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Effect of Parathyroid Hormone on Diffusion of Calcium into the Peritoneum. II.

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Two adult dogs, which had been subjected to repeated (7 times each) filling and emptying of the peritoneal space (dextrose, 2.5%-NaCl, 0.9% solution, 100 cc per kg) during the preceding 3 weeks, were treated as indicated in Fig. 1. The purpose of the repeated filling and evacuation of the peritoneum, particularly during the 24 hours preceding the injection of parathyroid hormone, was to determine whether the removal, by this means, of diffusible calcium

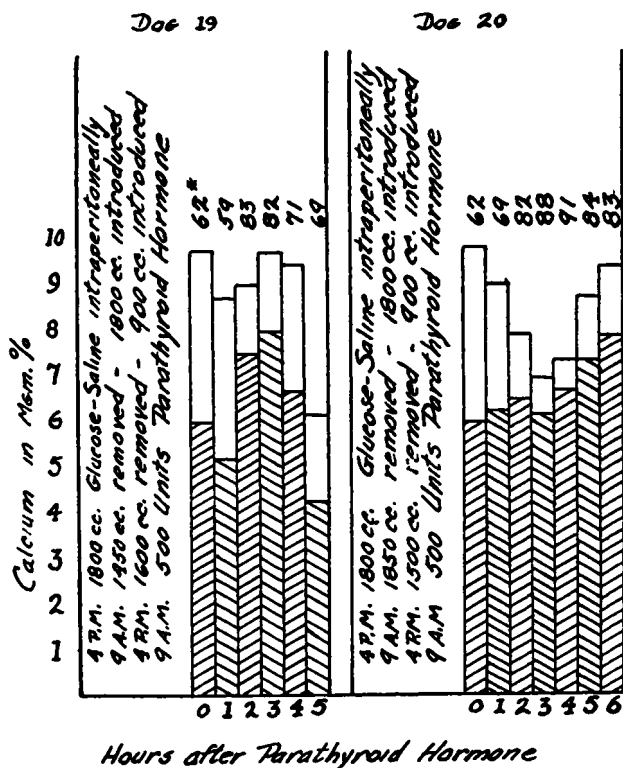


FIG. 1.

* Ratio (%) of peritoneal fluid calcium to total serum calcium concentration.

from the blood would influence the response to parathyroid hormone.*

In Dog 19 (18 kg), a total of 183 mg, and in Dog 20 (18 kg), 201 mg of calcium was removed in the peritoneal fluid in the 24 hours immediately preceding the intramuscular injection of parathyroid hormone. No food and only distilled water were allowed during the experimental period.

Three points of interest are revealed by these data.

(1) Under certain conditions, the administration of parathyroid hormone may result in hypocalcemia. That these animals were not refractory to the hormone was indicated by the fact that changes occurred in the serum and peritoneal fluid magnesium which were identical with those observed in a series of cases in which hypercalcemia was produced by the hormone.¹

(2) A fall in serum calcium may be accompanied by a fall in the peritoneal fluid calcium. This is of importance in view of the doubt as to whether the concentration of calcium in the fluid is capable of changing, and especially of decreasing rapidly simultaneously with corresponding changes in the diffusible fraction of serum calcium.

(3) An actual and significant increase in "diffused" calcium may occur following parathyroid hormone administration with a constant (Dog 19) or a falling (Dog 20) serum calcium concentration.

These findings suggest that the primary effect of the parathyroid hormone on serum calcium is to increase its diffusion from the blood into the tissue fluids. If the peritoneal fluid calcium concentration may be regarded as representing the level of the diffusible serum calcium fraction, the primary effect of the hormone on serum calcium appears to be to increase this fraction regardless of the occurrence or direction of simultaneous changes in the total serum calcium concentration.

Under normal conditions, this increase is believed to be the result of active mobilization of calcium from the bones, with consequent hypercalcemia. Under such circumstances the maintenance of the normal ratio of diffusible to total serum calcium is due perhaps to prompt "binding" of some of the mobilized calcium by serum protein or in a "colloidal calcium phosphate complex,"² masking the primary nature of the increase in the diffusible fraction. The fact that

* The parathyroid hormone was supplied by Dr. E. A. Sharp, of Parke, Davis and Company. Aided by a grant from Parke, Davis and Company.

¹ Cantarow, A., Hauray, V. G., and Whitbeck, C. G., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **89**, 15.

² Cantarow, A., Brundage, J. T., and Housel, E. L., *Endocrinology*, 1937, **21**, 368.

the peritoneal fluid-serum calcium ratio increased to 83% and 91% with a constant or a falling serum calcium concentration suggests the possibility that the parathyroid hormone may increase the diffusible calcium at the expense of the nondiffusible serum calcium fraction under certain conditions. Why the production of these phenomena should be effected by the removal from the organism of such relatively small amounts of calcium as 183 and 201 mg under the conditions of the experiment cannot be stated at the present time.

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Influence of Testosterone Propionate on Vaginal Opening in the Immature Albino Rat.*

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Butenandt and Kudzusz¹ observed that androgenic substances administered to immature female rats produced premature vaginal opening. Since then Salmon² has attempted to determine whether this effect (vaginal opening) was the result of a direct action of the androgenic substance upon the genitals or whether the effect was secondary to a stimulating action of the androgen on the ovary. Because Salmon observed follicle stimulation or luteinization (or both) in his test animals, he concluded that the premature vaginal opening which he noted was due to the effect of the testosterone propionate and androstenediol (which he used) upon the ovary. Since this author did not use spayed animals it is difficult to see how a direct effect of the androgenic substance upon the genital organs can be ruled out. For this reason, the following experiments which utilized both non-castrate and castrate animals as test objects are reported.

Fifty-two female albino rats (*Mus norvegicus*—var. *alba*) of Wistar Institute stock 26 days of age were divided into 4 groups consisting of (1) 16 non-spayed test animals; (2) 10 spayed litter-mate test animals; (3) 16 non-spayed litter-mate controls; and (4) 10 spayed litter-mate controls. Castrations were carried out at 22

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¹ Butenandt, A., and Kudzusz, H., *Hoppe-Seyler's Z. Physiol. Chem.*, 1935, **237**, 75.

² Salmon, U. J., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **35**, 49.