Center

Brookhaven National Laboratory

Upton, L. I., New York

P

BROOKHAVEN NATIONAL LABORATORY

725519

MEMORANDUM

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.

Principal Investigator	CIRC #
Dr. Cronkite	3
	4
	20
	23
	35
	35A
Dr. Dahl	5
	6
	14
	25
Dr. Jesseph	1
Dr. Robertson	9
	10
	16
	28
Dr. Schiffer	22

REPOSITORY Records Holding Area Bldg 494

COLLECTION Committee-Clinical Investigations and Uses of Radioisotop

BOX No. 4

FOLDER CIRC#3

EPC/ck

cc: CIRC Committee
Mr. Finn
Dr. Dahl

Routine text as adopted in Med Staff min of [illegible] 73

1179402

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

Studies of Iron Metabolism in Man

CIRC # 3 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 7, 1963

Place Medical Research Center
Brookhaven National Laboratory
Upton, New York

1179403

V.P.

FORM FOR INITIATION OR REVIEW OF CLINICAL

INVESTIGATIVE PROGRAMS

B

(Submit original only to Department Chairman)

A. Title of the proposal: STUDIES OF IRON METABOLISM IN MAN.

B. Sponsoring physician(s): E. P. Cronkite, L. M. Schiffer

C. Responsible investigator(s): E. P. Cronkite, L. M. Schiffer

D. Brief description of the study, including its general goals and purpose, and pertinent information on past studies: (Attach additional sheets if necessary.)

Iron metabolism in man is poorly understood. The factors that control iron absorption, in particular, require further investigation. We plan to approach these problems by investigating iron absorption in patients with very active erythropoiesis, no erythropoiesis, ineffective erythropoiesis and in normal individuals. It is planned to alter the pathologic course of individuals where possible, and at the same time to perform iron absorption studies before and after treatment. Ferrokinetic data will be obtained as further diagnostic and therapeutic aids. (See additional sheets)

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

The majority of disease states considered do not have known animal parallels.

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.):

1. Aplastic anemia - aregenerative anemia
2. Polycythemia vera - untreated
3. Thalassemia minor and major
4. Iron loading diseases
5. Normal individuals

Oral consent will be obtained by frank discussion with the patients.

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G. 1. Are drugs not in the U. S. Pharmacopoeia (USP) or the NNR being used or contemplated for use? Yes X No ____

2. Is an unusual use of a drug(s) accepted by the USP or NNR contemplated? (An example would be the use of an accepted drug in dosages far exceeding the recommended limits or for purposes distinctly different from the usual indications cited.) Yes ____ No X

3. Are any biological products to be administered that do not bear on their containers or labels notation of approval by the Biological Control Division of the National Institutes of Health? Yes ____ No X

4. Is external or internal radiation other than accepted diagnostic or therapeutic procedures to be administered? Yes X No ____

5. Are any (other) unusual procedures being performed or proposed which in your judgment may entail a special hazard - particularly a hazard above and beyond any imposed by accepted diagnostic and therapeutic measures for that patient? Yes ____ No X

6. Are any radioisotopes to be administered to human beings? Yes X No ____

a. If yes, are the radioisotopes to be used solely within the limits of procedures, specifically described in the USP? Yes ____ No ____

Describe the radioisotopic preparation(s):

b. Or are the radioisotopes to be used only in accordance with a project previously approved by the former Radioisotope Committee of this Department? Yes X No ____

Note the project number: H-62

IF ANY OF QUESTIONS 1 THROUGH 5 ARE ANSWERED AFFIRMATIVELY, a detailed analysis of the potential hazards must be appended, including pertinent bibliographic citations and other relevant information.

IF QUESTION 6 IS ANSWERED AFFIRMATIVELY, a completed supplementary form for Radioisotope Administration to Human Beings must be appended. However, this form need not be filed provided that question 6a or 6b is also answered affirmatively. A separate form must be submitted for each radioisotopic species to be administered.

Eugene P. Cronkite
Sponsoring Physician

Committee on Clinical Investigations and
Uses of Radioisotopes

Approval recommended ✓ Date 11/8/63

Disapproval _____ Date _____

V. P. Bond JUN 29 1964
V. P. Bond, M. D.
Chairman, Medical Department

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6/25/63
mlk

Additional sheets to Item D.

Investigators: E.P. Cronkite, L. M. Schiffer

Research Collaborators: L. Wasserman, P. Reizenstein

Experimental Background: The factors that control elemental iron absorption are still poorly understood. In the normal hemopoietic steady state, the amount and type of dietary iron and mucosal efficiency determine absorption. The development of iron deficiency by phlebotomy, chronic bleeding, inadequate dietary iron etc; is characterized by increased absorption of elemental iron. However, other factors are operative. In patients with anemic states other than iron deficiency that have been repeatedly transfused- the body iron stores are greatly increased (siderosis). In these cases iron absorption may be controlled by the hemoglobin level and by the body stores of iron. Saturation of transferrin bears no relation to iron absorption (Crosby-Blood). In other cases it appears that the activity of the marrow may control iron absorption by some undisclosed feed-back system - the more active the erythropoiesis, the more iron is absorbed. These factors are amenable to clinical study.

(a) Influence of hemoglobin level upon iron absorption can be determined in aplastic-aregenerative anemias by determining absorption when very anemic versus absorption after transfusion to high levels and after development of transfusion hemosiderosis.

(b) Influence of relative erythropoiesis in polycythemia vera by determining absorption: (1) before therapy (2) after induction of anemia by phlebotomy in patients given Imferon(R) to replace all iron lost in phlebotomy. (3) In anemic iron deficient PCV and (4) In polycythemic iron deficient patients with PCV.

(c) Study of iron absorption in compensated hemolytic states.

(d) Study of iron absorption in hemochromatosis, cirrhosis etc.

All of the preceding are based upon testing the absorption by using tracer doses of elemental labeled iron. Of great importance, also, is the determination of labeled iron from normal foodstuffs such as beef liver and muscle. This has been obtained by in-vivo injection of Fe59 into a calf and ingestion of its tissues.

PROPOSED AND CONTINUING CLINICAL RESEARCH PROJECTS CONCERNING IRON METABOLISM.

I. Aplastic anemia-Aregenerative anemia.

Objective: Determine influence of hemoglobin level upon iron absorption in the absence of new red cell production.

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Design: (a) Evaluation of patients clinical state and tolerance to anemia in hospital environment at rest.

(b) Constant diet, standard iron.

(c) Measure Fe59 absorption at a hemoglobin of 6-8 gm %.

(d) Transfuse to 12-13 gm. Hgb and do repeat absorption.

(e) Measure other parameters of iron metabolism such as red cell Fe59 uptake

(f) Erythropoietin assay.

Patients: now available. Approximately six more patients will be studied as they are found.

II. Polycythemia Vera

Objective: Determine role of relative rate of erythropoiesis upon iron absorption in PCV in various states of disease.

Design: a) Divide PCV patients into three categories:

1) No chemotherapy, no phlebotomy, nor radiotherapy

2) Phlebotomy and no other treatment

3) Phlebotomy plus chemo- or radio-therapy.

b) Reevaluate patients with respect to iron stores.

1. serum iron and TIBC
2. RBC sizing
3. Reticulocytes
4. iron absorption
5. iron stain in bone marrow
6. plasma iron clearance
7. red cell mass

c) They may then fall into the following groups.

A - Polycythemic iron replete

A1 - Polycythemic iron deficient

B - Normocythemic iron replete

B1 - Normocythemic iron deficient

C - Anemic iron replete

C1 - Anemic iron deficient

d) Alteration of their iron stores and hemoglobin levels may then be attempted.

Patients: New ones and those whom we have been following for several years. Patients with erythrocytosis but without PCV, may be used as subjects also. To study adequately this will necessitate at least six patients in each category and will take years to amass this number of patients.

III. Thalassemia

Objective: Determine iron absorption in patients with T. major and all members of their family and attempt to correlate absorptions with red cell production rates. It is planned to include both parents and as may sibs as practical for each T. major. In this way a representative proportion of T. minor, T. trait can also be studied.

Design: Contact has been made with several institutions who have large quantities of T. major patients (Coney Island Hospital, Albert Einstein Medical College).

IV. Iron-Loading Diseases

Objective: With the advent of Desferrioxamine (Ciba) we now have a new tool with which to study iron metabolism.

a) taken orally this drug prevents iron absorption

b) given intramuscularly or IV it binds iron and increases urinary excretion of this bound compound.

Design: The design of this experiment will depend on patient availability and drug availability.

V. Utilization of Iron in Fe59 Labeled Foodstuffs

Objective: Foodstuff iron is believed absorbed to a lesser extent than elemental iron. Precise data on absorption of iron from foodstuffs is needed. Some studies on vegetables, eggs, milk, chicken, have been performed by others.

Design: A calf labeled with 7 mc of Fe^{59} was slaughtered and the meat frozen for use. Preliminary iron absorption studies have been performed on normal individuals eating this meat and compared to the absorption of elemental iron of the same quantity as in the meat. These studies will be extended to more people and to appropriate patients with iron deficient states not due to bleeding.

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VI. Ferrokinetics

Objective: Complete ferrokinetic data will be obtained where possible, on all patients with anemia of obscure etiology, and those with other interesting illnesses.

1. Serum iron and TIBC
2. Plasma clearance of Fe^{59} (Fe^{52})
3. RBC uptake of Fe^{59}
4. Blood volumes and RCM measurements
5. Organ localization of Fe^{59} and Cr^{51}
6. All pertinent hematologic data.

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File

H-62

Investigators: E.P. Cronkite, L.M. Schiffer (1)
E.P. Cronkite, L.M. Schiffer and J. Cuttner (2)

Title: Proposed addendum (1) and (2) to authorization H-62 - Use of Fe^{59} in selected hospitalized patients.

Date: February 19, 1963

Project: H-62

APPROVED:

COMMITTEE ON USE OF RADIOACTIVE ISOTOPES IN PATIENTS:

George C. Cotzias MD.
George C. Cotzias, Chairman

Lewis M. Schiffer
Lewis Schiffer, M.D.

Eckart Schackow M.D.
E. Schackow, M.D.

V. P. Bond
V. P. Bond, M.D., PhD
(Ex-officio)

J. S. Robertson
J. S. Robertson, M.D., PhD
(Ex-officio)

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[redacted]

H-62

BROOKHAVEN NATIONAL LABORATORY

MEMORANDUM

DATE: 14 February 1963

PRIVACY ACT MATERIAL REMOVED

TO: Committee for the Use of Isotopes in Humans

FROM: E. P. Cronkite, M. D. and L. M. Schiffer

SUBJECT: Proposed addendum (1) and (2) to authorization H-62 - Use of Fe^{59} in Selected Hospitalized Patients.

(1) Investigators: E. P. Cronkite, L. M. Schiffer

The original protocol of December 1959 lists 3 compounds of Fe^{59} as available for administration to patients; Ferric Fe^{59} chloride, Fe^{59} globulin complex and Ferrous Fe^{59} citrate. It is proposed that a fourth compound Ferrous Fe^{59} sulfate be added to the list. It is available commercially in the same concentrations as Ferrous Fe^{59} citrate and in the same specific activity - namely 10 millicuries per milligram of Fe. The same dose of radiation to the blood and whole-body can be expected as that noted in the original protocol. The reason for the use of Ferrous Fe^{59} sulfate instead of Ferrous Fe^{59} citrate is 1) that the use of carrier iron for absorption studies has been changed from ferrous citrate to ferrous sulfate and 2) most investigations in the field of Fe metabolism are performed with Ferrous sulfate and this change would allow for more comparable results.

(2) Proposed addendum (2) to authorization H-62: Use of Fe^{59} in Patients with Thalassemia.

Investigators: E. P. Cronkite, L. M. Schiffer and J. Cuttner.

Patients with Thalassemia (Major, Minor and Trait) have been shown to have varying degrees of defects in iron metabolism. The plasma clearance, and red cell uptake and turnover have been studied extensively but adequate study of iron absorption in these patients is not available.

Inasmuch as many physicians treat the anemia of Thalessemia with iron preparations, it would be clinically very useful to have information regarding this parameter of iron metabolism. Aside from the basic data which may be obtained, prevention of oral iron overloading in patients not needing the excess iron can be achieved. The latter information will be particularly important in the future as new compounds are developed to either prevent iron absorption or to increase body iron excretion (eg. desoxyferramine). It is proposed to study the family of and their relations as the pilot study and perhaps to extend this to other families with

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the disease. It is planned to give 1 to 5 μc to the adult members of the group and 0.5 to 1.0 to the children. It is likely that absorptions will be low, but calculations are based upon complete absorption. Children at the age of 1 year or beyond will be considered as subjects. They will each receive 1 dose only. It is proposed to use 0.5 μc below the age of 10 and 1.0 μc above that age.

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(A) The calculations for total body dose are as follows:

For gamma dosage:

$$D_\gamma = 0.0346\ T\ C\ T\ \bar{g}$$

where

T = 45.1

$\bar{g}$ = as noted in table.

C = noted in table.

AGE	(cm)* HEIGHT	(cm*) RADIUS OF CIRCUMFERENCE	+ $\bar{g}$	Kg * Wt.	0.5 μc - C x 10^{-4}	1.0 μc - C x 10^{-4}
1	74.9	7.59	73.3	10.2	.490	.980
2	86.9	8.08	73.3	12.9	.388	.776
3	96.0	8.32	73.3	15.0	.333	.666
4	103.6	8.56	73.3	17.1	.292	.584
10	140.0	10.3	110	35.2	.142	.284
15	168.0	12.1	120	59.0	.085	.170

For beta dosage:

$$R_\beta = 73.8\ C\ \bar{E}_\beta\ T$$

T = 45.1

E_β = 0.12

C = as noted in table.

* Holt and MacIntosh - Texbook of Pediatrics - Average Values.

\+ Quimby, Feitelberg and Silver - Radioactive Isotopes in Clinical Practice.

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Therefore 0.5 μc oral dose

Age	γ Dose (mr)	β Dose (mr)	Total Body Dose (mr)
1	36.4	19.6	56.0
2	28.8	15.5	44.3
3	24.8	13.3	38.1
4	21.7	11.7	33.4
10	15.8	5.67	21.5
15	10.3	3.39	13.7

For 1.0 μc Oral dose

Age	γ Dose	β Dose	Total Body Dose (mr)
1	72.9	39.1	112.0
2	57.7	31.0	88.7
3	49.5	26.6	76.1
4	43.4	23.3	66.7
10	31.7	11.3	43.0
15	20.7	6.79	27.5

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(B) Dosage to organs which may concentrate iron in thalessemics:

1. Approximate organ weights at young ages:

	Age 1	Age 3
Spleen	30 g.	45 g.
Liver	330 g.	500 g.

2. Using Bertinchamps and Cotzias nomogram for β and γ dosimetry (Science 1958, Vol. 128, p. 988) and assuming total dose of 0.5 μc is concentrated in spleen or liver, then infinite dose of radiation using a sphere model is as follows:

	Age 1	Age 3
Spleen	5.44 rads	3.99 rads
Liver	.71 rads	.52 rads

LS:aw
copies to all members of the Committee

1179415

December 9, 1959

Committee for the Use of Isotopes in Humans:

Walton W. Shreeve, M. D., Ph. D., Chairman
Elmer E. Stickley, Ph.D.
Donald C. Borg, M. D.
John L. Bateman, M. D.
James S. Robertson, M. D., Ph. D., Ex Officio
Lee E. Farr, M. D., Ex Officio

Investigators: E. P. Cronkite, I. Brodsky, S-A. Killmann

Request is made for the authorization for the use of Fe^{59} in the form of Ferric Fe^{59} chloride, Fe^{59} Globulin Complex and Ferrous Fe^{59} citrate in selected hospitalized patients.

Fe^{59} has been used since 1949 as a research and diagnostic tool in studying patients[1]. It is at present used in many hospital centers primarily as a diagnostic tool. The two primary techniques used have been to study (1) the clearance rate of Fe^{59} from the plasma and (2) the rate of uptake of radioactive iron by the red blood cells.

(1) The clearance rate is usually expressed as the length of time required for one-half of intravenously injected Fe^{59}, in the form of globulinate, ferrous citrate or ferric chloride, to disappear from the circulation. Normally, this half-time is about ninety minutes and 95 per cent is cleared in six hours. It is accelerated in polycythemia, the leukemias, hemolytic anemia, pernicious anemia, the anemias of infection and malignancy and iron deficiency. It may return to normal as the basic disease is brought under control.[2]

(2) The rate of uptake of radioactive iron by the red blood cells can be obtained by the daily determination of the radioactivity of the circulating erythrocytes (cpm/ml whole blood).

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The formula used for this determination is:

$$\frac{\text{(counts per minute/cc red cells) x red cell volume x 100}}{\text{total counts of radioiron injected intravenously 1-20 days previously}}$$

In the normal about 85 per cent of the administered dose is incorporated into erythrocyte hemoglobin in 10 days. There is a markedly decreased utilization in aplastic anemia and an increased utilization in such conditions as polycythemia vera and iron deficiency anemia. The amount of radioactivity entering the circulating red blood cells over a period of 15-20 days is a composite of three interdependent mechanisms of iron metabolism: the serum iron transport mechanism, the quantity and mobility of the iron stores, and the rate of formation of hemoglobin by the bone marrow for production of red blood cells[3].

It is proposed to use , a patient on Pavilion 3, as a subject for Fe^{59} studies. This 46 year old female has a known daignosis of osteosclerosis and agnogenic myeloid metaplasia. She has a marked thrombocytopenia associated with episodes of severe bleeding plus anemia with a strong hemolytic component as determined by previous Cr^{51} studies. Although it is realized that the spleen is a active site of blood formation in this condition, it is felt that its role in blood destruction as determined by its markedly increased Cr^{51} sequestration and possible platelet destruction may greatly overshadow its role in blood production. Therefore, splenectomy in this patient is being strongly considered. However, before this decision is reached an evaluation of erythropoiesis by means of Fe^{59} would be of value. In particular <u>in vivo</u> counting over the spleen, liver and sacrum (bone marrow) immediately after an i.v. dose of Fe^{59} may give us some idea as to the possible role in blood formation that the liver and bone marrow are playing

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in this patient as compared to the spleen. In the normal, counting over the spleen, liver and bone marrow (sacrum), the first few hours after intravenous injection of Fe^{59} as $FeCl_3$ using a collimated scintillation crystal detector, shows a rapid rise of radioactivity reaching a peak within four hours and then falling off so that values of 25 per cent of the peak values are reached in five days and background values are reached in about ten days. It may even be desirable to repeat Cr^{51} study in conjunction with Fe^{59} in evaluating this patient[4].

Radioactive iron, Fe^{59}, has a physical half-life of 45.1 days, decaying with emissions of beta 0.27 mev (46 per cent), 0.46 mev (54 per cent) and 1.56 mev (0.3 per cent) and three gamma emission of 0.191, 1.098, 1.289. It is prepared (Fe^{58} (n, γ) Fe^{59} (target enriched in Fe^{58})) in Oak Ridge with a specific activity of 2000 mc of Fe^{59} per g of iron and shipped in 1 N HCl in a concentration of > 0.1 mc/milliliter[5]. The purity is >99 per cent (exclusive of Fe^{55}). Fe^{59} is now commercially available from Abbott Laboratories. It will probably also be available in the very near future from other pharmaceutical firms such as Squibb. It is prepared in either the form of ferric chloride, ferrous citrate or iron globulin complex. The cost of $Fe^{59}Cl_3$ and ferrous citrate is \$45.00/250 μc and \$58.00/500 μc. The cost of the globulin complex is \$200.00/mc which is the minimum shipment. The advantage of the globulin complex is that it does not have to be mixed with the patient's or a donor's plasma prior to administration. It is felt by some that the use of Fe^{59} globulin complex will give more reproducible and reliable results in the Fe^{59} clearance study[2]. The Abbott preparations are sterile and pyrogen free and ready for immediate patient use. Upon arrival the receipted material

(Fe^{59}) will be checked in the 100 channel pulse height analyzer and on aliquot assayed against known standards in a scintillation well counter prior to administration to a patient.

The proposed dose of Fe^{59} is 4-10 μc to be administered intravenously. $Fe^{59}Cl_3$ or Ferrous Fe^{59} citrate will be administered i.v. in 20 ml. of the patient's or donor serum, after it has been permitted to incubate with the serum for 15-30 minutes at room temperature. The amount of iron injected is so small (5 ug) that it may be considered a truly tracer dose. The amount of radioactivity administered to the whole-body is also well within permissible limits. Below is given a sample calculation of the total amount of radioactivity received by a 70 Kg. man, 170 cm. tall. For Fe^{59} given intravenously the critical organ is considered to be the blood[6]. Since Fe^{59} emits both beta and gamma irradiations and since the blood courses through the entire body, it was felt that irradiation should be expressed on the basis of <u>whole body irradiation</u> because the gamma irradiations would certainly not be restricted to only the blood stream. The dosage used in the calculations is 10 μc. The effective half-life (T) of Fe^{59} is 27 days[6]. The $\bar{E}_\beta$ is 0.120 mev[7] and $\bar{g}$ is 126 for a 70 Kg. man 170 cm. tall[3]. The point source γ-ray dose - rate constant, Γ, cm^2-r/mc-hr. is 6.13[7].

$$D_{\beta+\gamma} = C\,T\,(73.8 \times \bar{E}_\beta + 0.0346 \times \bar{g} \times \Gamma)^3$$

$$= \frac{10}{700000} \times 27\,(73.8 \times 0.120 + 0.0346 \times 6.13 \times 126)$$

$$= 0.137\ r = 137\ mr.$$

The above equation is given in reference 3, page 104. It gives the addition of beta and gamma doses expressed in rads.

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The above calculation of 137 mr for one dose of Fe^{59} of 10 μc is well within limits of safety. The maximum permissible total body burden for Fe^{59} is 13 μc[7].

Although the effective half-life of Fe^{59} is given as being 27 days[6], it is quite possible that this figure is in error. It has been well established from studies of iron metabolism, that iron is markedly conserved by the body and therefore very little is excreted. The effective half-life is therefore probably closer to the physical half-life. This point could be checked easily in the whole body counter. Using the physical half-life 45.1 days to represent the effective half-life, the dose administered in the hypothetical case above would be 0.229 rad or 229 millirads.

The question may be raised as to whether or not it is accurate to calculate the dosage delivered from the beta irradiations of Fe^{59} on the basis of whole body irradiations. The average energy of the beta irradiations ($\overline{E}_\beta$) is 0.120 mev[7]. The average range of the emissions is 0.2 mm.[7]. When one considers the size of the capillaries through which the blood courses, this represents in a sense total body irradiation. However, if one assumes that the entire beta emission is absorbed by the blood which is the critical organ for Fe^{59}[7], the total dose received by the blood from 10 μc would be 0.800 rads. This dose is well within limits of safety. The derivation of this figure is given below. The average weight of the blood is assumed to be 5400 Gm.[7].

$$D_\beta = 73.8\ C\ \overline{E}_\beta\ T$$

$$= 73.8 \times \frac{10}{5400} \times 0.120 \times 45.1$$

$$= 0.800 \text{ rad} = 800 \text{ millirads}$$

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The amount of beta irradiation delivered to the bone marrow is also of interest. However, this will be comparatively quite small because the amount of Fe^{59} taken up by the marrow is very rapidly utilized in the process of erythropoiesis and discharged with the newly produced red cells into the peripheral blood. As pointed out in the beginning of the paper approximately 85 per cent of the administered dose of Fe^{59} is incorporated in erythrocyte hemoglobin in ten days. The effective half-life of Fe^{59} for the bone marrow is therefore about 5 days. The total weight of the normal bone marrow is approximately 1500 Gm.[7] Assuming complete absorption of the beta irradiation by the marrow the dose delivered to bone marrow by 10 μc. of Fe^{59} injected intravenously would be 297 millirads.

$$D_\beta = 73.8\ C\ \overline{E}_\beta\ T.$$
$$= 73.8 \times \frac{10}{1500} \times 0.120 \times 5$$
$$= 297 \text{ millirads}$$

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The above calculation is also overestimated because a certain percentage of the administered dose in the normal individual will not be directly utilized in red cell production but will merely exchange with the fixed iron stores.

The irradiation dose delivered to the bone marrow of

will be much less than that calculated for the normal. In the presence of large numbers of circulating normoblasts and reticulocytes, a significant percentage of the initial dose will be taken up directly by the circulating blood. In addition there will be a greater exchange with fixed iron stores.

It is requested, therefore, that permission be given to use Fe^{59} as a diagnostic tool where indicated in certain hematological

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problems. As a rule repeat doses will not be necessary but this could be done because of the small amount of irradiation involved particularly if smaller doses such as 2-5 μc are used after waiting at least one physical half-life before repeating the dose.

Walton W. Shreeve

Walton W. Shreeve, M. D., Chairman

Elmer E. Stickley

Elmer E. Stickley, Ph.D.

Donald C. Borg

Donald C. Borg, M. D.

John L. Bateman

John L. Bateman, M. D.

J. S. Robertson

James S. Robertson, M. D., Ph. D.
Ex Officio

S. P. Cronkite Acting

Lee E. Farr, M. D.
Ex Officio

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6. Behrens, Charles F., Atomic Medicine. Williams and Wilkins, pp. 244-245, 1959.
7. Hine and Brownell. Radiation Dosimetry. Academic Press, 1956.

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