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METABOLISM AND BIOLOGICAL EFFECTS OF ALPHA-EMITTING RADIONUCLIDES

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INTRODUCTION

In recent years, the worldwide effort to understand the health implications of alpha-emitting radionuclides has greatly increased. Much of the effort has used new and improved techniques to refine and understand the results of earlier work. Increased emphasis has also been given to studying alpha emitters in the forms that may occur in work places and in the environment. I will briefly describe some of the more interesting and perhaps more important results of these recent studies. Some of these are raising intriguing questions which should stimulate a new generation of experiments. In this presentation, I have taken considerable liberty with published data in an attempt to consolidate and generalize the information. This includes rounding of numbers. The referenced publications should be consulted for details.

GASTROINTESTINAL-TRACT ABSORPTION

During the past 10 years much effort has been placed on estimating the dose to human populations predicting the potential health consequences from alpha-emitting radionuclides dispersed in various real and theoretical environments. This work has raised questions about the appropriateness and adequacy of existing data for application to these types of assessments. One of the first areas of concern was the reliability of predictions of gastrointestinal-tract absorption of alpha-emitting radionuclides incorporated in foodstuffs from environmental sources since all of the available data were from experiments with pure inorganic compounds of the radionuclides. Experiments were undertaken to measure the absorption of alpha emitters from ingested plants grown in contaminated soil and from ingested flesh from animals that had been given radionuclides. In addition, some of the earlier experiments were repeated under different conditions of food intake. Larson's report that plutonium in drinking water was likely to be oxidized to the more readily absorbable Pu(VI) oxidation state by chlorine introduced in water treatment plants [1] stimulated a repeat of some of these experiments. Figure 1 summarizes most of the experimental animal data on the absorption of alpha-emitting radionuclides from the gastrointestinal tract in adult and newborn animals. These data are shown as they relate to the absorption factors recently used by the ICRP in revising limits for intakes of radionuclides by workers [2]. The ranges of three or more observations are shown by the lines. Closed circles represent single published values. Dashed lines and open circles represent data obtained for newborn animals. This presentation of the data is modified from Stather [3].

Since oral intake of radionuclides rarely occurs in a work site, alpha emitters entering the gastrointestinal tracts of workers will almost always come from material cleared from the lungs following an inhalation exposure. Since few inhalation exposures will be to biologically incorporated alpha emitters or to the rare forms such as the higher oxidation states, citrates, and so forth, and since only adults are likely to be exposed, the absorption factors used by the ICRP appear to represent adequately the absorption of insoluble plutonium (class Y), soluble forms of plutonium (class W) and all other transuranics. However, these factors may not apply in all cases of ingestion of alpha emitters from environmental sources. Although the absorption of biologically incorporated plutonium is in the range of values obtained for plutonium nitrate (plutonium in the IV oxidation

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state), an absorption factor somewhat higher than the 10^{-4} for class W plutonium compounds seems more appropriate. On the other hand, biologically incorporated americium is absorbed about the same as americium oxide [3,4]. Thus, an ICRP absorption factor of 5×10^{-4} for transuranics other than plutonium would probably not underestimate the absorption of americium biologically incorporated in food. This is an important finding since americium is considered a major component of long-range environmental contaminants from nuclear power activities, and in areas where nuclear weapons tests were conducted 15 to 25 years ago.

Tests of plutonium in the Pu(VI) oxidation state, which Larson [1] believes may occur in drinking water, yield absorption values from 3×10^{-4} to 8×10^{-3}. In an early experiment, Weeks et al. [5] obtained a value of 1.75×10^{-2}, using rats deprived of food before and after the plutonium was administered. More recently, Sullivan et al. [6], using $^{238}Pu(VI)$, obtained a value of 2×10^{-4} for fed rats (about the same as for Pu IV) and 3×10^{-4} for fed guinea pigs. In fasted rats given $^{239}Pu(VI)$, the absorption factor was 5×10^{-3}. This increased to as much as 1.8×10^{-2} in another experiment where rats were both fasted and given Pu(VI) in nitrate solution containing an oxidizing agent, dichromate. Although further work needs to be done, especially to determine whether the very small mass of material that would be ingested from foodstuffs and drinking water behaves the same as the larger mass quantities of materials used in these experiments, 10^{-3} is a reasonable absorption factor for environmentally dispersed plutonium.

Many of the radionuclides shown in Figure 1 have been tested in newborn animals of several species including pigs, rats, and guinea pigs [7]. In nearly all cases, the absorption of alpha emitters in the gastrointestinal tract of newborn animals is one to two orders of magnitude greater than in adults. This could be an important factor in assessing radiation doses to the public from environmentally dispersed radionuclides, although it should be remembered that this high absorption factor rapidly decreases within a few months after birth [7]. Thus, it is unlikely that a very significant portion of an individual's life-time committed dose would occur as a result of ingestion of alpha emitters during the first few days or weeks after birth.

All of this information is from animal experiments of uncertain applicability to human beings. However, the data in Figure 1 are from many animal species: rats, guinea pigs, hamsters, dogs, and pigs. Such interspecies comparisons improve the credulity of applying the results to humans.

PULMONARY RETENTION AND TRANSLOCATION

The retention of several alpha-emitting radionuclides in lungs and the translocation from those sites to other tissues have been sufficiently well characterized to predict with confidence the qualitative behavior of most radionuclides deposited in the body (Figure 2). To develop the curves in this figure, I have taken considerable license with published data. The curves are based largely on data from experiments with dogs, modified somewhat by rodent data and data from a few human exposure cases [8]. No statistical or mathematical treatments were used in this rough attempt to represent this broad spectrum of data.

Of all the compounds represented in Figure 2, $^{239}PuO_2$ has the longest retention half time in the lungs, up to 1000 days or more. $^{238}PuO_2$ is less readily retained. Americium and curium oxides, as well as $^{239}Pu(NO_3)_4$ are cleared from the lungs rapidly compared with $^{239}PuO_2$. Even more rapidly cleared is $^{238}Pu(NO_3)_4$. The retention half-times are on the order of 100 to 200 days. It should be remembered that all of these retention rates decrease with time after exposure;

after several years, small fractions of all of these compounds may still be found in the lungs. The translocation of these elements from the lungs to other tissues in the body is similar in that the major tissues in which they are deposited are the same--liver, skeleton, and lymph nodes. The rates of translocation to liver and skeleton are inversely related to the retention in the lungs. Thus, translocation to these tissues is much less for inhaled $^{239}PuO_2$ and $^{238}PuO_2$ than for the other compounds shown in Figure 2. On the other hand, only small amounts of plutonium nitrate and even less of curium oxide and americium oxide accumulate in the thoracic lymph nodes. While results from individual experiments may vary quantitatively, evidence that different radionuclides and different compounds of the same radionuclide behave differently is conclusive. It should be concluded from the representative curves in Figure 2 that knowledge is sufficient to predict the behavior of alpha emitters under all situations where they might be inhaled. It is already known that factors such as particle size and the way aerosols are produced can influence deposition, retention and translocation. Current studies are providing more definitive information on these and other factors.

ISOTOPIC DIFFERENCES

Since there is no reason to believe that the chemical properties of the isotopes of these heavy elements are significantly different, it has usually been assumed that biokinetics information about one isotope applied to all other isotopes of that element when all other factors such as chemical compound, particle size, animal species, route of entry, and so forth are similar. The first suggestion that this was not always a valid assumption resulted from comparative studies of IV-injected ^{238}Pu and ^{239}Pu citrates in rats [9] and of inhaled $^{238}PuO_2$ and $^{239}PuO_2$ in rats and dogs [8-10]. In the latter case, translocation of inhaled $^{238}PuO_2$ to liver, skeleton and other tissues and excretion were much more rapid than for $^{239}PuO_2$. This finding, which challenged the existing practice of applying $^{239}PuO_2$ data to $^{238}PuO_2$, has since been confirmed at several laboratories in rodents and dogs [11-13]. Figure 2 and Table 1 show that inhalation of $^{238}PuO_2$ results in the body burden of plutonium being distributed among lung, liver, skeleton and lymph nodes; whereas, after inhalation of $^{239}PuO_2$, over the same period of time, the body burden is largely distributed between lungs and lymph nodes. The different behavior of these two plutonium isotopes in the body after inhalation of particles of their oxides has been attributed to the fact the specific activity of ^{238}Pu is so much higher than that of ^{239}Pu. Because of the high specific activity, $^{238}PuO_2$ particles tend to be reduced in size by radiolytic action. The resulting small particles may be transported to other tissues in the body [14] or they may be dissolved and the plutonium translocated [15]. However, neither mechanism explains the different behavior of inhaled ^{238}Pu and ^{239}Pu nitrates observed by Dagle [16] (Figure 3). In this experiment the retention and translocation of $^{238}Pu(NO_3)$ and $^{239}Pu(NO_3)_4$ were compared in beagle dogs. The radioactivity inhaled was about 70 nCi in both cases. Retention of $^{238}Pu(NO_3)_4$ in lungs was much less and translocation was much greater than for $^{239}Pu(NO_3)_4$. Similar differences reported earlier for ^{238}Pu and ^{239}Pu citrates [9] and for ^{237}Pu and ^{239}Pu nitrates [17] given intravenously were explained on the basis of large differences in mass for the same level of radioactivity; 280 and 2 x 10^5 larger mass of ^{239}Pu compared with ^{238}Pu and ^{237}Pu, respectively. The larger mass of ^{239}Pu injected possibly resulted in polymer formation in the blood leading to greater deposition in liver and less deposition in bone than for ^{238}Pu and ^{237}Pu. In the case of inhaled plutonium nitrate, the greater retention of $^{239}Pu(NO_3)_4$ in the lungs than of $^{238}Pu(NO_3)_4$ also may be due to its greater mass and thus higher probability of forming polymers which, if phagocytized, could lead to a longer retention time in the lungs.

Another example of such a mass effect is in Ballou's study of inhaled ^{232}U and ^{233}U nitrates (Table 2) [18]. There was no difference in long-term retention

of $^{233}UO_2(NO_3)_2$ after inhalation of amounts ranging over a 60-fold difference in mass. In other rats which inhaled an amount of $^{232}UO_2(NO_3)_2$ that represented a further reduction in mass by a factor of 24, long-term lung and kidney retention were the same as observed for ^{233}U, but retention in skeleton was a factor of 2 higher.

HETEROGENOUS PARTICLES

Although most experimental work with alpha emitters has been done with individual radionuclide compounds, it has long been recognized that in most human exposure situations, mixtures of radionuclides and other materials would be involved. A few early experiments were done with materials identified as a source of human exposure. Recent efforts have attempted to anticipate the kinds of mixtures to which humans could be exposed. This has included sampling of work environments by scientists planning animal studies [19,20] as well as efforts to duplicate in the laboratory aerosols that might be released in accidents.

The use of liquid sodium as a coolant in breeder reactors has posed questions about accidental releases of plutonium mixed with sodium. To investigate the behavior of plutonium-sodium mixtures deposited in the body, aerosols have been produced by burning plutonium wires coated with sodium at 450°C [21], by exploding sodium-coated plutonium wires [22], and by passing through sodium vapor an aerosol produced by pulsing a focused laser beam onto the surface of a rotating plutonium-uranium fuel pellet [23]. Representative results from experiments done with the plutonium-sodium aerosols are shown in Table 3. Inhalation of these aerosols resulted in much greater translocation to tissues outside the respiratory tract (primarily to liver and skeleton) than occurred after inhalation of plutonium free of sodium. Some authors consider the increased mobility of plutonium associated with sodium to be due to conversion of plutonium in the presence of the sodium to the more soluble Pu(VI) and Pu(VII) oxidation states [21]. Other authors report that the presence of sodium results in a larger proportion of the plutonium occurring as very small particles, $\sim$ 0.001 μm in diameter, which are readily transported to the blood circulating through the lungs--the higher the amount of sodium, the larger the fraction of very small particles [27]. Laser-produced plutonium-sodium aerosols, which also contained uranium, consist of chain aggregates of particles of PuO_2 on which sodium is condensed [23]. The primary particles were 0.003 to 0.1 μm in diameter. In a dry environment, there was no chemical interaction between PuO_2 and sodium, but interactions probably occurred in the presence of water vapor to form either a sodium-plutonium (IV) ternary oxide and Pu_2O_3, or a sodium-plutonium (III) ternary oxide, all of which are much more soluble than the laser-produced plutonium-uranium chain aggregates not exposed to sodium [26].

The data in Table 4 on the disposition of ultra fine PuO_2 particles support the concept that the greater mobility of plutonium inhaled as an aerosol produced from an exploding sodium-coated plutonium wire is due to the formation of very small, readily transportable particles. Inhalation of ultra fine 0.001 μm $^{238}PuO_2$ and $^{239}PuO_2$ particles, produced by calcining the oxalate at 750°, resulted in substantially greater translocation to liver and other tissues than inhalation of 0.025 to 0.22 μm PuO_2 particles [28,29]. The levels of plutonium excreted were greater than those observed after inhalation of soluble plutonium citrate, but the levels translocated were about the same. However, the mechanism of translocation may be different. Cooper et al. [14] report that 0.001-μm particles of plutonium react in the lung alveoli with acidic phospholipids in the surfactant, which may be involved in transport of the ultra fine particles to the blood. According to these authors, the particles in the blood rapidly form an intermediate species of low molecular weight which is readily filtered through the kidney, resulting in a

greater rate of excretion than occurred after inhalation of plutonium citrate.

In contrast to the results obtained with 0.001-μm particles are the results for ultra fine $^{239}PuO_2$ particles of 0.009-μm diameter [30] (Table 4). These particles were prepared by passing a vaporized plutonium chelate through a series of three furnaces at 200°, 280° and 1150°, respectively. The aerosol consisted of aggregates of < 0.01-μm primary particles. Inhalation of this aerosol resulted in less than 1 % of the plutonium being translocated from the lungs to other tissues. It is obvious that the interactions in the lung described for the 0.001-μm PuO_2 particles do not apply to this form of PuO_2 which consisted of primary particles about 10 times larger. This confirms earlier reports that the method of aerosol preparation and particle size are important influences on the behavior of radionuclides in the body.

The proposed use of mixed plutonium-uranium-thorium oxides in nuclear reactors has led to several studies of inhaled mixed oxides [31,32]. An example of results from these studies is given in Table 5. One year after inhalation of a mixed plutonium-uranium aerosol, retention and translocation of plutonium are very similar to retention and translocation observed after inhalation of PuO_2 alone. (At earlier times after exposure, the author observed a 2- to 3-fold increase in the transportable fraction of plutonium.) In another experiment, inhalation of a mixture of plutonium and americium did not appear to result in different pulmonary retention and translocation characteristics of either radionuclide from those that occur when the radionuclides are inhaled alone [33]. Because of the few data available, it is premature to draw conclusions about the behavior of mixed oxides deposited in the lungs. However, there is even less known about mixed oxides deposited in the gastrointestinal tract and in wounds. This is an obvious area needing further study.

BIOLOGICAL EFFECTS

Genetic Effects

Early studies emphasized the more obvious biological effects of alpha emitters, such as those leading to acute death and those, such as cancer, which might cause death later. The possibility of genetic effects as a consequence of internal depositions of alpha emitters was rarely considered, especially since tissue distribution studies showed that very small fractions of the alpha emitters in the body were in the gonads. In response to questions about the possibility of genetic effects, Richmond and Thomas [34] summarized available data on the deposition of plutonium in animal and human gonads. This report and additional data from several laboratories led to the ICRP's adopting uptake values of 3.5×10^{-4} for testes and 1.1×10^{-4} for ovaries (Table 6). Studies by Green et al. [35,36], Priest and Jackson [37] and Brooks et al. [38] have shown that the early random distribution of plutonium in testes and ovaries is followed at later times by accumulation in macrophages in the interstitial tissues of testes and in the medulla of ovaries. In rodents it has been estimated that this accumulation of plutonium could result in radiation doses 2.5 to 4 times the average testes dose. However, morphometric studies by Brooks et al. [38] indicate that because of microanatomical differences between the testes of rodents and humans, the radiation dose to spermatogonia in humans would probably be less than the average dose to the whole organ. It is unlikely that developing follicles in ovaries would receive a dose greater than the average dose to the ovaries because the plutonium migrates away from the cortex and the region of developing follicles [37]. Again however, this estimate is based on studies in rodents and it may not apply to human beings.

Grahn et al. [39] measured genetic effects of plutonium in male mice and found the frequencies of fragments, translocations and dominant lethals per gamete per rad were similar to those that occurred after weekly fission neutron irradiation

and were about 13 to 38 times higher than after continuous ^{60}Co gamma irradiation. Searle et al. [40] found alpha particles to gamma ray ratios of 24. Further information is needed on the genetic effects of plutonium and other alpha emitters, although genetic effects are expected to be very rare because only a small fraction of the body burden is deposited in the gonads. High body burdens, 5 and 10 μCi/kg, were used by Grahn to give average testes doses of 0.075 and 0.15 rad/day, respectively. Brooks et al. [38] found that levels of ^{239}Pu, 2×10^{-3} and 6×10^{-4} μCi/g body weight in hamsters, caused a shortening of life span and increased the incidence of bone and liver cancer. However, these levels did not cause a significant increase in the frequency of mitotic chromosome aberrations in spermatogonia.

Chromosome changes in somatic cells are other possible genetic effects of plutonium contamination. Early studies of chromosome aberrations in circulating lymphocytes of plutonium workers were inconclusive since external radiation exposures were considered to account for the frequencies of chromosome aberrations observed [41]. Recent studies by Brandom et al. [42] suggest a correlation between the frequency of structural aberrations and estimates of plutonium body burden (Figure 4). However, the authors are careful to stress the risks in interpreting these data with regard to possible health or genetic effects because of the relatively low frequencies of aberrations. Also, a clinical significance of chromosome aberrations in circulating lymphocytes has not been established. As in the Dolphin study [41], external radiation doses received by the subjects of the Brandom study [42] may have contributed to the aberrations observed.

Lymphocytopenia

Perhaps relevant to the observation of chromosome aberrations in circulating lymphocytes of persons with small plutonium burdens is the fact that in dogs, depletion of the numbers of circulating lymphocytes continues to be the most sensitive response to inhaled plutonium dioxide. Figure 5 shows the mean circulating lymphocyte levels in groups of dogs up to 80 months after inhalation of $^{239}PuO_2$ [43]. The time of onset and the degree of lymphocytopenia are dose-related. An initial lung deposition of 79 nCi caused a significant lymphocytopenia as early as 10 months after exposure. Lymphocytopenia also occurs in dogs after inhalation of $^{238}PuO_2$ [11] and $^{239}Pu(NO_3)_4$ [44].

The clinical significance of the lymphocytopenia, as well as the mechanism for its induction by plutonium, is unknown. A decreased antibody response in dogs exposed to plutonium may be related to the lymphocytopenia [45]. Lymphocytopenia has not been reported in persons who have inhaled PuO_2. Based on the dog experiment (Figure 5), lymphocytopenia probably would not be detectable in humans with lung burdens of less than about 1000 nCi. Because the large number of chromosomes in dogs makes chromosome studies very difficult, it has not been determined whether there is an increased frequency of aberrations in the chromosomes of circulating lymphocytes in the plutonium-exposed dogs having lymphocytopenia. This information would be very useful in interpreting the data of Brandom [42] and Dolphin [41], who have observed chromosome aberrations in plutonium workers.

Cancer

Knowledge of the carcinogenic properties of alpha emitters has been extended during the past several years by continued work on several exposed human populations. This includes uranium miners, Thorotrast-treated patients, radium dial painters, and patients given ^{224}Ra. Since continuing studies of plutonium workers have not revealed any health consequences that can be attributed to plutonium, it is still necessary to rely upon animal experiments for information about transuranic health

effects. Recent results from the University of Utah include osteosarcomas in dogs given single intravenous injections of doses as low as 0.0053 μCi/kg ^{239}Pu (average skeletal dose was 22 rad) [46]. Lung cancers and bone sarcomas have been observed in dogs after inhalation of levels of about 0.5 μCi/kg $^{238}PuO_2$ [11,47]. However, lung cancers are the only primary death-causing cancers that have occurred in dogs that inhaled $^{239}PuO_2$ [11]. Although insoluble alpha emitters accumulate in lymphatic tissues, the risk of lymphatic cancers appears to be much lower than the risk of bone and lung cancer. An occasional leukemia has been observed in the numerous rodent experiments with the transuranics. However, leukemia has been very rare in studies involving well over 1000 dogs. Thus, like lymphatic cancers, the risk of leukemia following exposure to the transuranics appears to be very low. While liver cancer is very rare in experimental animals that inhaled alpha emitters, it is more common in animals given plutonium by intravenous injection. Using data from Thorotrast-treated patients, Mays [48] estimated the life-time risk of liver cancer to be 1.27 per μCi of insoluble ^{239}Pu inhaled. This compares with his estimates of 0.6% for lung cancer and 0.3% for bone sarcoma.

In the last three years, attention has been directed toward the possibility that alpha emitters combined with other substances might increase the risk of cancer. In France, administration of cigarette smoke and benzo-5,6 flavone was found to increase the carcinogenic response to inhaled radon decay products [49,50]. Other experiments have been directed toward the possible combined effects of inhaled plutonium and chemical carcinogens [51]. In other studies, cigarette smoke and exposures to uranium ore dust did not appear to increase the carcinogenic effects of inhaled radon decay products in dogs [52]. Rodents exposed to diesel engine exhaust, radon decay products and ore dust did not appear to show a greater frequency of lung cancer than rodents that inhaled only the radon decay products and ore dust [53]. In other studies, exposures to benzo-α-pyrene or asbestos did not appear to raise the frequency of lung cancers in rats that had inhaled plutonium [54]. The results of these and the few other attempts to detect carcinogenic action of environmental pollutants in animals that have body burdens of alpha emitters are inconclusive in answering questions about the possibility that cigarette smoking and exposures to toxic chemicals increase the cancer risk to persons who become internally contaminated with alpha-emitting radionuclides. This is an area needing further research.

SUMMARY

To summarize briefly, the emphasis of much of the current and planned research on the toxicity of alpha-emitting radionuclides is directed toward the complexities of actual and potential conditions of occupational and environmental exposures of human beings. These, as well as the more limited studies on mechanisms of biological transport and effects, should increase our ability to predict health risks more accurately and to deal more confidently with human exposures, if and when they occur.

Table 1. Tissue Distribution of Pu in Dogs 4 Years After Inhalation of Polydisperse $^{238}PuO_2$ and $^{239}PuO_2$ (Percent of Body Burden at Death)[11].

TISSUE	^{238}Pu	^{239}Pu
LUNG	20.	55.
LIVER	16.	0.17
SKELETON	24.	0.43
TB LYMPH NODES	34.	44.
ABDOMINAL LYMPH NODES	0.36	0.02
BODY BURDEN	2nCi	6nCi

(a) AMAD = 1.8 μm, GSD = 1.9
(b) AMAD = 2.3, GSD = 1.9

Table 2. Distribution of ^{232}U and ^{233}U in Rats ~800 Days After an Inhalation Exposure (Percent of Initial Lung Burden) [18].

	$^{233}UO_2(NO_3)_2$			$^{232}UO_2(NO_3)_2$
	INITIAL LUNG BURDEN			
TISSUE	0.63 nCi (66. ng)	10 nCi (1050 ng)	36 nCi (3780 ng)	53 nCi (2.7 ng)
LUNG	1.2	.4	.2	.2
SKELETON	6.	2.	3.	10.
KIDNEY	.2	.07	.05	.25

Table 3. Lung Retention and Translocation of Plutonium-Sodium Mixed Aerosols ~180 Days After Exposure *[24], **[25].

AEROSOL	ANIMAL SPECIES	Pu:Na RATIO	PERCENT OF INITIAL LUNG BURDEN: LUNG	PERCENT OF INITIAL LUNG BURDEN: OTHER TISSUES
LASER VAPORIZED	RATS	0	15	0.8
PuO_2-UO_2		1:1	10	5.0
- Na *		1:12 TO 21	3	24
EXPLODED	HAMSTERS	0	10	.16
PuO-Am WIRE		1:27	27	27
- Na **		1:104	25	6

Table 4. Disposition of Ultrafine PuO_2 Particles Deposited in Rat Lungs; (Percent of Initial Lung Burden), a[30], b[28], c[29].

	$^{239}PuO_2$(a)	$^{239}PuO_2$(b)	$^{239}PuO_2$(b)	$^{238}PuO_2$(c) FRESH	$^{238}PuO_2$(c) AGED	^{239}Pu CITRATE(b)
	PARTICLE SIZE					
	.009 μm	.025-.22 μm	.001 μm	.001 μm	.001 μm	
TISSUE						
LUNGS	51.	92.	20.	20.	25.	7.
LIVER	0.55	<.05	5.	6.	7.	6.
ALL OTHER TISSUE	0.55	1.5	51.	39.	39.	69.
URINE	.25	<.05	9.	12.	9.	4.
FECES	48.	6.4	15.	24.	21.	14.

(a)16 DAYS AFTER INHALATION
(b)17 DAYS AFTER INTRATRACHEAL INTUBATION
(c)21 DAYS AFTER INTRATRACHEAL INTUBATION

Table 5. Distribution of Pu in Hamsters 360 Days After Inhalation of Mixed Pu-U Oxide Aerosols (Percent of Initial Lung Burden)[31].

TISSUE	Pu:U ATOMIC RATIO 1:0	1:1	1:4
LUNG	12.	4.9	11.
LIVER	.13	.12	.26
LYMPH NODES	.29	.1	.34
CARCASS	.31	.26	.62

PRODUCED FROM EXPLODING WIRE
AMAD = 1.3 μm, GSD = 1.6

Table 6. Plutonium in Genetic Tissues [34], [2], [39], [35], [37], [36], [40], [38].

	FRACTION TRANSLOCATED TO GONADS	DISTRIBUTION IN GONADS: EARLY	DISTRIBUTION IN GONADS: LATE	GERM CELL DOSE	RESPONSE (PER GAMETE PER RAD)
TESTES	3.5×10^{-4}	• SEMINIFEROUS TUBULES • INTERTUBULAR TISSUES	MACROPHAGES IN INTERSTITIAL TISSUES	SPERMATOGONIA (2.5 TO 4 TIMES AVERAGE)	5.8, 3.4 TRANSLOCATIONS 93, 120 FRAGMENTS 84, 190 DOMINANT LETHALS
OVARIES	1.1×10^{-4}	• ATRETIC FOLLICLES	MACROPHAGES IN MEDULLA IN CORPORA LUTAE	DEVELOPING FOLLICLES (POSSIBLY GREATER THAN AVERAGE)	

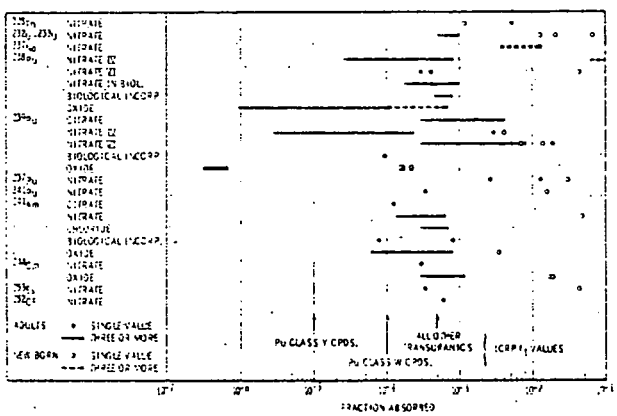

Figure 1. Composite of Data on the Absorption of Alpha-emitting Radionuclides from the Gastrointestinal Tract (after Stather [3]; see [3,4,5,6,7,8] for sources of data).

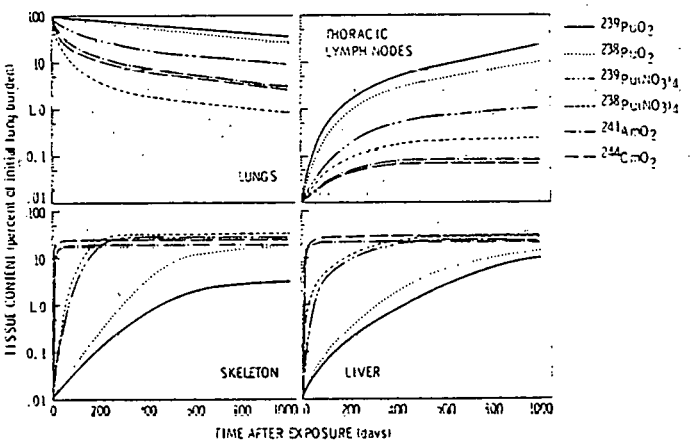

Figure 2. Representative Retention and Translocation Curves for Several Inhaled Alpha-Emitting Radionuclide Compounds.

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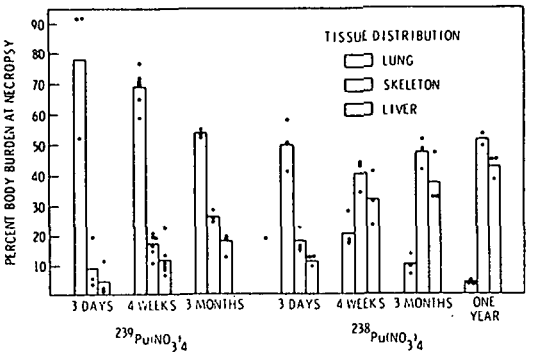

Figure 3. Comparison of Inhaled ^{238}Pu and ^{239}Pu Nitrate in Dogs [16].

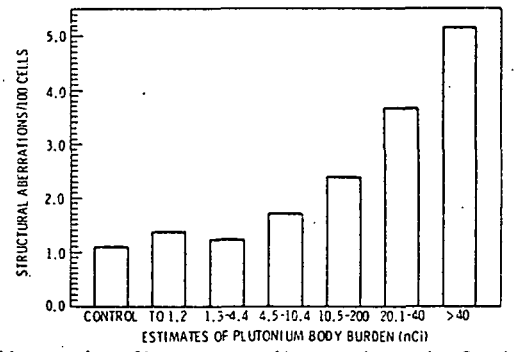

Figure 4. Chromosome Aberrations in Peripheral Blood Lymphocytes of Plutonium Workers (modified from Brandom [42]).

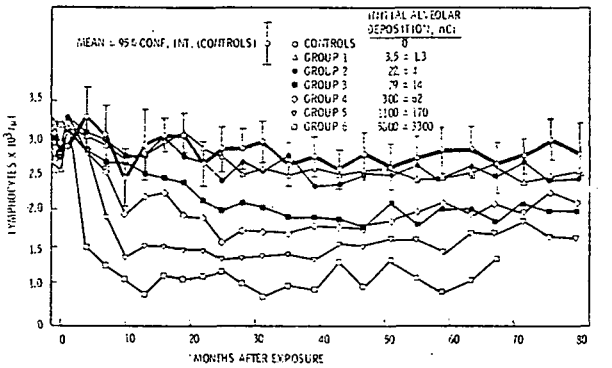

Figure 5. Mean Lymphocyte Values from Dogs After Inhalation of $^{239}PuO_2$ [43].

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