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Health Physics Vol. 46, No. 4 (April), pp. 839–844, 1984
Printed in the U.S.A.

0017-9078/84 $3.00 + .00
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PLUTONIUM PARTITIONING AMONG INTERNAL ORGANS

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(*Received* 7 *December* 1982; *accepted* 28 *February* 1983)

Abstract—An estimate of partitioning of plutonium among skeleton, liver, and other organs is needed to estimate the radiation dose to individual organs. This review was done to provide an analysis of the coefficients currently used for the translocation of plutonium from blood to other organs and excreta. Data from both experimental animals and human autopsy cases were used in our analysis. The analysis of data from 257 experimental animal and 169 human subjects led to a conclusion that a 70–30% split of plutonium distribution between skeleton and liver, respectively, would be appropriate for use in plutonium organ distribution models. Analysis of data from other organs and early excreta indicated that these other compartments generally comprised less than 3% of the total early body burden. The variability of plutonium distribution within all compartments is emphasized, with the conclusion that the coefficients of uptake to individual organs are adequate to estimate average organ doses for an exposed population but use for estimating doses for an individual will lead to uncertain results.

INTRODUCTION

In 1972, the International Commission on Radiological Protection (ICRP) recommended values to be used for the translocation of plutonium from the blood to other organs (ICRP72). By extension, the ICRP recommended that these same values be used for other transuranics. The values chosen were 45% of that in the blood moving to bone, 45% to liver and 10% to other tissues and excreta. In implementing these recommendations, the ICRP (ICRP79) allocated a small portion of the 10% that did not go to skeleton or liver to gonads and considered the remainder of this fraction to be excreted.

Durbin pointed out that the partitioning between skeleton and liver depends strongly on the ionic radius of the actinide (Du62). For plutonium in young female albino rats, she noted that twice as much plutonium went to the skeleton as to the liver.

The partitioning among skeleton, liver and other organs is important in estimating radiation dose to individual organs following intake of plutonium. There is also uncertainty in any choice of partitioning coefficients because of individual variation and differences in the form of the plutonium taken into the body. For these reasons, a review of available data was made to provide coefficients for the distribution from blood to different organs and some measure of the uncertainty in these coefficients. Both animal and human autopsy data were used in this review.

PLUTONIUM METABOLISM DATA

For the animal data, two compilations that presented the results of a large number of experiments were used (Bu70; ICRP72). These data represent tissue distribution studies with a number of species and plutonium compounds expressed on a per organ basis. For humans, information was obtained from two autopsy tissue analysis studies. The first was an autopsy study of members of the public from several regions in the United States who were exposed to fallout (Fo80; Mc79). The second source was unpublished data from a similar autopsy program for plutonium workers who were exposed during the course of their employment. Although the data used in this report are not all-inclusive, they are assumed representative of

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others that may be available, and it was not the intent to consider this a complete review of all the plutonium metabolism data that may exist.

In examining the animal data, it was found that the data from many experiments are insufficient to permit estimation of the total body content so that the quantity in an organ cannot be expressed as a fraction of that in the body. This limits the amount of useful data. To allow use of the maximum amount of data possible, the information was first analyzed as the ratio between quantity in the skeleton and quantity in the liver. This ratio was then converted to the per cent in the skeleton of the total amount contained in the skeleton plus liver. This approach requires an assumption that the fraction of the plutonium depositing in skeleton and liver is a constant. These two organs do take up a major portion of the plutonium entering the blood; investigation of a random sample of animal data from *ICRP Publication 19* (ICRP72) where sufficient data were available to estimate this fraction, showed that skeleton plus liver contents ranged from 93 to >99%, a reasonable confirmation of the assumption. A sample of 20 values from these data showed an average of 97.3% of that in the body to be in the skeleton plus liver with a standard deviation of 1.8%. Because the interest in this study was the initial uptake, only animal data from sacrificies prior to 33 days were used; this minimized problems due to loss from organs and interchanges among organs that occur much more rapidly in small animals than in man. An analysis of data from earlier sacrifices (at Day 1 or less) indicated little change in relative distribution in dogs out to the 33-day limit. For instance, the skeleton plutonium content as a fraction of the skeleton plus liver contents for 24 dogs exposed by inhalation to four different ^{238}Pu aerosols and sacrificed two per point at three different times, were as follows: *four hr*, 0.78, 0.57, 0.88, 0.78; *four days*, 0.33, 0.92, 0.94, 0.96; *32 days*, 0.59, 0.71, 0.70, 0.66 (Me77).

The human data from the autopsy program are given as concentration of plutonium in the organ. The predominant bone sample was the vertebrae and this was chosen as an indicator of plutonium in the skeleton. A factor of 0.65 was used for multiplying the plutonium concentration in vertebrae to derive a concentration for the entire skeleton; the vertebrae are known to accumulate more plutonium than many of the other bones (Lar81). The factor 0.65 was derived using information from three sources (Du72; ICRP75; St69). Durbin's formula for plutonium in the entire skeleton was used (Du72), assuming (1) the thoracic vertebrae conservatively weighed 407 g in a 10-kg male skeleton, including marrow (ICRP75); (2) a fraction of 0.135 for the total skeleton plutonium that was contained in the entire vertebral column (Du72); and (3) an estimate that the thoracic vertebal section contained 47% of the total vertebral column plutonium (St69). The combination of these values into Durbin's formula gave the factor of 0.65 for the concentration of plutonium in total skeleton as a fraction of that in the vertebral sample.

In this series of data both bone and liver samples were not taken from all individuals. Because of the interest in variation among individuals, only those cases in which both bone and liver values were available were used. This limited the amount of data used but did clearly provide information for the spread of individual values.

In analyzing the data, ratios of concentration in the skeleton to that in the liver were made. These ratios were converted to ratios of quantity in the organs by multiplying by the ratio of these two organ weights from Reference Man (ICRP75). This poses an undefined uncertainty because the organ weights vary and the influence of this weight variation on the uptake is not known. In the analysis of these skeletal samples, the marrow was included. For this reason the total weight of the Reference Man skeleton, including marrow, was used. Using the recommended reference skeletal weights for female and male (ICRP75) enabled a direct transition to total skeletal content from the plutonium concentration in the vertebral sample (sample dis/min/kg × 0.65 × 6.8 kg (female) or 10.0 kg (male) = dis/min in total skeleton). Reference liver weights used were 1.4 kg and 1.8 kg for female and male, respectively (ICRP75).

The human data from nonoccupationally exposed members of the public represent the accumulation after continuous intake over a period of about 20 yr with a higher level of exposure in

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the early part of the period. The occupationally exposed individuals were generally exposed at some indeterminate time in the past and some of them had several exposures. Although neither are ideal for assessing transfer from blood to organs, human data are usually preferred over animal data whenever available. In addition, the human data were considered relevant since the retention time in human organs has been assumed to be long.

The averages of the fractional plutonium deposition in skeleton for each of the species and type of administration are given in Table 1 along with the range of the values for each mean. The range was used rather than statistical analyses because the values approach upper and lower boundary conditions in the bone, as would be anticipated. A *t*-test, however, indicated the occupational and nonoccupational data to be sufficiently similar so that they were combined as one population in Fig. 1. The overall mean was 0.74 and the standard deviation was 0.21. Normal distribution statistics were used, recognizing the boundary conditions mentioned above (skeleton content/skeleton plus liver content cannot be greater than 1.0). About 10% of the values for skeleton content fall above the 98% point. The fraction of skeleton-plus-liver plutonium in the skeleton was also analyzed using lognormal distribution statistics and the geometric mean and standard deviations are given in Table 1. This compares very favorably with the values obtained using normal distribution analysis.

In addition to bone and liver, a complete assessment requires knowledge of plutonium uptake by other organs. A summary of a large number of animal experiments giving values for per cent of body burden in lung, spleen and kidney, as well as in skeleton and liver, is given by the ICRP (ICRP72). These data are from administration by a number of routes of a large number of plutonium compounds to several species of animals. A simple average of the per cent of body burden was obtained for these organs for all routes of administration except inhalation. The averages obtained from 182 animals were 0.9% for spleen, 0.2% for lung and 1% for kidney. Similar data for humans were obtained from the autopsy data from the oc-

Table 1. Fractional plutonium in the skeleton assuming 100% of the body burden was in liver plus skeleton

			Fraction Plutonium in Skeleton			
					Geometric	
Species	Route[a]	Number of Subjects	Arithmetic Mean	Range	Mean	Stnd. Dev.
Mouse	IV	25	0.41	0.02 - 0.86	0.28	3.0
Rat	IV	102	0.68	0.07 - 0.98	0.60	1.8
	IV	10	0.67	0.09 - 0.93	0.58	2.0
	INH	34	0.78	0.33 - 0.95	0.76	1.3
	SQ-ID	13	0.81	0.55 - 0.97	0.79	1.2
	IP	8	0.83	0.64 - 0.92	0.82	1.1
	IM	14	0.89	0.52 - 0.97	0.88	1.2
Dog	IV	5	0.48	0.07 - 0.73	0.38	1.5
	INH	27	0.63	0.09 - 0.98	0.56	1.8
Sheep	IV	6	0.76	0.45 - 0.88	0.74	1.3
Pig	SQ-ID	13	0.71	0.17 - 0.94	0.63	1.7
Human						
Occup. Accidents		59	0.65	0.15 - 0.99+	0.61	1.5
Non-Occ. Fallout		110	0.79	0.35 - 0.99+	0.76	1.4

[a] IV - Intravenous
INH - Inhalation
IP - Intraperitoneal
SQ-ID - Subcutaneous, Intradermal
IM - Intramuscular

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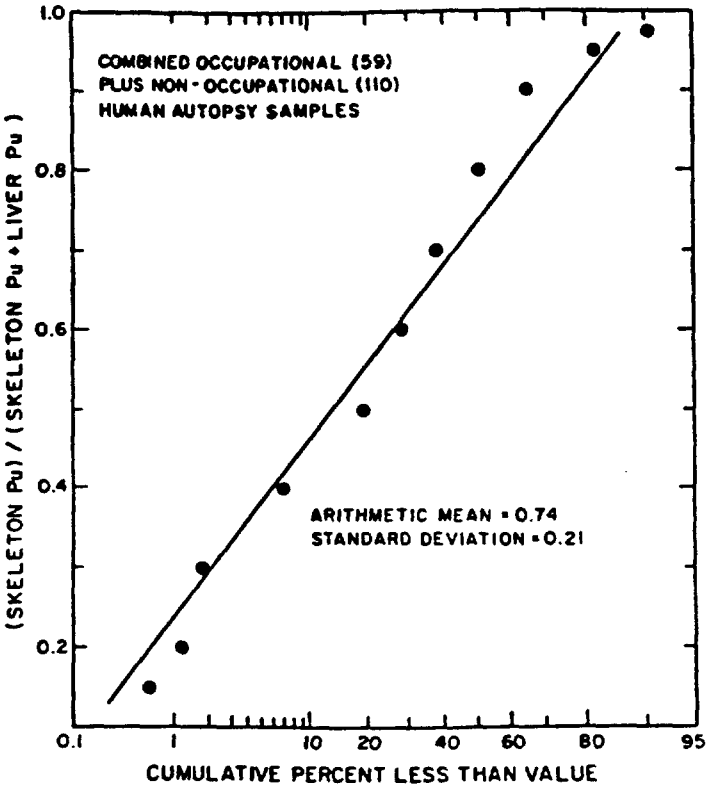

FIG. 1. The cumulative distribution of the quantity in skeleton of the occupationally exposed humans and the humans exposed to fallout.

cupationally exposed group. The interpretation of these data was more complex than that for the animal data because the values given were in the form of concentration in the organ rather than per cent of body burden. To provide a check on the reasonableness of the more extensive animal data, however, these concentrations were converted to per cent of the liver-plus-skeleton burden using the ICRP Reference Man organ weights (ICRP75). The lung was not considered in the human data because many of the individuals were exposed by inhalation. For the spleen, 12 values above the detection limit were available and averaged 0.7% of the liver-plus-skeletal burden. For the kidney 13 values above the detection limit were available with an average of 0.5% of this burden. These values are in good agreement with the animal data, particularly considering the many assumptions used in calculating the total body burden for humans.

DISCUSSION

The purpose of this study was to derive reasonable coefficients for the uptake of plutonium and some indication of their variability. A weighted arithmetic average of the animal data in Table 1 is 68% in skeleton and 32% in liver compared to the combined human results of 74% and 26% in Fig. 1. The geometric mean for the combined human data is 70% in the skeleton and 30% in the liver. These data suggest that the amount going from blood to skeleton is higher than that going to the liver. The exact distribution in these two organs is difficult to judge from the data available but a 70–30% split between skeleton and liver is reasonable for the average of a sizeable group of people.

The data presented for other organs indicate small quantities deposited in the spleen, lung and kidney. In addition, some of the plutonium will be excreted. To evaluate the excretion fraction, Langham's data on human subjects were used (La80). These data indicated about 0.6% of plutonium excreted in the feces and urine on the first day and a total excretion of only 2.5% within the first 40 days. These data were derived from intravenous injections. If the data are

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appropriately rounded, values of 1% in each the spleen and kidney, 0.2% in lung and an arbitrary value of 0.8% in excreta, are reasonable, amounting to 3% of the initial body burden.

Rather than presenting the final organ uptake values with more than justified significance, the 70% of plutonium to skeleton and 30% to liver is retained with the 3% in other organs added. This means that the uptake values add to 103%, but this is well within the error of any of the measurements used. Final values are given in Table 2 with any adjustments desired for the 103% to be made by any user. The ICRP (ICRP79) uses a combined liver and skeleton plutonium content totalling 90%; any reasonable value for this total may also be judged by the user, applying the recommended 70 : 30% skeleton : liver partitioning to the selected total.

An important observation in Table 1 is the range of the individual values that make up the average. Thus, even though the average uptake in bone is recommended in this paper as 70%, the ranges indicate that some people may have < 20% in the skeleton and > 80% in the liver, while others may have > 90% in the skeleton with < 10% in the liver.

These data indicate the difficulty of ascribing an uptake coefficient for a given organ in an individual. Strictly, these uptake coefficients should be used only to describe the plutonium distribution in the body for the average of a group large enough to provide a meaningful average. However, they may be used to derive concentration limits for controlling exposure with the understanding that these values should not be used for estimating dose to an individual.

Table 2. Values of uptake from blood as derived in this study

UPTAKE FROM BLOOD TO ORGAN	
ORGAN	*UPTAKE
Bone	70%
Liver	30%
Spleen	1%
Kidney	1%
Lung	0.2%
Excreta	0.8%

*Total exceeds 100% because of method of derivation.

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