METABOLISM OF URANIUM AND

TRANSURANIUM ELEMENTS

BIOMEDICAL FOLLOW-UP OF THE MANHATTAN PROJECT PLUTONIUM WORKERS

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Abstract

Long-term studies have been performed on 25 men who were exposed to plutonium during World War II at what is now the Los Alamos Scientific Laboratory. Almost all of the subjects had body burdens of plutonium ranging from 0.1-1.3 μg or 6-80 nCi of relatively pure plutonium-239 as estimated from the urine assay method for plutonium used at Los Alamos prior to 1950. This paper reconstructs the war-time exposure conditions, discusses the estimates of body and lung burdens based primarily on urine assay for plutonium, and recapitulates the medical studies that have continued during the intervening years.

Introduction

This is the story, first, of how 25 young men were heavily exposed to plutonium at what is now the Los Alamos Scientific Laboratory (at Los Alamos, New Mexico) in the days of the Manhattan Project during World War II and, second, of what has happened to them in the subsequent 27 years. All were sent to Los Alamos (Project Y) in 1944 or 1945 and given various technical jobs processing plutonium in the Chemistry and Metallurgy Research Division. All subjects had body burdens of plutonium estimated from the urine assay for plutonium used at Los Alamos before 1950 that ranged from 0.1-1.2 μg[1] (0.006-0.08 μCi).

With the production and processing of plutonium on a milligram scale early in 1944 and in kilogram lots in 1945, Manhattan Project workers were exposed to a new radioactive hazard on an unprecedented scale. Since there was no practical basis for the safe handling of plutonium, the experience of the radium industry was adapted to the processing of plutonium at LASL. However, the problem of protection against plutonium and radium in practice differed by many orders of magnitude. To complicate the safe handling of plutonium further, there were no sensitive portable alpha particle counters or air samplers. Laboratory and air-borne contamination could be detected only qualitatively by paper swipes of surfaces or external nares measured in a stationary proportional alpha counter, and finally there was no method of determining body burdens of plutonium until the spring of 1945.[2]

The first studies of the chemistry and metallurgy of plutonium were carried out in the now destroyed D Building, an old wooden temporary building shown in Fig. 1. The exhausts of individual hoods, most without filters, can be seen.

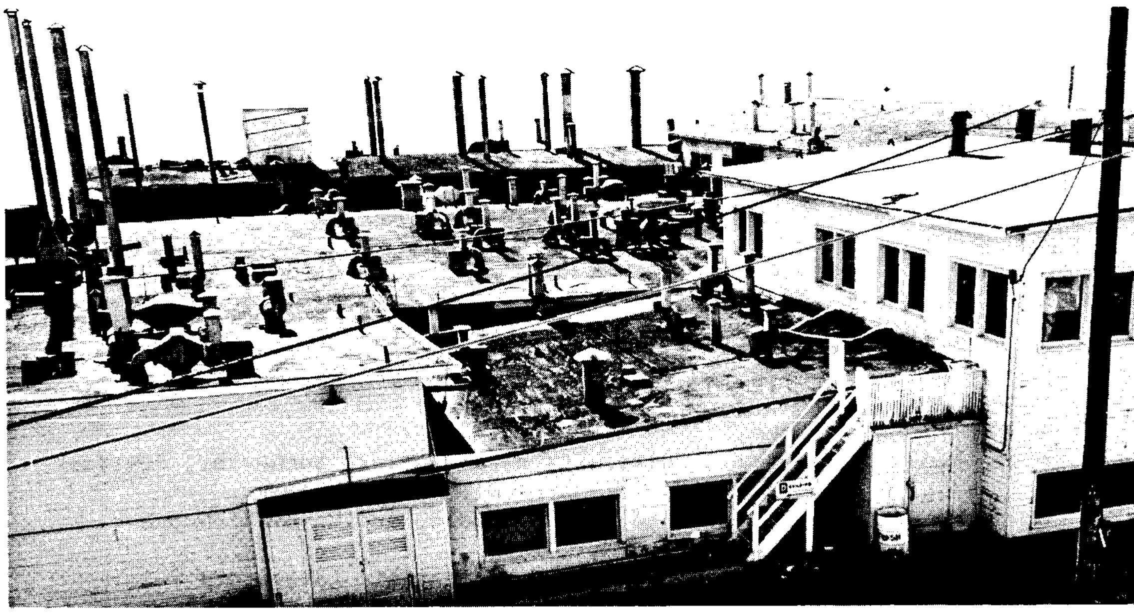

Fig. 1. The original wooden D Building which housed the chemists and metallurgists in CMR Division.

Although every known method of protecting the workers against inhalation or ingestion of plutonium was used, the exposure conditions were deplorable by present-day standards. The makeshift methods at hand were simply inadequate to prevent exposure of the workers despite the most stringent safety regulations. As an example, unsuspected contaminated areas at laboratory benches of up to 35 µg of plutonium were detected by the swipe method. Cumulative quantities of up to 0.5 µg were swiped out of the external nares of some workers despite conscientious use of respirators. The most dramatic accident occurred when the first 8 g of plutonium (all that existed at that time) were being processed. The sample was spilled once on the floor, recovered, and then spilled into a centrifuge cup.

By February 1945, when kilogram quantities of plutonium began to arrive at LASL for processing and fabrication into nuclear devices, protective measures had improved considerably, and a method of assaying the body burden of plutonium had been developed. When the war ended in August 1945, 29 workers had been removed from their jobs because they contained measurable body burdens up to 1.2 g as determined by the urine assay methods available at that time. Of the 29 men, one died of a coronary, and three were dropped because future lists showed no detectable body burden.

Clinical, Laboratory, and Radioactivity Observations

Medical Observations

In 1953, a program for periodic examination of these men (financed by the U. S. Atomic Energy Commission) was established. In 1953 and again in 1955, 22 and 25 subjects of the series, respectively, were examined by physicians associated with the U. S. Atomic Energy Commission. All 25 of the men were examined by their family physicians in 1960, 17 in 1966, and 24 in 1970. In late 1971 and early 1972, 22 of the 25 subjects traveled to Los Alamos for a complete study including urine assays for plutonium, *in vivo* measurements for plutonium-239 in the chest, pulmonary cytology, and chromosome analyses. The results of these studies will be reported in detail.[3] Roentgenograms were also taken of the chest, pelvis, and teeth. Except for the ailments that one would expect in a group of men mostly in their early fifties, all subjects examined were in remarkably good health. One man had died in 1959 of a coronary at age 38. All men were actively working, most as successful executives. No roentgenographic changes in the lungs or bones were apparent. The lamina dura of the jaws were intact in all cases.

Estimates of Plutonium Body Burdens from Urine Assay

The estimates of body burden of plutonium as determined by assay of the urine of the subjects made during the 20-yr observation period (1953-1972) are shown in Table I. The 1972 version of the PUQFUA (Plutonium Body Burden From

TABLE I

Plutonium Body Burden Estimates Based upon Urine Assay Data for the Subjects[a]

Case Code No.	1953	1962	1972
1	0.03 - 0.06	0.01	0.206
2	0.006 - 0.032	--	0.03
3	0.08	0.13	0.42
4	0.08	0.14	0.26
5	0.08	0.14	0.18
6	0.06	0.07	0.14
7	0.06	0.08	0.15
8	0.04	0.05	0.11
9	0.06	0.11	0.11
10	0.05	0.03	0.10
11	0.03	0.03	0.05
12	0.03	0.02	0.12
13	0.02	0.04	0.005
16	0.006	0.002	0.03
17	0.04	0.09	0.13
18	0.04	0.04	0.10
19	0.03	0.06	0.02
20	0.02	0.02	0.05
21	0.02	0.03	0.04
22	0.02	0.02	0.05
23	0.02	0.04	0.04
24	0.006	0.01	0.03
25	0.006	0.01	0.01
26	0.02	0.03	0.006
27	0.02	0.03	0.05

[a]Microcurie ± approximately 50%.

Urine Analysis) code was used to estimate what is considered to be the best value for the body burden of the subjects.[4] In all but 2 cases, the current estimates of body burden are higher than those in 1953, usually by a factor of 2-3 and sometimes by a factor of 5-6. Values in the last column of Table I range from 0.005-0.42 μCi plutonium-239,240, or from approximately 1/8-10 times the current maximum permissible body burden (0.04 μCi) for occupational workers. Eighteen of the 25 values listed for 1972 are equal to or exceed the 0.04 μCi value. Comparing the relatively small quantities of plutonium deposited in the body (excluding the lungs) with the large amounts to which the subjects had been exposed, we can only conclude that the gastrointestinal tract has a remarkable ability to exclude plutonium from entering the body. Had plutonium been as readily absorbed as radium, all subjects would unquestionably have lethal body burdens of radioactivity.

To evaluate the possible consequences of bone doses of this magnitude, we must refer to animal data. The most extensive of these studies has been carried out at the University of Utah Medical School since December 1, 1952, when the first group of 6 beagles were injected intravenously with plutonium-239 citrate.[5] Injected doses ranged from 0.016-2.9 μCi/kg body weight for 6 groups of about 12 dogs each. To date, the 0.016 μCi/kg dose level is of interest, as 4 dogs developed osteosarcomas, giving a tumor incidence of 33%.[5] Average time from injection to death for these animals was 9.9 yr, and the average skeletal dose from injection to death was estimated to be about 80-90 rads delivered at about 8-9 rads/yr.[6]

It is difficult to estimate even crudely bone and liver doses from the data in Table I. However, some estimates can be obtained if numerous simplifying assumptions are made. For example, the average body burden for 1972 in Table I is about 0.10 μCi which, if equally divided between bone and liver, would deliver about 0.7 rad/yr and 2.9 rads/yr, respectively, to these tissues. If no loss occurred during the 27 yr since exposure, the corresponding total doses to bone and liver would be about 19 and 78 rads. For the highest body burden listed in Table I (case No. 3), the estimated dose rates for bone and liver would be ~2.9 and 12.2 rads/yr, respectively. If the entire average burden to the group was limited to bone, the dose rate would be 1.4 rads/yr and the 27-yr dose, using the same assumptions, would be about 38 rads to the skeleton. For case No. 3, the comparable values would be about 5.9 rads/yr and 195 rads. These estimates, as indicated above, are very crude and should not be considered as being otherwise.

Determination of Plutonium in the Body by *In Vivo* Measurements

During the most recent medical examinations at Los Alamos, estimates were made of the amount of plutonium in the chest (lung and respiratory lymph nodes) of each subject using an *in vivo* lung counter. Measurements also were made of the liver region in several subjects and of the hands of persons known to have had skin wound contaminated by plutonium. Positive counts suggesting chest burdens ranging from 3 to about 10 nCi were obtained for 14 of 21 persons measured. However, in no case did the estimated chest burden exceed the minimum detectable level at the 95% confidence level. Seven of the 14 subjects with positive chest counts had estimated chest burdens of 7 nCi or greater and may be considered (at the 68% level of confidence) to have statistically significant chest burdens of from 7-10 nCi.

The only direct measurement of plutonium in the lungs in this study was made on the operative specimens of subject No. 2 who had surgery for a benign lung tumor. Table II shows results of analyses for plutonium-239. The concentration of plutonium-239 was approximately the same in the tumor and lung tissue, while the concentration of plutonium-239 in bone was approximately half.

TABLE II

Plutonium-239 Content of Tissues Removed from Subject No. 2 in May 1971[a]

Tissue	pCi/g Wet Weight
Lung	3.85
Lymph node	205.00
Hamartoma	3.40
Rib	1.61

[a]After ashing and dissolution of tissue.

The highest concentration, observed in the lymph node tissue, is consistent with experimental findings in dogs exposed to PuO_2 by inhalation, as mentioned above. It is well established that the concentration in lymph nodes relative to that in lung tissue increases as a function of time following exposure If one assumes a homogeneous distribution of plutonium-239 throughout the l' g and lymph nodes and a total lung weight of 1000 g and respiratory lymph node weight of 20 g, the total plutonium burden of the lungs and respiratory lymph nodes is approximately 8 nCi roughly equally divided between lung and lymph node. For reference, the total amount of plutonium in the lung of case No. 2 (estimated by tissue assay to be 3.85 nCi) is approximately 550 times contemporary total lung burdens in humans in the United States exposed to fallout resulting from plutonium dispersed by atmospheric weapons tests. Estimates of the chest burden of plutonium-239 of subject No. 2, based on extrapolation from analysis of lung and lymph node tissue, are in reasonable agreement (a factor of about 2) with estimates based on chest-counting.

Chromosome analysis of lymphocytes in the peripheral blood revealed no abnormalities, and studies of exfoliated pulmonary cells showed mild to marked dysplastic changes particularly in heavy smokers.

Vital Statistics Information

Although our study group is relatively small, about 25 men, the magnitude of their plutonium burdens, the long time since exposure, and their cooperativeness collectively make them a unique and extremely valuable group. However, because something like 16-20% of all deaths annually in the United States are from cancer, one might be concerned about the size of the group as 4 or 5 might be expected to die from "naturally occurring" cancer had they never been exposed to plutonium. However, evidence obtained from experimental animal studies very strongly indicates that the kinds of cancer induced by plutonium are not all increased in a nonspecific way but, rather, consist primarily of lung carcinomas, liver cancer, and bone sarcomas from the modalities of exposure involved.

We have used vital statistics data[7] to estimate the probabilities of death from certain cancer types over a 65-yr period from age 20 to age 85. The total probabilities per 100,000 deaths for tumor type 23 (bronchus, trachea, and lung, specified as primary), type 16 (liver), and type 48 (bone) are 3023, 578, and 152, respectively, for United States white males. Thus, for a group of 25, we would expect 0.76, 0.15, and 0.04 deaths from tumor types 23, 16, and 48, respectively. Therefore, in lieu of other information, the occurrence of one lung cancer could be ascribed to nonradiation factors, whereas the occurrence of one liver cancer might be considered suggestive of plutonium induction, and the occurrence of one bone sarcoma would be statistically significant.

One also needs to consider the individual smoking histories because of the difference in lung cancer incidence history between smokers and nonsmokers. In addition, these subjects have been exposed to a large number of chemicals, some of which are known to cause biological effects, both during the Manhattan Project and subsequent employment. The following is a list of materials to which one person has been exposed: organic plasticizers, xylene, toluene, urea, formaldehyde, sulfonic acid, sodium thiosulfate, tetraethyl lead, freon, ethyl chloride, fluorinated hydrocarbons, and industrial sludges containing lead and mercury. It is also known that several of our subjects could have been significantly exposed to beryllium at a time when virtually no safety precautions were observed because of its alleged lack of toxicity. Hopefully, these follow-up studies will be continued throughout the lifetime of these subjects. This information, even though very limited, is human experience of the most relevant kind for establishing value judgments where inadequate data exist for formulating risk evaluations.

Acknowledgments

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This report covers information and work that has been carried out over a period of many years and has involved persons too numerous to mention who have contributed to the success of the project.

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