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ADDITIONAL SHORT-TERM PLUTONIUM URINARY EXCRETION DATA FROM THE 1945-1947 PLUTONIUM INJECTION STUDIES

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A recent publication by Rundo[1] on the long-term urinary excretion of plutonium, 10,000 days after intravenous injection of known amounts, has shown that the amount of plutonium excreted per day is significantly higher than predicted by the Langham power function model.[2] The Langham equation for daily urinary (Y_u) excretion rates, in percent/day of the injected dose at time t (days) after the intake, follows:

$$Y_u = 0.2t^{-0.74}$$

Complete details on the Langham experiment are given in the Langham report and in a follow-up publication by Durbin.[3]

A review of the original injection experimental records was made because the published 10,000-day excretion data and observations made at Los Alamos[4] and at the Oak Ridge National Laboratory[5] have shown that at long times after occupational exposure, the urinary plutonium excretion deviates from the Langham power function model. Each of the

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Los Alamos National Laboratory notebooks used to record the analytical data was taken from storage and was studied for details that could influence the published findings. The most interesting discovery from this review was that there were additional urine excretion data for case HP-3. This case was one of the two cases from which Rundo obtained the 10,000 day excretion rate. The reason the data were not used in the original Langham publication is unknown, but remarks included in the notebooks suggest that there were some questions about the analytical methodology and an uncertainty with regard to the collection order. These two remarks may have influenced the exclusion of the data from the Langham report. The other case considered by Rundo was HP-6.

Table I lists the results for case HP-3, recorded in the Los Alamos notebooks, starting with day 1 through day 23 and for days 321 through 324. Additional urine excretion data referenced in the Langham[2] publication from day 1645 (reported as four daily samples showing an average daily urinary excretion of 0.0008% for the injected dose) and the Rundo data at day 9934 are also listed in Table I. The Los Alamos notebook records did not identify the data from day 1645, but two samples collected on day 1674 are noted in the notebook and are included in Table I. The recorded values for these two samples are 1.29 and 0.83 counts/min and correspond to 0.0004% and 0.0002% of the injected dose. These values do not relate to the percent excreted value of 0.0008% reported by Langham. There were no records of spiked control samples analyzed concurrently with the injection study samples, and there is no record of correction factors being applied to the recorded results to

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correct for chemical losses. Each of the samples through day 324 was analyzed in duplicate. When a serious procedural problem was noted with either of the aliquots, the result was not utilized by Langham in the mathematical treatment of the data to calculate his model.

The data for case HP-6 are given in Table II. The samples collected on day 523 and day 1610, referred to in the Langham report, were not identified in the notebooks. Two results for days 1626 and 1627 are identified and are listed in Table II along with the 10,008-day data. All remarks relative to each sample's collection and analysis are also included in this table.

The excretion data for HP-3 and HP-6 are plotted in Figs. 1 and 2. Power function least-square curve fits for these data from day 3 to day 22 or 23 are also shown in the figures. The first data points for the HP-3 and HP-6 cases were not used to calculate the curve fit because they do not represent 24-h collection periods. The second data points were also excluded because of the influence of the short first-day collection period. Also shown on this graph is the Langham power function curve that was derived from the use of all the published data including data collected from occupationally exposed workers. The occupational exposure data were used by Langham to extend the power function fit to 1750 days of postexposure.

It is apparent in Figs. 1 and 2 that a power function fit is a good choice to describe the early urinary plutonium excretion. The later

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period (300-,500-, and 1600-day) results, along with the 10,000-day results, however, show a significant departure from the single power function model used to describe long-term plutonium excretion. The 300-, 500-, 1600-, and 10,000-day data may represent a distinctly different segment of the Pu excretional model for humans. This would be in keeping with the observations made by Stover[6] and Clark[7] that there were two distinct excretion segment rates for dog and swine plutonium excretion as a function of time following injection of plutonium (IV) citrate. The dog data showed a change in the first segment after 20 days and the swine data changed after 10 days. Durbin has concluded that within the Langham published data, there is evidence of two to four distinct segments in the excretion data and that the segments were dependent on how long the excretion data were collected. The evidence from the animal data, the additional results on day 324 for case HP-3, on day 523 for case HP-6, and on the 10,000-day data for both cases support the evidence of at least a two-segment model for the two human cases. The 1600-day data for cases HP-3 and HP-6, however, appear to be a departure from a simple two-segment model for the human excretion data.

Because the 1600-day data are inconsistent with a simple two-segment model to describe human plutonium excretion, the notebook records for this time period (1950) were reviewed for identifiable events that could have affected the reported results. As previously stated, only two results for each case at the 1600-day period were identified by the patient's name in the notebook records. The HP-3 results did not relate

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to the percentage given by the Langham report; therefore, we cannot identify the source of the reported 0.0008% of dose excreted on day 1645 for case HP-3. The notebook records, 4.54 and 4.26 counts/min, for case HP-6 are equivalent to the 0.0011% excretion values reported by Langham. These results can be assumed to be one of the sources of the data reported by Langham for the 1610-day excretion for case HP-6. The notebook records indicate that these "special" samples were analyzed along with other routine bioassay samples and that no special attention was given to the samples. However, these samples were analyzed by a different analytical procedure than was used to report results analyzed before the year 1950. In October 1949, the bismuth phosphate analytical method replaced the cupferron procedure that had been used since 1945.[8] The lower chemical recovery and wider standard deviation of the bismuth phosphate procedure are significant variables that could have influenced the 1600-day HP-3 and HP-6 results. The influence of this lower recovery and larger precision is also evident within the routine bioassay sample data obtained from personnel with histories of positive plutonium excretion.[9]

In contrast to the data collected and analyzed through day 1600, which may be low because of losses associated with the analytical procedure, the 10,000-day data reported by Rundo are corrected by the use of ^{242}Pu tracer to 100% of the excreted amount of ^{239}Pu in each 24-h collection.

The 10,000-day data, therefore, are the only data we have from the injection study cases that have a reliable estimate of analytical sources

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of error associated with the excretion data. The correction of the other data for the appropriate chemical recovery factors would change the estimates of the amounts excreted and will significantly bring the day 1600 data closer to the profile of long-term plutonium excretion for the two cases, as evidenced by the data on either side of the 1600-day data. We have not introduced these factors into the data listed in Tables I and II. We do, however, suggest that the 1600-day results be used with caution because of possible errors introduced by the analytical method used in 1950 and because of the available evidence, which shows that samples analyzed in 1950 were not as carefully supervised as were the samples analyzed during the period when the injection study samples were first under investigation in 1945-47 and again in 1973.

The previously unreported additional plutonium excretion data from HP-3 at day 324 and the evidence of the reported HP-6 data at day 524, plus the 10,000-day data on each case, support the conclusion that for these two cases, plutonium excretion departs from a power function curve fit as early as 300 days' postinjection. These data also support the evidence seen in occupationally exposed workers that the long-term excretion of plutonium deviates from the Langham power function model after the early excretion period.

We have refrained from the development of a new mathematical model to describe plutonium excretion using these data because of the limited data and possible sources of error noted. We do feel that the use of the Langham equation to predict plutonium body burdens from long-term

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excretion data should be discouraged. It is obvious that the use of the 523- and 1600-day data from the HP-3 and HP-6 cases influenced the mathematical development of the Langham power function equation, and application of this equation to occupational exposure excretion data will bias the resulting estimates of plutonium body deposition.

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TABLE 1. Individual Urinary Excretion Values for Case HP-3 Expressed as Counts per Minute per Aliqout Analyzed and as Per Cent of Dose Excreted per Collection Period

Days Post-Injection (11/27/45)		Counts per Aliquot[a] 1 (counts/min)	2 (counts/min)	Per Cent of Dose[b] 1	2	Remarks from Notebook
0.4	9h	563.9	509.1	0.3281	0.2962	
0.9	12h	437.0	446.8	0.2543	0.2600	
1.9	24h	299.1	496.6	--	0.2890	Aliquot No. 1 discarded
3	24h	191.4	lost	0.1114	--	
4	24h	190.3	176.7	0.1107	0.1028	
5	24h	138.7	129.0	0.0807	0.0751	
6	24h	73.1	74.6	0.0425	0.0434	Shipping material moist
7	24h	70.0	77.0	0.0407	0.0448	
8	24h	74.3	94.1	0.0432	0.0548	
9	24h	45.2	32.9	0.0263	0.0191	
10	24h	46.6	lost	0.0271	--	
11	24h	46.8	45.2	0.0272	0.0263	
12	24h	26.5	23.7	0.0154	0.0138	
13	24h	34.1	33.9	0.0198	0.0197	
14	24h	34.2	34.1	0.0199	0.0198	
15	24h	49.5	45.6	0.0288	0.0265	
16	24h	41.9	43.3	0.0244	0.0252	
17	24h	30.4	41.3	0.0177	0.0240	
18	24h	34.3	23.1	0.0200	0.0134	
19	24h	29.5	31.6	0.0172	0.0184	
20	24h	17.6	24.1	0.0102	0.0140	
21	24h	32.1	31.8	0.0187	0.0185	
22	24h	23.6	24.0	0.0137	0.0140	
23	24h	23.6	23.5	0.0137	0.0137	
321	24h	3.1	4.5	0.00180	0.00262	Ran these two bottles separately, both with same date, as we understood four 24-h samples had been sent.
322	24h	5.0	4.3	0.00291	0.00250	
323	24h	7.4	4.5	0.00431	0.00262	
324	24h	8.2	8.0	0.00477	0.00471	
				(X1)		
1645	c			0.0008		Ref. 2
1674	d		1.29			
1674	d		0.83	0.0002		
9934	e		8.6±1σ,0.9	0.00252		Corrected for tracer recovery

Note: Dose, 343 725 counts/min; injection time, 11:00 a.m.
[a]Each aliquot=one-half of sample.
[b]Counts per aliquot/doseX2X100=per cent of dose excreted per sample.
[c]Four 24-h daily collections.
[d]Collection period not recorded.
[e]The 14- to 24-h samples.

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TABLE 2. Individual Urinary Excretion Values for Case HP-6 Expressed as Counts per Minute per Aliqout Analyzed and as Per Cent of Dose Excreted per Collection Period

Days Post-Injection (11/27/45)		Counts per Aliquot[a] 1 (counts/min)	2 (counts/min)	Per Cent of Dose[b] 1	2	Remarks from Notebook
0.26	6.3h	312.3	331.9	0.1690	0.1800	
0.76	12.0h	324.2	315.2	0.1755	0.1706	Splattering in oven, Aliquot No. 2, broken pipette
1.76	24h	404.9	391.8	0.2192	0.2121	
3	24h	225.8	241.8	0.1222	0.1309	
4	24h	206.0	135.7	0.1115	lost	Aliquot No. 2 splattered
5	24h	138.3	140.7	0.0749	0.0762	Sample ignited, vigorous reaction
6	24h	99.5	112.3	0.0539	0.0608	
7	24h	80.5	81.7	0.0436	0.0442	Spilled in centrifuge, indicator trouble
8	24h	81.3	80.1	0.0440	0.0434	
9	24h	63.3	54.0	0.0343	0.0292	
10	24h	48.1	66.4	0.0260	0.0359	
11	24h	lost	lost	--	--	Great loss in ashing
12	24h	43.4	45.9	0.0234	0.0248	Leakage
13	24h	43.3	40.9	0.0235	0.0221	
14	24h	36.9	35.3	0.0200	0.0191	Burned in oven
15	24h	40.7	39.0	0.0220	0.0211	
16	24h	30.4	33.2	0.0164	0.0180	
17	24h	25.0	23.0	0.0135	0.0124	
18	24h	27.7	28.2	0.0150	0.0153	
19	24h	29.0	27.4	0.0157	0.0148	
20	24h	23.7	22.7	0.0128	0.0123	
21	24h	23.7	20.2	0.0128	0.0109	Approximately 100 cc lost
22	24h	23.3	20.6	0.0126	0.0111	
				(X1)		
523	c			0.002		Ref. 2
1610	c			0.0011		Ref. 2
1626	d		4.54	0.0012		
1627	d		4.26	0.0012		
10 008	e		5.45±1σ,0.6	0.00141		Result corrected for tracer recovery

Note: Dose, 369 500 counts/min; injection time, 1:40 p.m.
[a]Each aliquot=one-half of sample.
[b]Counts per aliquot/doseX2X100=per cent of dose excreted per sample.
[c]Four daily samples.
[d]Collection period not recorded.
[e]Eight 24-h samples.

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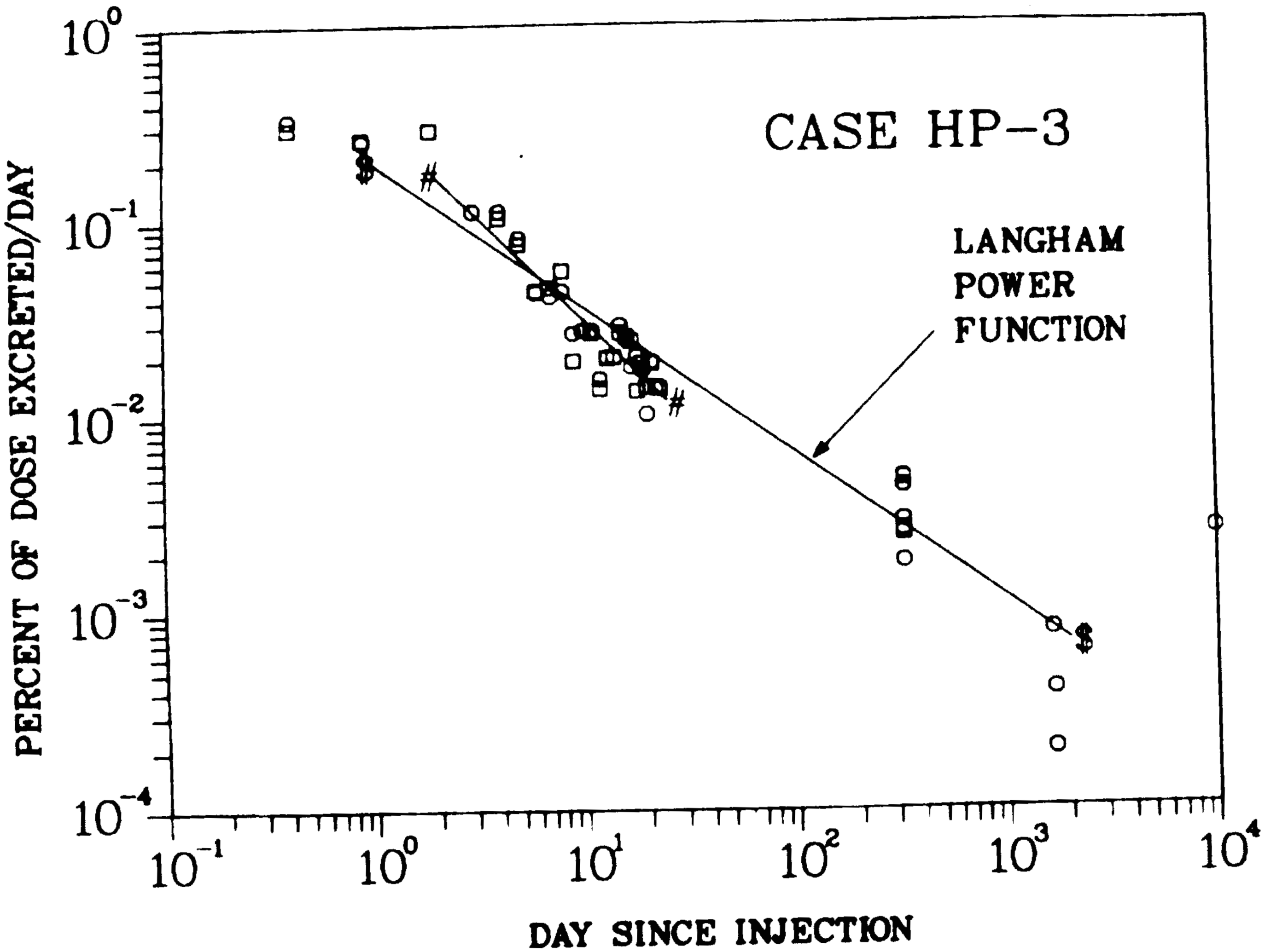

FIGURE 1. Excretion Data for Case HP-3. A power function curve for data collected on days 3 to 23 is shown by the solid line between the # symbols. The power function for these data, days 2 to 23, where t = days of postexposure, is percent excreted per day = $0.34t^{-1.04}$, r = 0.92. The Langham power function model through day 1750 is indicated by the solid line drawn between the $ symbols.

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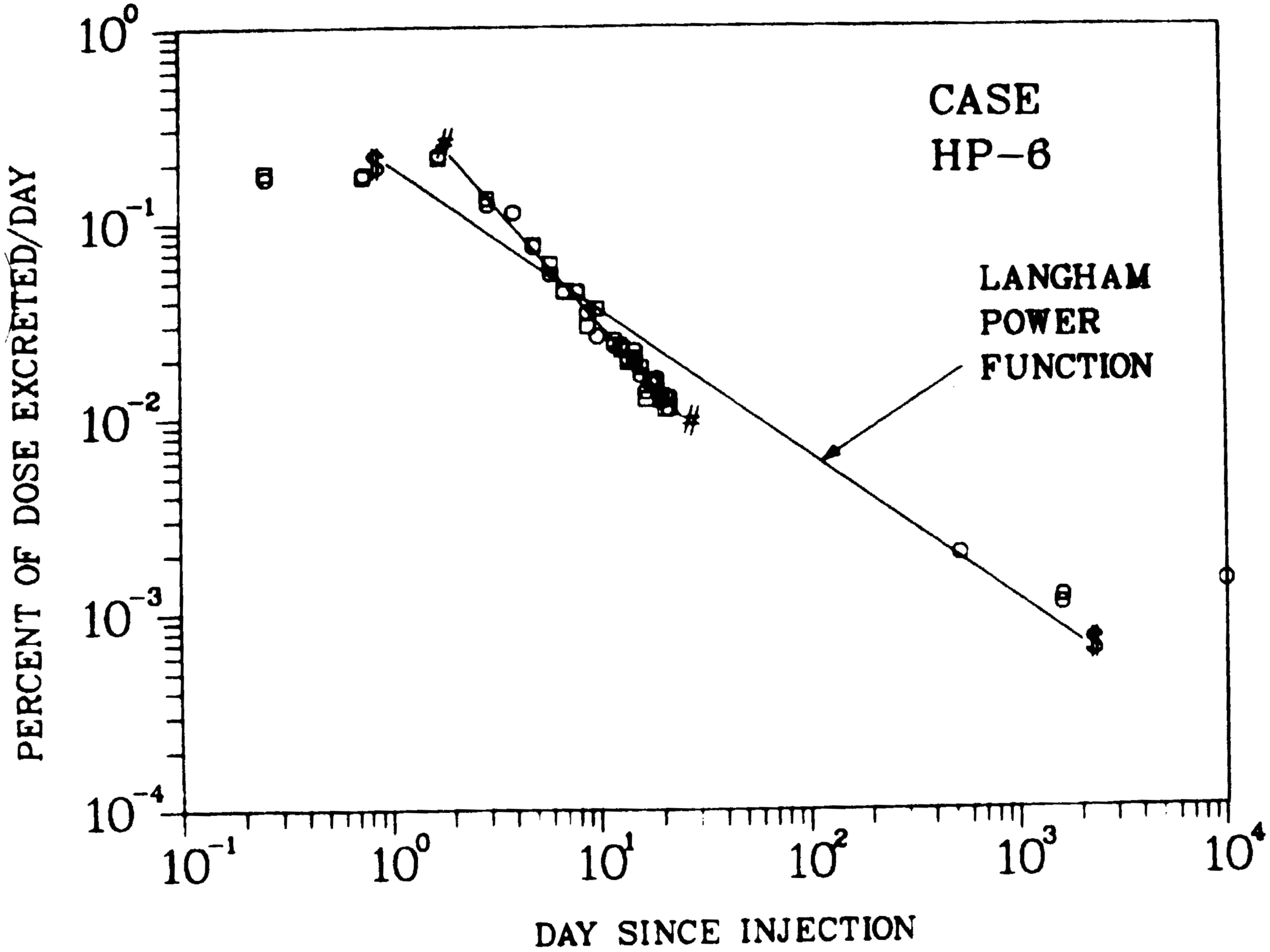

FIGURE 2. Excretion Data for Case HP-6. A power function curve for data collected on days 3 to 23 is shown by the solid line between the # symbols. The power function for these data, days 2 to 23, where t = days of postexposure is percent excreted per day = $0.53t^{-1.24}$, r = 0.99. The Langham power function model through day 1750 is indicated by the solid line drawn between the $ symbols.

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