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GASTRO-INTESTINAL ABSORPTION OF PLUTONIUM

III. COMPARISON BETWEEN RAT AND PIG

November 15, 1954

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By

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ABSTRACT

In single-feeding experiments the absorption of plutonium from the gastro-intestinal tract of three pigs averaged 0.0022 per cent, with 95 per cent confidence limits of ± 0.0013. This figure did not differ significantly from the results of more extensive single feeding and chronic feeding experiments on rats.

Plutonium absorbed and excreted in the urine of rats amounted to less than 20 per cent of the total plutonium absorbed. Less than one per cent of plutonium fed to rats remained in the animals two days after feeding.

GASTRO-INTESTINAL ABSORPTION OF PLUTONIUM
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INTRODUCTION

The preceding papers in this series reported the results of long-term chronic feeding experiments in which the gastro-intestinal absorption of plutonium in the rat was found to average 0.0028 per cent, and to be constant over a wide range of plutonium concentrations in the solution fed.[1, 2] The extrapolation of any experimental result from rat to man is fraught with considerable uncertainty. Additional data were therefore sought from a larger animal. The pig was chosen for study because of its similarity physiologically to the human.

Because of the experimental difficulties involved in the intra-gastric administration of radioactive materials to animals as large and obstreperous as the pig, chronic feeding was considered impractical. Single doses of relatively high plutonium content were administered to the pigs and single doses of smaller volume to rats. Thus a comparison was obtained between pigs and rats receiving acute dosage; and, combined with earlier data, a comparison between rats chronically exposed and rats acutely exposed. The results should be of value in establishing the most probable value for gastro-intestinal absorption of plutonium in the human.

EXPERIMENTAL PROCEDURE

The three pigs employed were female Chester-White x Danish Landrace hybrids weighting between 30 and 45 kg. The 15 rats were young adult females of the Sprague-Dawley strain weighing between 210 and 265 g. All animals were housed in individual cages and maintained on their normal

diets of dried rations with water ad libitum. A single dose of plutonium-239 nitrate solution, pH 2, containing 0.45 mg Pu per ml was administered by stomach tube to each animal; 20 ml to each pig, and 1 ml to each rat. Single rats were sacrificed at 2, 3, 4, 5 and 7 days after plutonium administration. The 10 remaining rats and the 3 pigs were sacrificed 9 days after plutonium administration. Urine and feces were collected daily from the 10 rats sacrificed at 9 days.

Pelt and gastro-intestinal tract were removed from all animals at sacrifice, care being taken to prevent contamination of other tissues from these sources. A blood sample and the liver were analyzed separately for each animal. In addition, kidneys, spleen, heart and lungs were separately analyzed for the pigs. Organs from the pig were analyzed in toto, except for the liver and blood, where an average result was obtained from three or four aliquots. Skeletons were separated from the soft tissue and analyzed in toto in the case of the rats. Soft tissues and skeletons from the pigs were thoroughly ground and three or four aliquots analyzed. Analytical procedures have been previously described.(1)

RESULTS AND DISCUSSION

Plutonium retention in the three pigs sacrificed nine days after intra-gastric administration is shown in Table I. Comparable plutonium concentrations were observed in skeleton and liver; other tissues exhibited considerably lower concentrations. On a total tissue basis the skeleton contained from two to three times as much plutonium as the remainder of the animal. Samples from the intestinal tract (contents removed) were analyzed from one pig. The results indicate no appreciable holdup of plutonium on the intestinal tract. In general, agreement between samples from the three animals was quite good.

TABLE I

ABSORPTION AND RETENTION OF PLUTONIUM IN THE PIG NINE DAYS FOLLOWING INTRA-GASTRIC ADMINISTRATION

	Per Cent of Administered Dose Retained					
	Per Gram (x 10^8)			Per Tissue (x 10^4)		
Tissue	Pig #1	Pig #2	Pig #3	Pig #1	Pig #2	Pig #3
Skeleton	38	58	40	16	20	10
Blood	1.1	1.7	1.4			
Liver	52	52	34	4.7	3.8	2.3
Kidney	5.2	6.5	2.3	.09	.11	.06
Spleen	2.5	3.6	3.6	.02	.03	.03
Heart	0.5	1.5	0.3	.008	.009	.004
Lung	4.1	4.1	4.1	.13	.10	.10
Duodenum[1]	40					
Jejunum[1]	8.1					
Ilium[1]	5.9					
Other Soft Tissue[2]	2.2	1.8	1.8	4.0	3.1	2.7
Total Soft Tissue[1]				9.0	7.1	5.2
Total Animal[1]				25.0	27.1	15.2

[1]Plutonium content of gastro-intestinal tract and skin not included in totals.

[2]Includes blood and all tissues not separately listed, except gastro-intestinal tract and skin.

Table II shows the results obtained from the 15 rats. Three animals, numbers 3, 7, and 15, show consistently a much lower plutonium retention in all tissues than do the other animals. Excretion of plutonium by rats 7 and 15 (feces were not collected from rat 3) was comparable with that from the other animals, so the low retention values can only be attributed to an impaired absorption. Individual variations in absorption of this magnitude were not noted in previous chronic feeding experiments,[1, 2] and it is therefore probable that the low values observed for these animals were due to some temporary disturbance in gastro-intestinal function. Excluding animals 3, 7, and 15, the results were reasonably consistent. There was no significant difference between animals sacrificed from 2 to 7 days following administration, and those sacrificed 9 days following administration.

Plutonium excretion data obtained from rats 6-15 are summarized in Table III. There is little holdup of plutonium in the intestinal tract, less than one per cent of the administered dose being excreted after the second day. The very small amounts of plutonium excreted in the urine are evidence that most of the plutonium absorbed from the gastro-intestinal tract is retained by the animal. Total urinary excretion amounted to only about one-fourth of the plutonium retained in the animal. All figures for urinary excretion should be considered as maximum values, since the slightest contamination of the collected urine with the much more radioactive feces would result in higher apparent urinary excretion. That such contamination probably did not occur to any very significant degree is indicated by the fact that the measured plutonium content of the urine remained at a relatively constant level for the first three days in the face of a sharp decrease in fecal plutonium excretion. The difference of 12 per cent between plutonium administered and total plutonium recovered from the excreta is not considered a serious discrepancy in view of the

TABLE II

ABSORPTION AND RETENTION OF PLUTONIUM IN THE RAT FOLLOWING INTRA-GASTRIC ADMINISTRATION

Rat No.	Time of Sacrifice (Days after Admin.)	Per Cent of Administered Dose Retained						
		Per Gram (x 10^6)			Per Tissue (x 10^4)			
		Skeleton	Liver	Other Soft Tissue	Skeleton	Liver	Other Soft Tissue	Total[1]
1	2	115	137	4.8	22	10.5	5.3	38
2	3	65	109	1.3	14	6.9	1.4	22
3	4	15	21	0.3	3	1.3	0.4	5
4	5	99	133	1.8	20	9.3	1.9	31
5	7	159	154	2.2	32	10.3	2.3	45
6	9	87	92	3.7	15	6.1	4.3	25
7	9	14	8	0.2	3	0.5	0.2	4
8	9	100	145	1.7	18	10.1	2.1	30
9	9	100	110	1.8	20	7.3	2.1	29
10	9	108	192	1.5	20	12.1	1.9	34
11	9	147	98	2.0	24	8.7	2.3	35
12	9	131	135	1.7	23	15.6	2.0	41
13	9	88	47	1.0	16	4.7	1.2	22
14	9	154	86	2.7	27	9.4	2.9	39
15	9	9	7	0.1	2	0.7	0.1	3

[1] Gastro-intestinal tract and skin not included.

TABLE III

EXCRETION OF PLUTONIUM BY RATS FOLLOWING INTRA-GASTRIC ADMINISTRATION

Days Following Feeding	Per Cent of Administered Dose Excreted	
	In Feces[1]	In Urine (x 10^4)[2]
1	75	2.2
2	12	3.7
3	0.6	1.2
4	0.02	0.03
5	0.002	0.2
6	.0008	0.06
7	.0006	0.02
8	.0005	0.09
9	.0006	0.2
Cumulative Total	88	7.7

[1]Figures for first five days are averages of values obtained on 24-hour feces collection from each of 10 animals. Figures for last four days obtained from analysis of pooled collection from all animals.

[2]Figures are the average of results on 2 samples, each representing the pooled 24-hour urine collection from 5 animals.

difficulties inherent in the intra-gastric administration of an accurately measured volume of solution, and the general problems of plutonium analysis in biological materials.

A summary of gastro-intestinal absorption of plutonium in the pig (single feeding) and the rat (single feeding and chronic feeding) is given in Table IV. With the possible exception of liver deposition, the singly fed rats and pigs show no significant differences. Because of the smaller number of animals employed, results on the singly fed animals have wider confidence limits than the results from the chronically fed rats. Certainly there is no significant difference in total absorption between the singly and chronically fed animals. It does appear that plutonium retention in soft tissue is greater in the singly fed animals and deposition in the skeleton correspondingly lower, than in the chronically fed animals. Such a difference is reasonably explained on the basis of a gradual shift of plutonium, with time, from the soft tissues to bone. Evidence for such a shift was not obtained from the rats sacrificed at intervals from 2 to 7 days following feeding. The number of animals employed was, in any case, too small to have given significant results, and the time interval too short to have proven or disproven this point.

The demonstrated close similarity in extent of gastro-intestinal absorption of plutonium in the rat and pig is presumptive evidence for a similar behavior in the human. The presently recommended maximum permissible concentration of plutonium in drinking water (1.5×10^{-6} μc/ml)[3] is based on an assumed absorption of 0.1 per cent. In view of the evidence here presented this figure would seem to be unnecessarily conservative by a factor of at least ten.

TABLE IV

COMPARISON OF GASTRO-INTESTINAL ABSORPTION OF PLUTONIUM IN THE RAT AND PIG

Tissue	Per Cent of Administered Dose Retained (Average with 95% Confidence Limits ($\times 10^4$))		
	Single Feeding		Chronic Feeding
	Pig (3 Animals)	Rat (8 Animals)[1]	Rat (360 Animals)[2]
Skeleton	15 ± 7.6	20 ± 7.4	25 ± 3
Liver	3.6 ± 2.6	9.3 ± 6.3	--
Other Soft Tissue[3]	3.3 ± 1.0	2.1 ± 1.5	--
Total Soft Tissue[3]	7.1 ± 4.1	11.4 ± 6.2	3.3 ± 7.2
Total Animal[3]	22 ± 13	32 ± 12	28 ± 8

[1] Animals 7 and 15 (Table II) omitted (See text).

[2] Data from ref. (2).

[3] Gastro-intestinal tract and skin not included.

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