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Influence of Cattle Ant. Pituitary Extract on the Joints of Thyroidectomized Guinea Pigs.

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In the joints of young guinea pigs changes corresponding to those seen in acromegalic arthropathy may occur under the influence of anterior pituitary extract of cattle. The lesions consist in a hypertrophy and hyperplasia of the cartilage cells, proceeding from the transitional zone towards the sliding or pressure zone and finally producing ulceration of the surface of the joint.¹ The newly formed cartilage may or may not undergo calcification. Inasmuch as thyroidectomy does not counteract the action of anterior pituitary on the epiphyseal line² and on bone repair,³ we wished to investigate what effects thyroidectomy would exert on the changes produced by anterior pituitary extract on the joints.

The investigations were made on 16 young guinea pigs which had already been used for study of the behavior of the epiphyseal line² and bone repair.³ Method and technique have been described previously. As a rule, the changes produced on knee and hip joints were studied by us.

As early as after 7 injections of the extract a proliferation of the cartilage cells is seen within the transitional zone of the thyroidectomized animals. The cells become hyperplastic, assuming a longitudinal arrangement in contradistinction to the flat horizontal position which they show normally. The cytoplasm of these cells hypertrophies, the nuclei of the cells are distinctly turgescient and mitotic figures are seen here and there. After 10 to 21 injections the cells have become still more numerous and the stroma between the cells is diminished. Their nuclei take on a more deeply bluish stain with hematoxylin as an indication of the relative immaturity of the growing cells. The distinct columnar arrangement of the cartilage cells is thus associated with these changes in the cells. The cell proliferation gradually extends towards the sliding zone of the cartilage and the surface of the joint. In addition, liquefaction of the cartilage takes place. Small ridges are formed, and in advanced

¹ Silberberg, M., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 333.

² Silberberg, M., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **33**, 554.

³ Silberberg, M., and Silberberg, R., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 108.

cases we may even find gaps within the rapidly growing zone of cartilage. As soon as true ulceration has occurred, vascularization and ingrowth of bone-marrow into the cartilage cell layers is seen together with further destruction of the surface of the joint. These latter processes are especially frequent in the neighborhood of the insertion of the ligaments, where the cartilaginous covering of the joint is comparatively thin. However, these changes are also to be found more or less pronounced elsewhere on the surface of the joint. In addition, in some instances disturbances of calcification and of endochondral ossification are seen as revealed by a rapid calcification of the growing cartilage. Inflammatory changes are missing.

As to the arthropathic changes the following statement may be made: The greater the tendency to calcification of the newly-formed cartilage is, the more distinct is the ossification and the less is the ulceration which is to be expected. On the other hand, if the growth tendency of the cartilage predominates over calcification, the formation of ulcers will be more pronounced. Why in one case one effect is seen and the other effect in another case, is uncertain. However, the reaction does not depend upon the sex of the animals nor on the number of injections given. We see then that the changes observed in the cartilage of the joint under the influence of anterior pituitary extract in thyroidectomized guinea pigs take a course parallel to that seen in the epiphyseal line and in the chondrophyte under the corresponding conditions. Obviously, the cartilage of the epiphyseal line, of the chondrophyte and of the surface of the joint show the same growth reactions.

Conclusions. In thyroidectomized young guinea pigs anterior pituitary extract of cattle exerts its growth-promoting effect on the cartilage of the joint as well as in non-thyroidectomized animals, and the same arthropathic changes characteristic of acromegaly develop in both. Lack of the thyroid gland does not only not prevent the growth-promoting effect of anterior pituitary extracts, but in thyroidectomized guinea pigs the phenomena are even more pronounced than in normal animals which were treated with the extract. These experiments provide, therefore, further evidence for the conclusion that the extract exerts its influence on bone, epiphyseal line and joint cartilage without the intermediation of the thyroid gland.