SOLUBILITY CHANGES OF ^{238}Pu OXIDE IN WATER SUSPENSION AND EFFECT ON BIOLOGICAL BEHAVIOR AFTER INHALATION BY BEAGLE DOGS*

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Abstract -- Beagles were exposed to aerosols of $^{239}PuO_2$ or $^{238}PuO_2$ prepared by identical methods of calcining the oxalate at 750°C for 2 hours. The PuO_2 was stored in water suspensions of 2 to 3 mg PuO_2/ml for various periods until required for exposure at which time suspensions of suitable concentrations were prepared by dilution of the stock. Aerosols were generated by nebulizing these suspensions. Ultrafilterability of the $^{239}PuO_2$ suspension remained stable ranging from 0.1 to 0.2% over a 16 month period. Dogs exposed to $^{239}PuO_2$ during this time and sacrificed 30 to 140 days postexposure had more than 98% of the body burden at death in the lungs and thoracic lymph nodes. Dogs exposed to $^{238}PuO_2$ 6 months after preparation of the stock suspension had 64% and 50% in the lungs and thoracic lymph nodes, with 23% and 34% in the skeleton and 8% and 11% in the liver at 30 and 90 days postexposure, respectively. Ultrafilterability of the stock $^{238}PuO_2$ suspension was 25%. X-ray diffraction analyses of the $^{239}PuO_2$ and of freshly prepared $^{238}PuO_2$ yielded the expected peaks, but the $^{238}PuO_2$ that had been in water suspension for 9 months showed no X-ray peaks. Dogs exposed to freshly prepared $^{238}PuO_2$ with 0.2% ultrafilterability showed more than 98% of the Pu in the lungs and thoracic lymph nodes 30 and 60 days postexposure, while the ultrafilterability of the water suspension changed from 0.2% to 16% during the 60-day postexposure period. Radiation damage to $^{238}PuO_2$ may be responsible for the differences in the behavior of $^{238}PuO_2$ and $^{239}PuO_2$ in water suspension and in vivo.

INTRODUCTION

In preparation for a life-span dose-effect-relationship study with beagle dogs comparing inhaled $^{239}PuO_2$ and $^{238}PuO_2$, small groups of dogs were exposed to compare the short-term retention and translocation of the two isotopes before exposing the larger group of dogs. The dogs that inhaled $^{238}PuO_2$ showed much more translocation of Pu to the liver and skeleton during a 3-month postexposure period than dogs exposed to $^{239}PuO_2$. Results of preliminary studies to investigate the difference in behavior of the two isotopes are the subject of this paper.

METHODS

Eighteen month-old beagle dogs were exposed for 5 to 30 minutes to aerosols of $^{238}PuO_2$ or $^{239}PuO_2$. These oxides were prepared by identical methods, involving calcining plutonium oxalate at 750°C for 2 hours. After calcining, the PuO_2 was stored in water at a concentration of 2 to 3 mg PuO_2/ml. This suspension was stored (i.e., aged) until required for exposure of dogs, when suspensions of suitable concentrations were prepared by dilution of the stock suspension and aerosols were generated by nebulizing these suspensions[1]. Dogs

were exposed via a mask from an aerosol exposure chamber as described previously[2].

Table 1 shows the groups of dogs available for comparison. The aged $^{238}PuO_2$ stock suspension had been in water suspension for 6 months when the dogs were exposed. Ultrafilterability, measured by the methods of Lindenbaum and Westfall[3], using 24 Å pore-size visking-type membrane, of this aged stock suspension was 25% and the aerosolized particle size distribution, determined using a cascade type impactor[4], was smaller than that of the freshly prepared $^{238}PuO_2$ or the aged $^{239}PuO_2$.

Table 1. Experimental Groups for Comparison of the Behavior of Inhaled $^{238}PuO_2$ and $^{239}PuO_2$ in Beagles

Pu Suspension	Number of Dogs	Sacrifice (Days After Exposure)	Age of Stock Suspension	Ultra-filter-ability of stock Suspension	Particle Size AMAD* (μm)	GSD**
Aged $^{238}PuO_2$	3	27-37	6 mo	25%	0.8	2.5
Aged $^{238}PuO_2$	3	91-92	6 mo	25%	0.9	2.5
Fresh $^{238}PuO_2$	1	29	48 h	0.2%	2.3	2.3
Fresh $^{238}PuO_2$	2	54	48 h	0.2%	2.0	2.3
Fresh $^{238}PuO_2$	2	78	48 h	0.2%	2.2	2.3
Aged $^{239}PuO_2$	3	28-30	16 mo	0.2%	2.6	1.7
Aged $^{239}PuO_2$	4	140-142	3 mo	0.2%	2.5	1.8

* AMAD Mean activity median aerodynamic diameter
** GSD Mean geometric standard deviation

The freshly prepared $^{238}PuO_2$ was stored in water suspension only 48 hours before exposing the dogs. Ultrafilterability of this suspension was about 0.2% and the aerosolized particle size distribution was more like the distribution for the $^{239}PuO_2$ aerosols.

The $^{239}PuO_2$, prepared in the same way as the $^{238}PuO_2$, was in suspension for 16 months prior to exposure of one group of dogs and for 3 months prior to exposure of the other group. The ultrafilterability and particle size distribution of the aerosols for both $^{239}PuO_2$ groups was similar.

Dogs were sacrificed from 1 to 5 months after exposure. Tissues and excreta were analyzed for Pu content by liquid scintilation counting following ashing and dissolution in HNO_3-HF[5].

RESULTS

Table 2 shows the distribution of plutonium in the dogs at sacrifice expressed as mean % final body burden. The final body burden ranged from 0.01 to 4.8 μCi in the dogs. No influence of dose on Pu tissue distribution was observed. The dogs exposed to $^{239}PuO_2$ had nearly all of the Pu in the lungs and thoracic lymph nodes (98-99%) at 30 and 140 days after exposure with very little translocation to other tissue, except the thoracic lymph nodes, regardless of the age of the suspension.

Table 2. Tissue Distribution of Inhaled Pu in Beagles

Pu Suspension	Sacrifice (Days After Exposure)	Mean % Final Pu Burden			
		Lungs	Thoracic Lymph Nodes*	Liver	Skeleton
Aged $^{238}PuO_2$	27-37	63	1.0	7.5	23
Aged $^{238}PuO_2$	91-92	43	6.7	11	34
Fresh $^{238}PuO_2$	29	98	0.7	0.3	0.5
Fresh $^{238}PuO_2$	54	93	5.0	0.6	0.9
Fresh $^{238}PuO_2$	78	91	5.0	0.8	1.8
Aged $^{239}PuO_2$	28-30	97	0.8	0.07	0.2
Aged $^{239}PuO_2$	141-142	96	4.0	0.01	0.05

* Tracheobronchial, mediastinal and sternal lymph nodes

The Pu tissue distribution in the dogs exposed to fresh $^{238}PuO_2$ was similar to the dogs exposed to $^{239}PuO_2$ with 96 to 98% of the final body burden in the lungs and thoracic lymph nodes at 29 to 78 days after exposure. Translocation was primarily to the thoracic lymph nodes. These dogs had more Pu in the skeleton and liver than the dogs exposed to $^{239}PuO_2$. There was a trend toward ^{238}Pu translocation from the lung and accumulation in the thoracic lymph nodes, liver and the skeleton with time after exposure.

The Pu tissue distribution in the dogs exposed to aged $^{238}PuO_2$ suspension was very different from the dogs exposed to aged $^{239}PuO_2$ suspensions or dogs exposed to fresh $^{238}PuO_2$ suspensions. There was much more translocation to liver, 8 to 11% of the final body burden; and skeleton, 23 to 34% of the final body burden in the dogs exposed to aged $^{238}PuO_2$. This appeared reasonable, since the particle size of the aged $^{238}PuO_2$ aerosols was smaller than that of the fresh $^{238}PuO_2$ and $^{239}PuO_2$ and since the ultrafilterability of the aged $^{238}PuO_2$ suspension was 25% compared to 0.2% for the fresh $^{238}PuO_2$ suspension and aged $^{239}PuO_2$ suspension. A higher solubility of the aged $^{238}PuO_2$ was expected because of the relatively greater surface area with smaller particles.

Table 3 shows the fraction of total plutonium deposited in the dog that was retained in the body or excreted in urine or feces. The fraction retained was largest for inhaled $^{239}PuO_2$ followed in descending order by aged $^{238}PuO_2$ and fresh $^{238}PuO_2$. Both ^{238}Pu-exposed groups excreted a larger fraction in the feces than did the $^{239}PuO_2$-exposed dogs. The fraction excreted in the urine of the dogs exposed to aged ^{238}Pu was about 10 times larger than the fraction excreted in the urine of the other two groups but still represented less than 0.5% of the plutonium initially deposited.

It seemed surprising that storage in water for 6 months could so markedly change the physical and biological behavior of the $^{238}PuO_2$. X-ray diffraction analyses of 19 month old suspensions of $^{239}PuO_2$ and freshly prepared 72 hour old $^{238}PuO_2$ suspensions showed the expected peaks but $^{238}PuO_2$ that had been in water suspension for 9 months showed no X-ray peaks, indicating an alteration in crystal structure. We measured the ultrafilterability of $^{238}PuO_2$ suspensions at periodic intervals following their preparation with the results shown in Table 4. Electron micrographs of the aerosolized aged $^{238}PuO_2$ particles collected on thermal precipitator[6] grids were much smaller and more regularly shaped than the fresh $^{238}PuO_2$ and $^{239}PuO_2$ particles (Figure 1).

Table 3. Retention and Excretion of Inhaled Pu in Beagles

Pu Suspension	Sacrifice (Days After Exposure)	MEAN % INITIAL PU BURDEN Final Body Burden	Fecal Excretion	Urinary Excretion
Aged $^{238}PuO_2$	31	67	32	0.36
Aged $^{238}PuO_2$	92	64	36	0.48
Fresh $^{238}PuO_2$	29	27	73	0.04
Fresh $^{238}PuO_2$	54	25	75	0.02
Fresh $^{238}PuO_2$	78	18	81	0.06
Aged $^{239}PuO_2$	29	85	16	0.05
Aged $^{239}PuO_2$	141	92	8	0.07

* Tracheobronchial, mediastinal and sternal lymph nodes

Table 4. Ultrafilterability of $^{238}PuO_2$ Suspension

Age of Stock Suspension (Days)	Ultrafilterability Mean ± SD (%)
1	0.17 ± 0.04
3	0.38 ± 0.04
9	1.70 ± 0.17
26	8.1 ± 2.3
35	12.1 ± 0.49
65	15.8 ± 0.70

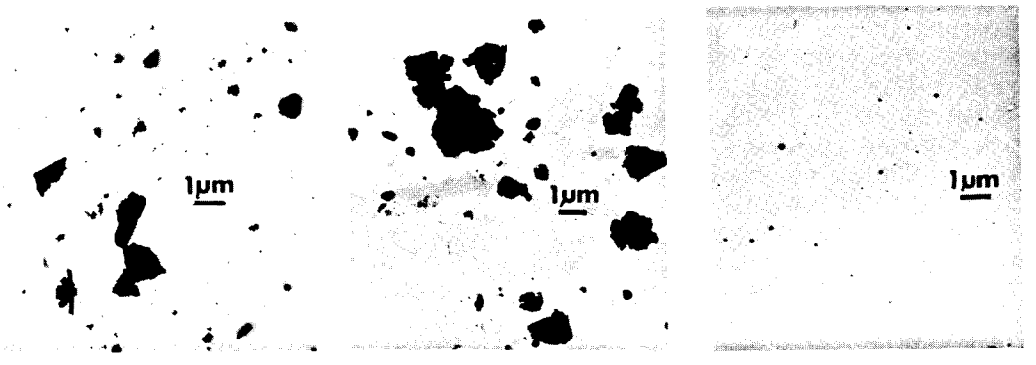

Figure 1. Electron Micrographs of (a) Aged $^{239}PuO_2$ Aerosol, (b) Fresh $^{238}PuO_2$ Aerosol and (c) Aged $^{238}PuO_2$ Shadowed at 26°.

DISCUSSION

The smaller AMAD of the aged $^{238}PuO_2$ may have influenced the fraction translocated to the liver and skeleton; however, the lack of X-ray defraction peaks, the size and shape of the particles and the higher ultrafilterability indicate a change in the chemical form of the $^{238}PuO_2$ during storage in water. The trend with time after exposure toward increased translocation from the lung and accumulation of Pu in the liver and skeleton of the dogs exposed to freshly prepared $^{238}PuO_2$, suggest that similar changes in chemical form of $^{238}PuO_2$ may occur in the animals. Rats exposed to $^{238}PuO_2$ showed a high rate of translocation to the skeleton - 11% of the body burden at 20 days and over 20% at a year or more after exposure - compared to less than 2% in the skeleton of rats exposed to $^{239}PuO_2$. In other studies, dogs exposed to $^{238}PuO_2$ aerosols have shown higher rates of translocation to skeleton, up to 13% of the body burden after 6 months, compared to less than 1% for $^{239}PuO_2$-exposed dogs[8]. Table 5 shows distribution of ^{238}Pu in the tissue of dogs 5 to 6 years after inhalation of $^{238}PuO_2$, compared to dogs sacrificed at similar times after inhalation of $^{239}PuO_2$. The much greater translocation of ^{238}Pu to the skeleton and liver, despite the low ultrafilterability and fresh state of the water suspension employed in generating the aerosol, suggest that solubilization of the $^{238}PuO_2$ occurs to a significant degree within the dog, as well as in water suspension. The $^{239}PuO_2$-exposed dogs died due to lung tumors and the $^{238}PuO_2$-exposed dogs died due to bone tumors[9,10].

Table 5. Tissue Distribution of Pu in Beagles After Inhalation of $^{238}PuO_2$ and $^{239}PuO_2$

	Percent of Final Body Burden+					
	$^{238}PuO_2$*			$^{239}PuO_2$**		
Tissue	58***	60	62	54	57	68
Lung	6	7	17	55	49	35
Lymph Nodes	10	11	9	24	27	37
Liver	23	33	22	16	15	19
Skeleton	55	43	47	3	5	4
All Other Tissues	6	6	5	2	4	5
Final Body Burden (μCi)	2.5	2.3	2.2	1.8	1.2	1.4

\+ Values are for individual dogs
* Calcined 350°C, ultrafilterability 1-2%, CMD 0.1 μm, animal exposed 2 days after preparation of the water suspension
** Calcined 350°C, ultrafilterability <1%, CMD 0.1-0.5 μm
***Months after exposure

The chemical and physical differences between $^{238}PuO_2$ and $^{239}PuO_2$, which caused the differences in their behavior in water suspension and in vivo, are not completely understood. Higher in vitro solubility of respirable $^{238}PuO_2$ particles, as compared to $^{239}PuO_2$ particles, has also been reported by Raabe, et al.[11].

Due to the small amount of information on the biological behavior of $^{238}PuO_2$, it has generally been assumed that $^{238}PuO_2$ would behave like $^{239}PuO_2$. This is quite evidently not the case in the animal and it may not be the case in environmental contamination.

Since both isotopes are present in varying proportions in reactors, and in the wastes from fuel reprocessing, we should learn how the ratio of ^{238}Pu to ^{239}Pu influences the physical and biological behavior of mixtures. We should

also learn if this is related to the high specific activity of ^{238}Pu and whether other alpha-emitting, high specific activity radionuclides present in the fuel cycle may influence the chemical, physical and biological behavior of the mixture of radionuclides.

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