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Changes in the Anterior Pituitary Gland of Rats With Experimental Goiter. II.

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In a previous communication[1] cellular changes in the anterior lobe of the pituitary gland of rats reared on a goitrogenic diet[2] were described. In male rats fed for 3 to 12 months on the Steenbock and Black diet[3] supplemented by viosterol, nests of large cells were seen in the anterior lobe of pituitary glands fixed in Bouin solution and stained with hematoxylin-eosin. We report now the results of histologic examinations of pituitaries which had been fixed in Regaud

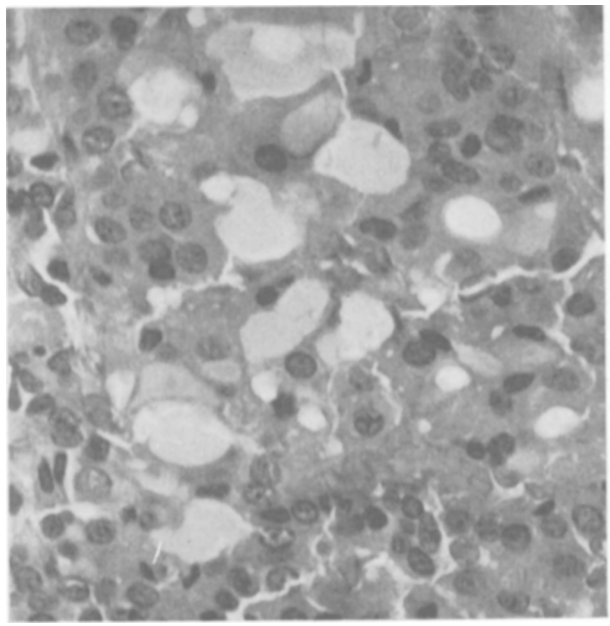

FIG. 1.
Section of anterior hypophysis of rat 130 Y (10.5 months on goitrogenic diet), showing a nest of large cells containing vacuoles. (Regaud fixation; Hematoxylin-Eosin stain; × 800.)

1 Nelson, R. C., and Warkany, J., PROC. SOC. EXP. BIOL. AND MED., 1938, **39**, 66.

2 Krauss, W. E., and Monroe, C. F., *J. Biol. Chem.*, 1930, **89**, 581; Thompson, J., *J. Nutrition*, 1932, **5**, 359.

3 Steenbock, H., and Black, A., *J. Biol. Chem.*, 1925, **64**, 263.

solution and were stained with methods which permit the identification of granules as well as that of other elements contained in the cytoplasm of the abnormal cells. During life the rats had been treated for 4 to 12 months in the same way and fed the same diet as the animals described before.

On sections of pituitaries fixed with Regaud solution and stained with hematoxylin and eosin, groups of large cells can be recognized with the low power objective of the microscope; the picture resembles that of pituitaries fixed with Bouin solution. With the high power magnification the large cells appear to contain vacuoles of different sizes. In animals on the diet 4 to 6 months numerous small vacuoles can be seen which give the cytoplasm a spongy appearance. In older animals the large cells often contain but a single large vacuole which is filled with a pale hyaline or colloid material (Fig. 1). Mitotic figures are occasionally seen in these cells (Fig. 2) suggesting a process of cellular hyperplasia.

In order to identify the cell granules similar sections were stained by the Cleveland and Wolfe method.[4] The sections of the pituitary of a male rat (137 B) reared on the diet for 9 months, whose weight was 284 g and whose hypertrophic and hyperplastic thyroid weighed

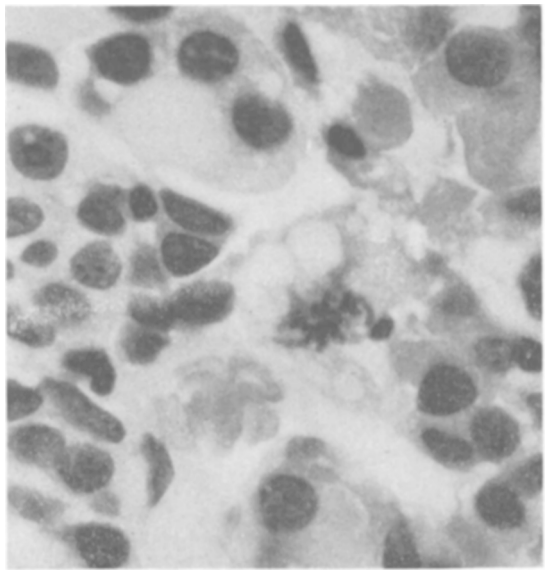

FIG. 2.

Section of anterior hypophysis of rat 129 Y (10.5 months on goitrogenic diet), showing large vacuolated cells, one of which is undergoing mitosis. (Regaud fixation; Hematoxylin-Eosin stain; about × 1800.)

4 Cleveland, R., and Wolfe, J. M., *Anat. Rec.*, 1932, **51**, 409.

154 mg when sacrificed, revealed the following findings which are typical: The large cells could be recognized as basophilic cells, some densely packed with blue granules and others containing, in addition, vacuoles of different sizes (Fig. 3). The vacuoles were filled with hyaline material in varying amounts. The larger hyaline areas usually stained light blue; small vacuoles often took a dark blue stain. However, there were numerous large cells in the same part of the section containing hyaline which had taken a red stain. Orange staining hyaline material could be seen in intercellular spaces as well as in the residual cleft. The sections also contained areas of normal appearance made up of cells of normal size and normal granular structure. It should be emphasized that numerous eosinophilic cells can be seen in such areas.

The weight of the testes of the animal whose pituitary is reproduced in Fig. 1 was approximately normal and the epithelium of the prostate was tall, columnar in type and the secretory vacuoles could be plainly seen. This animal successfully fathered 2 litters of living young; the second breeding taking place shortly before the animal was sacrificed.

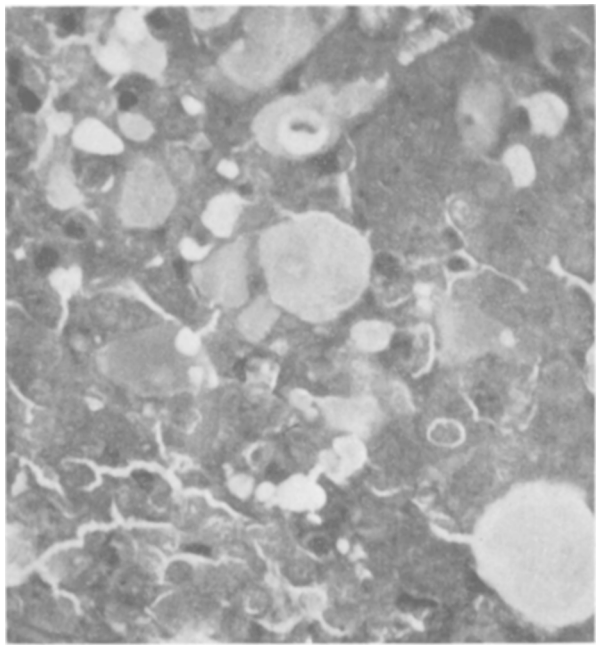

FIG. 3.
Section of anterior hypophysis of rat 137 B (9 months on goitrogenic diet), showing large vacuolated cells and areas of hyaline material. (Regaud fixation; Cleveland and Wolfe stain; × 800.)

As a rule, however, the reproductive organs of animals reared on this diet are slightly retarded in development[1] and breeding occurs infrequently. One could suspect, therefore, that the pituitary changes described by us are secondary to the impaired sex function frequently observed in these animals. Furthermore, the growth of these animals is retarded and one might consider a possible relationship between the impairment of growth and the changed pituitary morphology.[5]

In order to rule out the reproductive irregularities and the retardation of growth as factors in our experiments, we have made use of an improved goitrogenic diet devised by Remington.[6] This diet results in normal, or nearly normal, growth, maturity and reproduction of the experimental animals. The thyroids of these rats, however, resemble in every respect those found in animals fed the supplemented Steenbock and Black diet, which was used in our previous experiments.

Remington's improved goitrogenic diet consists of wheat gluten 18, yellow corn meal 78, calcium carbonate 1, sodium chloride 1, dried pig liver 2. (We added 60 U.S.P. units of vitamin D as viosterol every 10 days.)

The results of Remington were corroborated and we were thus enabled to examine the pituitary glands of goitrous male rats which were satisfactory with regard to growth and reproductive function.

The histological picture of these anterior pituitaries is, as far as we can determine, identical with that seen in animals on the Steenbock and Black diet supplemented with viosterol. Marked pituitary changes were found in 10 male rats fed Remington's improved goitrogenic diet for 27-54 weeks. In pituitaries of 5 animals fed the diet for not more than 14-18 weeks the changes were present in a moderate degree only. This was also true for one rat which was on the diet for 35 weeks. The morphology and the microscopic picture of the testes and prostatic glands of these animals appear to be normal.

In summary it can be stated that in male rats reared on goitrogenic diets, nests of large vacuolated cells filled with a hyaline material are seen in the anterior pituitaries. Mitotic figures are not infrequently found in such cells. These changes seem to be causally related to the changes of the thyroid gland[7] and not to impairment of growth and reproduction.

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5 Erdheim, J., *Frankfurt. Z. f. Path.*, 1936, **49**, 452; Zeckwer, I. T., *Arch. Path.*, 1938, **25**, 802.

6 Remington, R. E., *J. Nutrition*, 1937, **13**, 223.

7 For review of pituitary following thyroidectomy see: Altschule, M. D., and Cooper, P., *Arch. Path.*, 1937, **24**, 443; Zeckwer, I. T., Davison, L. W., Keller, T. B., and Livingood, C. S., *Am. J. Med. Sc.*, 1935, **190**, 145; Severinghaus, A. E., *Sex and Internal Secretions*, p. 1045, Williams & Wilkins, 1939.