

MEMORANDUM

R DATE: 24 March 1971

TO: A. Harrison
FROM: E. P. Cronkite, M.D. E.P. Cronkite
SUBJECT: CIRC Numbers

The following CIRC #s are inactive. Except for completing old records, they should not be used for identifying patient activity until reactivation is formally approved.

Table with 2 columns: Principal Investigator and CIRC #. Rows include Dr. Cronkite (3, 4, 20, 23, 35, 35A), Dr. Dahl (5, 6, 14, 25), Dr. Jesseph (1), Dr. Robertson (9, 10, 16, 28), and Dr. Schiffer (22). An arrow points to the '5' in Dr. Dahl's row.

EPC/ck
cc: CIRC Committee
Mr. Finn
Dr. Dahl

REPOSITORY: Records Holding Area, Bldg. 494
COLLECTION: Committee-Clinical Investigations and Uses of Radioisotopes
BOX No. 4
FOLDER: CIRC #5

The Committee on Clinical Investigations and Uses of Radioisotopes
hereby approves the program with the following title:

Whole Body Potassium Determination and Turnover Study

CIRC # 5 has been assigned to this program.

Walton W. Shreeve

Walton W. Shreeve, M.D., Ph.D., Chairman

E. P. Cronkite

Eugene P. Cronkite, M.D.

E. Schackow

Eckart Schackow, M.D.

M. H. Van Woert

Melvin H. Van Woert, M.D.

J. S. Robertson

James S. Robertson, M.D., Ph.D. (ex officio)

Date November 8, 1963

Place Medical Research Center
Brookhaven National Laboratory
Upton, New York

1179445

FORM FOR INITIATION OR REVIEW OF CLINICAL
INVESTIGATIVE PROGRAMS

V3

(Submit original only to Department Chairman)

- A. Title of the proposal: Whole Body Potassium Determination and Turnover Study.
- B. Sponsoring physician(s): Dr. L. K. Dahl
- C. Responsible investigator(s): Drs. L. K. Dahl, L. C. Lax, and E. Schackow
- D. Brief description of the study, including its general goals and purpose, and pertinent information on past studies: (Attach additional sheets if necessary.)

The aim of the study is to investigate the turnover of total exchangeable body potassium together with the mass of this potassium pool, as to how it is related to or dependent on the total exchangeable body sodium and its turnover rate in normotensive and hypertensive human subjects.

- E. Reasons why the investigation(s) are to be performed on human subjects.

Hypertension is a disease of humans^{beings} and all hypotheses as to the role played by salt in hypertension must, therefore, be tested in human subjects.

- F. Type of patient in which the study is to be done (including approximate number of subjects, if known; special restrictions or requirements; method of obtaining consent; etc.):

Subjects with hypertensive cardiovascular disease and no secondary complications such as renal disease, and normotensive controls which are hospitalized for some other disease but not for hypertension (approximately 40 subjects per year). Subjects are to be placed on restricted salt diets and on varying salt intake regimens. Consent is obtained directly from the patient.

SUPPLEMENTARY FORM FOR RADIOISOTOPE
ADMINISTRATION TO HUMAN BEINGS

A. Radioisotope

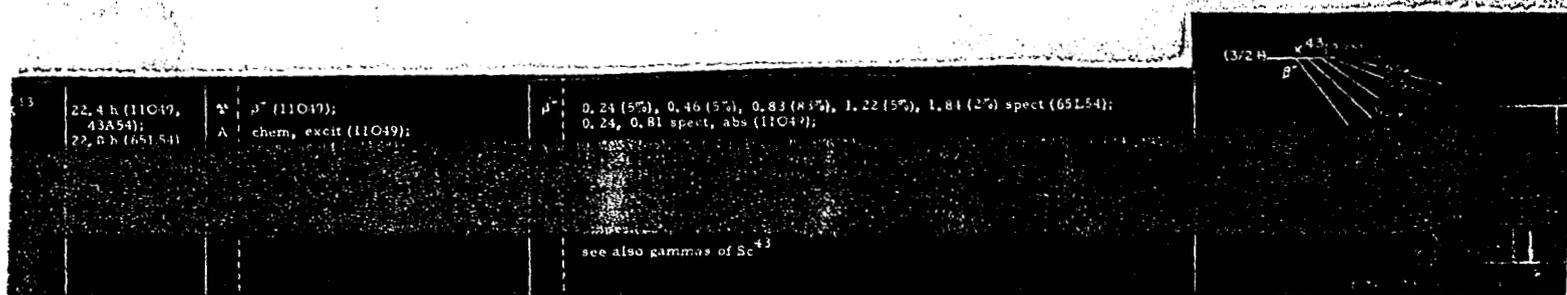
1. Species: (Radioisotope or labeled compound, eg. Na^{24}Cl or $1\text{-C}^{14}\text{-glucose}$)
 K^{43}Cl
2. Physical characteristics: (Physical half-life; decay scheme (or type, energy and relative frequency of major emissions)
Physical half-life = 22.4 hours. (See attached sheet for decay scheme)
3. Source: (BNL reactor, cyclotron, hot lab.), commercial supplier, etc.)
BNL cyclotron
4. Preparation: (Target material, quantity, special problems)
Alpha particles bombarding argon.
5. Specific activity and isotopic purity of administered material:
1 curie/gm K - only trace impurities other than potassium isotope.
6. Radioassay and calibration procedures: (Include validation to be performed at BNL prior to use) Dilution to desired strength on arrival at Medical Research Center and calibration on well counter #2, BNL #37172 in the Medical Research Center.
7. Vehicle and route of administration:
Isotonic glucose.
8. Procedures for control of sterility and pyrogenicity: (Or note that commercially supplied isotopes are certified as ready for administration to human beings.) Sterilized at 20 lbs. pressure for 1 hour prior to intravenous administration.
9. Extraneous effects, if pertinent: (Such as pharmacological or toxic actions of the parent compound or vehicle, etc.) None.

B. Radiation Dosage

1. Biological half-life or half-lives, including slow components:
20 - 40 days depending on dietary potassium intake.
2. Organ, cellular, or subcellular localization: (Should account for the effects of special drugs or agents on altering the natural distribution of the radioisotope)
 - a. Critical or "target" organ(s): No specific one.
 - b. Gonadal exposure: As for any other organ - See attached sheet

DECAY SCHEME OF K^{43}

(See reference #1)



K^{43} will be administered orally or parenterally as may be necessary. Prior to use, each shipment will be suitably calibrated and the amount of isotope required will be removed. Suitable sterilization will be done when parenteral routes of administration are used and the precautions appropriate to such procedures will be followed.

It is anticipated that between 2 and 10 μc of K^{43} will be administered to the average patient at any one time. If repetitive doses are administered, the maximal radiation doses received will be well within the tolerance limits proposed by both the International Committee on Radiological Protection (2) and the National Committee on Radiological Protection (3), respectively.

Radiation Dose from K^{43} :

The maximal radiation dose delivered to an individual has been calculated on the assumption that none of the K^{43} was excreted, i.e. an infinite biological half-life was assumed.

Calculations are based on a 70 kg man, 160 cm tall, receiving a dose of 10 μc K^{43} .

Formulae for these calculations are generally accepted, as in Quimby, et al (4) and Hine and Brownell (5).

Radiation from beta radiation:

$$D_{\beta} = 73.8 C \bar{E}_{\beta} T_{1/2} \text{ rads}$$

where D_{β} = dose due to β radiation in rads

$$\begin{aligned} \bar{E}_{\beta} &= \text{average } \beta \text{ ray energy per disintegration} \\ &= 0.29 \text{ Mev for } K^{43} \end{aligned}$$

$$\begin{aligned} C &= \text{conc. of isotope in body tissues assuming uniform} \\ &\quad \text{distribution} \\ &= \frac{10}{70,000} \quad \mu\text{c/gm} \end{aligned}$$

$$T_{1/2} = \text{half-life in days} = 0.925 \text{ days}$$

$$D_{\beta} = 0.0029 \text{ rads for } 10 \mu\text{c } K^{43}$$

Radiation from gamma radiation:

$$D_{\gamma} = 0.0346 \bar{\Gamma} C T_{1/2} \bar{g}$$

where D_{γ} = dose due to γ radiation in rads

$$\begin{aligned} \bar{\Gamma} &= \text{dose rate in roentgens per hour at 1 cm distance} \\ &\quad \text{in air from 1 mc} \\ &= 5.8 \text{ for } K^{43} \end{aligned}$$

C = as for D_{β} calculation

$$T_{1/2} = \text{as for } D_{\beta} \text{ calculation}$$

$$\begin{aligned} \bar{g} &= \text{an average geometrical factor for a } \gamma \text{ ray emitter} \\ &\quad \text{uniformly distributed in the total body} = 129 \text{ for} \\ &\quad \text{a 70 kg man 160 cm long.} \end{aligned}$$

$$\therefore D_{\gamma} = 0.0034 \text{ rads}$$

and Total cumulative dose =

$$D_{\beta} + D_{\gamma} = 0.0029 + 0.0034 = 0.0063 \text{ rads for } 10 \mu\text{c } K^{43}$$

Thus about 46% of the radiation is from β radiation and 54% from gamma radiation.

Supplementary Sheet #3

If it is further assumed that none of the K^{43} is in extracellular fluid but is confined to an intracellular locus, the amount of β radiation would be increased by about 20 per cent.

But in any event, the total amount of whole body radiation is very small.

Supplementary Sheet #4

Bibliography

1. Strominger, D., Hollander, J.M., and Seaborg, G.T. The Table of Isotopes, Reviews of Modern Physics, 30 (No. 2) Part 2, p. 619 (April) 1958.
2. Report on Permissible Dose for Internal Radiation, by I C R P Committee II: 1959, Health Physics, 3: 3-4, 11-27, 41, 1960.
3. Recommendations of the National Committee on Radiation Protection: Maximal Permissible Body Burdens and Maximal Permissible Concentrations of Radionuclides in Air and Water for Occupation Exposure, Washington, D.C., National Bureau of Standards Handbook 69, U.S. Gov't. Printing Office, 1959, p. 24.
4. Quimby, E.H., Feitelberg, S., and Silver, S. Radioisotopes in Clinical Practice, Lea and Febiger, Philadelphia, 1958, Ch. 8.
5. Hine, H.J., and Brownell, G.L. Radiation Dosimetry, Academic Press, New York, 1956.

1179451

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: Sept. 17, 1952

TO: BNL Committee on Use of Radio-
active Isotopes in Human Subject

FROM: Lewis K. Dahl, M. D.

SUBJECT: Proj. H-28 - Use of Na-24 in
Hypertensive Patients

It is proposed to measure the 24 hour total exchangeable sodium in hypertensive patients by the isotope dilution technique, using Na-24. Measurements will be made before and after restriction of sodium intake and will be repeated at two to three week intervals throughout the period of hospitalization.

The dosage of Na-24 will be kept within the limit of 0.3r/wk by using a maximum dose of 3 μ c/kg body weight.

Lewis K Dahl

Lewis K. Dahl, M. D.

Approved:

Lee E. Farr

Lee E. Farr, M.D.

J. S. Robertson

J. S. Robertson

J. T. Godwin

J. T. Godwin, M.D.

R. A. Love

R. A. Love, M.D.

W. M. Hale

W. M. Hale, M.D.

F. M. Sinex

F. M. Sinex

D. L. Jellinger

D. L. Jellinger, M.D.

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