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Effect of Cattle Anterior Pituitary Extract on Bone and Cartilage of the Joint (Acromegalic arthropathia).

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In previous investigations[1, 2] we have established a stimulating influence of acid extract of cattle anterior pituitary gland on the growth of cartilage and bone of young guinea pigs. In the epiphyseal line, hypertrophy and hyperplasia of the various cell layers of cartilage took place. In the majority of cases, as a result of subsequent rapid calcification a premature closure of the epiphyseal line occurred, but in about 20% only proliferation of the cartilage cells was noticeable. This effect was likewise exerted on the cartilage of the chondrophyte. There was, therefore, good reason for assuming that, under the influence of the extract, growth of bone and cartilage of the joint might likewise be stimulated. Correspondingly, we wished to analyze the changes which take place within the joints.

The observations were made in the 30 guinea pigs which had also been used for the study of endochondral ossification under the influence of the extract. As to the technique, we refer to our previous paper.[1] In the present investigations, we studied the effects of the extract on the knee joint and on the upper part of the femur.

After 6 to 7, but still more pronouncedly after 10 injections, proliferation of the cartilage is seen, the first changes being observed within the transition cell zone: here the cells become hypertrophic and hyperplastic; more and more they become arranged in a longitudinal direction in contradistinction to their flat horizontal position under normal circumstances. After 14 injections these cells have become still more numerous, and at the same time they assume a distinct columnar arrangement, and are stained dark bluish with hematoxylin, as an indication that they are still relatively immature; the stroma between them is diminished in amount. The proliferation within the transitional zone extends gradually in the direction towards the sliding zone of cartilage on the surface of the joint. This proliferative process is followed by liquefac-

1 Silberberg, M., PROC. SOC. EXP. BIOL. AND MED., 1935, **33**, 1033.

2 Silberberg, M., *ibid.*, 1936, **34**, 177.

tion and degeneration of the growing cartilage. Subsequently small vacuolar ridges are formed, and in later stages we may even find gaps within the rapidly growing zone of the cartilage. Finally, the surface of the joint is reached and here microscopic ulceration occurs. The pressure zone of the cartilage participates in these processes as well: Vascularization and ingrowth of bone-marrow into the cartilage cell layers penetrating up to the surface are noted. In addition, within the cartilage cell layers disturbances of calcification and of endochondral ossification are found.

After 21 injections, ulceration is seen especially in the neighborhood of the insertion of the ligaments. Here the covering of the surface of the cartilage by cells is comparatively thin; it is therefore to be expected that here also the most marked changes should take place, but to a less marked extent they are noted everywhere in the joint.

We may then conclude that the behavior of the cartilage of the joint corresponds to that observed within the chondrophyte and at the epiphyseal line. The growth phenomena in these 3 places (1) epiphyseal line, (2) chondrophyte, and (3) joint have to be considered as an entity. One may state the rule that the greater the proliferation of the cartilage, the more pronounced will be the ulceration of the surface of the joint and the less the calcification, the greater the tendency to ossification, the more extensive will be the calcification of the cartilage cells, and the less the ulceration.

Our experimental findings correspond in every respect to the "acromegalic arthritis" as described by Erdheim[3] at the "Knorpelknochengrenze." Inasmuch as in our experimentally produced conditions, any marked inflammatory reaction was missing, our findings would better be designated as "acromegalic arthropathia."

Conclusions. In young guinea pigs, under the influence of acid extract of cattle anterior pituitary, the growth-promoting effect manifests itself as acromegalic arthropathia in 2 directions: (1) Hypertrophy and hyperplasia starting in the transitional zone of cartilage then proceeding towards its sliding and pressure zone, and in a later stage leading to its liquefaction and to ulceration of the surface. (2) This stimulation of the growth of cartilage may be followed by calcification. In the latter case the ulcerative processes are less pronounced than in the former. Whether the one or the other of these 2 effects occurs does not depend upon the number of injections given to the animals.

[3] Erdheim, J., *Veroeffentlich, a. d. Gebiete d. Pathol. in Einzeldarstellungen,* 1931, Julius Springer, Berlin.