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Subject: Proposed Experiments with Alpha Emitting Elements.

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U. S. Engineer Office, Manhattan District, Oak Ridge, Tenn., 4 November 1944
To: The Area Engineer, Rochester Area, Rochester, New York

The attached "Proposed Experiments with Alpha Emitting Elements" has been reviewed. The proposals are adequate and are approved. Investigations should be initiated without delay and completed as rapidly as possible.

For the District Engineer:

Incl. N/C (1 cy w/d)

STAFFORD L. WARREN
Colonel, Medical Corps
Chief, Medical Section

Distribution:

Cys 1 & 2 - addressee
Cys 3 & 4 - Classified Files
Cy 5 - Medical Section w/d

PROVENANCE

REPOSITORY:	OFFICE OF HUMAN RADIATION EXPERIMENTS (OHRE)
COLLECTION:	PLUTONIUM INJECTION INVESTIGATION FILES (OHRE 1)
BOX:	3
FOLDER:	IRRELEVANT MATERIAL

[redacted] 5 a

Proposed Experiments with Alpha Emitting Elements.

Background.

Plutonium and other very active alpha-emitting elements are being handled by personnel of the Special Engineering Corps on an increasing scale. Therefore the hazards to personnel of alpha-emitting material absorbed internally is of growing concern to the Medical Section.

From long experience with naturally occurring alpha-emitting elements, especially with radium, and its disintegration products, it is known that the effect of alpha-emitting elements may be considered in three separate phases. Amounts large enough to be quickly lethal produce death by blood dyscrasias or possibly by acute kidney injury. Amounts of radium great enough to produce death in a few months apparently do so by damage to the blood-forming organs. There is some evidence that polonium may occasionally produce chronic kidney damage sufficient to cause death in a few months, although here too the damage to the blood organs probably predominates.

At least with radium, however, dosage too low to cause death by the above mentioned effects is known to cause bone necrosis and malignant changes, leading to death by cancer. The dosage known to be routinely fatal because of changes of this type produced, is severalfold lower than that causing death by a more direct injury, such as has been mentioned above.

It is possible experimentally to study in animals the more acute types of injury mentioned above, with a reasonable expectation of determining the dosage of any alpha-emitting material necessary to produce acute damage in the human. The time needed, however, to carry out any series of experiments which are of the order of the lifetime of the experimental animal in duration is considerable; probably measured in terms of many months or several years. Also the legitimacy of extrapolating such an effect as the production of malignant changes from an animal with a short life-span to the human is open to question.

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There is one approach to this problem that seems capable of providing a reasonably satisfactory answer to the question of the chronic toxicity of an alpha-producing element in the space of a few months. The rationale behind this approach is as follows: If another alpha-emitting element of long halflife is distributed in the body, in a manner quantitatively similar to that of radium, then one may suppose that the tissue injury produced, when compared with that produced by radium, will be equal, if the alpha-activity, measured in terms of ionization per gram of tissue, is equivalent.

In order to make this calculation, it is necessary to know as a function of time the distribution in the body, both of radium including its daughter substances, and of plutonium or any other alpha-emitting element for which one wishes to determine the hazard after absorption into the body. Also, for this information to be of any practical usefulness, one needs to have a quantitative method for estimating the amount of the alpha-active element in the human body. Moreover, a very useful check upon the accuracy of the above calculations should be a knowledge of the acute and semiacute toxicity (experiments extending over 2 or 3 months) of these alpha-emitting elements compared with radium.

Certain of this information is already known, or is in the process of being obtained by research groups associated with the Medical Section. We understand that the group at Chicago and groups associated with Dr. Hamilton and Dr. Hampelmann are doing animal tracer work with plutonium. At Rochester a thorough survey of the literature concerning the metabolism of radium and radium poisoning, both of humans and experimental animals, is being made.

Adequate data are not yet available concerning the acute and semiacute lethal doses of plutonium and polonium. Also, from a preliminary survey

of the literature, it seems probable that data concerning tissue distribution and metabolism studies, as well as the acute and semiacute effects of radium, are not adequate. Adequate facilities for obtaining these data mentioned above are available at Rochester. We therefore propose to carry out the experiments listed below. Also we propose to check the quantitative methods for plutonium being developed by Dr. Hempelmann and his associates and, if opportunity arises, to check on humans the experiments he is scheduled to carry out concerning the relation between plutonium content of the body and amounts found in excreta and blood samples.

Proposed Experiments.

A. Lethal dosage of postum in rats.

Isotonic postum chloride will be administered in single intravenous doses to rats. After a preliminary experiment with 12 rats, in which the approximate dose, 50% lethal in 20 days, is determined, 5 groups of 20 rats each will be given doses around this point with sufficient spread to determine the approximate shape of the lethal curve. About 15 of these rats will be kept for a period of 3 months. Complete autopsy and hematological studies will be made on about one-fourth of these animals, including several living at the end of the 3-month period.

B. Tracer studies with radium.

We now have precise quantitative methods available for radium determinations in tissues by the radon emanation method. Also sensitive apparatus for gamma ray measurements is easily available. Since, however, our radon apparatus is in almost continuous use, any extensive program will make necessary construction of duplicate apparatus. The actual tracer work done with radium will depend to a certain extent upon our survey of the literature concerned with radium metabolism and poisoning. We tentatively propose, however, to carry out complete tracer studies, including balance experiments, on rats kept

in metabolism cages for periods of one, ten and 50 days. The total number of rats used will probably not exceed 15.

C. Lethal studies with radium.

The exact extent of this program again will depend upon the results of our survey of the radium literature. We tentatively propose to carry out work upon the same scale and over the same ground as suggested for postum in Part "A" above.

D. Lethal studies with plutonium.

We propose here to cover, using the rat as the experimental animal, about the same ground as suggested for the lethal postum experiment.

E. Tracer studies with plutonium.

We do not propose an extensive tracer study with plutonium, since this is being carried on by other groups associated with the Medical Section. It seems desirable, however, to have an independent check upon the quantitative methods being developed by Hempelmann and his coworkers. This we propose to do. We are particularly interested in assays of urine, and excreta as a measure of plutonium concentration in the body. Also it may be possible, at some future time, because of our hospital connections, to carry out a limited number of tracer studies on human subjects. This seems to us important work to be carried out if possible, because of the pertinent information it will give.

This tracer work with plutonium is tentatively scheduled for a time when our work with postum is essentially complete, and the tracer work with radium is well under way, so that our somewhat limited personnel with wide experience and skill in chemistry will be used efficiently.

F. Proposed work with dogs.

Data available to the Rochester project indicate that dogs are considerably more sensitive to radioactive injury than rats, and possibly closer to the human in this respect. We therefore propose to carry out lethal dose experiments on dogs with the above elements to the extent to which the elements

and animal facilities can be supplied. It seems probable that cages for fifteen to twenty dogs will be available for this work.