of FFA by skeletal muscle was influenced by the FFA concentration of the medium, but not by the presence of epinephrine.

Summary. An intravenous infusion of labeled palmitic acid was repeated after an interval of about 90 minutes on the same intact anesthetized dog. During the second period, an infusion of NE (0.2 or 0.4 μg/kg/min) was also given. Arterial FFA, CS-A difference for FFA and myocardial uptake of FFA were increased by the higher dose of NE; the specific activity of arterial FFA, the extraction ratio of FFA and myocardial R.Q. were decreased. Infusion of nicotinic acid, preceding administration of NE eliminated the above changes. It appears that myocardial FFA oxidation is indirectly influenced by NE, through FFA mobilization and the elevated arterial level of this metabolite.

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Some Criteria for Removal of Skeletally Bound Radioactive Strontium.* (29996)

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It has been demonstrated that magnesium ions, in excess of normal requirement, can increase the overall elimination of radioactive strontium from the skeletons of rats. This occurs whether the isotope was administered 1 or 30 days previously. The increased elimination is by way of the kidney since fecal elimination is decreased(1). Magnesium ions also decrease uptake and retention of radioactive strontium by skeletons of rats fed a diet containing the isotope(2). Moreover, it has also been shown that the phosphate content of the diet has a marked influence on the removal of skeletally bound Sr^{89}(3,4,5). Since magnesium metabolism is intimately involved with that of calcium and phosphorus the following studies were designed to determine the mechanism whereby alterations in the dietary Ca/P ratio and in supplemental magnesium increase radiostrontium elimination and decrease skeletal uptake of the isotope.

Experimental. Male Holtzman rats weighing 90-100 g were injected with 30 μc of carrier free Sr^{89} intravenously and fed laboratory stock diet for 30-50 days before they were fed the experimental diets. During the balance period, the animals were housed in individual metabolism cages designed to separate urine and feces. They were kept in these cages for 16 days during which time their food, water and magnesium consumption were measured daily. The first 4 days were considered a pretreatment period to allow the rats to adjust to the different diets and the individual cages. From day 5, half of the animals received 10% glucose solution and the other half 10% glucose solution containing 2% $MgCl_2 \cdot 6H_2O$. The glucose solution

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TABLE I. Total Strontium^{89} Excretion for 12-Day Period.

Groups	Dietary calcium (%)	Dietary phosphorus (%)	Ca/P ratio	Supplemental mg++	Relative counts of Sr^{89}* Urinary	Fecal	Total
1	1.6	traces	very large	—	1193[1]	66[1]	300[1]
2	1.6	”	” ”	+	875[1,2]	42[1]	216[1]
3	.8	”	large	—	321[1]	37[1]	160[1]
4	.8	”	”	+	212[1,2]	23[1]	102
5	1.6	.4	4	—	224[1]	83[2]	145[1]
6	1.6	.4	4	+	143[1,2]	75[1]	104[2]
7	.8	.4	2	—	100	100	100
8	.8	.4	2	+	159[1,2]	74[1,2]	110[3]
9	.8	.8	1	—	92	110	104
10	.8	.8	1	+	121	82[1,2]	98
11	traces	.4	small	—	103	103	104
12	”	.4	”	+	222[1,2]	100	137[1,2]
13	”	.8	very small	—	144	87	104
14	”	.8	” ”	+	298[1,2]	106	104

[1] $p < .01$ when compared to excretion by rats fed control diet.
[2] $p < .01$ when compared to group fed same diet but without supplemental magnesium.
[3] $p < .05$ when compared to group fed same diet but without supplemental magnesium.
* For ease of comparison of data, excretion of Sr^{89} by animals fed the control diet (0.8% calcium and 0.4% phosphorus) was arbitrarily set at 100 and all other values are relative to this.

was used to insure sufficient quantities of urine for analysis. The average magnesium intake by the unsupplemented rats, over the 12-day period, was about 65 mg and that of the supplemented rats between 7 to 10 times greater. Urines and feces were collected every 2 days. There were 5 rats in each group and they were fed a synthetic diet composed of the following ingredients: 4.0% Salt mix, 60% Cerelose, 10% Mazola oil, 24% blood fibrin and 2% alphacel. Alterations in dietary calcium/phosphorus ratios were made by varying the calcium and phosphorus contents of the salt mix. The diets contained adequate amounts of all the known vitamins and the indispensable trace elements.

Calcium was determined by the method of Berger(6) and phosphorus by a modification of the Fiske-Subbarow procedure(7). Aliquots of urine were plated out in stainless steel planchets, air dried, dried in an oven at 70-80°C and counted in a flowgas counter containing a micromil window. Feces were ashed in a muffle furnace at 600°C; the residue dissolved in a small volume of 1 N HNO_3 and made up to a suitable volume. Aliquots were analyzed by the same procedures used for urine. Suitable corrections were made for decay and the samples were counted long enough to ensure a statistical accuracy of at least 1%. An analysis of variance according to Snedecor was made on all data(8).

Results. Effect of alterations in dietary calcium and phosphorus on removal of skeletally bound Sr^{89}. In Table I may be seen the effects of alterations in dietary Ca/P ratios on Sr^{89} excretion. When the Ca/P ratio was 4 or greater, urinary Sr^{89} was increased significantly above that of the controls. The greater the Ca/P ratio, the more Sr^{89} was excreted. Urinary Sr^{89} was unaltered if the Ca/P ratio was below 2. Fecal Sr^{89} was decreased when the Ca/P ratio was 4 or greater and unchanged at the other ratios. The net excretion of Sr^{89} (urinary plus fecal) was significantly greater only by those animals fed diets whose Ca/P ratio was 4 or more.

Effect of supplemental magnesium on removal of skeletally bound Sr^{89}. The effects of increasing the intake of magnesium ions on elimination of Sr^{89} is reported in Table I. Supplemental magnesium decreased urinary Sr^{89} by rats fed diets whose Ca/P ratio was 4 or greater and increased it if the diets had Ca/P ratios of 2 or less. The increased magnesium intake also tended to decrease fecal Sr^{89} by those animals whose diets contained calcium. However, the decrease was statistically significant only in those groups fed diets whose Ca/P ratio was 2 or less.

Effect of alterations in dietary Ca/P ratios and supplemental magnesium on calcium and phosphorus balance. Since radioactive strontium is handled by the body in a manner similar to radioactive calcium(9), it was felt

TABLE II. Calcium and Phosphorus Excretion During 12-Day Balance Period.

Groups	Supplemental magnesium	Dietary ratio Ca/P	Calcium intake (mg)	Urinary calcium (mg)	Fecal calcium (mg)	Calcium balance	Phosphorus intake (mg)	Urinary phosphorus (mg)	Fecal phosphorus (mg)	Phosphorus balance
1	—	very large	1660	232[1]	729	+ 699	traces	2.0	37	— 39
2	+	" "	2500	250	703[2]	+1547[2]	"	5.0	41	— 46
3	—	large	600	200[1]	204	+ 196	"	1	62	— 62
4	+	"	1420	241	161[2]	+1018[2]	"	1	67	— 67
5	—	4	1920	172[1]	935	+ 813	480	18	142	+320
6	+	4	2400	114	871[2]	+1415[2]	600	8	215	+370
7	—	2	1020	27	503	+ 490	510	36	137	+337
8	+	2	1120	72[2]	384[2]	+ 659[3]	560	26	173	+361
9	—	1	1020	29	428	+ 563	1020	211	243	+566
10	+	1	1340	42	297[2]	+1001[2]	1340	106[2]	366	+868[2]
11	—	small	traces	10	55	— 65	720	457	61	+202
12	+	"	"	8	29	— 37	570	142[2]	80	+348[2]
13	—	very small	"	5	16	— 21	1250	968	48	+243
14	+	" "	"	8	27	— 35	1370	515[2]	184[2]	+671[2]

Same animals and legend as Table I.

that an examination of urinary and fecal calcium might help explain the mechanism for the increased urinary and decreased fecal Sr^{89} under certain dietary conditions. Table II shows the calcium and phosphorus balance of the animals described in the previous Table. The unsupplemented rats (Groups 1, 3 and 5) which excreted more Sr^{89} in their urines than the controls (Group 7) also had an elevated urinary calcium. Groups 1 and 3, whose diets contained insufficient phosphorus for growth or maintenance were in negative phosphorus but in positive calcium balance while both balances were positive in Graup 5. The animals in Groups 11 and 13 did not have an elevated urinary calcium nor was their urinary Sr^{89} above the normal values despite their being in negative calcium balance.

The effect of supplemental magnesium on calcium and phosphorus excretion was also dependent on the Ca/P ratio in diet. Although the absolute urinary calcium of Groups 2 and 4 was slightly greater than their controls (Groups 1 and 3), it was significantly less if calculated as percent of intake since the magnesium supplemented groups ate considerably more calcium. In actuality, urinary calcium by rats fed diets with high Ca/P ratios was decreased with increasing magnesium intake. The strontium excretion paralleled that of calcium (Table I). Urinary calcium was increased by mag- urinary Sr^{89} since animals with a positive less as was urinary Sr^{89} (Groups 8 and 10 as compared to 7 and 9). Although urinary Sr^{89} was significantly elevated by Groups 12 and 14, no changes in urinary calcium could be detected by the method of analysis used(6) which was too insensitive to detect with any degree of accuracy the small amounts of calcium excreted by rats on a calcium 'free' diet.

Increasing the magnesium intake decreased fecal calcium by all groups of animals regardless of the dietary Ca/P ratio. In other words magnesium increased the absorption of calcium by all animals fed diets containing more than traces of calcium. It also made the calcium balance more positive.

Increasing the intake of magnesium consistently decreased urinary phosphorus and increased fecal phosphorus provided the diet contained adequate phosphorus. It made phosphorus balance significantly more positive in most groups (Table II).

Discussion. No satisfactory measures exist for removal of a 'bone-seeking' isotope once it has been deposited in the skeleton. Low phosphorus diets(3,4,5) will increase the rate of removal of radioactive strontium from the skeleton in part, as a result of the deleterious effect that such diets have on bone mineral composition(4) and in part as a result of the increased urinary calcium which results from increased absorption of calcium from the gut (10). It is apparent that a negative phosphorus balance is not essential for increased urinary Sr^{89} since animals with a positive phosphorus balance, but fed a diet containing a Ca/P ratio of 4, excreted more Sr^{89} than did their controls (Table I). These animals did, however, have an increased urinary calcium. The animals which were in negative calcium balance had a depressed urinary calcium and excreted no more Sr^{89} than the controls. Thus, it would appear that alterations in the dietary Ca/P ratio such that they result in an increased urinary calcium will cause an acceleration of the release of skeletally bound radioactive strontium.

The effectiveness of magnesium ions in increasing the elimination of skeletally bound isotope is also dependent on its ability to increase urinary calcium.

If the diet contains calcium, increased magnesium intake decreases fecal calcium, *i.e.*, increases absorption from the gut and makes the calcium balance more positive. In these experiments, the magnesium supplemented rats consumed more calcium than their controls and it is conceivable that increase in the calcium balance may in part be derived from the increased calcium intake. However, despite the increased calcium intake by the magnesium supplemented rats, fecal calcium was always less. Moreover, in a series of experiments in which magnesium supplemented rats were pair-fed with their controls the effect of magnesium was to decrease consistently fecal calcium and to increase the balance regardless of the dietary Ca/P ratio, provided the diet contained more than traces of calcium (to be published). The decreased fecal Sr^{89} observed previously(1) and in these experiments must be the result of increased absorption of this ion which resulted from the excess magnesium intake. The rate of renal elimination must be greater than that of absorption to account for the increased overall elimination (Table I).

Summary. The removal of skeletally bound Sr^{89} is accelerated by diets whose Ca/P ratios are 4 or greater. Also, supplemental magnesium increases the removal of isotope if the dietary Ca/P ratio is 2 or less. Large dietary Ca/P ratios and supplemental magnesium produce hypercalciuria which is essential for increased Sr^{89} elimination. Increased intake of magnesium ions routinely decreases urinary phosphorus and fecal calcium causing their balance to become more positive.

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The Activating Effect of Lead on the Precipitation of Calcium Phosphate.* (29997)

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For many years one of the most puzzling features of calcification has been how hydroxyapatite crystals can form *in vivo* at a

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