The results of average weight at 13 weekly intervals shows that while at 20°C. there is relatively little difference in the growth curves of the 2 sets of rats, at 28°C. the difference is quite marked.

At the end of the experiment these rats were infected with *Tr. evansi.* The results, summarized in Table I show that the duration of the infection parallels the growth curves. The animals showing a better growth curve are more resistant, while those showing a retarded growth curve manifested a lower resistance.

These experiments indicate that not only does the external temperature influence the resistance of animals directly[2] but that it may do so indirectly by its effect on metabolism. These experiments are also suggestive in connection with the whole problem of climate and nutrition—a problem which has heretofore not been a subject of experimentation.

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Experimental Ostitis Fibrosa Cystica in Dogs.

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In previous reports the production in the guinea pig of fibrous bone lesions by injection of parathyroid extract was described, as well as its effects on the serum calcium and phosphorus.[1,2] The production in dogs of *ostitis fibrosa cystica* is possible, but more difficult. The difficulty lies in the fact that in the dog doses of parathyroid extract (Parathormone Collip) necessary to produce marked resorption of the bone and marrow injury, are liable to lead to fatal hypercalcemia before there is much fibrous repair.

We studied eleven growing puppies for periods from 10 to approximately 180 days. They were under the influence of increasing doses of parathormone. We produced, depending upon the dosage and the length of time under parathormone, all degrees of change from mild bone resorption and slight fibrous replacement of the marrow to severe bone resorption and degeneration of the marrow with hemorrhage, when the animals died from overdosage. Finally,

[2] Kligler, I. J., and Olitzki, L., *Science,* 1929, lxx, 45; *Am. J. Hyg.,* in press.

[1] Jaffe, H. L., Bodansky, A., Blair, J. E., PROC. SOC. EXP. BIOL. AND MED., 1930, xxvii, 710.

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

we produced typical *ostitis fibrosa cystica* in 3 dogs that were injected for 5 to 6 months. In these we gradually increased the daily dose of parathormone. At the end of the experimental period they were receiving 20 units daily.

The dogs with the more pronounced lesions showed: (1) resorption of the existing spongy and cortical bone, (2) invasion of the enlarged haversian spaces and of the marrow canal by fibrous tissue, (3) the presence of Howship's lacunae, containing osteoclasts, on the walls of the haversian spaces, on the inner and outer surfaces of the compacta, and on the surfaces of the spongy trabeculae, (4) new bone formation (osteoid tissue), as a substitute for the original lamellar bone, and (5) cysts and hemorrhages in the marrow cavity. Some of the bones were deformed, particularly those of the forelegs.

One of the most marked clinical features in all the dogs was the stunting of their growth, which was referable to a cessation of bone formation and growth at the epiphyseal cartilage plates. The bone changes were generalized, and the ribs offered very satisfactory material for study. In the long tubular bones, the changes were most marked in the diaphysis and metaphysis. During the study frequent blood examinations were made, particularly in regard to the serum calcium and phosphorus, but we found that loss of appetite was a very good indication of the existence of hypercalcemia and parathormone overdosage. If these existed the parathormone was omitted for short periods, allowing the dogs to recover.

The diet consisted of lean meat, which was fed daily in ample quantity. This was supplemented with 1 cc. of cod-liver oil, tomato juice, and during various phases of the experiment calcium was given in the form of calcium lactate by stomach tube or calcium lactate and bone meal were added to the meat. This is an adequate diet.

It takes several months to produce fibrous changes in the bones of the dogs. These fibrous changes may be produced even when the calcium intake is high. In one dog, receiving 650 mg. of calcium daily in the form of calcium lactate administered by stomach tube, fibrous replacement of the bone was observed even on 8 units of parathormone daily. The production of *ostitis fibrosa cystica* was enhanced in the dogs by depleting their calcium stores through the diminution of the calcium intake, which permits giving larger doses of parathormone without danger of hypercalcemia.[3] That the

[3] Bodansky, A., and Jaffe, H. L., PROC. SOC. EXP. BIOL. AND MED., 1930, xxvii, 797.

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.

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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.