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PLUTONIUM ACCUMULATION FROM LONG-TERM OCCUPATIONAL EXPOSURE*

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Abstract—Analyses of tissue aliquots from a plutonium process operator, who had been exposed to Pu^{239} largely via chronic low-level inhalation for approximately 6 out of $11\frac{1}{2}$ years of employment, showed that he had accumulated a body burden of approximately 0.018 μc. Estimations of his body burden from his urine assay record ranged from 0.019 to 0.034 μc. The highest plutonium concentration (125 dis/min per g) was found in pulmonary lymph nodes, followed by liver (9.9 dis/min per g), lungs (4.8 dis/min per g) and bone (average of sternum, rib and vertebra, 1.4 dis/min per g). Some implications of these findings to chronic low-level inhalation exposures and to estimation of body burden from urine assays are discussed.

THE occurrence of a fatal criticality accident at the Los Alamos Scientific Laboratory provided an opportunity to obtain data on plutonium accumulation in an individual who had spent a total of approximately 6 years of an $11\frac{1}{2}$-year employment period working with this potentially hazardous material.

These data are of interest because they provide, for the first time, limited information on (a) the efficacy of industrial hygiene and engineering practices in plutonium processing operations; (b) body distribution of plutonium in an individual, exposed primarily by inhalation of low-level plutonium aerosols over a prolonged period; and (c) reliability of estimates of bc burden from urinary excretion data, wl exposure has been primarily via inhalati

The individual involved was a 75-kg m 38 years of age at the time of death. The fa accident occurred during a plutonium recov procedure. Details of the accident and operation are described elsewhere.[1] De resulted from an over-dose of radiation. plutonium contamination occurred and, c sequently, the conditions of the accident did influence the findings in this study.

The individual's employment and assignment history is shown in Table 1.

Table 1. Employment history of the subject

Period	Job assignment	Time (days)
17 June 1946—24 January 1949	Pu^{239} recovery operator	947†
24 January 1949—4 June 1954	U^{235} recovery operator	1987
4 June 1954—8 June 1955	Resigned—no exposure	369
8 June 1955—31 December 1958	Pu^{239} recovery operator	1297†
Total plutonium exposure time		2244

* Work performed under the auspices of the U.S. Atomic Energy Commission.
† Between first and second plutonium exposure periods, exposure conditions had been greatly improved.

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Table 2. Average concentration of airborne plutonium in areas in which employee was assigned

Year	Room 308 (dis/min per m³)	Room 313 (dis/min per m³)	Room 408 (dis/min per m³)	Room 413 (dis/min per m³)	Rooms 212, 213, 218 (dis/min per m³)
46	6	16	188	15	
47	11	25	77	98	
48	Not used	24	35	69	
49	Not used	19	30	72	
49–1954	Worked with enriched uranium				
55					3
56					3
57					4
58					4

During the first period of plutonium exposure 7 June 1946—24 January 1949), his work onsisted of chemical processing involving utonium nitrate solutions, plutonium oxalate id, occasionally, plutonium fluorination. uring the second period (8 June 1955—31 ecember 1958), his work consisted largely of quid–liquid extraction of plutonium under eatly improved exposure conditions.

Detailed exposure records were kept during ie periods when the employee was working ith plutonium. These records included pluto-ium air concentrations in the processing rooms, ie operator's nose swipe counts done several mes a week up to the end of 1955 and frequently ut irregularly thereafter, daily hand counts, id frequent plutonium assays of 24-hr urine ecimens. Average plutonium air concentra-ns to which the individual was exposed are sented in Table 2. The instances when his swipe counts went above 50 dis/min bitrarily chosen as the limit of significance) e listed in Table 3, and his urine assay record given in Table 4. No tabulation of hand unts is given, since they were consistently low significant levels. Results of fecal analyses re not available. Because of the analytical id sampling difficulties involved, fecal analyses e not a routine practice at the Los Alamos cientific Laboratory.

There were no specific accidents to which ie individual's exposure could be attributed. however, as might be expected, a number of

*Table 3. Record of high nose swipe counts**

Date		Right/Left nostril (counts/min)
1946	29 July	189/320
	30 July	87/70
	5 September	149/19
	25 September	55/4
	1 November	61/15
	10 December	57/68
	30 December	164/106
1947	21 January	192/61
	1 April	91/135
	7 July	144/40
	3 October	120/78
1948	10 February	0/59
	26 April	86/3
	9 June	33/50
	10 June	244/72
	2 July	72/1
	2 August	65/0
	1 December	50/38
After 1948 (none)		

* Technique consisted of rotating a piece of dampened filter paper (on an applicator) in each nostril, after which the paper was unrolled, flattened, dried and counted. Fifty counts/min was arbitrarily taken as the limit of significance.

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Table 4. Results of periodic plutonium urine assays for entire period of employment

Date	dis/min per 24 hr specimen	Date	dis/min per 24 hr specimen
9 August 1946	1.2	1 August 1955	1.2
19 September 1946	1.7	12 August 1955	0.6
18 December 1946	1.7	19 August 1955	0.0
18 April 1947	0.7	30 September 1955	0.7
23 May 1947	0.7	14 November 1955	0.7
26 June 1947	0.7	27 December 1955	0.6
30 July 1947	0.0	9 February 1956	0.0
27 August 1947	1.0	5 April 1956	0.7
2 October 1947	1.5	30 April 1956	0.0
7 November 1947	0.8	8 June 1956	0.4
8 December 1947	4.0	20 July 1956	0.6
13 January 1948	1.0	23 August 1956	0.5
13 February 1948	0.0	25 September 1956	0.0
19 March 1948	0.0	24 October 1956	0.0
22 April 1948	2.0	23 November 1956	0.0
23 June 1948	3.7	17 December 1956	0.1
22 July 1948	0.0	31 January 1957	0.23
19 August 1948	0.8	28 February 1957	0.68
20 September 1948	3.0	12 April 1957	0.22
26 October 1948	2.0	14 May 1957	0.12
22 November 1948	2.5	14 June 1957	0.11
21 December 1948	0.0	15 July 1957	0.03
24 January 1949	Uranium	19 August 1957	0.00
31 January 1949	2.0	20 September 1957	0.20
14 July 1949	1.2	22 October 1957	0.21
8 February 1950	0.8	31 October 1957	0.39
1 September 1950	0.1	14 November 1957	0.51
28 February 1951	0.8	10 January 1958	0.00
4 September 1951	0.7	21 February 1958	0.65
19 May 1952	0.3	25 March 1958	0.51
14 December 1952	0.0	7 May 1958	0.25
4 September 1953	0.0	19 June 1958	0.55
4 June 1954	Off uranium	30 July 1958	0.49
18 June 1954	0.0	15 September 1958	0.79
8 June 1955	Back on plutonium	28 November 1958	0.47

minor mishaps occurred during the period of employment. The detailed record of such minor incidents is summarized in Table 5.

At the time of autopsy, tissues were taken specifically for plutonium assay. The specimens taken and their plutonium contents are shown in Table 6. The assays were carried out using the alpha track counting method.[2] Two independent analyses of aliquots from each tissue sample were made by the analytical section of the Los Alamos Industrial Hygie Group, and aliquots or samples of rib, sternu vertebrae, lungs, liver and lymph nodes we sent to the Hanford Atomic Products Oper tion, where they were analyzed independent by both the Biological Laboratory and t Bioassay Group. The values given in Table are averages and standard deviations for t four independent analyses. The standard devi tion for the lymph nodes includes variation

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Table 5. Summary of minor exposure incidents during period of employment

Date	Type of incident	Potential exposure
26 August 1946	Minor laceration on thumb	No alpha activity detected
30 December 1946	Helped clean up spill of plutonium solution	Air concentration 52 dis/min per m^3 for 8-hr day; nose count 164/106 dis/min
22 April 1947	Received nitric acid burns on arm	No record of contamination
3 September 1947	Small cut on hand, received while making material transfer	No alpha activity detected
14 December 1947	Puncture wound on right hand from a screw point on an instrument panel	No contamination reported
17 March 1949	Helped clean up spill of enriched uranium	No air concentration or nose swipe data recorded
22 April 1950	Exposed to fumes of oxides of nitrogen	No contamination involved
10 August 1953	Helped clean up spill of enriched uranium	Room air concentration 8 dis/min per m^3; nose count 4 dis/min
9 August 1955	While adding caustic to a plutonium and americium solution, materials sprayed out of reaction vessel. Operator was wearing face shield and respirator	No body contamination detected; nose count 22/28 dis/min; room air concentration 175 dis/min per m^3
25 November 1958	Maintenance work involving removal of plutonium-contaminated insulation from an evaporator–condenser	Nose swipe count 0 dis/min; room air concentration 1070 dis/min per m^3. Operator was wearing Wilson 800 respirator

Table 6. Plutonium concentration in autopsy samples (based on actual analytical data)

Organ or tissue	Gross weight at autopsy (g)	Plutonium concentration (dis/min per g wet wt.)
[illegible]oos muscle		0.01
[illegible]idneys	270	0.05
[illegible]art	400	0.06
[illegible]rtilage		0.14
[illegible]leen	116	0.18
[illegible]anium		1.0 ± 0.2
[illegible]bs		1.2 ± 0.3
[illegible]ertebrae		2.1 ± 0.6
[illegible]ungs (minus major [illegible]ronchii)	350	4.8 ± 0.6
[illegible]iver	1950	9.9 ± 1.4
[illegible]ronchial lymph [illegible]odes		125 ± 57*

* Includes variation in different lymph-node samples, [illegible]s well as analytical variation.

sample, as well as variation in analysis, since different lymph-node samples were used in the independent determinations. The highest plutonium concentration was found in the pulmonary lymph nodes (125 ± 57 dis/min per g), followed by the liver (9.9 ± 1.4 dis/min per g), lungs (4.8 ± 0.6 dis/min per g) and then vertebrae (2.1 ± 0.6 dis/min per g). The average of all bone samples was 1.4 ± 0.7 dis/min per g, for which the standard deviation includes the variation among the different bone samples plus the analytical variation.

The total organ and body content, calculated from the data in Table 6, are shown in Table 7. The estimated total body burden was 0.018 μc.

As a result of changes in production methods, the Pu^{238}/Pu^{239} ratio of plutonium processed at the Laboratory increased considerably between 1946–1948 and 1955–1958. Determination of the Pu^{238}/Pu^{239} ratios in bone, lymph node, liver and lung samples indicated bone and lymph nodes had the lowest ratio (corresponding generally to material produced in 1946–1948),

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Table 7. Total body burden estimated from tissue or organ weight and plutonium content

Organ or tissue	Weight (g)	Total content (dis/min)
Liver	1950	1.930×10^4
Skeleton (average)	10,000	1.400×10^4
Lungs(minus bronchii)	850	0.408×10^4
Respiratory lymph nodes	10	0.125×10^4
Muscle	30,000	0.030×10^4
Heart	400	0.002×10^4
Spleen	116	0.002×10^4
Kidney	270	0.001×10^4
Balance*	26,400	0.026×10^4
Total	70,000	3.924×10^4 (0.018 μc)

* Assuming plutonium content of the balance is the same as that of muscle.[3]

and lung samples had the highest (corresponding roughly to more recently produced material). The Pu^{238}/Pu^{239} ratio in the liver was intermediate.

DISCUSSION

The data in Tables 2 and 3 show that all high plutonium air concentrations to which the employee was exposed and all high nose swipe counts recorded occurred during his earlier period of exposure. It is very likely that most of his plutonium burden was accumulated during this period. The record summarized in Table 5 shows that there were no specific incidents to which his plutonium exposure could be attributed. The summary is given principally to point out the close attention given to all potential modes of exposure and thereby emphasize the certainty with which a contaminated accident can be ruled out as the source of the subject's plutonium burden. It is most likely that the body burden, in this case, resulted from chronic inhalation exposure to a low-level plutonium contaminated atmosphere. The above speculations regarding time and mode of exposure are supported also by the indication that the Pu^{238}/Pu^{239} ratio in lymph nodes and bone appeared to correspond to that of plutonium being processed during the early period of the subject's exposure.

Three different urine assay procedures were used during the 12-year period over which th urine data shown in Table 4 were collected Each change resulted in somewhat greate reliability of the data. In 1957, the method was changed to the Hanford alpha trac counting procedure.[2] Urine assays from thi time onwards have considerably higher relia bility than previously. Even during 1957 an 1958, however, there was considerable variatio in the assays, which is probably due both t analytical limitations and to normal physio logical fluctuations. The employee's systemi plutonium burden was estimated from th urine assays using empirical equations derive from human excretion data.[3] Following a acute exposure occurring at known time, th retained plutonium body burden (D_R) is give by the expression

$$D_R = 435\ Ut^{0.76} \qquad (1)$$

in which U is the plutonium (counts/min, dis/min, μc) in a 24-hr urine sample collected days after the time of exposure. D_R is given in the same units used to express U. Since this equation is applicable to relatively acut exposure occurring at known time, it is necessar in protracted exposure cases to assume a effective time of exposure which, to a firs approximation, may be taken as the midpoint of the work period. Following chronic invariant

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xposure to plutonium, the total systemic ntake (D_t) is given by the expression

$$D_t = \frac{130 \times m \times U}{(n + 1/2)^{0.26} - (n - m + 1/2)^{0.26}} \quad (2)$$

n which m is the duration of exposure (days), nd U is the average dis/min per 24-hr urine ample taken n days from the beginning of xposure. D_t is the sytemic exposure and it is igorously necessary to subtract the amount xcreted in order to obtain the amount retained D_R). However, since only about 10 per cent of plutonium burden is excreted in 10 years,[3] uch a correction is insignificant in most cases. The above expressions indicate the determinaion of body burden from a single 24-hr urine ssay. Analytical limitations of the assay nethods and normal physiological variations n urinary plutonium excretion make such stimates completely unreliable, and in practice t is better to use the average of several onsecutive assays (even though they may be veeks or months apart).

Because of the nature of the exposure, either of the above equations is specifically pplicable to the case under consideration. Application of equations (1) and (2) to the verage of all urine assays run during 1949–51 during which time there was no exposure to lutonium) gives 0.033 and 0.031 μc, respecively, for the employee's body burden at that ime as a result of his first period of exposure. During 1957–58, frequent urine assays were un using the more sensitive and reliable alpha rack counting method. Estimations based on quations 1 and 2 (assuming all his exposure ccurred during the earlier work period, and sing the average of the 1957–58 urine assays) ave 0.034 and 0.031 μc, respectively, for the ody burden at the time of death. The latter stimates may be high, since they are predicated n the assumption that the entire body burden as accumulated during the earlier work period and that exposure during the second period ade no contribution to the 1957–58 average rine assay value. That this assumption is pproximately correct is borne out by the stimates of burden at the end of the employee's irst period of exposure. A method of estimating plutonium body burden employing IBM-704 Fortran programming of all urine assay data has been developed by LAWRENCE[4]. His estimate of the subject's body burden at time of death was 0.019 μc. The burden derived from tissue analyses (Tables 6 and 7) was 0.018 μc, which is 45 per cent of the maximum permissible level of 0.04 μc.[5]

The above agreement between body burden from tissue analyses and estimated burden from urine assays is so very satisfactory that it is undoubtedly fortuitous. Determination of body burden from tissue analyses is subjected to considerable sampling uncertainty. Since it is not possible to analyze the entire body, it is necessary to analyze aliquots of the various organs and, on the assumption of uniform distribution and representative sampling, calculate the total body content from the organ weights. This assumption is particularly uncertain with regard to the skeleton, as shown by the analytical data for sternum, rib and vertebra (Table 6).

Some uncertainty in the body burden estimated from urine assays may be expected also from the uncertainty in the exponents of the time parameters in equations (1) and (2). When $t = 10$ days, a 10 per cent error in the exponent of [equation (1)] would make an 18 per cent error in the body burden estimated from the urine assay. The error would increase with time, approaching a factor of about 2 at $t = 3500$ days. Indication that the exponent of t in the [illegible] urinary excretion equation[3] may be in error by about 10 per cent), in the direction resulting in overestimation of the body burden, was obtained recently by re-estimation of the plutonium burdens of workers exposed at the Laboratory during 1944–45 and who had received no subsequent exposure. When estimated from a urine sample collected approximately 10 years after termination, their systemic burdens were, in most cases, about a factor of 2 higher than the estimates based on samples collected during or immediately after exposure. Most of the cases, however, were believed to be inhalation exposures and it is possible although seemingly unlikely, that their systemic burdens did increase as a result of absorption of plutonium deposited in the lungs and pulmonary lymph nodes.

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The distribution of plutonium in the various tissues and organs was somewhat surprising. Approximately 50 per cent of the body burden was found in the liver and 36 per cent in the skeleton (Table 7). A hundred and fifty days after intravenous injection of Pu^{239}-citrate in man, approximately 65 per cent of the administered dose was found in the skeleton and 22 per cent in the liver.[6] Rat experiments show that the relative concentration of plutonium in bone and liver following intravenous injection is dependent on the chemical form and valence state of the material administered.[7] It is quite possible, in the present case, that the partitioning of plutonium between the liver and skeleton was influenced both by the chemical or physical nature of the plutonium and by the route of exposure. The respiratory route of exposure was radiologically responsible for the high plutonium concentrations found in the lungs and pulmonary lymph nodes.

Some interesting qualitative speculations regarding relative deposition and clearance rates of plutonium in various tissues may be drawn from the Pu^{238}/Pu^{239} ratios in bone, lymph nodes, liver and the lungs. The Pu^{238}/Pu^{239} ratios of the plutonium deposited in bone and lymph nodes appeared to correspond with that of plutonium produced in 1946-1948 (which was the subject's earlier and greater period of exposure). The Pu^{238}/Pu^{239} ratio of the material deposited in the lungs, however, appeared to correspond to that of more recent production. The above observations suggest (a) a relatively rapid clearance rate for plutonium in the lungs, compared to that in bone and lymph nodes; and (b) that a relatively small percentage of the material deposited in the lungs must migrate to the latter tissues. Since the Pu^{238}/Pu^{239} ratio of material in the liver was intermediate between that deposited in the bone and lymph nodes and that in the lungs, the rate of clearance from the lungs to the liver must be relatively fast and the retention time in the liver must be longer than in the lungs.

The biological effective dose rate to the various tissues of the subject may be estimated from the observed plutonium concentrations (Table 6) and the following expression derived from the Recommendations of the International Commission on Radiological Protection.[8]

$$R = \frac{C \times \Sigma E(\mathrm{RBE})n}{2.8 \times 10^{-3}}$$

In this expression, R is the dose rate in rems/week, C is the plutonium concentration in $\mu c/g$ and $\Sigma E(\mathrm{RBE})n$ is an effective energy weighted for the RBE of alpha particles and the nonhomogeneity of energy distribution and absorption in the tissue. The weighted energy terms for plutonium in soft tissue and bone are 53 and 270, respectively. Calculated in the above manner, the pulmonary lymph nodes were subject to the highest biologically effective dose rate (~1 rem/week), the liver next (0.08 rem/week), followed by the bone and lungs (0.06 and 0.04 rem/week, respectively). The estimated alpha radiation dose to the lymph nodes may be considerably too high because of shrinkage in lymphoid tissue mass as a result of the acute radiation dose (~10,000 rads of fast neutrons plus gamma rays incident to the chest) received during the criticality accident.

No definite conclusions can be drawn from a single case, but these observations again bring up the troublesome questions of choice of the critical organ following chronic inhalation exposure, the size of the critical tissue volume and the relative sensitivity of various tissues to chronic radiation damage.

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REFERENCES

1. H. C. Paxton, R. D. Baker, W. J. Maraman and R. Reider, Los Alamos Scientific Laboratory Report, LAMS-2293 (1959).
2. L. C. Schwendiman, J. W. Healy and D. L. Reid Hanford Atomic Products Operation Report HW-22680 (1951).
3. W. H. Langham, *Brit. J. Radiol.*, Suppl. No. 7 95 (1957).
4. J. N. P. Lawrence, Los Alamos Scientific Laboratory Report, LA-2329 (1959).

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5. *Maximum Permissible Body Burdens and Maximum Permissible Concentrations of Radionuclides in Air and in Water*, National Bureau of Standards, Handbook No. 69, U.S. Govt. Printing Office, Washington (1959).
6. W. H. LANGHAM, *Health Phys.* **2,** 172 (1959).
7. J. CARRITT, R. FRYNELL, J. KLEINSCHMIDT, W. LANGHAM, A. SAN PIETRO, R. SCHAFFER and B. SCHNAP, *J. Biol. Chem.* **171,** 273 (1947).
8. Recommendations of the International Commission on Radiological Protection. *Brit. J. Radiol.* Suppl. No. 6 (1955).

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