BNL 7041
To file (20)

700196

EVALUATION OF PLUTONIUM EXPOSURES IN MAN*

J. S. Robertson and S. H. Cohn

Medical Research Center
Brookhaven National Laboratory
Upton, L.I., N. Y.

25 May 1963

*Research supported by the U.S. Atomic Energy Commission.

OFFICIAL USE ONLY

0001821

occurred in a dog injected with 0.048 μc/kg and one in another injected with 0.016 μc/kg. Further studies of the toxicity of Pu^{239} at the lower dose levels are planned (22).

VI. PLUTONIUM EXPERIENCE IN MAN

A. Body burdens

Langham (24) has reviewed the problem of occupational exposure to Pu^{239} at Los Alamos, Hanford, Chalk River, and in England. Altogether, several thousand employees have been studied by means of urinalysis for plutonium. However, insofar as providing the basic data relating known body burdens to excretion rates is concerned, there are only three principal sources of data on the behavior of plutonium in man:
1) Sixteen patients given tracer doses of plutonium intravenously,
2) employees occupationally exposed to plutonium during the Manhattan project, and 3) autopsy data on a few formerly occupationally-exposed employees.

The patient data were originally reported by Langham, Bassett, Harris and Carter (25) and have been added to and re-examined in subsequent reports (6,3,26,27,28,29). An outline of what transpired follows.

In a joint project of Los Alamos and the University of Rochester beginning in April 1945, twelve patients were injected intravenously with 4.6 to 6.5 μg Pu^{239} prepared by dissolving Pu metal in nitric acid and then diluting to volume with 0.41 per cent sodium citrate (25). Three patients at Chicago were injected with PuO_2^{++} in doses of 6.5 to 95 μg Pu^{239} (25), and one at Berkeley was given a mixture of 5 μg Pu^{239} and 0.3 μg Pu^{238}, regarded as a total of 120 μg Pu^{239} equivalent, as PuO_2^{++} (28).

At the last survey, two, and possibly four, of the patients were still living (28). Autopsy material was obtained in seven cases who died in the first few months, and the tissue Pu^{239} distributions, regarded as approximately 5 months after injection, were in substantial agreement with the comparable distribution in beagles, as indicated in the following table (6):

TABLE VI

Pu^{239} DISTRIBUTIONS FIVE MONTHS AFTER INTRAVENOUS INJECTION

	Per cent of injected dose per tissue	
	Beagle	Man
Skeleton	60	66
Liver	21	23 (Range 2.7-42.8 (22))
Spleen	0.2	0.4
Kidneys	0.2	0.4

In no case was any radiation injury attributable to plutonium found.

In the kinetic studies, 64 blood samples were obtained from among 11 patients over the first 23 days after injection, and 6 samples from among 5 patients during the 29- to 46-day period (25, Table 5). Although the individual values varied widely, the means fell on a fairly smooth curve from 35.7 per cent of the injected plutonium in the bood volume at 4 hours after injection to 15.7 per cent at one day, 1.2 per cent at 10 days, and 0.3 per cent at 30 days.

The urinary excretion of plutonium was followed in 11 of the Los Alamos patients; two for 22 days and one each of the other nine for 23, 25, 27, 30, 34, 36, 37, 58 and 65 days. One Chicago patient was followed for 16 days. The Berkeley patient and two of the Chicago patients were followed for 138 days.

These data were pooled and fitted by a smoothed curve described by the power function (25):

$$Y_u = 0.0023\ t^{-0.77} \tag{9}$$

Where Y_u is the fraction of the injected dose excreted per day, and t is in days after injection. The standard error of the estimate was ± 32 per cent.

Similarly, the total excretion rate (urine plus feces) was described by:

$$Y_{u+f} = 0.0079\ t^{-0.94} \tag{10}$$

with the standard error of the estimate being 17 per cent.

Later, urinary samples obtained from one of the patients on the 523rd to 526th days, and another group of samples beginning on the 1610th day after injection had 0.002 per cent of the injected dose per day and 0.0011 per cent per day, respectively. Four daily samples from another patient beginning at 1645 days had an average of 0.0008 per cent per day.

The patient data were further extended by data obtained from three employees who had accumulated body burdens of plutonium resulting in measurable urinary plutonium excretion rates and who had been removed from further exposure to plutonium. Although their body burdens had been achieved through chronic exposure by inhalation, an attempt was made to express their dose in terms of an "effective" single dose given at some "effective time" between the limits of exposure, calculated by fitting equation (9) to two values for the excretion rates taken an appreciable time apart. Using this procedure, effective doses of 1.3 μg, 1.2 μg, and 1.0 μg at 37, 53 and 42 days prior to the first urine assay used in the calculation were assumed. In this manner the urinary plutonium excretion curve was extended to 1750 days and the final adjusted fit was:

$$Y_{ua} = 0.0020\ t^{-0.74} \qquad (11)$$

with the standard error of the estimate for the adjusted expression being 42 per cent.

Equations (9) and (11) are significant because they have been used as the basis for estimating body burdens from urinary plutonium excretion rates in man in almost all subsequent calculations (26,30,31,32,33).

Unfortunately no fecal data are given for the period after 138 days in these studies (25) because it was considered that contamination of the feces by plutonium removed from the lungs by ciliary action and ingested would disturb the results.

For a total excretion rate after 138 days an equation is given which sums the 138-day fecal rate and the adjusted urinary rate:

$$Y_{ua+f} = 0.0020\ t^{-0.74} + 0.0063\ t^{-1.09} \qquad (12)$$

Integration of this expression and evaluation at 5 years indicates that a total of only 8.7 per cent of a single injected dose of Pu^{239} would be excreted in this period.

A "biological half-time" was calculated (25) by assuming that after 1750 days the excretion rate would remain constant at 0.001 per cent of the injected dose per day, so that to increase the total amount excreted from 8.7 per cent at 5 years to 50 per cent would take another 113 years, for a total of 118 years. (It had evidently been assumed that this procedure was equivalent to assuming an exponential excretion rate after 5 years, but in exponential excretion it is the fraction of the amount remaining which would be constant and the biological half-time would be even longer: $\frac{0.69315}{.00001}$ = 69315 days = 190 years. For practical purposes, the result is the same - plutonium remaining in the body after 5 years is, effectively, there permanently.)

The problem of estimating the Pu^{239} lung burdens in employees has been considered by Langham (26,27) and described as appearing, "almost hopelessly complex." An attempt was made, however, to use the urinary to fecal ratios as a measure of lung burden. The following table represents data obtained in studies of Los Alamos employees (26)

TABLE VII

COMPARISON OF FAECAL AND URINARY EXCRETION OF PLUTONIUM BY LOS ALAMOS WORKERS IN RELATION TO MODE OF EXPOSURE

Subjects	Type of exposure	Approximate time after exposure (months)	Faeces (c/m/24 hour)	Urine (c/m/24 hour)*
Average of 25	No exposure	-	0.9 ± 0.4	0.7 ± 0.4
	Slight, general	1	0.7	1.1
	Moderate, general	1	25	1.0
	High, general	6	68	0.9
	Dry box explosion	6	7	0.7
	Dry box explosion	6	23	0.7
	Burning Pu metal	6	2	0.8
	Burning Pu metal	6	19	0.5
	Burning Pu metal	1/2	1190	1.3
	Burning Pu metal	1/2	70	0.8
	Burning Pu metal	1/2	950	0.6
	Spray of $PuO_2(NO_3)_2$	1	3400	5.0
	Spray of $Pu(NO_3)_4$	9	196	2.6
	Spray of $Pu(NO_3)_4$	10	130	7.3
	Spray of $Pu(NO_3)_4$	12	21	4.9
	Spray of $Pu(NO_3)_4$	11	237	4.3
	Spray of $Pu(NO_3)_4$	10	24	3.6

*Counts of less than one have no statistical significance.

**Used to calculate values for lung burden.

Data on the five subjects indicated by double asterisks in Table VII were used to estimate the lung burdens, using kinetic data obtained in rats by Abrams <u>et al</u>. (cited in refs (26,27)). The estimated Pu^{239} lung burdens given by two methods were about ten times the systemic burden. A model for evaluating the lung burden hazard was proposed, based largely on rat data and assuming an elimination half-time of about six months for the insoluble particles deposited on alveolar surfaces, with the rest being much more rapidly disposed of.

The lung burden problem has also been considered by Healy (31). As he points out, "Relatively insoluble quantities of plutonium in the lung may be regarded as a pool of material isolated from the normal metabolism of the body but continually injecting plutonium into the blood stream at a rate dependent upon the character of the deposited material and relevant physiological processes." In deriving equations to relate the lung burden to the urinary excretion rate, he assumes a constant fractional removal per unit time for the lung burden, so that the quantity, Q, remaining in the lung at a time, t, following acute fixation of a quantity, Qo, is given by: $Q = Qo\ e^{-\lambda t}$.

The λ in this equation includes the rate of loss due both by solubilization and by ciliary action, so the rate of transfer to the circulation is some fraction, λ_s, of Q. It was then assumed that Langham's equations were applicable for obtaining the urinary and fecal excretion rates of the systemic plutonium, and the combined functions were integrated to predict urine and feces excretion rates of plutonium deposited in the lungs. In an application to an exposure case, the rate of fall of the excretion rate was not sufficient to provide an accurate estimate of λ, although samples were obtained for 1600 days.