S^{35} \longrightarrow Cl^{35} + \beta^-$ (E_{max} 0.167 MEV.).
- B. When inorganic S^{35} is injected intravenously in human or intraperitoneally in animals, 90-95 per cent of the dose injected is excreted in the urine by the end of the fifth day.

The fate of the 5-10 per cent which is not excreted has been thoroughly studied in animals: A very small part of it (5 per cent) is incorporated in S-containing amino acids. The remainder is incorporated in S-containing mucopolysaccharides.

S^{35} as inorganic sulfate has been repeatedly used in humans for the determination of the extracellular fluid volume (Walser, Reid, and Seldin, Arch. Biochem. 45, 91, 1953).

In calculating radiation exposure, the dose injected may be divided into three compartments:

- (A) 90 per cent which is excreted by the end of the fifth day ($T/2 = 1.5$ days)
- (B) 5 per cent x 10 per cent incorporated into amine acids ($T/2 = 87$ days)
- (C) 95 per cent x 10 per cent incorporated into mucopolysaccharides ($T/2 = 17$ days)

Assuming an initial whole-body distribution of the isotope, administration of $\mu c/gm$. would deliver the following amounts of radiation:

<u>Compartment</u>	<u>rad total (∞)</u>	<u>rad first day</u>
A	5.45	2.02
B	1.76	0.01
C	6.55	0.26
<u>Total</u>	<u>13.76</u>	<u>2.29</u>

If 200 μc were administered to a patient of 50 kg., (corresponding to 0.004 $\mu\text{c}/\text{gram}$), the total exposure at ∞ would be 0.05 rad and the total exposure at the first day would be 0.008 rad.

II. Specific Proposal

It is proposed to inject 200 μc of S^{35} as inorganic sulfate intravenously into patients with rheumatoid arthritis and into a few selected patients hospitalized for conditions different from rheumatoid arthritis.

The amount of radioactivity associated with the plasma α_1 globulins at different times after the injection and the specific activity of urinary mucopolysaccharide in the days following the injection will provide a measurement of the rate of synthesis of S-containing mucopolysaccharide.

Patients with rheumatoid arthritis will receive more than one single dose of the isotope, in order to secure data before and during treatment of the condition. However, we do not foresee the necessity of giving more than three single doses to each patient.

Patients hospitalized for other conditions will be used as controls. A fraction of the urine excreted by the patients will be used for determining the specific activity of the urinary mucopolysaccharide; the remainder will be disposed of in the plumbing system of the Hot Laboratory.

It is requested, therefore, that permission be given for administration of 200 μc of S^{35} , as inorganic sulfate, in patients with rheumatoid arthritis and in patients hospitalized for other conditions.

L. E. Farr

L. E. Farr, M.D.

J. S. Robertson

J. S. Robertson, M.D.

L. K. Dahl

L. K. Dahl, M.D.

R. A. Love

R. A. Love, M.D.

E. E. Stickley

E. E. Stickley, Ph.D.

E. P. Cronkite

E. P. Cronkite, M.D.

V. P. Bond

V. P. Bond, M.D.

1176330