Normal Blood Calcium Homeostasis in Response to Calcium Infusion in Pseudohypoparathyroidism and Idiopathic Hypoparathyroidism* (32930)

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The pathway of the action of thyrocalcitonin has not been completely elaborated but the hormone apparently decreases the blood calcium level by decreasing bone resorption. It may act directly on bone and indirectly by antagonizing the action of parathyroid hormone (1, 2). One could then speculate that pseudohypoparathyroidism—a disease associated with resistance to parathyroid hormone and often with hypocalcemia—and "idiopathic hypoparathyroidism" are caused by increased secretion of or sensitivity to thyrocalcitonin. Since thyrocalcitonin secretion is stimulated by hypercalcemia (3) we have measured the blood calcium homeostasis of several of these patients in response to a rapid infusion of calcium. The rapid rather than the prolonged infusion of calcium was selected so that the maximal effect of thyrocalcitonin which is seen within 60 min (4) would be more apparent.

Materials and Methods. Five tests were performed on 4 subjects with pseudohypoparathyroidism, and 1 test on a patient with "idiopathic hypoparathyroidism." All the patients with pseudohypoparathyroidism had the classical physical stigmata of the disease, and 3 had significant hypocalcemia. MA was a 40-year-old woman. Her blood calcium level was once 7.2 mg/100 ml but usually ranged between 8.5 and 9.5 mg/100 ml. She had never received treatment for hypocalcemia. CA was a 35-year-old woman who had had tetany as a child (5). She was being treated with 50,000 units of vitamin D and 6 gm of calcium gluconate daily at the time of the test. SO was a 66-year-old woman. She had never had tetany and was not receiving treatment at the time of the test. RH was a 42-year-old male who had had tetany and was receiving 50,000 units vitamin D daily at the time of the test. KO was a 9-year-old girl who had had tetany at the age of 3 years. The diagnosis of "idiopathic hypoparathyroidism" was made on the basis of hypocalcemia, hyperphosphatemia, normal phosphaturic response to parathyroid extract, and the absence of the physical defects of pseudohypoparathyroidism. At the time of the test she was receiving 50,000 units of vitamin D daily.

Calcium infusion tests were performed twice on MA and once each on the other subjects. The tests were done in the morning or in the afternoon after at least a 6 hour fast. Ten per cent calcium gluconate (containing approximately 9 mg of calcium per ml) was injected in a dose of 0.33 ml/kg of body weight over a 10-min period. Bloods were drawn before and immediately after the infusion, and at 30, 60, 120, and 180 min. Plasma was analyzed for calcium (6) and phosphorus (7).

The same test was done on 6 normal control subjects.

Results. The average initial plasma calcium level was lower in the patients with parathyroid disease than in the normal subjects (Table I). The increase immediately after infusion, calculated either as mg/100 ml or percent was also slightly higher; 2.2 mg/100 ml or 24% compared to 1.7 mg/100 ml or 17%. The level remained slightly higher in the patients during the 3-hour period, but the difference in mg/100 ml was not statistically significant (i.e., $p > .05$) from the normal subjects. The rate of decrease was the same in the two groups (Fig. 1). In none of the patients did the plasma calcium fall below the initial level.

The average initial plasma phosphorus was 4.4 mg/100 ml in the patients, and 3.5 mg/100 ml in the normal subjects ($p < .05$). In both groups the level started to increase 30 min after the infusion. It reached a peak increase of 0.6 mg/100 ml (12%) at 120 min in the

* Supported in part by NIH Grant No. 1 RO1 AM10632-01A1.

TABLE I. Plasma Calcium Levels in Response to Calcium Infusion in Experimental and Normal Subjects.

Time[a]:	Plasma calcium										
	Initial	0		30		60		120		180	
	(mg/100 ml)	(mg/100 ml)	Incr (%)	(mg/100 ml)	Incr (%)	(mg/100 ml)	Incr (%)	(mg/100 ml)	Incr (%)	(mg/100 ml)	Incr (%)
Subject											
MA	9.0	10.4	16	9.8	9	9.8	9	9.8	9	9.8	9
	8.8	12.2	39	11.2	27	11.0	25	10.8	23	10.6	20
CA	9.8	11.6	19	11.0	12	10.6	8	10.0	2	10.4	6
SO	10.2	11.8	16	11.4	12	11.4	12	11.0	8	10.6	4
RH	8.6	11.2	30	10.2	16	9.6	12	9.2	7	9.4	9
KO	9.2	11.6	26	11.2	22	10.4	13	10.0	9	9.6	5
Mean	9.2	11.5	24	10.8	16	10.5	13	10.1	10	10.1	9
SE	.23	.23	3.41	.24	2.57	.26	2.28	.25	2.62	.20	2.18
p[b]	<.05		<.10				<.05				
Increase[c] (mg/100 ml)											
Mean		2.2		1.6		1.2		.9		.8	
SE		.28		.23		.19		.23		.19	
p[b]											
Normal (6)											
Mean	9.9	11.6	17	11.1	12	10.7	8	10.4	4	10.5	5
SE	.10	.26	2.4	.18	2.6	.11	1.4	.05	.4	.13	1.8
Increase[c] (mg/100 ml)											
Mean		1.7		1.2		.8		.4		.5	
SE		.24		.25		.13		.05		.15	

[a] Initial and 0 levels immediately before and at end of infusion; other times refer to minutes after end of infusion.

[b] p values compared to normal subjects, given only if <.10.

[c] Increase over initial level.

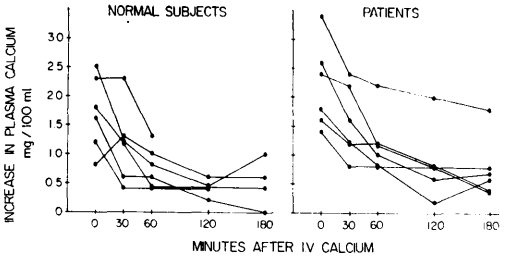

FIG. 1. Response of patients and normal subjects to calcium infusion. The 0 blood was obtained immediately after end of infusion.

patients and of 0.9 mg/100 ml (26%) at 80 min in the normal subjects. The increase in mg/100 ml was not statistically different from the normal subjects.

Discussion. The average increase of 17–24% in the plasma calcium level obtained by the infusion corresponds to the 20% increase that induces thyrocalcitonin secretion in animals (8,9), though the duration of the infusion used in the latter experiments was longer. The normal response to hypercalcemia in our patients is evidence against the concept that excessive thyrocalcitonin secretion is responsible for the hypocalcemia in this disease. Increased amounts of thyrocalcitonin have been found in the thyroid glands of 2 patients with pseudohypoparathyroidism (10,11), but this may well be secondary to long-term hypocalcemia (3).

It is noteworthy that the changes in plasma calcium we observed in normal subjects are similar to those recently reported in which a standard injection of 20 ml or 10% calcium gluconate was used (12). Those investigators found that hypothyroid or hypoparathyroid subjects had normal blood calcium homeostasis when tested in this fashion.

Summary. Blood calcium homeostasis after calcium infusion was measured in 4 pseudohypoparathyroid patients and in one patient with "idiopathic hypoparathyroidism"—as a reflection of possible excessive thyrocalcitonin secretion. The response was similar to that of normal subjects, and in no patient did the postinfusion level fall below the initial level. This is evidence against the concept that excessive thyrocalcitonin secretion produces the hypocalcemia in these diseases.

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Received Dec. 11, 1967. P.S.E.B.M., 1968, Vol. 128.