(meat) diet produces (1) no change in systolic blood pressure; (2) a hypertrophy of the renal substance; and (3) certain histological changes of a pathological nature which are not, however, analogous to chronic nephritis in man.

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## Serum Calcium and Phosphorus of Guinea Pigs after Administration of Single and Repeated Doses of Parathormone.

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The tendency has been to assume that hyperparathyroidism is consistently associated with hypercalcemia. We emphasize that frequently this is not the case, that hypercalcemia is not a sole criterion of hyperparathyroidism. Recorded instances of absence of hypercalcemia after parathyroid administration have sometimes been noted as merely paradoxical. The suggestion of "immunity" to parathormone is not supported by the data. On the other hand, the suggestion that an increased rate of excretion may prevent the accumulation of calcium in the blood is plausible. And a generalization (based on work with rodents) that herbivora are very resistant to parathormone injections implies an effect of diet on serum calcium response. However, the resistance of the cat would have to be explained on a different basis.

It has been established that in mice, rats and rabbits relatively small, if any, effects upon serum calcium are produced by administration of relatively huge doses of parathormone. Negative results in guinea pigs were reported by Macleod and Taylor[1] and Taylor.[2]

We found that in guinea pigs consistent effects upon serum calcium and phosphorus could be produced only by very large doses; that these effects could be brought out more prominently, in young animals, after starvation; and that with doses not sufficiently great to produce effects on serum calcium and phosphorus, calcium mobilization and excretion could be demonstrated.

*Controls.* Normal guinea pigs, young and adult, fed and starved, showed a serum calcium of $10.4 \pm 1.0$ mg. per 100 cc. The serum phosphorus varied from about 8.0 mg. in guinea pigs weighing

[1] Macleod, J. J. R., and Taylor, N. B., *Trans. Roy. Soc. Can.*, 1925, xix (Sect. V), 27.

[2] Taylor, N. B., *Am. J. Physiol.*, 1926, lxxvi, 221.

about 300 gm. to about 4.0 mg. in adults. Starvation for about 70 hours lowered the serum phosphorus of the young animals to between 5.0 and 6.5 mg.

*Effects of a Single Administration of a Large Dose: 1. Calcium.* With doses of 10 to 20 units per 100 gm., injected subcutaneously into *adult* guinea pigs, the serum calcium rose to a maximum of about 16.0 mg. about 24 hours after injection and returned within the normal range before 48 hours. Starvation did not intensify the effect. *Young* animals, if fed, showed high serum calcium 24 to 36 hours after injection, and normal values at the 48 hour interval. After about 70 hours' starvation, calcium values were relatively higher at all intervals after injection. Maximum values (15 to 16 mg.) were found between the 18 and 36 hour intervals. High values persisted after 48 hours. Thus, the influence of starvation on the parathormone effect upon serum calcium is shown strikingly not only by the higher values attained but also by their persistence.

2. *Phosphorus.* The serum phosphorus of young *starved* guinea pigs, after injection of parathormone, rose high beyond the range of values in starved controls—an indication of overdosage, in our opinion. In the *fed* young guinea pigs the effect of parathormone was moderated. In starved *adult* guinea pigs the serum phosphorus was generally raised; the effect was less in the fed adults.

*Effects of Repeated Administration of Parathormone.* The effect upon serum calcium of single doses of parathormone has been shown to last for more than 24 hours. Daily injections, therefore, result in pyramiding their effect. Six guinea pigs were injected about 7, 14 and 20 units per 100 gm. respectively, on 3 successive days. All of the animals died on the third day. When dosage as large as 30 units per 100 gm. were injected daily for several days, after a previous gradual stepping up from smaller doses, the animals survived until the termination of the experiment. Their serum calcium rose to as high as 20 mg., and the high phosphorus indicated overdosage.

When doses less than 5 units per 100 gm. were injected daily for 10 and 16 days, no clearly recognizable or consistent effects upon the serum calcium or phosphorus were produced. Histological examination, however, showed bone resorption, proving mobilization and excretion of bone calcium in the absence of hypercalcemia.

Thirty-three animals were used as controls, 70 were used for the study of the effects of single injections and 23 for the effects of repeated injections.

Our acknowledgement is due to Eli Lilly and Company for their generous cooperation in supplying most of the parathormone used in these experiments.