REMOVAL OF PLUTONIUM FROM RATS BY PROLONGED ADMINISTRATION OF CHELATING AGENTS

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In our previous work (1) we investigated the effect of single chelate doses and suggested the combination of calcium diethylenetriaminepentaacetate (Ca-DTPA) with desferrioxymine-B methane sulfonate (DFOA) for early decorporation of ^{239}Pu. The present data concern the efficacy of prolonged chelate administration as a function of the time elapsed since ^{239}Pu citrate injection, the choice and dosing of chelating agents, and the rate and duration of their administration. Results obtained can be summarized as follows:

1. An early initiated treatment, continued for a month, involving an equivalent of the commonly employed human chelate dose (Tab. 1):

1.1 Prolonged administration of a combination of Ca-DTPA and DFOA was superior to the use of either of these two chelating agents alone.

1.2 The chelate combination could be replaced after the first two injections by zinc diethylenetriaminepentaacetate (Zn-DTPA) without reduction of the overall decorporation effect.

1.3 The first two chelate injections virtually exerted the same effect as prolonged chelate administration; they prevented more than 90 % of injected ^{239}Pu from deposition in the bone and liver.

1.4 The effect of only one single chelate injection was, however, substantially less, although a chelate combination was injected immediately after ^{239}Pu incorporation.

2. Treatment initiated 4 days post ^{239}Pu injection and continued for another 5 days, involving varying amounts of Zn-DTPA (Fig. 1):

2.1 Decorporation of ^{239}Pu increased with increasing amount of Zn-DTPA; this was most pronounced as far as ^{239}Pu in the bone is concerned.

2.2 When Zn-DTPA was administered only once a week, the decorporation effectiveness was in general less pronounced than that after the same total weekly chelate dose had been divided into two or more fractions.

2.3 A continuous subcutaneous infusion of Zn-DTPA was in general not more effective than single daily injections of the same chelate amount.

2.4 When the number of Zn-DTPA fractions per week was decreased and, simultaneously, the total chelate dose per week was increased, an equal decorporation effect was achieved.

3. Treatment initiated 4 days post ^{239}Pu injection and continued for 1 or 4 weeks, involving 5 injections of varying amounts of Zn-DTPA per week

3.1 With 30 $\mu mol \cdot kg^{-1}$ Zn-DTPA the decorporation of ^{239}Pu was least pronounced and could be significantly improved by protraction of treatment only as far as ^{239}Pu in the liver is concerned.

3.2 With 100 $\mu mol \cdot kg^{-1}$ Zn-DTPA the contents of ^{239}Pu in the skeleton, liver and kidneys decreased by 50, 80 and 75 %, respectively, after 4 weeks of treatment, as compared with controls. This is significantly better than the effect of treatment continued for 1 week only.

3.3 With 1000 $\mu mol \cdot kg^{-1}$ Zn-DTPA the best decorporation results were achieved in the skeleton and liver after one week of treatment. There was surprisingly no further improvement due to protraction of treatment so that after 4 weeks of treatment the ^{239}Pu removal from the skeleton and kidneys was equal and in the liver even smaller than after administration of 100 $\mu mol \cdot kg^{-1}$ Zn-DTPA.

CONCLUSION

a. When a prolonged treatment can be initiated early after ^{239}Pu incorporation, the effect of the first few injections is most important.

b. If delays occur, Zn-DTPA becomes the treatment of choice, since it can be administered at higher doses which entail a higher reduction of ^{239}Pu contents in the organs than can be obtained by the human Ca-DTPA dose.

c. A sufficiently long period of administration and fractioning of the weekly, rather than of the daily Zn-DTPA dose seem to be the most important factors influencing the effectiveness of a delayed prolonged chelate treatment of incorporated ^{239}Pu.

REFERENCE

(1) VOLF, V., "Diagnosis and Treatment of Incorporated Radionuclides" IAEA, Vienna (1976), p. 307.

Treatment schedule[a]		N	Percentage of injected ^{239}Pu dose[b]		
Injection 1-2	Injection 3-6		Skeleton	Liver	Kidneys
Controls		24	60.8 ± 0.9	4.0 ± 0.1	0.35 ± 0.01
Ca-DTPA	Ca-DTPA	6	11.0 ± 2.7	0.49 ± 0.08	0.061 ± 0.009
DFOA	Zn-DTPA	6	5.4 ± 1.7	0.67 ± 0.08	0.13 ± 0.01
Ca-DTPA+DFOA	Ca-DTPA+DFOA	6	3.6 ± 0.6	0.41 ± 0.03	0.070 ± 0.010
Ca-DTPA+DFOA	Zn-DTPA	6	3.3 ± 0.4	0.27 ± 0.01	0.060 ± 0.010
Controls		14	57.7 ± 1.7	4.1 ± 0.1	0.33 ± 0.01
Ca-DTPA+DFOA[c]	-	6	3.2 ± 0.4	0.36 ± 0.02	0.10 ± 0.01
Ca-DTPA+DFOA[d]	-	10	7.7 ± 1.1	0.55 ± 0.06	0.15 ± 0.02

TABLE 1 Organ retention of ^{239}Pu affected by repeated administration of chelating agents, beginning early after ^{239}Pu incorporation.

[a] Chelating agents (30 $\mu mol \cdot kg^{-1}$ each) were injected i.p. at 1.5 min and on days 1, 8, 15, 22 and 29 after i.v. injection of ^{239}Pu citrate. Rats were sacrificed 36 days after ^{239}Pu administration.

[b] Arithmetic means ± S.E.; N - number of animals

[c] Only two chelate injections, at 1.5 min and on day 1 post ^{239}Pu

[d] Only one chelate injection, at 1.5 min post ^{239}Pu

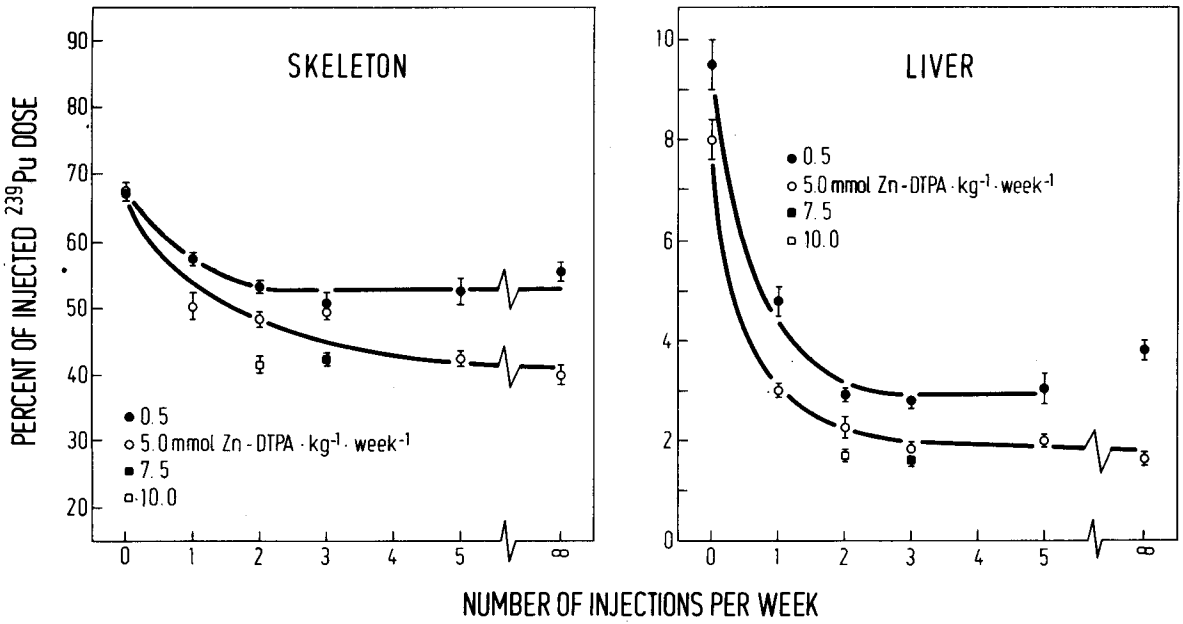

Fig. 1. Organ retention of ^{239}Pu as a function of the total Zn-DTPA dose and its fractioning. Zn-DTPA was injected or infused s.c. on days 5 to 9 after i.v. injection of ^{239}Pu citrate. Rats were sacrificed 15 days after ^{239}Pu administration. Values are geometric means ± S.E., on the average 6 rats per group.