THE IN VIVO SOLUBILITY OF PLUTONIUM-239 PRODUCED IN PLUTONIUM-SODIUM AEROSOLS

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1. INTRODUCTION

Fast Breeder reactors use liquid sodium as a coolant. Under certain accidental conditions there is a probability that mixtures of the oxides of plutonium and sodium (mixed oxides) could be released into the environment as a polydisperse aerosol. It has been shown previously that in rodents a significant fraction of the plutonium-239 (Pu) associated with these mixed oxides is readily transportable from the lungs to other body tissues (1,2,3). The objectives of this work are threefold. Firstly, to further characterise the transportable fraction; secondly, to evaluate the reactions that occur between this fraction and naturally occurring constituents of blood and urine; and thirdly, to investigate the relationship between the amount of Pu excreted in the urine and the body content in the early period after an intake.

2. MATERIALS AND METHODS

Mixed oxides were prepared as described previously (2,4). Two mixed oxides, with Pu to Na atomic ratios of 1:3 and 1:20 were used. These ratios were chosen because they have been shown to contain a small and a large transportable fraction of Pu respectively (1). The plutonium in these mixed oxides has the physico-chemical characteristics of plutonium-239 dioxide (PuO_2) (1,4,5). Various particle size fractions between 0.001 μm and 0.22μm were isolated by an ultrafiltration technique (4). Negligible amounts of plutonium were found in the nominal particle size range from 0.004 to 0.025 μm. The amount of plutonium found in the 0.001 μm diameter fraction varied with the Na content from 1.6% (atomic ratio 1:3) to 48% (atomic ratio 1:20). For comparison, the 0.001 μm diameter fraction isolated from high temperature calcined PuO_2 contained about 0.1% of the total Pu in suspension (4). The mixed oxides aerosol fractions were suspended in water and contained about 1.4×10^5 dpm ml^{-1}; aliquots of this suspension were administered to rats either by pulmonary intubation (0.05 ml) or intravenous injection (0.2 ml). Plutonium citrate prepared as described previously (4) was used to provide control data on a known soluble form of Pu. The rats were young mature females, about 10 weeks old, weighing 150 g to 200 g, obtained from an inbred strain (Medical Research Council, Radiobiological Unit, Harwell). The animals were given food and water ad libitum. Radiochemical analysis for Pu and sampling and gel filtration separation techniques to determine the physico-chemical form of Pu in blood and urine were performed as described elsewhere (7).

3. RESULTS AND DISCUSSION

3.1 Transportability of mixed oxides

The enhanced transportability of Pu following the uptake of mixed oxides relative to PuO_2 has been demonstrated in vivo (1,2,3). This could be due either to the presence of small particles of PuO_2 or hexavalent or heptavalent Pu, all of which have been observed in vitro (1,2,6,7,8). Recent studies with PuO_2 suggest that the transportability of Pu could be primarily dependent on the presence of small particles of PuO_2 about 0.001 μm in diameter (4). The tissue distribution and excretion pattern of Pu following the intubation of the 0.001 μm particle fraction of mixed oxides is summarised in Table 1. The metabolic behaviour of Pu after 1 day is broadly similar to that observed after the pulmonary intubation of Pu citrate. About two-thirds of the Pu on the 0.001 μm diameter fraction of the mixed oxides is behaving as a Class D compound according to the

classification of the Task Group Lung Clearance Model (9). However, after 21 days, Pu remaining in the lungs is behaving as a compound with long term retention. During the 21 day period the extra pulmonary tissue deposition of Pu is similar for the two mixed oxides and Pu citrate, e.g. the amounts of extrapulmonary Pu present in the skeleton (remaining carcass) is 85% and86% (atomic ratios 1:3 and 1:20) for the mixed oxides and 86% for Pu citrate. The lung clearance and tissue destribution of Pu is independent of the Na content of the aerosol. It is postulated therefore that the primary effect of Na is to influence the particle size distribution of PuO_2 during the preparation of the aerosol and in particular the amount of the 0.001 μm fraction. Thus, when mixed oxides of Pu and Na contain appreciable quantities of 0.001 μm diameter PuO_2 particles the amount of Pu transferred to blood would be greater than that proposed in the Task Group Lung Clearance Model which considered PuO_2 as a Class Y (insoluble) compound (9). In contrast, there was negligible translocation (<0.5%) to extrapulmonary tissue of Pu associated with

Tissue/ Excreta	Period (days)	Plutonium administered as		
		Pu citrate	Mixed oxide suspension (0.001 μm diameter)	
			Pu:Na, 1:3[c]	Pu:Na, 1:20[c]
Lungs	1	28.2 ± 1.7	34.2 ± 1.2	32.2 ± 1.8
	6	7.40 ± 0.45	27.6 ± 2.4	25.0 ± 1.4
	21	5.43 ± 0.38	21.3 ± 0.9	18.0 ± 0.9
Liver	1	11.0 ± 1.0	8.37 ± 0.69	10.1 ± 1.1
	6	12.4 ± 0.4	7.67 ± 0.46	7.50 ± 0.52
	21	9.79 ± 0.33	6.30 ± 0.56	6.25 ± 0.22
Blood	1	3.07 ± 0.38	2.56 ± 0.26	3.53 ± 0.22
	6	0.32 ± 0.05	0.31 ± 0.04	0.19 ± 0.02
	21	0.06 ± 0.01	0.06 ± 0.01	0.09 ± 0.02
Other tissues[a]	1	1.69 ± 0.14	2.70 ± 0.20	2.58 ± 0.19
	6	3.20 ± 0.12	1.87 ± 0.15	2.12 ± 0.21
	21	1.63 ± 0.12	1.40 ± 0.12	1.42 ± 0.13
Remaining carcass	1	51.7 ± 2.6	42.5 ± 1.6	42.1 ± 1.2
	6	64.2 ± 0.6	44.1 ± 1.8	46.4 ± 0.6
	21	64.7 ± 0.7	46.3 ± 1.3	46.9 ± 0.7
Urine[b]	1	1.41 ± 0.14	6.80 ± 0.18	7.71 ± 0.22
	6	3.18 ± 0.22	8.33 ± 0.37	9.01 ± 0.21
	21	3.84 ± 0.24	10.7 ± 0.3	11.3 ± 0.2
Faeces[b]	1	2.93 ± 0.40	2.84 ± 0.28	1.78 ± 0.16
	6	9.40 ± 0.80	10.2 ± 0.7	9.85 ± 0.33
	21	14.6 ± 0.8	14.0 ± 0.3	16.0 ± 0.3

TABLE 1 Metabolic fate of plutonium administered to the rat by pulmonary intubation

Results, Mean ± SEM, expressed as % of initial lung content
Number of animals per group, 4

a kidneys, ovaries, adrenals, thymus, spleen and gastrointestinal tract
b cumulative excretion
c atomic ratio of Pu:Na in mixed oxide aerosol

mixed oxides particles between 0.025 μm and0.22 μm diameter. After 21 days more than 94% of the Pu was present in the lungs.

3.2 The physico-chemical form of Pu in blood and urine

Monomeric Pu when injected into the blood is known to be complexed rapidly by the high molecular weight protein transferrin, and the low molecular weight anion citrate (10,11). The glomerular filteration of Pu citrate probably accounts for the presence of Pu in the urine. However, the data summarised in Table 1 shows that the urinary excretion of Pu is appreciably greater following the administration of 0.001 μm diameter mixed oxides particles than after Pu citrate. This increase can be attributed principally to Pu excreted within the first 24 hours. Gel filtration studies showed that at early time intervals, a low molecular weight "intermediate" complex, thought to be a reaction product involving PuO_2 and the citrate anion, was circulating in blood and being filtered simultaneously through the kidneys. The clearance half time from blood was about three minutes (5). This species which has also been observed with high temperature calcined PuO_2 (4) probably explains the enhanced urinary excretion of Pu relative to administered Pu citrate. Ultimately Pu was found to be complexed by transferrin and citrate in blood and by citrate in urine.

3.3 The relationship between tissue deposit and urinary excretion

It has been suggested by Lafuma (12) that for a limited period of time following the inhalation of Pu compounds, a constant relationship exists between cumulative excretion of Pu and the amount translocated to tissue. This hypothesis is supported by data obtained following the intubation of Pu citrate and Pu nitrate into rats which showed that the systemic content of Pu after 1 week was about 25 times the amount appearing in urine (1).

Intubated material	T/U		
	0 - 1 days	0 - 6 days	1 - 6 days
Pu citrate (control)	47.8 ± 5.1	24.8 ± 1.8	44.6 ± 6.6
Mixed oxide (Pu:Na 1:3, 0.001 μm)	8.3 ± 0.3	6.4 ± 0.4	34.6 ± 9.4
Mixed oxide (Pu:Na 1:20, 0.001 μm)	7.6 ± 0.3	6.2 ± 0.3	43.0 ±10.0

TABLE 2 Relationship between extrapulmonary tissue deposit (T) and cumulative urinary excretion (U) of plutonium

In contrast, the factors obtained following the intubation of the transportable fraction of oxide suspensions were lower and variable, viz. 18-20 for PuO_2, 10-19 for mixed oxides (1). In the experiments with mixed oxides described here, the factor relating extrapulmonary tissue deposit and total urinary excretion is independent of the Na content of the suspension and about 4 times less than that for monomeric Pu after the first week (Table 2). Moreover these results are in agreement with the corresponding value obtained for PuO_2, viz. 7.7 ± 0.4 (4). It is therefore concluded that an empirical fixed factor cannot be arbitrarily assigned to the interpretation of urine analysis data although it would appear that when the enhanced excretion due to the "intermediate" is complete, i.e. essentially after the first day, the factor is reasonably independent of the physico-chemical form of the Pu intake (Table 2).

4. SUMMARY

The amount of plutonium transported from the lungs to blood in the early clearance phase following the intubation of mixed oxide suspension obtained from polydisperse aerosols depends primarily on the presence of plutonium dioxide particles of about 0.001 μm diameter. When these particles are

present in significant quantity, the lung clearance characteristics are different from those defined for insoluble (class Y) compounds; the Task Group Lung Model would therefore require modification. Furthermore, the enhanced urinary excretion of plutonium relative to administered plutonium citrate invalidates the use of an empirical fixed factor to determine systemic burden.

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