UDC 615-092.21 : 615.92 : 546.42

Effect of Phosphorus-deficient Diet with Excess of Calcium or Strontium on the Excretion of Radiostrontium and Its Possible Mechanism

It has been reported by several workers that the excretion of injected radiostrontium is greatly enhanced in phosphorus-deficient rachitic rats[1,2,3] and in rats fed with low-phosphorus, rachitogenic diet[2] or non-rachitogenic diet mildly deficient in phosphorus.[4] Mechanism of the action of phosphorus deficiency has also been discussed by some of us[4] and others.[1,2] The present experiment was carried out to obtain further information on this problem.

Thirty male rats, two months old, were divided into two groups. One group of rats were fed a normal diet consisting of corn starch, dextrin, cooked egg albumin, peanut oil, and powdered filter paper with a suitable mixture of inorganic salts (Ca, 0.56%, P, 0.45%) and vitamins A, B, and D (Diet I); the other group was placed on a diet which was very low in both calcium (0.016%) and phosphorus (0.025%) (Diet II). Each group was further divided into three, i.e., the first was injected with Ca in three doses of 5 mg. as lactate (Ca-I and Ca-II groups), the second was injected with Sr in three doses of 11 mg. as lactate (Sr-I and Sr-II groups), and the third was injected with 0.9 % solution of NaCl (N and E groups). Detail of the grouping of the rats is shown in Table I. The first injection was made 30 mins. before the subcutaneous injection of radiostrontium, and the second and the third injections were respectively carried out 30 and 150 mins. after the radiostrontium injection.

The diets in the groups Ca-I and Ca-II were changed into very low phosphorus one (Diet III) 9 hrs. after the administration of radiostrontium, and the diets in the groups Sr-I and Sr-II were changed into a diet very low in both Ca and P, containing $SrCO_3$ (Sr : 1.12%) (Diet IV). N and E groups were continuously fed the original diets (Diets I and II). Forty-eight hours after the administration of radiostrontium all the animals were sacrificed by cutting the carotid artery, and the blood was drawn and centrifuged to separate the serum for radioassay and analysis of alkaline earth metals. Urine and feces after the injection of radiostrontium were collected separately as described below :

The first collection of the urine (U-I) was carried out 6 hrs. after the radiostrontium injection. The second (U-II) was collected at 33rd hr. of the experiment, and the third (U-III) at sacrifice. Feces were collected at sacrifice throughout the experimental period.

Table I.

Group	No. of animals	Diet		Excretion of *Sr[a] %			Alkaline earths		*Sr in U-III / *Sr in Serum	*Sr in Serum[d] / Residual *Sr
		0~9th hr. of expt.	9~48th hr. of expt.	In U-I	In U-III[e]	Total	In U-III[c] (mg.)	In Serum[b] (m.mol.)		
N	5	I	I	15.06	3.24	36.61	9.22	2.53	474	7.16×10^{-2}%
E	5	II	II	15.87	4.49	38.73	5.19	2.44	419	11.19×10^{-2}
Ca-I	5	I	III	16.49	6.66	41.53	83.2	2.81	1015	7.16×10^{-2}
Ca-II	6	II	III	16.90	6.99	50.58	106.8	2.73	1012	7.51×10^{-2}
Sr-I	5	I	IV	18.08	6.71	48.83	66.0	1.73	688	10.80×10^{-2}
Sr-II	4	II	IV	27.89	10.56	61.45	79.0	2.32	1209	10.80×10^{-2}

a) Radioactivity is expressed as per cent of the injected dose.
b) Serum alkaline earth metals were titrated with $KMnO_4$ after precipitating them as oxalates.
c) Alkaline earth metals in the urine were weighed as $M(COO)_2\cdot H_2O$.
d) Serum radioactivity was determined in 1 cc. serum, and the activity in total serum was calculated by assuming the total volume of the serum to be 2.5 cc./100 g. body wt.
e) Values of radiostrontium excreted into U-III are expressed as per cent of total body burden of radiostrontium at 33rd hr. of the experiment.

1) D.C. Jones, D.H. Copp : J. Biol. Chem., **189**, 509(1951).
2) D.H. Copp, J.G. Hamilton, D.C. Jones, D.M. Thompson, C. Cramer : Transactions of 3rd Conference on Metabolic Interrelations, Josiah Macy, Jr. Foundation, New York, 226(1951).
3) D.H. Copp, J.G. Hamilton, D.C. Jones, D.M. Thompson, C. Cramer : U.S. AEC Documents, UCRL-146(1951).
4) Y. Ito, S. Tsurufuji, M. Shikita, Y. Matsushima : Yakugaku Zasshi, **78**, 76(1958).

Some of the results in which we are especially interested are summarized in Table I. In order to indicate the actual rate of transit of radiostrontium through the kidneys and the rate of its liberation from the bones, radioactivity ratio of Sr in U-III to that in the total serum was calculated and is shown in Table I, as well as the ratio of radiostrontium in the serum to that in the carcasses. According to these data, it is apparent that the diet with excess Sr is as effective as that with excess Ca in increasing the urinary excretion. The P-deficient diets III and IV significantly increase the probability of passage of radiostrontium in serum through the kidneys $\left(\frac{\text{*Sr in U-III}}{\text{*Sr in Serum}}\right)$ with simultaneous increase of urinary alkaline earth metals. It is most interesting, but incomprehensible, that parenterally introduced excess of Ca failed to elevate urinary excretion of radiostrontium (U-I).

Examination of the ratio of serum radiostrontium to that in residual carcass indicates the following facts:

1) Deficiency in both Ca and P increases removal of radiostrontium from the bones, but does not increase its urinary excretion because of slight decrease in its clearance from the kidneys.

2) The effect of P-deficiency with excess Ca results chiefly from the elevated passage of radiostrontium through the kidneys.

3) The effect of excess Sr with P-deficiency results both from elevated transit through the kidneys and from increased liberation from the bones.

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December 23, 1957