changes observed could not be attributed to calcium deficiency alone is evident from examination of bones of control dogs kept for months on a low calcium diet. These animals developed osteoporosis, which is histologically quite different from *ostitis fibrosa cystica.*

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Experimental Chronic Hyperparathyroidism in Dogs Without Hypercalcemia.

AARON BODANSKY AND HENRY L. JAFFE.

From the Laboratory Division, Hospital for Joint Diseases, New York City.

The rate at which the elimination of tissue and bone calcium proceeds in the dog under the influence of parathormone depends, among other factors, upon the dosage. However, the dose of parathormone that may be administered to the dog is limited by the danger of fatal hypercalcemia.

Serum calcium is obviously one term in an equilibrium. Some of the other terms affecting it, under given physico-chemical conditions of the blood, are: tissue calcium and other salts, bone salts, their availability, and the rate of calcium excretion, particularly by the kidneys. The rapid rate of excretion of calcium, as well as dietary factors, are probably largely responsible for the phenomena observed by us in the guinea pigs after parathormone. We have shown[1, 2] that this animal tolerates large doses of parathormone, although it reacts to the extract both by an elevation of serum calcium and by formation of bone lesions. In our belief, this "tolerance" is the reason for the ease with which the typical changes of *ostitis fibrosa* were produced in guinea pigs. We have succeeded, after having depleted bone and tissue calcium in dogs, in administering to them relatively large doses of parathormone without producing hypercalcemia. By thus increasing the "tolerance" of the dog to parathormone it was possible to produce *ostitis fibrosa cystica* in this animal.[3]

This report is based on a study of 11 growing dogs in which experimental chronic hyperparathyroidism was produced by daily in-

[1] Bodansky, A., Blair, J. E., and Jaffe, H. L., PROC. SOC. EXP. BIOL. AND MED., 1930, xxvii, 708.

[2] Jaffe, H. L., Bodansky, A., and Blair, J. E., *Ibid.*, 710.

[3] Jaffe, H. L., and Bodansky, A., PROC. SOC. EXP. BIOL. AND MED., 1930, xxvii, 795.

jections of parathormone. The diet of the dogs consisted of an adequate quantity of fresh raw meat with additions of cod-liver oil, bone meal, calcium lactate and tomato juice. Parathormone was injected at first in a daily dose of 2 units per kilo, which was raised gradually in some dogs to as high as 5 units toward the end of the experimental period of 5 to 6 months.

The first injections of parathormone raised the serum calcium to about 15 or 16 mg. per 100 cc. It was sometimes necessary to interrupt the treatment because of vomiting, loss of appetite and other symptoms of overdosage. As the treatment was continued, the serum calcium fell to normal values or lower, and larger doses could be given with only a temporary elevation of serum calcium. This condition was produced most rapidly in one dog on a low calcium intake. In that dog, indeed, serum calcium dropped to as low as 7.8 mg. per 100 cc., and seemed to be associated with a tissue calcium lowered sufficiently to account for the tremors and tetany observed in that dog. In other dogs the serum calcium was maintained at a "normal" calcium level when increasing doses of parathormone were administered, with only temporary increases after an increase of dose. These normal values, as well as the hypocalcemia observed in one instance, cannot be explained by "immunity" acquired as a result of previous parathormone treatment. When the calcium reserves were allowed to replenish after discontinuance of parathormone for a short period, parathormone injection had its usual effect of raising the serum calcium. An increased rate of excretion of calcium in the urine produced in the course of parathormone treatment is a possibility which we have not yet tested, but which we suggest tentatively.

We have found in the literature of parathormone therapy instances in which we suspect the presence of hyperparathyroidism, although hypercalcemia was not observed. In view of the reliance that is frequently placed upon hypercalcemia as a sole criterion of hyperparathyroidism we should be justified in designating hyperparathyroidism without hypercalcemia as *crypthyperparathyroidism.* This condition is to be recognized by a negative calcium balance and other evidences of hyperparathyroidism in the absence of hypercalcemia.