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MUC-ERR-209
This document consists of 34 pages and 0 figures.
No. 10 of 50 copies. Series A.
DOE-A30887

700241

Date: June 11, 1946

Subject: Distribution and Excretion of Plutonium

Chapter VII, Volume 20 A, PPR

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Acknowledgement

It has been difficult to give credit to specific individuals for their contributions which are included in this chapter. Some of the work was done at other sites and privately communicated to us.

Specifically, we are indebted to Dr. Wright Langham and associates for information concerning the cupferron-chloroform procedure, to Dr. K. G. Scott and his associates for the information on the hexone and T.T.A. extraction procedures and to Dr. M. D. Taylor, Mr. L. E. Motta, Mr. D. Hovinson, Mr. Harold Delaney, Miss J. A. Jackson, Miss Cordelia Brown, and Miss Wilana Monroe, all of our group, for testing and working out most of the procedures.

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1. Introduction

Following the discovery of plutonium, the determination of its half life as 24,300 years, and the fact that the material is alpha active, it became obvious that elaborate precautions were necessary if the worker was to be protected from harm. Experience in the radium industry had indicated clearly that very small amounts of the radium element deposited in the body were capable of producing serious illness or death. As a result of these considerations, the conditions under which plutonium is handled in the laboratory have been ringed about with elaborate protective regulations and devices.

In addition, however, it seemed highly desirable, if not essential, to know as precisely as possible the amount of plutonium in the individual worker. Animal experimentation indicated that the plutonium content of the urine and feces would be a useful guide to the total amount of plutonium in the body. It was decided to use urine for the routine determination(3) primarily because of the greater ease in handling urine samples. As will be discussed below, it appears that in humans the amount of plutonium excreted per day is greater in the urine than in the feces.

Initially, a tentative maximum permissible body content of plutonium was established on an arbitrary basis. From purely physical considerations it seemed that plutonium,

weight for weight, should be approximatoly one-fiftieth as toxic as radium. Since the tolerance amount of radium is generally accepted as 0.1 microgram in the body, the plutonium tolerance value was initially set at 5.0 micrograms in the body.

In order that one might estimate the plutonium content of the body through analysis of the urine, it was necessary first to establish the excretion rate. Preliminary experiments[1] with rabbits indicated that after the first two or three weeks of plutonium intake, approximately 0.01% of that retained in the body is excreted in a 24-hour urine specimen. Many excretion experiments with other animals and man have shown that this is nearly the correct value for the sub-acute excretion rate. Recent work discussed elsewhere indicates that this figure may be greater than the true excretion rate of plutonium which has been in the body for a year or more. It is possible that the figure of 0.01% may have to be reduced in the future.

If 5 micrograms is to be the body threshold, and 0.01% excretion is assumed, then analytical procedures capable of detecting 28 alpha counts per minute (plutonium) in a 24-hour urine specimen, or 2 counts per minute in a 100 ml specimen should be adequate. An adsorption procedure, described later, was designed specifically to assay 100 ml specimens. Any specimen showing less than 2 alpha counts per minute was not considered significant. This procedure

served its purpose well. However, when it became apparent that the factor of fifty between radium and plutonium toxicity was too high, it was evident the method was not sufficiently sensitive. Comparative toxicity studies with these two elements showed that a factor of ten would be much safer and therefore the plutonium tolerance threshold was lowered to one microgram.

If the tolerance threshold is 1.0 microgram, the analytical procedure should detect at least 0.2 micrograms in the body, therefore 0.2 x 10^{-4} microgram in a 24-hour urine specimen would be significant. Since the average urine specimen used in Chicago is approximately 1/3 of a 24-hour sample, the method must then be sufficient to detect 0.7 x 10^{-5} microgram or 0.4 alpha counts per minute of plutonium. Smaller samples present an even more difficult problem.

The problem of detecting such small quantities of plutonium was mainly one to be solved by the development of adequate counters. Dr. Jesse and associates have produced counters with backgrounds of less than 0.1 count per minute. With such counters 0.2 counts per minute can be detected with fair accuracy. Counting times are long, of course.

It should be pointed out that contamination is one of the greatest sources of error in the determination of low alpha [illegible]. This will be demonstrated very clearly in the results of the survey of project personnel. It is necessary that collection, handling and assaying of the

urine be carried out under "sterile" conditions.

It is the purpose of this chapter to present a detailed description of the methods used in the detection of plutonium in humans and to briefly discuss the results. In closing, suggestions are given for the establishment and operation of a laboratory for the detection of plutonium in individuals working with or in areas contaminated by the element.

2. Estimation of Plutonium in the Body

2.1 Methods of Urine Analysis: A survey of the analytical methods for plutonium used by the chemistry division revealed that with certain modifications some of those might be used to assay urine. A direct lanthanum fluoride precipitation from a small volume of acidified urine is adequate for many purposes. Where the volume is large and the concentration of plutonium is exceedingly small, such a method is not applicable as too large a quantity of lanthanum is required. In addition, certain salts in the urine may cause difficulty.

In the development of analytical methods applicable to urine analysis the time element as well as manpower requirements to assay a given number of samples were considered. It was felt that an adsorption procedure would offer the greatest possibility of routinely assaying daily the largest number of specimens with a minimum of personnel. As was

It was previously mentioned that plutonium is eliminated from the body in the urine at a fairly constant rate--the rate being approximately 0.01% per day. This figure was proposed on the basis of some very preliminary excretion studies on rabbits(1). Subsequent experiments on mice, rats, and dogs showed that the excretion rate may vary by a factor of five in the different species(11) It was felt necessary to establish independently the excretion rate of humans.

The fecal plutonium excretion, however, varied as much as a thousand fold from species to species. This made it difficult to assign any rate for human fecal plutonium excretion.

4.1 Results of Human Excretion Studies:

Urinary excretion of plutonium. Three experiments were begun within a few weeks (one at Chicago) in which plutonium was injected into a human and the plutonium excretion followed daily. During the first 15 days of the experiments there was less than 10% difference between the daily urinary plutonium excretion of the individual studied by Dr. W. Langham and associates at Los Alamos and the individual studied by Dr. J. J. Nickson, E. R. Russell and associates at Chicago. The individual studied by Dr. J. G. Hamilton at Berkeley showed a slightly lower excretion but not by a factor of 2. Following the initial period where a rapid decrease in the excretion rate is observed, there was a slight divergence in the results obtained from the three subjects. The individual

studied at Los Alamos showed an average daily excretion of slightly less than 0.02%, the one at Chicago slightly above 0.012% and the individual at Berkeley slightly less than 0.006%. These values persisted over a 100-day period. Since these experiments were completed, two additional studies have been made at Chicago. The excretion rate of one of these individuals after the first two weeks has remained between 0.010 and 0.015% per day. The other individual was not available for further study after the 16th day.

In view of the fact that the majority of the urinary plutonium excretion studies on humans have indicated that a sub-acute excretion rate of 0.01% per day is very nearly correct, this value appears to be at this time a reasonable one to use in determining the concentration of plutonium in the body of workers. It may be pointed out that the urinary plutonium excretion of dogs[13] parallels that of man.

Fecal excretion of plutonium. In addition to following the urinary excretion of plutonium of the above individuals, the plutonium content of the daily fecal specimens was also determined. It has been predicted by several workers on the basis of animal excretion studies, that the plutonium fecal excretion rate would be greater than the urinary excretion rate. It therefore appeared that stool determinations would be easier to interpret. All of the human studies that have been made have failed to confirm this thesis. Plutonium in

a 24-hour fecal specimen is from 2 to 4 times less than that in a corresponding 24-hour urine specimen.

The average daily fecal plutonium excretion for the four cases studied is 0.003% ranging from 0.001% to 0.006% of that contained in the body. From the difficulties encountered in detecting 2×10^{-5} micrograms of plutonium, it would appear that surveys of personnel through fecal analysis would be difficult.

4.2 Distribution of Plutonium in the Body: The development and understanding of any satisfactory means of plutonium therapy is dependent upon a knowledge of the distribution of the element in the organism. Since nearly 90% of the plutonium finding its way in the body is retained there for many years it is vitally important that we week some means of increasing the excretion rate. The first step in devising means of therapy is to learn in what organs the plutonium is concentrated.

There have been many experiments involving animals in which plutonium was injected and at some later date its distribution determined. The majority of these tests have shown that the liver, spleen, bone marrow, and lymph nodes are the principle sites of deposition. The same general distribution has been found for the one fairly normal human which was studied. The distribution data is given in Table I. In addition the distribution of plutonium in a female containing

approximately 90 micrograms was determined (see Table II.) This individual had many abnormally functioning organs and therefore the distribution may not be representative. It is interesting to note that even under these conditions the marrow and bone are among the principle sites of deposition.

Chicago Case 1: RER 12/19/72

Table I

Distribution of Plutonium in a 68-year, White Male (155 days after injection of 6.5 ug of plutonium as the citrate)

Tissue	Grams of tissue analysed	Cts/gram of tissue	*Relative Affinity for Plutonium
Marrow (rib)	0.8292	70.9	10.13
Liver	34.11	59.8	8.54
Sternum	5.38	20.6	2.94
Periosteum	0.1215	20.0	2.86
Spleen	32.12	11.1	1.59
Tumor (lung)	2.03	7.4	1.06
Cancer Tissue	2.87	7.2	1.03
Rib (cortex)	1.0125	7.0	1.00
L.Nodes (aorta)	0.63	6.7	0.96
Lung	15.39	2.6	0.37
Testicle (glandular)	4.3425	2.3	0.33
Kidney	27.35	1.7	0.24
Heart	4.9435	1.2	0.17
Diaphragm	35.73	1.0	0.14
Abdominal Fat	17.05	0.2	0.03
Bile	8 cc	?	---

* = cts/gram found ÷ cts/gram assuming equal distribution throughout the body.

Chicago Case 2:
RER 12/14/

Table II

Distribution of Plutonium in a 54-year, White Female
(16 days after injection of 94.91 µg of plutonium citrate)

Tissue	Grams of tissue Analysed	cts/gram of tissue	*Relative Affinity for Plutonium
Marrow (rib	0.2065	1399	8.49
Rib (cortex)	0.430	1299	7.88
Callus and bone	0.1933	828	5.02
Callus (bone free)	0.262	534	3.17
Kidney	6.00	360	2.18
Thyroid	2.64	226	1.37
Contents (lower bowel)	10.05	183	1.11
Liver	8.70	162	1.00
Pancreas	6.045	148	0.90
Periosteum (rib)	0.461	123	0.75
Lung	14.40	107	0.65
Fat	5.850	96	0.58
Spleen	10.850	94	0.57
Tumor (liver)	1.97	71	0.43
Heart	).40	70	0.42
Ovary (l.)	1.975	63	0.38
L. Node (abd.)	1.53	48	0.29
Intestines (small)	3.40	45	0.27
Intestines (large)	6.87	43	0.26
Muscle (striated)	15.32	40	0.24
Blood (heart clot)	1.835	22	0.13

* = cts/gram found ÷ cts/gram assuming equal distribution throughout the body.