

58th injection, at which time the animals kept on the other diets showed amyloid grossly and in large amounts, as well as the secondary pressure effects of the amyloid.

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### Influence of Age on the Effect of Parathormone on Guinea Pig Bones.

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We have already indicated the striking difference in the response of young and adult guinea pigs to relatively large single doses of parathormone.<sup>1, 2</sup> *For the purposes of this study we consider a guinea pig fully adult when the major epiphyseal cartilage plates of the humerus, tibia and femur are closed.*

We produced the essential lesions of osteitis fibrosa in young guinea pigs by daily administration of 10 to 20 units of parathormone for 10 to 34 days. It is usually assumed that a more prolonged period of treatment would produce a greater effect. However, the animals' increasing age during the period of treatment had to be considered. Four guinea pigs were treated daily, beginning at the age of 2 to 7 days, with daily doses increasing to 20 units during the last 2 to 3 months. The total length of the treatment was about 110 days, at the end of which time the epiphyses were not closed. In the treated animals the bones showed no marked changes when compared with their normal litter-mate controls, and the changes were insignificant when compared with those previously reported in younger animals. While the number of animals was small, the data were consistent enough to warrant the conclusion that the serum calcium is lowered toward the end of a long course of treatment of guinea pigs with parathormone.

We believe that for a time the severity of the lesions increased in these animals. However, when the animals reached a certain age the effect of parathormone on the bone was decreased, and healing actually occurred after that time in spite of the continued administration of parathormone. This is not to be interpreted as evidence of immunity developed in the course of the treatment.

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<sup>1</sup> Bodansky, A., Blair, J. E., Jaffe, H. L., *J. Biol. Chem.*, 1930, **88**, 629.

<sup>2</sup> Jaffe, H. L., Bodansky, A., Blair, J. E., *Arch. Path.*, in press.

Three guinea pigs about 3 weeks old were injected increasing doses (60 to 140 units) of parathormone at intervals of 7 to 11 days, after a preliminary short period on smaller doses. Two guinea pigs killed at the age of about 145 days (5 days after the last dose), showed healing fractures at the costochondral junctions indicating effects of only the last previous dose. An interval of 10 days between the doses seems sufficient to allow for almost complete healing. One guinea pig died at the age of 96 days, (48 hours after the last dose). The animal being younger, the bone changes were more definite, and the effects of other previous doses probably still persisted.

We tested the limits of resistance of adult guinea pigs to parathormone, in view of our earlier findings of absence of bone changes after single doses of 20 units per 100 gm. A 900 gm. guinea pig received 900 units of parathormone, and a guinea pig weighing 1040 gm. received 2080 units. The first animal was killed 48 hours after the injection, at which time it was apparently well; the serum calcium was 15.7 mg., but serum phosphorus and blood urea nitrogen were normal. The second died 40 hours after the injection. *In contrast to our results with young animals, it was shown that enormous and fatal single doses may be given to adult guinea pigs without producing bone lesions.*

We administered to an 860 gm. guinea pig 2580 units of parathormone in 3 equal doses pyramided within 48 hours. Urgent symptoms were absent 24 hours after the last injection, with a serum calcium of 19.6, and a serum phosphorus of 4.7 mg. per 100 cc. But 24 hours later urgent symptoms developed, associated with a serum calcium of 18.9, a serum phosphorus of 8.4 and a urea nitrogen of 40 mg. per 100 cc. The epiphyseal cartilage plates in this animal were not fully closed, as the cartilage cells were still arranged in columns. It is therefore all the more significant that only very slight bone resorption occurred in this animal. The evidence of bone resorption consisted chiefly in the appearance of numerous Howship's lacunae containing osteoclasts, especially beneath the endosteum.

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