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Effect of Feeding Thyroid on Anterior Hypophysis of the Female Albino Rat.*

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It has been reported that feeding thyroid to rats increases the gonad-stimulating complex of the anterior hypophysis.[1, 2] In an attempt to obtain a morphologic basis for this increased physiologic effect, we have studied serial sections of the anterior pituitaries of 28 female rats which were fed varying amounts (250 to 1,000 mg.) of thyroid daily for periods of 30 to 71 days. Twelve of these rats were placed on experiment when immature; the others were fully mature when thyroid feeding was initiated. Confirming studies of other investigators,[2, 3, 4] it was found that feeding thyroid in sufficient amounts suppressed the oestral cycle resulting in prolonged periods of dioestrus. However, it was also found that by varying the dosage of thyroid the oestral cycle could be regulated almost at will. In rats receiving the smaller amounts, the oestral cycles were usually regular, occasionally interspersed with cycles the length of pseudo-pregnant cycles. Weichert and Boyd[5] consider that such cycles represent a true lutein phase. Larger dosage resulted in prolonged periods of dioestrus, ranging up to 40 days. In some animals, oestrus was suppressed for periods of time ranging up to 72 days, which covered the entire period of observation. The heavier thyroid dosages fed in these experiments were sufficient to decrease the growth rate slightly, but never to a marked degree. Animals receiving smaller dosages exhibited a normal rate of growth.

At autopsy it was found that the weight of the ovaries and the pituitaries of those animals which had exhibited oestral cycles of normal or pseudo-pregnant length were normal in appearance and weight. In those rats in which the oestral cycle had been suppressed to a more marked degree, the ovaries were decreased in weight and

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1 Evans, H. M., and Simpson, M. E., *Anat. Rec.*, 1930, **45**, 215 (Supplement).

2 Van Horn, H. N., *Endocrinol.*, 1933, **17**, 152.

3 Reiss, M., and Pereny, S., *Endokrinologie*, 1928, **2**, 181.

4 Weichert, C. K., *Physiol. Zool.*, 1930, **3**, 461.

5 Weichert, C. K., and Boyd, R. W., *Anat. Rec.*, 1933, **58**, 55.

the accessory reproductive organs approached a castrate condition. In these rats the weight of the pituitary was also decreased. Considering the group as a whole, the mean pituitary weight was 7.8, while that in 69 control females was 10.9 mg.

The pituitaries were prepared for study by means already described.[6] The ovaries and accessory organs were fixed in Bouin's fluid and the sections stained with hematoxylin and eosin. Serial sections of the pituitary and the ovaries were cut. Cell counts were made on representative sections of the anterior pituitary; a total of 89,535 cells was counted.

Histologically the ovaries and the accessory organs of those animals in which the oestral cycles were moderately to markedly suppressed exhibited definite changes. The ovaries exhibited a normal number of follicles, mostly small and moderate in size, but a few were as large as those found in the ovaries of late prooestral rats. However, much follicular atresia was evident which involved most of the follicles. The large amount of interstitial tissue and the small number of corpora lutea were the outstanding characteristics. Some rats exhibited only one or 2 periods of oestrus, or none at all during the 71 days of observation. In the ovaries of these animals corpora lutea were almost entirely absent, only follicles and interstitial tissue being present. The uteri and vaginae of these rats approached a castrate condition.

Histologically the anterior pituitaries presented certain changes which varied from normal to a degree proportional to that in which the oestral cycle and the reproductive tract varied from normal. The basophiles were increased very slightly in percentage, the mean level in the experimental rats was 5.3%, while the mean level in 69 virgin control rats was 4.8%.

The basophiles were consistently different in appearance from those found in normal females. They were larger and well filled with granules, which took a purple-red stain, varying to a brick red. The granules of basophiles in the anterior pituitaries of normal females take a deep blue stain and often are so closely packed that they give the impression of a dense blue cytoplasm. It is important to emphasize that the basophiles in the anterior pituitaries of the thyroid-fed rats were packed full of granules, while in normal rats these cells exhibit varying degrees of granular depletion. The changes in the basophiles described above were remarkably constant and were most marked in rats in which the oestral cycle had been most markedly suppressed.

[6] Cleveland, R., and Wolfe, J. M., *Anat. Rec.*, 1932, **51**, 409.

In 8 rats which exhibited normal oestral cycles of 5 or 6 days in length, or cycles of pseudopregnant length, the level of the eosinophiles ranged from 30 to 40%, which is the normal level (the mean level of these cells in 69 controls was 33.6%, with a standard deviation of 4.5). The remaining 20 experimental rats exhibited varying degrees of suppression of the oestral cycle. In the anterior pituitaries of these rats the level of the eosinophiles ranged from 24.1 to 28%; such a low level is found only occasionally in normal females.

It is known from the work of the investigators mentioned above that the capacity of the anterior hypophysis to increase the size of the ovaries of immature test animals is increased by thyroid feeding. Our morphologic studies would indicate that there were definite structural changes in the anterior pituitaries of such rats; most notable was some increase in size and definite increase in granular content and change in appearance of the basophilic elements. Changes in the eosinophiles were less constant and where such changes did occur, they were in the nature of a decrease in the percentage of these cells. Our data would indicate, therefore, that the increased capacity of the anterior pituitaries of thyroid-fed rats to increase the weight of the ovaries of immature test rats was probably due to the changes in the basophiles noted above.

One interesting point should be noted; the basophiles in these animals are very similar to those found in the anterior pituitaries of rats killed during the last half of pregnancy. As pointed out previously,[7] during the first 6 days of pregnancy the basophiles are markedly reduced in percentage and granular content, but from the 7th day to delivery they increase gradually in percentage and size and become filled with purple-red granules which vary to brick-red in color. The reason for the similarity of the appearance of the basophiles in these 2 groups of rats is unknown.

The mechanism by which thyroid feeding disturbs the oestral cycle has been discussed fully by Van Horn and Weichert and Boyd. The view that the increased metabolic rate in some way keeps the level of oestrin below the threshold for oestrus is upheld by a certain amount of evidence presented by these workers and by Reiss and Pereny.

Summary. Twenty-eight female rats were fed amounts of desiccated thyroid ranging from 250 to 1,000 mg. daily. The oestral cycle was suppressed to varying degrees, dependent on the dosage of thyroid. The pituitaries were subnormal in weight. Histologically the anterior lobes exhibited certain changes: most notable was

[7] Wolfe, J. M., and Cleveland, R., *Anat. Rec.*, 1933, **56**, 33.

a slight increase in the percentage of the basophiles and a definite increase in the size and granular content of these cells. The granules stained a purple-red which varied to a dull brick-red; in normal female rats (virgin and killed during the normal oestral cycle) the basophiles take a deep blue stain. The changes in the basophiles were most marked in those animals in which the suppression of the oestral cycle was most evident.

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Variations in Contour of the Records Found in Serial Electrocardiograms of the Dog.

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In the course of some studies we had occasion to take serial electrocardiograms on 3 normal dogs twice a week over a period of 4 months. The dogs were trained to lie on their right sides while the electrocardiograms were taken. The limbs were shaved and flannel bandages soaked in concentrated saline bound around them. Copper wire spiral was then applied tightly over the bandage and connected with the electrodes. The skin resistance was found to be low with this procedure (below 1000 ohms) and no polarization was encountered.

The serial records obtained in each dog over the period of 16 weeks revealed irregular fluctuations in the form of the electrocardiograms. These variations were not progressive, could not be related to environmental factors, and varied within the wide limits illustrated in Fig. 1. These results were obtained in spite of the fact that every effort was made to take the successive electrocardiograms under identical conditions as regards the position and posture of the animal. These normal variations in the electrocardiogram of the dog are probably due to variations in the position of the heart at different times. The relative mobility of the dog's heart as compared to the human is such that it is almost impossible to manoeuver it into exactly the same position time after time. These effects of position involve changes in the amplitude and even direction of all the complexes of the electrocardiogram, especially the T wave. Sim-

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