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INDUSTRIAL MEDICINE ON THE PLUTONIUM PROJECT

Survey and Collected Papers

Edited by

ROBERT S. STONE, M.D.

Professor of Radiology and Chairman of the Division of Radiology, University of California School of Medicine; formerly Associate Project Director for Health, Metallurgical Project, University of Chicago; Consultant, Argonne National Laboratory

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Chapter 8

DISTRIBUTION AND EXCRETION OF PLUTONIUM*

By E. R. Russell and J. J. Nickson

1. INTRODUCTION

Following the discovery of plutonium and the observation that it is an active alpha emitter with a half-life of 24,300 years, it became obvious that rigid precautions are necessary for the protection of workers handling plutonium. Experience in the radium industry had shown that very small amounts of radium deposited in the body could produce serious illness or death. Since plutonium could have similar effects, provision was made for elaborate protective regulations and devices in the laboratories where plutonium was handled.

As a basis for the health-protection work it was necessary to establish the maximum permissible body content of plutonium. At first a tentative limit was established on an arbitrary basis. From purely physical considerations it seemed that plutonium, weight for weight, should be approximately one-fiftieth as toxic as radium. Since the tolerance amount of radium in the body is generally accepted as 0.1 μg, the body tolerance for plutonium was initially set at 5.0 μg. Later, on the basis of experimental evidence, the plutonium tolerance limit was lowered to 1.0 μg.

It was essential to devise a means of detecting and measuring in an individual quantities of plutonium less than the tolerance limit. It appeared that this might be feasible through the analysis of excreta. The analysis, however, presented difficult problems, for, as will be seen, it was necessary to measure the plutonium in 100 ml of urine when only about 0.01 per cent of somewhat less than 1 μg is excreted in a 24-hr period. The analytical methods that were developed are still considered secret and cannot be described in full here; nevertheless,

*Based on Metallurgical Laboratory Memorandum MUC-ERR-209.

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the problems encountered and the results of personnel surveys are presented in this chapter. For a complete understanding of plutonium poisoning it is necessary to know the distribution of plutonium in the various organs of the body. Results of certain experiments bearing on this problem are also given in the latter part of the chapter.

2. ESTIMATION OF PLUTONIUM IN THE BODY

In order to estimate the plutonium content of the body by analysis of excreta, it was first necessary to determine the rate of excretion of plutonium. Some very preliminary urinary excretion studies with rabbits indicated that plutonium is eliminated from the body at a fairly constant rate after the first two or three weeks from the time the plutonium enters the body.[1] This stable excretion rate was found to be approximately 0.01 per cent per day. Subsequent experiments with mice, rats, and dogs showed that the excretion rate may vary by a factor of 5 among the different animals.[3] This made it necessary to establish the plutonium excretion rate for man by direct experiments with human beings.

Experiments with human beings were conducted at the several sites where plutonium was handled. During the first 15 days after exposure to plutonium there was less than 10 per cent difference between the daily urinary plutonium excretion of the individual studied by Wright Langham and associates[4] at Los Alamos and that of the person studied by J. J. Nickson, E. R. Russell, and associates at Chicago. An individual studied by J. G. Hamilton[5] at Berkeley showed a slightly lower excretion rate. Following the initial period, in which a rapid decrease in the excretion rate was observed, there was a slight divergence in the values obtained from the three subjects. The individual studied at Los Alamos showed an average excretion rate of slightly less than 0.02 per cent per day; the individual at Chicago showed a rate slightly above 0.012 per cent per day; and the rate for the individual at Berkeley was slightly less than 0.006 per cent per day. These rates persisted over a 100-day period. In two additional studies made later at Chicago, one individual showed an excretion rate that remained between 0.010 and 0.015 per cent per day after the first two weeks.

From the results of these studies it appears that the value 0.01 per cent per day is nearly correct for the urinary plutonium excretion rate for subacute concentrations of plutonium in human beings. Recent work discussed elsewhere in this volume indicates that this value may be greater than the true excretion rate of plutonium retained in the body for a year or more. Although the value 0.01 per cent per day may have to be reduced in the future, it appeared to be a reasonable figure for use at the time in determining the plutonium in the bodies

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of the workers. It may be pointed out that the urinary plutonium excretion of dogs[2] parallels that of man.

On the basis of animal excretion studies several workers predicted that the fecal plutonium excretion rate would be greater than the urinary excretion rate. If this were the case, stool determinations might be easier to interpret. In the animal excretion studies mentioned before, fecal analyses showed excretion rates that varied as much as a thousandfold among the different species, which made it difficult to approximate any rate for human fecal plutonium excretion. All four of the human experiments in which fecal as well as urine analyses were made failed to confirm the prediction. In general, the plutonium in a 24-hr fecal specimen is only one-fourth to one-half the amount in a corresponding 24-hr urine specimen. The fecal plutonium excretion rate for the four human studies averaged 0.003 per cent per day, ranging from 0.001 to 0.006 per cent of the plutonium in the body. Thus plutonium determination by fecal analysis appeared more difficult than by urinalysis.

Because a greater amount of plutonium is excreted in the urine than in the feces and because of the greater ease of handling urine samples, urinalysis was considered to be the better method for determining plutonium in personnel. The development of analytical methods for determining submicro amounts of plutonium in urine and other biological materials involved both the development of precise counting instruments and chemical procedures for concentrating the plutonium. Perhaps full details of these methods can be published later, but for the present it must suffice to note that the chemical methods were based on the general principles of adsorption, solvent extraction, and coprecipitation as described in the Smyth Report.[6]

When 5 μg was considered to be the body tolerance limit and 0.01 per cent per day was considered the correct urinary excretion rate, an analytical procedure that could detect 28 alpha counts per minute from plutonium in a 24-hr specimen or 2 counts per minute in a 100-ml specimen was believed to be adequate. A method was developed which met these requirements, and it served its purpose well. When the tolerance limit was lowered to 1.0 μg, an analytical procedure making possible the detection of 0.2 μg of plutonium in the body was needed. This meant that 2×10^{-5} μg in a 24-hr sample would be significant, and, since the average urine specimen used in the survey work at the Metallurgical Laboratory was approximately one-third of a 24-hr sample, the method had to be sensitive enough to detect 7×10^{-6} μg or 0.4 alpha count per minute from plutonium. Smaller samples presented even more difficult problems. The original analytical method was not sufficiently sensitive to detect such small y plutonium ex-

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W. P. Jesse and associates produced counters with backgrounds of less than 0.1 count per minute. With such counters 0.2 count per minute could be detected with fair accuracy. Counting times were long, of course.

In the utilization of the analytical methods in personnel survey work, alpha contamination proved to be one of the greatest sources of error in the determination of low alpha activity. Experience proved the necessity of collecting, handling, and assaying the urine under "radioactively sterile" conditions.

3. RESULTS OF ROUTINE URINE SURVEYS

Routine personnel surveys were made by urinalysis at both the Metallurgical Laboratory and at Clinton Laboratories. In each case the results for the first year or so were of value principally in determining the methods and conditions necessary for obtaining significant results. A breakdown of results according to methods and condition of analysis demonstrated clearly that alpha contamination was continually causing high results. The survey work at the Metallurgical Laboratory during the period from August 1944 through October 1945 served mainly to eliminate difficulties caused by contamination and problems in the procedure. From this work four conditions were determined which were considered necessary for accurate and significant urine analysis. These are:

1. An isolated laboratory free from alpha contamination must be provided for the analyses.
2. An analytical method capable of handling large volumes of urine must be used.
3. Alpha-counting instruments capable of detecting 0.1 alpha count per minute must be provided.
4. Very definite rules of collecting and handling the specimens must be followed.

In November 1945 routine urinalysis was begun under conditions as near as possible to those outlined above. By Feb. 1, 1946, 216 individual urine specimens had been analyzed. Less than 1 per cent indicated more than 0.4 μg of plutonium in the body; 6.5 per cent showed 0.1 to 0.4 μg; and the remainder indicated less than 0.1 μg. Twelve 1,000-ml blank controls were run. The maximum result on these blanks was equivalent to a body plutonium content of 0.02 μg, which may be regarded as the lower limit of sensitivity of the method.

Contamination was encountered in the early work at Clinton Laboratories, just as it was at Chicago. One of the chief difficulties with a method used for a considerable period was that one of the reagents contained alpha-active material. The source of the alpha activity in the various specimens was not determined, but some samples were found to contain as much as 1.6 alpha counts per minute per milligram. In general, this activity followed through with plutonium in the method used. This difficulty necessitated a change in methods and reagents.

Accurate and significant results were obtained subsequently. Of 148 specimens assayed, 18 per cent showed negative counts but none below −0.1 count per minute. Eighty-two per cent showed zero or significant positive counts. Excluding the negative results, the average estimated body content was 0.063 μg of plutonium.

In the final analyses at both Clinton Laboratories and at Chicago, frequent blank controls were run. The results on the blanks ranged from 0.01 to 0.08 alpha count per minute. Such counts are not detrimental but rather serve to indicate that the reagents used in the analysis were not contaminated and that the external contamination was considerably reduced. The low blanks also lend weight to the high results obtained on specimens.

4. DISTRIBUTION OF PLUTONIUM IN THE BODY

The excretion studies have shown that nearly 90 per cent of the plutonium entering the body is retained for many years. To achieve a comprehensive understanding of plutonium toxicity, it was necessary to find out in which of the body organs and tissues plutonium was concentrated and deposited. This knowledge may suggest means for increasing the excretion rate and other possible therapeutic treatments for plutonium poisoning. Such possibilities are not discussed in this chapter, but the results of several distribution studies are reported.

A number of experiments with animals have been performed in which plutonium was administered and distribution was later determined by analysis of the various tissues and organs. These experiments showed the general pattern of plutonium distribution within the system, but confirmatory human experiments were needed. It was possible to conduct human experiments in two instances. In both cases a plutonium compound was administered to an incurably ailing individual, and the plutonium distribution was determined by postmortem examination. One study was made upon a 68-year-old white man whose system was considered to be fairly normal. The other study involved a 54-year-old white woman. Because of her ailment many of her organs were functioning abnormally. Her system contained approximately 90 μg of plutonium at the time of death, but because of the organic malfunctions the distribution may not be representative.

The animal experiments showed that the liver, spleen, bone marrow, and lymph nodes are the principal sites of plutonium deposition. The distribution found in the 68-year-old man (Table 8.1) was, in

Table 8.1 — Distribution of Plutonium in a 68-year-old White Male (Death Due to Other Causes 155 Days after Exposure)

Tissue	Amount of tissue analyzed, g	Counts per 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
Lymph nodes, aortic	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 (ml)	?	

*Counts per gram found ÷ counts per gram assuming equal distribution throughout the body.

general, the same. The distribution found in the 54-year-old woman is shown in Table 8.2. It is interesting to note that, even with the differences in the physical condition of the two subjects, the marrow and bone were among the principal sites of deposition in both cases.

5. SUMMARY

Plutonium has proved to be a radiotoxic material approximately as hazardous as radium. Accordingly, stringent health precautions are necessary to protect workers who are exposed to the element. At the time of writing, a body tolerance limit of 1.0 μg was established for the Project, and means for personnel examinations were provided to determine the actual body plutonium content. The personnel examinations were based on urinalysis, fecal analysis having proved unsatisfactory for the purpose. Actual plutonium content was calculated on the basis of a urinary plutonium excretion rate of 0.01 per cent per day. This rate had been fairly well confirmed through a number of human experiments.

Table 8.2 — Distribution of Plutonium in a 54-year-old White Female (Death Due to Other Causes 16 Days after Exposure)

Tissue	Amount of tissue analyzed, g	Counts per gram of tissue	Relative affinity for plutonium*
Marrow	0.2065	1,399	8.49
Rib, cortex	0.430	1,299	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	0.40	70	0.42
Ovary, left	1.875	63	0.38
Lymph nodes, abdominal	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

*Counts per gram found ÷ counts per gram assuming equal distribution throughout body.

Analytical methods for routine personnel survey work have been developed. The chief requirements for significant analyses are (1) alpha counters that can detect 0.1 count per minute in a sample and (2) absolutely "radioactively sterile" conditions for collecting, handling, and assaying the samples. Judging from personnel surveys of workers at the Metallurgical Laboratory and at Clinton Laboratories, it appears unlikely that any individual tested had accumulated an above-tolerance amount of plutonium.

The distribution of plutonium in the various organs and tissues had been determined by a number of experiments, including two with human subjects. These experiments showed that the bone and marrow and several organs, including the liver, spleen, and lymph nodes, are the principal sites of plutonium deposition.

ACKNOWLEDGMENTS

It has been difficult to give credit to specific individuals for their contributions 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 his associates and to Dr. K. G. Scott and his associates for information concerning certain analytical procedures.

Contributions were also made by M. D. Taylor, E. E. Motta, J. A. Jackson, and C. Brown.

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