



ANL

CENTER FOR HUMAN RADIOBIOLOGY August 27, 1971

719177

MEMO TO: R. J. M. Fry BIM

F R O M: A. F. Stehney afst RPY

SUBJECT: Revised Research Proposal for Study of Radium Patients

Attached is a revision of the Research Proposal for the Study of Effects of Internal Radiation on Humans, referring to diagnostic procedures proposed for radium patients, originally submitted June 28 and revised and expanded in accordance with suggestions made by your Committee. The comments below refer to queries bearing the corresponding numbers in your memorandum of 27 July 1971.

- 1.) A detailed analysis of radiation dose from skeletal radiographic examination has been made by L. D. Marinelli (Attachment 3). Risk-benefit and frequency of examination for radium patients are discussed by A. M. Brues (Attachment 4).
- 2.) The sentence in question has been stricken from the proposal.
- 3.) Your suggested consent form is a great improvement on the original form we proposed and has been adopted almost word for word (Attachment 1).
- 4,5.) The comparison of X-ray techniques described in Attachment 3 indicates that the ANL and MIT procedures are in keeping with good practice elsewhere. We plan to measure skin doses and to explore possible improvements when new X-ray equipment now on order is delivered.

AFS/cf  
Enclosures

BEST COPY AVAILABLE

- cc: A. M. Brues - RPY  
D. M. Givens - H. D.  
L. D. Marinelli - RPY  
R. E. Rowland - RPY  
F. W. Strehl - H. D.

1145012



PROVENANCE

REPOSITORY: OFFICE OF HUMAN RADIATION  
EXPERIMENTS (OHRE)

COLLECTION: PLUTONIUM INJECTION INVESTIGATION  
FILES (OHRE 1)

BOX: 2

FOLDER: EXTRA COPIES

1145012A

Project Title: EFFECTS OF INTERNAL RADIATION ON HUMANS

1. Objectives

The research objective is to obtain quantitative relationships between radiation dosage and effects on humans by study of radium-dial painters and other people with body burdens of radioactive isotopes. From another point of view, the objective is to detect individuals whose body burden and physical condition are such as to indicate the need for close medical attention; early detection of pathological conditions should increase the probability of cure for the patient and may aid in developing improved therapy.

2. Scope and Location of Proposed Research

This proposal covers medical studies and radioactivity measurements of humans exposed to internal radioactivity under circumstances beyond our control. In general, the subjects come to our attention because of previous industrial medical, accidental or natural exposure to radioactive isotopes. Procedures which require administration of medication or radioactive materials are included in this proposal only when used as normal diagnostic techniques in medical practice.

Patients will be examined in facilities associated with Argonne National Laboratory or with the Massachusetts Institute of Technology. Work at the latter site is funded under a subcontract in order to handle patients who live in the eastern part of the United States. We also maintain a small field office at St. Mary's Hospital, East Orange, New Jersey, for the purpose of locating and contacting patients in that area.

ANL: Medical examinations, including complete skeletal X-rays will be done in facilities of the Health Division. It may be necessary to have patients admitted to local hospitals for procedures requiring several days of observation, such as measurements of metabolic balance. In addition, we anticipate that medical studies will be made at the Argonne Cancer Research Hospital for patients with high body burdens of radioactivity or with indications

of malignant growths. Radioactivity measurements will be made in the low-background facilities and laboratories of RPY in Building 203 at Argonne.

MIT: Medical examinations will be done in the student Health Center or at the Clinical Research Center at MIT. Complete skeletal X-rays are to be taken at the Mount Auburn Hospital. Radioactivity measurements will be made in the laboratories of the Radioactivity Center at MIT.

3. Description of Radium Patients

Our immediate concern is with a large group of people who were exposed to intake of radium as dial painters or received radium as a therapeutic measure. Some information on the age and sex distribution in this group may help the Committee in evaluating this proposal. The table below provides such data for 725 patients in our study who were living in 1969 and have had radioactivity measurements made:

RADIUM PATIENTS LIVING IN 1969

Dose Range (1) (Rads)	Women (2)			Men (2)		
	No.	Age Range	Av. Age	No.	Age Range	Av. Age
1000 or more	62	58-92	68.5	9	57-86	68.2
100 - 1000	142	43-92	67.2	15	46-91	68.2
1 - 100	255	11-90	63.9	85	20-88	65.3
Less than 1	131	14-83	62.8	26	32-83	64.0
Sum	590	----	----	135	----	----

(1) Doses calculated to 1969

(2) Years of age in 1971

It should be mentioned that the dose is calculated as the total alpha-particle energy released (from isotopes of radium and their radioactive descendants) from intake to 1969, averaged over the skeletal mass. A present



body burden of about 0.5  $\mu$  Ci Ra corresponds to 1000 rads accumulated in 40 years. Included in the above are 7 women and 2 men under 30 years of age and all these have dose accumulations of less than 3 rads.

4. Principal Staff

Center for Human Radiobiology, ANL

R. E. Rowland, Director

Ph.D., Radiation Biology, University of Rochester, 1964

A. F. Stehney, Scientific Coordinator

Ph.D., Chemistry, University of Chicago, 1950

Austin M. Brues, Medical Consultant

M. D., Harvard University, 1930

Henry F. Lucas, Jr., Group Leader, Radiochemistry

B. S., Chemistry, University of Chicago, 1950

John H. Marshall, Group Leader, Bone Metabolism

Ph.D., Physics and Biology, Massachusetts Institute of Technology, 1952

Mary Rallo, Staff Assistant (New Jersey Field Office)

R.N., St. James School of Nursing, 1936

Elizabeth Rhoads, Staff Assistant

M.A.T., Biology, Notre Dame, 1970

John Rundo, Group Leader, Body Radioactivity

Ph.D., Biophysics, London University, 1958

Harvey A. Schultz, Custodian of Patient Records

Ph.D., Physics, University of Illinois, 1937

Health Division, ANL

Francis W. Strehl, Director

M. D., University of Illinois, Chicago, 1951

Dingess M. Givens, Staff Physician

M. D., Duke University, Durham, 1957

Radioactivity Center, MIT

Robley D. Evans, Principal Investigator  
Ph.D., Physics, California Institute of Technology, 1932

Mary Margaret Shanahan, Deputy Principal Investigator  
A. B., Chemistry, Radcliffe College, 1936

Samuel D. Clark, Associate Director, MIT Medical Department  
M. D., Harvard University, 1935

Melvin H. Chalfen, Staff Physician, MIT Medical Department  
M. D., Tufts University School of Medicine, 1954

Part-Time Medical Consultants, ANL

Melvin H. Chalfen  
M.D., Tufts University School of Medicine, 1954

Jan Lieben  
M. D., University of Liverpool, 1943

E. David Nordberg, Radiologist, (Mount Auburn Hospital)  
M. D., Jefferson Medical College, Philadelphia, 1960

R. Harrison Ryder  
M. D., College of Physicians and Surgeons, Baltimore, 1913

William D. Sharpe, Pathologist  
M. D., Johns Hopkins University, 1958

5. Procedures to be Performed

The procedures covered in this submission are diagnostic in nature. They are intended to evaluate the health of the patient, to measure body radioactivity and to study metabolic patterns. All procedures will be performed at the direction of a physician except for radioactivity measurements and measurements of bone mineral mass.

1) Physical Examination. A medical history will be taken and normal examination procedures will be done by a physician or technicians under his direction. A tentative protocol for the examination is attached.

2) Skeletal X-rays. Complete skeletal X-rays will be made at intervals of not less than two years for most patients. More frequent exposures, especially of the skull, pelvis, and long bones, may be requested when deemed advisable for diagnostic purposes by the responsible physician. Exposures are estimated to be less than 0.5R (mean marrow dose) and about 0.7R (mean to endosteum). A sample work-sheet of X-ray exposures is attached.

3) Special Blood Samples. Some patients will be asked to contribute 10-20 ml of blood which we shall examine for chromosome changes in cells. High-level patients may be asked to give 200 ml of blood, if deemed capable of doing so by the physician in charge. This quantity is required for measurements of the concentration of circulating radium.

4) Excreta. We will attempt to measure the rate of excretion of radioactivity for some patients. In order to obtain complete collection of urine and feces over a period of several days, it may be necessary to make special arrangements such as residence in the metabolic ward of a hospital.

5) Bone Mineral Mass. Each patient will have a measurement made of the bone mineral mass in the forearm. This will be done by measurement of the transmission through the arm of soft X-rays from a source, e.g.,  $^{125}\text{I}$ . The total dose delivered by the beam, collimated to a 2 mm width, is 1.5 mr to the bone and 0.3 mr to soft tissue above the bone.

6) Body Radioactivity. The patient sits or reclines for periods of about 30 minutes while a detector is nearby. This is done in heavily shielded rooms and may require special (clean) clothing and a shower. The total counting time required will normally be about one hour.

7) Breath-Radon. The patient breathes into a mouthpiece and exhaled air is collected in a flask or plastic bag. Back pressures are less than 0.5 lb per square inch, and the effort required is considerably less than that to inflate a toy rubber balloon. The time required for breath equilibration and collection will normally be less than one hour.

#### 6. Risks and Benefits

Patients participating in this program will gain the benefits of regular physical examinations. They will be studied by medical and scientific personnel well acquainted with symptoms of exposure to radioactivity and will be aided in seeking appropriate medical treatment should the occasion arise. It is already known that patients with body burdens in excess of 0.5  $\mu$ Ci Ra have increased incidence of bone sarcomas and carcinomas of head tissues; such patients should be examined frequently. Also, many of the patients are old, and some live far from urban medical centers, so even those with low burdens of radioactivity should benefit from the diagnostic facilities made available to them.

The risks involved are no more than those acceptable in routine medical examination with the possible exception of the X-ray examination. Since a skeletal dose of about 0.5 - 0.7 roentgen is delivered in a single complete survey, one may question the advisability of this procedure for patients already burdened with radioactivity. However, the additional risk, if any, is small compared to the high probability of serious bone disorders for patients with large burdens of radium, and the use of X-rays is justified by the need for thorough diagnostic examinations. The frequency and scope of skeletal radiographic examinations will depend upon the age and radium burden of the individual patient. Calculations of the X-ray dosages, and a description and explanation of the proposed limits of X-ray exposure for the various categories of patients, are attached.

#### 7. Informed Consent

Attached is a copy of a consent form ("Consent for Medical and Research Studies") which indicates the nature of information to be given patients on a

routine basis. The oral explanation of the nature, demands, and foreseeable risks will include simple descriptions of the type given above under "Procedures to be Performed" and any other information which the examining physician may consider appropriate to individual patients.

As a practical matter, it will usually be necessary to bring the patient to the place of examination and obtain preliminary information about the patient before the physician can explain the tests and obtain the signature of the patient. Also, time schedules may require that radioactivity measurements or other procedures be performed before a physician is available to see the patient. In this case, the explanation will be given by a qualified person designated by the Director of the Center for Human Radiobiology or his Deputy.

Patient contacts will usually be as follows:

1) Reasons for the study and the general nature of the tests will be described to the patient by the case worker who contacts the patient and schedules the appointment. These contacts may be entirely by telephone, although personal visits will be made when feasible.

2) A letter confirming appointment dates and travel arrangements will be sent to the patient. A copy of the consent form with the list of procedures to be performed will be attached, and the patient will be informed that he will be asked to sign the form when he comes for the examination. In this way, there will be a record of what is expected of the patient and he will not be surprised by the request for a release.

3) Explanations will be given and the consent form signed prior to any test listed on the form. If tests other than those listed in the confirmation letter appear to be advisable, the consent of the patient must be obtained and the additional items initialed by the patient prior to signing by the investigator. If new tests are scheduled at a later time, a new consent form must be signed.

#### 8. Rights and Welfare of the Patients

As former radium workers, many of the patients have lived most of their adult lives with a sense of vulnerability to terrible diseases from radiation. Our program offers help and guidance, but in great part they are accepting personal

inconvenience in order to make a valuable contribution to knowledge of radiation effects. We feel quite strongly that such patients are to be treated gently and respectfully, and that every effort should be made to avoid offending their sense of propriety.

Procedures to ensure the privacy of patients are already in operation. All records identifying the patient by name are kept in locked files in locked rooms. Access to such records requires the approval of the Director of the Center for Human Radiobiology or his Deputy. Each patient is assigned a case number which is the only type of identification to be used in publications. Interviews and tests are conducted in non-public offices and laboratories with only necessary personnel present.

A very capable, mature woman with hospital experience has been designated to look after the patients. Her main responsibility is to ensure that suitable arrangements for travel and accommodations have been made, and to provide for the safety and well-being of the patient. The patients are permitted to choose a traveling companion, or nurse, whose expenses are paid by us. If necessary, we will provide an escort for the entire trip.

As indicated earlier, the physicians and facilities of the Health Division are to be employed for medical procedures involving the patients at ANL. If an emergency should arise, the 24-hour ambulance service at ANL is available by dialing 13. During the day, the fire department ambulance picks up a physician at the Health Division. At night, the ambulance goes to the victim while the ANL Security Office telephones for a physician from a list which has been provided. Emergency treatment is given at ANL for heart attacks, shock, acute asthma, and accidents. Then the patient is taken to La Grange Memorial Hospital, about 10 miles distant, and specialists are called if needed.

9. Attachments

1. Consent form .
2. Suggested protocol for medical examination.
3. Estimate of dose to marrow from ANL X-ray survey -- L. D. Marinelli.
4. Risk and exposure considerations for skeletal X-rays -- A. M. Brues.

CENTER FOR HUMAN RADIOBIOLOGY

Argonne National Laboratory

VOLUNTARY CONSENT FOR MEDICAL AND RESEARCH STUDIES

I, \_\_\_\_\_, do hereby acknowledge that I have volunteered to participate personally in the clinical and research studies listed below. I have been fully informed of the research procedures to be followed, their possible benefits and attendant risks and discomforts, and the reasons for pursuing the research and its general objectives. I understand that I may withdraw from the studies at any time.

Further, I understand that these studies are for the purpose of evaluating my health and body content of radioactivity, and I confirm that no promise of subsequent medical treatment has been given or implied. I hereby give permission for emergency treatment by qualified personnel at no expense to me for conditions which may arise at places or time periods associated with these studies.

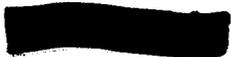
Date \_\_\_\_\_ Patient's Signature \_\_\_\_\_

Witnessed by \_\_\_\_\_

CLINICAL AND RESEARCH STUDIES TO BE PERFORMED

Investigator's Statement:

I have explained fully to the patient the research procedures to be followed, their possible benefits and attendant risks and discomforts, and the reasons for pursuing the research and its general objectives.

Date \_\_\_\_\_ Investigator's Signature \_\_\_\_\_ 

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CENTER FOR HUMAN RADIOBIOLOGY

Argonne National Laboratory

Suggested Protocol for Medical Examination at ANL Health Division

- 1) Patient fills out questionnaire.
- 2) Nurses take preliminary data: weight, height, etc.
- 3) Physician goes over questionnaire with patient.
- 4) Standard ANL examination is given, plus special tests considered advisable.
- 5) Neurologic test (reflexes, muscle power, etc.).
- 6) Audiogram.
- 7) Blood and urine samples for clinical tests.
- 8) X-ray examination of skeleton.

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