

## MAN LUNGS

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## THE DISTRIBUTION OF $^{239}\text{Pu}$ IN THE BODY FOLLOWING EXPOSURE BY INHALATION\*

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(Presented by W. S. SNYDER)

**Abstract**—Applying the standard lung model, a soluble aerosol deposited in the lung is absorbed into the blood, but some fraction of the more insoluble deposits remains in the lung for long periods of time. Conventionally, an elimination half-time of 120 days is assumed for these "insoluble" deposits, and it is assumed further that ultimately most of this material is eliminated via the gastrointestinal tract. As a result, bone is not considered to be the critical organ for most insoluble aerosols of  $^{239}\text{Pu}$  or other heavy metals. Recent work indicates that there may be a significant fraction of these "insoluble" deposits reaching the blood, and thus there is the possibility of a significant bone burden. At first glance, the available autopsy data on human exposure might seem to conflict with the above interpretation. However, a detailed data analysis of a human exposure record indicates that the above interpretation may be correct. Although the subject's skeleton showed a smaller concentration than did the liver, lung, or pulmonary lymph nodes, this does not exclude the skeleton as the critical organ. Applying the metabolic model, the lung would be expected to have a higher concentration than bone in the early years of exposure, although the latter would continue to increase and might become the limiting criterion governing continuous exposure for a working life. The evidence for and against this hypothesis is discussed in some detail.

EXPOSURE to rather insoluble aerosols of  $^{239}\text{Pu}$  poses a very serious problem for the atomic energy program and, particularly, to the health physicist who must cope with the problem of assessing such exposure. Animal experiments have demonstrated that  $^{239}\text{Pu}$  which is injected and deposits in bone may produce malignancies, and, on the basis of equal average doses to the skeleton,  $^{239}\text{Pu}$  is generally considered to be more hazardous than  $^{226}\text{Ra}$ .

The maximum permissible concentration, MPC, or, equivalently, the permissible quarterly intake is a derived standard, not a primary one; that is, it is intended to limit the dose to various body tissues. The ICRP and the NCRP base their recommendations for MPC values in air and water on the assumption that exposure is continuous and at a constant level; however, the recommendations permit dose and intake to be averaged over 13 weeks.

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In practice, exposure seems to occur more often by sporadic intakes that result from faulty equipment or failure to follow procedures. However, if the quarterly intakes can be controlled within the recommended limits, the resulting dose to body tissues should not exceed the recommended limits on dose equivalent provided the metabolic model used to estimate body burdens and organ burdens is substantially correct. Thus, it is of great importance to assess the accuracy of the metabolic model.

There is in the literature only one case of chronic exposure of man to  $^{239}\text{Pu}$  for which reliable data on distribution in the body are available. This case, studied extensively by FOREMAN *et al.*,<sup>(1)</sup> will be referred to as employee E822 in this paper in accordance with the terminology used in Ref. (2).

In Fig. 1 the urinary excretion record of this employee is indicated graphically. The lines connecting the points are merely to indicate the ordering of the points and to emphasize the fluctuations of the data. There are two extensive periods of 258 and 264 days, respectively,

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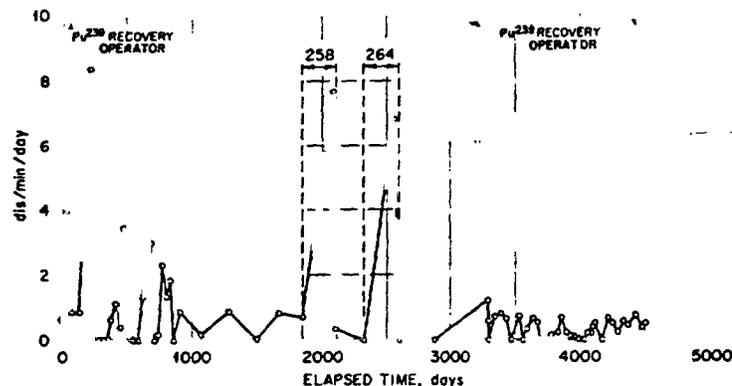


FIG. 1. Urinalysis data of case E822.

during which no samples were taken. The times when the employee was working as a  $^{239}\text{Pu}$  operator are indicated. There are three urine samples that indicated an unusually high concentration of  $\text{Pu}^{239}$ . Those most familiar with the analytical procedure used at LASL during this period have indicated that these and perhaps other values are considered as spurious, the high values probably resulting from contamination of the sample.

In Table 1 the estimated organ burdens and corresponding average concentrations in certain

Table 1. Estimated organ burdens and average concentrations in certain tissues for case E822<sup>(1)</sup>

Organ or tissue	Concentration (dis/min/g wet wt.)	Organ burden ( $\mu\text{c}$ )
Liver	$9.9 \pm 1.4$	0.0087
Skeleton (average)	$1.4 \pm 0.7$	0.0063
Lung (minus bronchii)	$4.8 \pm 0.6$	0.0018
Pulmonary lymph nodes	$125 \pm 57$	0.00056

tissues as reported in Ref. (1) are shown. In Ref. 1 the authors state "it is most likely that the body burden, in this case, resulted from chronic inhalation exposure to a low-level plutonium contaminated atmosphere." They also indicate that the distribution of plutonium in the various tissues and organs was somewhat

surprising since the liver burden exceeded the skeletal burden, whereas  $\text{Pu(IV)-citrate}$  injected in man gave higher skeletal burdens. They conclude "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 undoubtedly responsible for the high plutonium concentrations found in the lungs and pulmonary lymph nodes." Therefore, it is important to examine carefully the evidence on this unique case to glean whatever information or suggestions one can concerning the model for assessing exposure of man to plutonium by inhalation.

In Fig. 2 the growth of organ burden of plutonium according to the exponential model used by ICRP<sup>(3)</sup> is shown as a function of the period of exposure at a constant level. The curves in Fig. 2 were computed using  $T_b = 365$  days for lung,  $T_b = 3 \times 10^4$  days for liver and  $T_b = 7.3 \times 10^4$  days for bone. For clarity of presentation, the level of intake per day has been taken differently in the three cases, being chosen so as to produce the maximum permissible organ burden in each case after 50 years of exposure at a constant level. If the level had been the same, the curves for lung and liver would be much lower, but the reduction factor to be applied would depend on a number of factors which are largely unknown (e.g. the data on the chemical form of the plutonium as inhaled and as it reached the blood, the particle size and

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Table 2. Estimated intake to blood for case E822\*

Date	Amount (μc)	Date	Amounts
7-25-46	0.00096	9-9-55	0.00105
10-10-46	0.00135	10-23-55	0.00074
11-24-46	0.00100	5-20-56	0.00003
8-13-47	0.00059	6-29-56	0.00061
10-20-47	0.00017	10-27-57	0.00007
4-5-48	0.00187	1-31-58	0.00076
9-4-48	0.00302	3-9-58	0.00008
10-8-48	0.00035	5-29-58	0.00038
11-30-50	0.00333	7-10-58	0.00002
6-2-51	0.00134	8-23-58	0.00088

\* As estimated by J. N. P. LAWRENCE, LASL, private communication.

obtained prior to 1-24-57,<sup>(5)</sup> LAWRENCE indicates that these estimates may differ somewhat from others given previously. The author has obtained estimates of intake based upon the data of Fig. 1, rejecting the three highest values as spurious. LAWRENCE's method of estimation excludes these values and also others. Whereas LAWRENCE's method estimates a series of discrete intakes, the author's method<sup>(2)</sup> assumes a continuous process of intake and excretion and estimates the total intake to blood from the beginning of exposure to any specified date. The total intake as a function of time following

the beginning of exposure is shown graphically in Fig. 3, the step-function corresponding to LAWRENCE's estimates and the continuous dashed curve to the estimates by the author. The dashed curve should, by definition, not decrease, and the fact that it does decrease slightly merely reflects the fluctuations of the excretion data. According to the model, which assumes urinary excretion to be given by a power function  $0.0023t^{-0.77}$ ,<sup>(6)</sup> the excretion will never be zero following the first exposure. Yet frequently, the data shown in Fig. 1 indicate no excretion of <sup>239</sup>Pu. Such discrepancies of the actual data and the model account for the somewhat anomalous behavior of the estimated intake function. The discrepancy, however, is not serious, and the data presented in Fig. 3 indicate a remarkably close agreement of the two methods. Perhaps this is not surprising since both are based on the assumption that urinary excretion following intake to blood is governed by the formula  $0.0023t^{-0.77}$ . However, the mathematical treatment is different, and this agreement merely indicates the essential correctness of either method, provided the input data are accurate. Unfortunately, the hospital patients reported by LANGHAM<sup>(6)</sup> showed rather large differences in the power function that best represented their urinary excretion. The choice of the above function is merely an average over

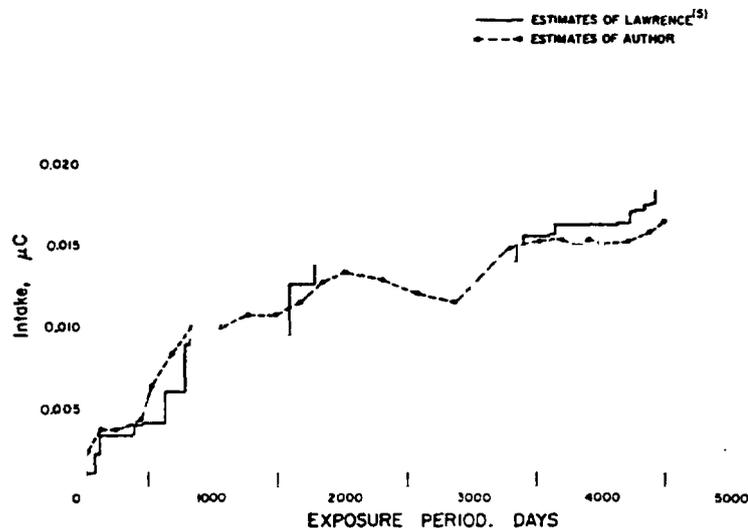


FIG. 3. Estimates of cumulative intake of <sup>239</sup>Pu to blood (case E822).

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is shown graphically on corresponding to and the continuous rates by the author. l, by definition, not at it does decrease e fluctuations of the to the model, which to be given by a .77,<sup>(6)</sup> the excretion g the first exposure. wn in Fig. 1 indicate discrepancies of the el account for the rior of the estimated pancy, however, is presented in Fig. 3 e agreement of the s is not surprising re assumption that intake to blood is 123t<sup>-0.77</sup>. However, t is different, and cates the essential provided the input ately, the hospital M<sup>(6)</sup> showed rather function that best etion. The choice ly an average over

many cases, and it is quite possible that E822 might have been better approximated by a different function. There does not seem to be any known procedure for adjusting to individual differences.

If one assumes that intake to blood is given by Fig. 3, he can then calculate the organ burdens for liver and bone. Since the ratio of <sup>238</sup>Pu/<sup>239</sup>Pu indicated long retention in these organs, the biological half-lives given by ICRP<sup>(3)</sup> were used, i.e. 3 × 10<sup>4</sup> days for liver and 7.3 × 10<sup>4</sup> days for bone. It is immediately apparent that the choice of these values does not significantly affect the resulting estimate of the organ burden provided these biological half-lives are long compared with 12 years, the total time during which exposure could occur. However, the use of the values of *f*<sub>2</sub>' which represents the fraction of material reaching blood which deposits in a specified organ, will result in the bone showing a markedly greater burden than will liver. Since this is contrary to the autopsy findings, it is suggested that *f*<sub>2</sub>' should have approximately the same value for liver and for bone.

As is noted by FOREMAN *et al.*,<sup>(1)</sup> the assumption that liver and bone absorb approximately equal amounts of inhaled plutonium that reaches the blood is at variance with the uptake in the organs following injection of Pu(IV)-citrate. BAIR *et al.*,<sup>(7)</sup> using plutonium in 0.14 N HNO<sub>3</sub>, found that inhalation produced approximately equal burdens of Pu in liver and in bone of dogs, whereas by injection the same material deposited predominately in liver. The same experimenters found that inhaled PuO<sub>2</sub> aerosols lead to approximately equal translocation to liver and bone. There were rather marked fluctuations in individual animals, however, with liver being predominant in some cases and bone in others. In some instances this excess was 1 order of magnitude. From the data of E822, it is suggested for inhaled plutonium aerosols that *f*<sub>2</sub>' might have the same value for liver and for bone, but this one case is obviously not enough to establish this hypothesis for standard man.

The pattern of intake to blood indicated by Fig. 3 can be used to estimate a possible pattern of intake to lung, admittedly on very tenuous evidence. If one postulates, for simplicity, that

a single intake to lung occurred at the beginning of exposure and immediately following each urine sample day, then he can estimate successively the magnitude of these intakes and the rate of accumulation of the lung burden. This particular intake day is somewhat arbitrary, of course, and the pattern could be varied in many ways. However, to account for a relative high value in a urine sample one must postulate material moving from the lung to blood during the preceding period.

Assuming, then, an intake of *l<sub>i</sub>* μc to the deep lung on day τ<sub>*i*</sub>, the contribution to blood during a period *t<sub>i</sub>* days to *t<sub>i+1</sub>* days would be

$$l_i f \int_{t_i}^{t_{i+1}} dt \lambda e^{-\lambda(t-\tau_i)} = l_i f [e^{-\lambda(t_i-\tau_i)} - e^{-\lambda(t_{i+1}-\tau_i)}] \quad (5)$$

Here *f* represents the fraction of material removed from the lung that goes to blood, and λ is the half-time removal from the lung. For this analysis the day of the supposed intake to lung, τ<sub>*i*</sub>, was taken to be the first day of exposure or the first day following collection of a urine sample. The intakes *l<sub>i</sub>* were estimated successively. When estimating the intake occurring on day *t<sub>i</sub>* + 1, that is, on the first day of the sampling period *t<sub>i</sub>* to *t<sub>i+1</sub>*, the intakes to blood during the time *t<sub>i</sub>* to *t<sub>i+1</sub>* from all lung intakes calculated previously were subtracted from LAWRENCE's estimate for this period. If the difference was zero or negative, *l<sub>i</sub>* was set equal to zero, for the previous intakes already accounted for this amount of absorption to blood. If the difference was positive, then *l<sub>i</sub>* was estimated by equating formula (5) to this difference. This calculation was programmed for the 1604 computer, and the resulting organ burdens were calculated also under various assumptions concerning λ and λ<sub>*c*</sub>. Since *f* is not known, formula (5) only determines *l<sub>i</sub>**f*, and the sums of these values for all intakes are tabulated in Table 3 with λ = (ln 2)/*T* and *T* = 60, 120, 240, 365, 730 and 1095 days. Similarly, only the product of organ burden and *f*<sub>2</sub>' was calculated in an attempt to obtain some guidance concerning the value of *f*<sub>2</sub>'. Values of organ burden and *f*<sub>2</sub>' were calculated for *T<sub>c</sub>* = 10<sup>3</sup>, 3 × 10<sup>3</sup>, 10<sup>4</sup>, 3 × 10<sup>4</sup>, and 7.2 × 10<sup>4</sup> days with λ<sub>*c*</sub> = (ln 2)/*T<sub>c</sub>*. Table 3 includes the values of *f* and *f*<sub>2</sub>' obtained if one

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Table 3. Calculated estimates of organ burdens and deposition factors

T (days)	T <sub>e</sub> (days)	Total deposition in deep lung × f	Lung burden × f	f	Organ burden × f <sub>2</sub> '	Liver f <sub>2</sub> '	Bone f <sub>2</sub> '
60	10 <sup>3</sup>	3.57 × 10 <sup>-2</sup>	3.55 × 10 <sup>-4</sup>	0.20	7.88 × 10 <sup>-3</sup>	1.10	0.80
	3 × 10 <sup>3</sup>				1.87 × 10 <sup>-2</sup>	0.47	0.34
	10 <sup>4</sup>				2.89 × 10 <sup>-2</sup>	0.30	0.22
	3 × 10 <sup>4</sup>				3.30 × 10 <sup>-2</sup>	0.26	0.19
	7.2 × 10 <sup>4</sup>				3.44 × 10 <sup>-2</sup>	0.25	0.18
120	10 <sup>3</sup>	5.28 × 10 <sup>-2</sup>	1.52 × 10 <sup>-3</sup>	0.84	1.10 × 10 <sup>-2</sup>	0.79	0.57
	3 × 10 <sup>3</sup>				2.69 × 10 <sup>-2</sup>	0.32	0.23
	10 <sup>4</sup>				4.17 × 10 <sup>-2</sup>	0.21	0.15
	3 × 10 <sup>4</sup>				4.78 × 10 <sup>-2</sup>	0.18	0.13
	7.2 × 10 <sup>4</sup>				4.98 × 10 <sup>-2</sup>	0.17	0.13
240	10 <sup>3</sup>	7.84 × 10 <sup>-2</sup>	4.45 × 10 <sup>-3</sup>	2.5	1.52 × 10 <sup>-2</sup>	0.57	0.41
	3 × 10 <sup>3</sup>				3.87 × 10 <sup>-2</sup>	0.22	0.16
	10 <sup>4</sup>				6.02 × 10 <sup>-2</sup>	0.14	0.10
	3 × 10 <sup>4</sup>				6.89 × 10 <sup>-2</sup>	0.13	0.091
	7.2 × 10 <sup>4</sup>				7.18 × 10 <sup>-2</sup>	0.12	0.088
365	3 × 10 <sup>4</sup>	9.75 × 10 <sup>-2</sup>	7.69 × 10 <sup>-3</sup>	4.3	8.40 × 10 <sup>-2</sup>	0.10	0.075
	7.2 × 10 <sup>4</sup>				8.73 × 10 <sup>-2</sup>	0.10	0.072
730	3 × 10 <sup>4</sup>	1.55 × 10 <sup>-1</sup>	1.74 × 10 <sup>-2</sup>	9.7	1.29 × 10 <sup>-1</sup>	0.067	0.049
	7.2 × 10 <sup>4</sup>				1.34 × 10 <sup>-1</sup>	0.065	0.47
1095	3 × 10 <sup>4</sup>	1.97 × 10 <sup>-1</sup>	2.72 × 10 <sup>-2</sup>	15	1.59 × 10 <sup>-1</sup>	0.056	0.040
	7.2 × 10 <sup>4</sup>				1.65 × 10 <sup>-1</sup>	0.053	0.038

(ln 2)/T<sub>e</sub> = λ<sub>e</sub> = elimination half-time for the organ of reference.

(ln 2)/T = λ = elimination half-time for the lung.

f<sub>2</sub>' = fraction of material entering the blood that deposits in the organ of reference.

f = fraction of material eliminated from lung that goes to blood.

equates the resulting organ burdens to the autopsy estimates. Half-times in lung much in excess of 120 days yielded values of f greater than 1 and, therefore, must be rejected, unless one would assume that some of the plutonium eliminated rapidly from the lung was soluble to a very high degree and reached the blood in significant amounts. This hypothesis is not considered a very likely one.

The values assumed for T and T<sub>e</sub> in Table 3 yield estimates of f<sub>2</sub>' which are possible except when T<sub>e</sub> = 10<sup>3</sup> days where the sum of f<sub>2</sub>' for bone and f<sub>2</sub>' for liver is inadmissibly high. When the biological half-time in lung is 240 days or more, the value of f is inadmissible.

The use of the values for T<sub>e</sub> given in ICRP Publication 2 and of T = 60 or 120 days yields approximately equal burdens in liver and bone with admissible values for f<sub>2</sub>'. Again, it seems that only more precise studies can decide the question of the proper value of f<sub>2</sub>' to use for inhaled plutonium aerosols.

ICRP Publication 2 does not indicate a quantitative model governing deposition in the pulmonary lymph nodes, and this, perhaps, is the major deficiency of the model. BAIR *et al.*<sup>(7)</sup> found that from 0.2 to 2 per cent of alveolar deposits had translocated to lymph nodes of dogs 30 days after inhaling PuO<sub>2</sub> aerosols; an elimination rate from these sites is not indicated

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Liver $f_2'$	Bone $f_2'$
1.10	0.80
0.47	0.34
0.30	0.22
0.26	0.19
0.25	0.18
0.79	0.57
0.32	0.23
0.21	0.15
0.18	0.13
0.17	0.13
0.57	0.41
0.22	0.16
0.14	0.10
0.13	0.091
0.12	0.088
0.10	0.075
0.10	0.072
0.067	0.049
0.065	0.47
0.056	0.040
0.053	0.038

given in ICRP for 120 days yields in liver and bone. Again, it seems we can decide the value of  $f_2'$  to use for

indicate a quantification in the data, perhaps, is that of alveolar lymph nodes of  $^{239}\text{Pu}$  aerosols; an estimate is not indicated

nor is such a rate well documented from other sources. The total intake to the deep lung is given in Table 3 for elimination half-times in lung of 60 days and 120 days—the only admissible values in view of the corresponding values of  $f$ . The ratio of these intakes to the autopsy estimate of the burden in lymph nodes is within the range of deposition values observed by BAIR. In the absence of any estimate of an elimination rate, this is, perhaps, as detailed as one can be in interpreting the data on the pulmonary lymph nodes.

In summary, the analysis of the data on E822 presented here suggests that (1) it is possible to construct patterns of exposure which bring the autopsy data of E822 and the organ burdens estimated by the ICRP model into substantial agreement except for the values of  $f_2'$  for liver and bone; (2) the values of  $f_2'$  for deposition in liver and bone of inhaled plutonium aerosols need to be re-examined, and, in view of the wide differences found in individual experimental animals, may require more experimentation; and (3) the shorter half-times for elimination from the lung are not grossly at variance with the standard lung model in view of our ignorance of the solubility and particle size of the inhaled material.

Perhaps this elaborate and circuitous method of analysis on the basis of very tenuous evidence is unwarranted, and the author does not regard any of the values or hypotheses used in the course of the analysis as more than a bare suggestion of possibility. But, one should not necessarily assume that the data on E822 are grossly at variance with the ICRP model. The author has no intention of asserting that the ICRP model is correct and has still less intention of implying that the above analysis establishes its correctness. Rather, the intent is to suggest that the data on E822 do not grossly contradict that model in view of our ignorance of so many important characteristics of the exposure. The author regards the discrepancy of the  $f_2'$  values for liver and bone as the point most deserving of attention on the basis of these data, but in view of the wide fluctuations shown by individual experimental animals, even this must be regarded as only a suggestion. Review of the human data as well as data on experimental animals suggests that the uptake of plutonium

by liver and by bone may be significantly different following i.v. injection and exposure by inhalation. More data and experience may very well show that the ICRP model requires substantial revision, but, other than the suggestion concerning the values of  $f_2'$ , the data of E822 do not provide a firm basis for such a revision nor even a strong indication of the direction in which the revision should be made.

*Acknowledgment*—The author acknowledges the very valuable assistance of J. N. P. LAWRENCE as mentioned above and the efficient help of M. R. FORD in carrying out exploratory calculations and supervising the computer calculations and preparation of the figures and tables. Mr. FRED ROBERTS and the Mathematics Panel at ORNL were responsible for programming the codes used in these calculations.

REFERENCES

1. H. FOREMAN, W. MOSS and W. LANGHAM, *Health Phys.* **2**, 326 (1960).
2. W. S. SNYDER, *Argonne National Laboratory, ANL-6637*, p. 13 (1961).
3. ICRP Publication 2, *Report of Committee II on Permissible Dose for Internal Radiation*. Pergamon Press, London (1959); *Health Phys.* **3**, 1 (1960).
4. J. N. P. LAWRENCE, *Health Phys.* **8**, 61 (1962).
5. J. N. P. LAWRENCE, Los Alamos Scientific Laboratory, Private communication.
6. W. H. LANGHAM, S. H. BASSETT, P. S. HARRIS and R. E. CARTER, *Los Alamos Scientific Laboratory, LA-1151* (1950).
7. W. J. BAIR, D. H. WILLARD, J. P. HERRING and L. A. GEORGE, II, *Health Phys.* **8**, 639 (1962).

DISCUSSION

KORNBERG, H. A.: Was the comparison of the two curves showing intake of  $^{239}\text{Pu}$  to blood based on any measurements other than excretion, or were they both estimates?

SNYDER, W. S.: Both the curves represented total intake to blood to time  $t$  as estimated from urinalysis data of the subject. In both cases, Langham's power function model for urinary excretion following iv injection was the basis of the estimation, but the calculation was programmed for a digital computer along rather different lines. There are no direct measurements which, to my knowledge, would provide an estimate of intake to blood.

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BAIR, W. J.: I would like to comment on our  $\text{PuO}_2$  inhalation studies with dogs although they are not really comparable with the case in point since the dogs were given only a single exposure. Although  $^{239}\text{Pu}$  is appearing in the skeleton of dogs more than 4 years after exposure, the rate of translocation is so

low that before the skeleton receives a harmful amount, the lungs will have already suffered severe pathology.

SNYDER, W. S.: The tables include data for many different possibilities we have explored. There are definite suggestions that some of the deposition factors should be changed.