Effect of High Phosphorus Intake on Sr^{85} Excretions in Man.* (29496)

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Changes in dietary calcium and phosphorus intake have been shown to affect radiostrontium excretion and retention in experimental animals. A phosphorus deficient diet has resulted in reduced retention of radioactive strontium(1-3); however, this dietary regimen led to severe demineralization of the skeleton(2,3). On the other hand, an increase in dietary phosphorus and calcium intake resulted in reduction of the Sr^{90} body-burden in rats(4).

Little is known concerning the influence of dietary factors on absorption of radioactive strontium in man. In view of the changes in radiostrontium retention induced by changes of dietary phosphorus intake levels in animals, the effect of different amounts of phosphorus was investigated on radiostrontium metabolism in man under controlled dietary conditions. To determine the influence of the calcium intake level in the presence of a high phosphorus intake the studies were performed during low and high calcium intake.

Material and methods. Six patients were studied under controlled dietary conditions on the Metabolic Research Ward (Table I). The effect of phosphorus added to the diet was studied during low calcium intake in 4 patients (Patients 1-4) and during high calcium intake in 4 patients (Patients 1, 4, 5 and 6). The diet was a constant analyzed low calcium diet which contained an average of 202 mg calcium and 656 mg phosphorus per day. During the studies in which the effect of increased phosphorus intake was studied on Sr^{85} excretion, the intake of phosphorus was raised to an average of 1628 mg per day by addition of 972 mg phosphorus as glycerophosphate to the low calcium diet. High calcium intake was attained by adding calcium gluconate tablets containing 1522 mg calcium per day to the low calcium diet. All other constituents of the low calcium diet remained unchanged during addition of phosphorus and/or calcium to the diet. The Ca:P ratio during low calcium-low phosphorus diet was approximately 1:4, during low calcium-high phosphorus intake 1:10, during high calcium-low phosphorus intake 2:1, and during high calcium-high phosphorus intake 1:1.

A single tracer dose of Sr^{85} as the chloride was given orally on the first day of each control and experimental study. Sr^{85} plasma levels, urinary and fecal excretions were determined throughout each study. On the day of Sr^{85} administration, plasma levels were determined at 1, 4, 8 and 24 hours, daily for 6 days and at less frequent intervals thereafter. The urinary Sr^{85} excretion was determined daily on aliquots of 24-hour urine collections. Each stool specimen was radioassayed separately. Administration of Sr^{85} and methods of urinary and fecal Sr^{85} analyses has been previously described(5,6). Urinary calcium and phosphorus were determined on aliquots of each 24-hour urine collection and fecal calcium and phosphorus on dry ashed aliquots of 6-day metabolic stool pools. Calcium was determined by the method of Shohl and Pedley(7), phosphorus by the method of Fiske and SubbaRow(8).

Results. Fig. 1 shows Sr^{85} plasma levels of Patient 1 in the control study and during addition of phosphorus to the low and high calcium diet. During low calcium intake, the Sr^{85} plasma level reached a peak at 4 hours after ingestion of the dose and decreased with time thereafter. Although a similar pattern was noted when phosphorus was added to the low calcium diet, the plasma levels were distinctly lower than during the low calcium-low phosphorus intake.

During high calcium-low phosphorus intake, Sr^{85} plasma levels were lower than those during low calcium-low phosphorus intake (Fig. 1). On the addition of phosphorus to

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the high calcium intake, a further decrease of Sr^{85} plasma level was noted. Plasma levels in all 4 studies in Patient 1 showed a similar pattern reaching a peak at 4 hours after ingestion of the dose and decreasing with time thereafter.

Table II shows Sr^{85} plasma levels of the other patients during low and high calcium intake. During the addition of glycerophosphate to the low calcium intake, Sr^{85} plasma levels were lower than in the control study for 24 hours after ingestion of the dose in 2 patients (Patients 2 and 3), while they were slightly higher in one patient (Patient 4).

TABLE I. List of Patients Studied.

Patient	Age, sex	Diagnosis	Study	Study days
1	77, ♀	Osteoporosis	Low calcium - low phosphorus	18
			Low calcium - high phosphorus	18
			High calcium - low phosphorus	42
			High calcium - high phosphorus	20
2	41, ♂	Osteoarthritis	Low calcium - low phosphorus	68
			Low calcium - high phosphorus	24
3	70, ♀	Multiple myeloma	Low calcium - low phosphorus	16
			Low calcium - high phosphorus	20
4	70, ♀	Hypothyroidism	Low calcium - low phosphorus	18
			Low calcium - high phosphorus	18
			High calcium - low phosphorus	18
			High calcium - high phosphorus	20
5	43, ♂	Peripheral neuropathy	High calcium - low phosphorus	42
			High calcium - high phosphorus	36
6	67, ♀	Osteoporosis	High calcium - low phosphorus	42
			High calcium - high phosphorus	30

Avg low calcium intake, 202 mg/day; avg high calcium intake, 1522 mg/day.
Avg low phosphorus intake, 656 mg/day; avg high phosphorus intake, 1628 mg/day.
A tracer dose of Sr^{85} as chloride was given orally on first day of each control and experimental study.

TABLE II. Sr^{85} Plasma Levels During High Phosphorus Intake.

	Low calcium intake					
	Sr^{85}, % dose/total plasma volume					
	Patient 2*		Patient 3		Patient 4	
Hour	Control	Glycerophosphate	Control	Glycerophosphate	Control	Glycerophosphate
1	.33	.36	1.21	.92	.66	1.14
4	1.53	1.14	1.40	1.09	2.47	2.56
8	1.23	.96	1.19	1.02	1.80	2.06
24	.84	.72	.88	.76	1.18	1.52
48	.60	—	.57	.57	.81	1.30
72	—	—	.47	.57	.64	1.18
	High calcium intake					
	Patient 5*		Patient 6		Patient 4	
Hour	Control	Glycerophosphate	Control	Glycerophosphate	Control	Glycerophosphate
1	.24	.00†	2.11	2.03	.23	.34
4	1.14	.78	1.74	2.15	1.16	1.22
8	1.02	.81	1.35	1.41	1.15	.87
24	.66	.72	.90	.97	.78	.62
48	—	—	.53	.78	.54	.48
72	—	—	.48	.67	.44	.38

* Calculated on an assumed plasma volume of 3000 ml. † Counts too close to background.

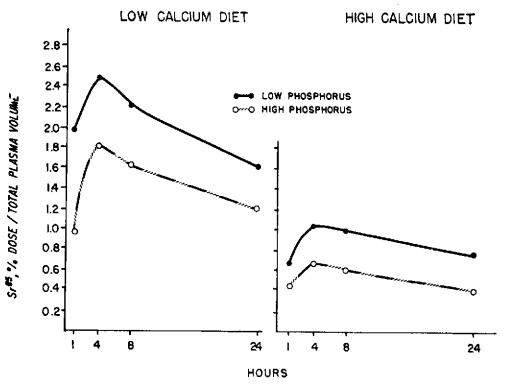

FIG. 1. Sr^{85} plasma levels during high and low phosphorus intake.

On high calcium intake, Sr^{85} plasma levels were lower during the addition of glycerophosphate for the first 8 hours in Patient 5, after the 8th hour in Patient 4; they were slightly higher than in the control study in Patient 6 from 4 hours to 24 hours.

Table III shows that urinary Sr^{85} excretions decreased in all 4 patients during the addition of glycerophosphate to the low calcium intake, the fecal Sr^{85} excretion being variable. It remained unchanged in Patients 1, 2 and 4 and was higher than in the control study in Patient 3. During the addition of phosphorus to the high calcium intake, a decrease of urinary Sr^{85} excretion was noted in all 4 patients, although this decrease was slight in Patient 6. Fecal Sr^{85} excretion was higher than in the control study in Patients 4 and 5 and remained unchanged in Patients 1 and 6.

Urinary calcium excretion decreased slightly in 3 of 4 patients on addition of phosphorus to the low calcium diet (Table IV). The average calciuria was 61 mg/day in the control phase and 47 mg/day in the experimental phase. During the addition of phosphorus to the high calcium intake, the average calciuria was 117 mg/day as compared to an average urinary calcium excretion of 150 mg/day in the corresponding control phase. The decrease in urinary calcium for the 8 studies during low and high calcium intake was highly significant, $P<0.001$. On the other hand, the changes in fecal calcium were not significant on the addition of phosphorus to the low and high calcium diet, fecal calcium increasing in some cases and decreasing in others.

Urinary phosphorus excretion increased in all patients on addition of phosphorus to the low and high calcium intake. This increase averaged 745 mg/day during low calcium intake and 409 mg/day during high calcium intake. The increase in fecal phosphorus was considerably greater on addition of phosphorus to the high calcium intake than to the low calcium diet, 291 *vs* 91 mg per day, respectively.

Discussion. The effect of different calcium intake levels, the phosphorus intake remaining constant, has been investigated on radio-

TABLE III. Urinary and Fecal Sr^{85} Excretion During Low and High Phosphorus Intake.

	Low calcium intake							
	12-day cumulative Sr^{85} excretion, % dose							
	Patient 1		Patient 2		Patient 3		Patient 4	
Excretions	Control	Glycerophosphate	Control	Glycerophosphate	Control	Glycerophosphate	Control	Glycerophosphate
Urine*	6.1	4.9	7.4	5.9	6.1	1.4	12.4	5.6
Stool*	79.2	79.8	83.2	86.4	83.3	95.4	62.7	55.9
	High calcium intake							
	Patient 1		Patient 5		Patient 6		Patient 4	
Excretions	Control	Glycerophosphate	Control	Glycerophosphate	Control	Glycerophosphate	Control	Glycerophosphate
Urine*	6.0	2.4	3.5	2.7	11.4	10.8	6.4	3.1
Stool*	93.5	97.3	81.0	97.1	84.0	76.0	74.4	92.5

* Cumulative urinary and fecal excretions in 12 days.

TABLE IV. Calcium and Phosphorus Excretions During Low and High Phosphorus Intake.

Patient	Study	Low calcium intake						High calcium intake					
		Calcium, mg/day			Phosphorus, mg/day			Calcium, mg/day			Phosphorus, mg/day		
		Intake	Urine	Stool	Intake	Urine	Stool	Intake	Urine	Stool	Intake	Urine	Stool
1	Control	140	49	175	519	345	210	1483	97	1281	519	266	225
	Glycerophosphate	146	34	199	1758	1336	325	1475	64	1193	1419	591	628
2	Control	272	78	308	795	268	276	—	—	—	—	—	—
	Glycerophosphate	259	65	394	1674	762	462	—	—	—	—	—	—
3	Control	140	64	191	552	463	236	—	—	—	—	—	—
	Glycerophosphate	145	36	133	1424	1192	297	—	—	—	—	—	—
4	Control	186	53	168	668	328	261	1180	152	782	678	244	296
	Glycerophosphate	188	53	125	1635	1094	232	1181	123	962	1383	568	498
5	Control	—	—	—	—	—	—	2111	127	1508	748	239	262
	Glycerophosphate	—	—	—	—	—	—	2080	86	1780	1658	725	583
6	Control	—	—	—	—	—	—	1496	224	1152	681	442	224
	Glycerophosphate	—	—	—	—	—	—	1515	194	1118	1422	1093	268

strontium metabolism in man(9), but no information has been available on the effect of different phosphorus intake levels.

Glycerophosphate used in this study was well absorbed, during low and high calcium intake, as evidenced by the prompt increase in urinary phosphorus excretion, phosphate being presumably released from glycerophosphate by the action of enzymes in the intestine. Added phosphorus consistently lowered urinary Sr^{85} excretion during low and high calcium intake; urinary calcium decreased also, in agreement with previously reported results(10-12).

Sr^{85} absorption decreased in 3 patients on addition of glycerophosphate to the low calcium diet and in 3 patients on a high calcium-high phosphorus diet, judging from the lower Sr^{85} plasma levels. However, fecal Sr^{85} excretion was not consistently increased. The slightly higher Sr^{85} plasma level and the lower fecal Sr^{85} excretion in Patient 4 during low calcium-high phosphorus intake represent physiological variations rather than increased Sr^{85} absorption. In Patient 1, any increase in fecal Sr^{85} excretion during high calcium-high phosphorus intake would have been difficult to detect, since the excretion was very high in the control study (93.5% *vs* 97.5%). The relatively high plasma level at 8 hours in Patient 4 during high calcium-high phosphorus intake may have been due to slow intestinal absorption in this hypothyroid patient.

Addition of calcium to the diet, the phosphorus intake remaining unchanged, decreased the absorption of Ca^{45} more than that of Sr^{85} in man(13), in agreement with results obtained by Palmer *et al* in mature rats(14). These investigators have shown that dietary phosphate affects Sr^{90} uptake by bone(15). Increase in dietary phosphate and calcium reduced the Sr^{90} body burden in rats more than addition of calcium alone(4), an effect also demonstrated by Wasserman and Comar(16,17). Large amounts of calcium phosphate reduced Sr^{85} absorption in fasted rats but the effect of calcium alone was not compared(18).

Summary. The effect of high phosphorus intake on radiostrontium absorption was in-

vestigated in 6 patients. Two of these were studied during low calcium diet, 2 during high calcium intake, and 2 patients during low and high calcium intake. Addition of phosphorus to the diet led to a decrease in Sr^{85} absorption in 3 of the 4 patients each studied during low and high calcium intake, respectively. Urinary Sr^{85} excretion and urinary calcium excretion were decreased during high phosphorus intake in both the low and high calcium studies.

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Histamine and Mast Cells in Human Fetal Skin.* (29497)

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In 1879 Ehrlich(1) pointed out that mast cells appear in connective tissue during the later phase of fetal development. Lombardo (2) found mast cells in the subcutaneous connective tissue of the human embryo from the second fetal month. Holmgren(3) reported the first mast cells in skin in a 9.0 cm long human fetus. In the adult human, mast cells produce histamine(4). The human fetus produces histamine(5), and histamine-forming capacity has been demonstrated in a variety of human fetal tissues including skin(6).

The present investigation was undertaken because no studies seem to disclose the time of appearance of measurable amounts of histamine nor the relationship between histamine and mast cells in human fetal skin. Histamine determinations were made by the fluorometric assay method(7). The histologic identification of mast cells was carried out by metachromatic staining for acid mucopolysaccharides.

Methods. The material consisted of skin from 14 human fetuses, removed by legally approved induced abortion in gynecologic departments in Greater Copenhagen. The pregnancies were interrupted by hysterotomy through inferior median laparotomy. The skin specimens were obtained a few hours after the operation. If not determined immediately the skin specimens were frozen down at —20°C.

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