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SUMMARY OF THE RESEARCH PROGRESS MEETING

of November 10, 1949

H. P. Kramer

December 12, 1949

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SUMMARY OF THE RESEARCH PROGRESS MEETING

of November 10, 1949

H. P. Kramer

Recent Studies on Decontamination and Bone Metabolism. D. H. Copp.

For several years past, the group at the University of California Radiation Laboratory under the direction of Dr. J. G. Hamilton has been engaged in an investigation of the biological behavior of radioactive materials in the skeleton. When certain radioactive elements are injected into the body, a substantial portion may become lodged in the bones, and there constitute a permanent source of destructive radiation similar to that encountered in radium poisoning. Accordingly, the program of research was considered from two aspects. First, it was desired to learn how these radioactive elements were deposited in the skeleton; and second, for purposes of therapy, means were sought for increasing the elimination of these materials from the bones and from the body.

I. Deposition of Radiostrontium in the Skeleton. Since radiostrontium is easily absorbed from the intestinal tract, it presents a serious hazard from fission product contamination of food or water. For this reason, the factors involved in its deposition in bone were studied. In addition, because of its close similarity to calcium in chemical and biological behavior, it was hoped that information might be obtained on the basic process of bone calcification. Hodges showed that bone ash would take up radiostrontium from solution by simple exchange with the calcium of the mineral. Such a mechanism may account for the deposition of radiostrontium in mature adult bone. However, as may be seen from Table I young growing animals show a much higher retention of radiostrontium, associated with the active formation of new mineral in the growing bone.

Table I

Test Animals	Hours after injection of Sr*	Percent of administered dose of Sr*		
		Skeleton	Urine	Feces
Adult rats	96 hrs.	29.1	42.7	26.9
Young rats (normal)	96 hrs.	71.9	16.4	12.8
Young-normal	1 hr.	86.1	0.3	-
Normal	72 hrs.	68.5	13.5	8.7
Young rachitic	1 hr.	81.5	8.2	-
	72 hrs.	16.3	81.3	3.6

To compare the manner in which this deposition of radiostrontium took place, curves showing the bone uptake of Sr* during the critical first hour following injection were obtained using mature adult rats, young actively growing rats, and young rachitic rats in which mineralization of the new bone was inhibited by lack of phosphate. These curves are shown in Fig. 1.

The uptake by adult bone is slow and steady, and can be explained by a physical process of ion exchange. In contrast, the initial uptake by both normal and rachitic young animals is very rapid, and appears to reach equilibrium within an hour or so. This suggests that there is a very minute labile fraction in young growing bone which rapidly attains equilibrium with the blood Sr*. In the normal animals, this Sr* is retained in the skeleton - presumably by fixation in the depositing mineral in the new bone. In the rachitic rats, in contrast, this Sr* is rapidly lost from the skeleton and appears in the urine. In these animals,

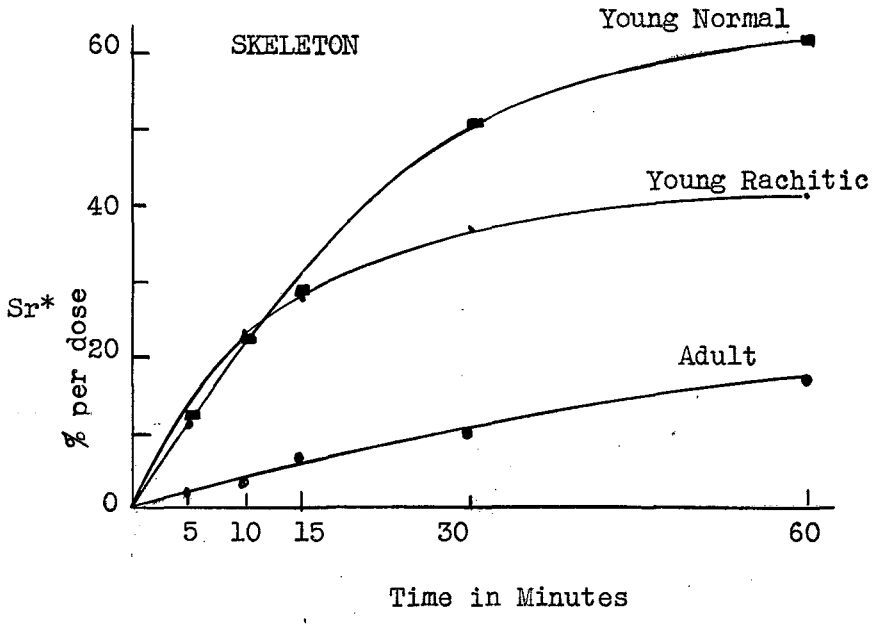
SKELETON
Young Normal
Young Rachitic
Adult
60
40
20
0
Sr*
% per dose
5
10
15
30
60
Time in Minutes

Fig. 1

calcification is inhibited, and permanent fixation of Sr* does not occur. It is possible that these experiments may give some clue as to means of eliminating Sr* from bone.

It was concluded that Sr* uptake in the adult bone is largely by adsorption and ionic exchange, while in the young growing bone, there is rapid uptake of Sr* into a labile fraction, which becomes permanently fixed in normal animals, but is rapidly lost from rachitic bone.

II. Effect of Large Doses of Zr-citrate in Eliminating Y^{*90} and Pu from the Body. One of the most effective means of increasing the elimination of heavy metals from the skeleton is the method, first developed by J. Schubert at Argonne, of prompt administration of massive doses of zirconium citrate. Table II shows that administration of Zr citrate immediately after the injection of Pu will actually flush out considerable Pu as evidenced by increased urinary Pu and decreased Pu in the bone. Similar effects were obtained with Y^{*91}. However, when the treatment was given 3 days after the injection of Pu or Y*, there was no significant decrease in the bone content, and the absolute value of the increased urinary excretion was small.

Table II

Effect of Zirconium Citrate on the Bone retention and Excretion of Y, Pu (From J. Schubert, AECD-2358)

Treatment	Percent of dose in: Femur	Urine
Controls Pu	7.29	1.41
Early Zr treated Pu	1.20	51.3
Late Zr treated - Pu	6.05	7.0
Controls Y	4.2	27.0
Early Zr treated - Y-	1.6	63.7
Late Zr treated Y	4.3	33.4

A comparison was made between the bone uptake and excretion of carrier-free Zr^{95}, and Zr^{95} mixed with the therapeutic dose of Zr citrate. The results in Table III show a tremendous increase in the urinary excretion of Zr^{95} when carrier was present, indicating a flushing action of Zr citrate. Similar results were obtained with Y^{90}, suggesting that the action in this case may also be of a "carrier" nature.

Treatment with Zr citrate two days before or two days after the injection of Y^{90} had very little effect on the bone uptake and excretion of this element, compared to the dramatic effect when administered immediately after the Y^{*} (Table IV) This suggests that the mechanism is not of an ion exchange nature, nor does there appear to be saturation of the reactive bone groups.

Table III

"Carrier" Effect of Zirconium Citrate

	Percent of administered dose in:	
Group	Femurs	Urine
Zr^{95} - carrier free	4.8 4.8	4.3
Zr^{95}-plus 40 mg. Zr citrate	0.4	86.6
Y^{90} - carrier free	5.8	9.7
Y^{90}-plus 40 mg. Zr citrate	0.4	91.3

Table IV

Effect of Pretreatment; Immediate Treatment, and Posttreatment with Zr. Citrate

Groups	Percent of administered dose of Y^{90} Skeleton	Urine
Controls	44.9	12.5
Pretreated with Zr. Citrate 48 hrs. prior to Y^{90}	43.0	12.8
Treated with Zr. Citrate immediately after the injection of Y^{90}	20.2	71.3
Treated with Zr. Citrate 48 hrs. after injection of Y^{90}	43.0	12.7

An attempt was made to combine the flushing action of zirconium citrate with the action of parathormone in promoting bone resorption. It was hoped that the latter might release bound Pu or Y from the bone, so that it might be swept out with the Zr citrate. The results in Table V indicate that this is not the case, and parathormone-Zr citrate therapy appears to be quite ineffective for decontamination.

Table V

Effect of Parathormone and Zirconium Citrate on Y* and Pu*

Groups	Y* % of administered dose in Femurs	Urine	Pu* % of administered dose in Femurs	Urine
Controls	6.0	9.9	10.8	13.9
Zr- immediate	3.2	28.0	6.0	18.9
Zr- 2 days after Y*,Pu*	5.0	16.4	8.8	11.7
Parathormone	6.6	8.4	7.6	14.1
Parathormone-Zr 2 days after Y*, Pu*	5.4	13.8	8.4	9.2

Formation of Cl^{38} from Cu. R. Batzel.

It was found that ${}_{17}Cl^{38}$ is obtained from bombardment in the cyclotron with 350 Mev protons with a yield corresponding to 10^{-4} barns. If the reaction can be represented by

$$ {}_{29}Cu^{63,65} + {}_{1}H^{1} \longrightarrow {}_{17}Cl^{38} + {}_{1}H^{1} + 6\ {}_{2}He^{4} + n $$

its calculated threshold is 100 Mev of which 51 Mev account for the increase in mass and 49 Mev for the energy required by the ejected particles to overcome the Coulomb barrier. The production of Cl^{38} at bombarding energies below 100 Mev, to 85 Mev, 50 Mev, and even 40 Mev demonstrated that Cl^{38} was either produced as a spallation product of an impurity contained in the copper target or else that the assumed reaction and the associated calculated threshold are not correct.

The possibility of the production of Cl^{38} from impurities contained in the copper was investigated by determining the impurities present in the target, measuring their cross sections for the production of Cl^{38} and deciding whether yields predicted on this basis corresponded to the observed yields of Cl^{38}. Since the amount of impurities was too small for chemical or spectrographic analysis (the copper was found to be 99.999 percent pure) the target was bombarded in the cyclotron at energies below the thresholds for the production of contemplated impurities and a search was made for typical reaction products that would indicate the presence of K, Ca, Sc, Ti, Va, and Cr. From this investigation the conclusion was drawn that Cl^{38} was not produced from impurities and must therefore have come from a copper-proton reaction.

The relative yields of Cl^{38} at energies below 100 Mev were determined by measuring the ratio of the β^- activity of this isotope to the β^+ activity of Cl^{34} which was observed at all bombarding energies. This method of measuring relative yield is valid since Cl^{34} arises from a (p,n) reaction on sulfur impurity in the copper target and is therefore produced in fairly constant amounts in the energy

range under discussion. The results displayed in the table below indicate that the actual threshold for the production of Cl^{38} falls below 60 Mev. The cross section at 85 Mev is 1/3 - 3 x 10^{-8} barns.

Bombarding Energy (Mev)	Cl^{38}activity/Cl^{34} activity
85	2
75	1.2
70	0.5
65	0.1
60	$\ll$0.1

The presence of Cl^{38} as a spallation product from Cu at low energies may conceivably be explained by postulating that large particles are emitted from the copper nucleus together with Cl^{38}. The emission of ${}_8O^{16}$ instead of 4 α-particles requires a threshold of only 81 Mev. If Mg^{25} were ejected, a bombarding energy of only 48 Mev would be needed. The hypothesis that heavy particles are emitted is strengthened by recent observations that demonstrate the emission of Li^8 nuclei from light elements.

A search for similar effects will be extended to the spallation of other elements.

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