CONNECTION BETWEEN CHANGES IN THE PARAFOLLICULAR SYSTEM OF THE THYROID AND IN BONE TISSUE IN EXPERIMENTAL THYROTOXICOSIS

A. I. Briskin, V. A. Odinokova,
V. F. Kondalenko, V. N. Ershov,
and M. N. Bayandurova

UDC 616.441-008.61-092.9-07:[616.441+616.71]-091-07

The connection between changes in the parafollicular system of the thyroid gland and in the bone marrow was studied in rats with experimental thyrotoxicosis induced by administration of thyroid and triiodothyronine. In experimental thyrotoxicosis bone metabolism is increased, and a pale-cell hyperplasia, leading to increased production of thyrocalcitonin, which fixes calcium in the bone tissue, develops in the tissues of the thyroid gland.

A connection between the state of thyroid function and changes in the structure and metabolism of bone tissue has now been demonstrated [2, 5, 6, 8]. It was in 1891 that Von Recklinghausen [12] first drew attention to skeletal decalcification in hyperthyroidism. Convincing evidence [3, 9, 11] of changes in the calcium and phosphorus metabolism in lesions of the thyroid gland and, in particular, in thyrotoxic goiter has subsequently been published.

The reasons for the relative stability of the calcium level in thyrotoxicosis became clear after the discovery of a new thyroid hormone, thyrocalcitonin, produced by the pale parafollicular cells and inhibiting resorption of bone tissue [7].

The object of the investigation described below was to study, by histological, histochemical, and electron-microscopic methods, changes in the pale parafollicular thyroid cells and in the bone tissue during prolonged administration of thyroid or triiodothyronine to animals.

EXPERIMENTAL METHOD

In the first experiment, thyroid was given by mouth to ten male rats weighing 180-190 g by adding it to the diet at the rate of 300 mg per animal daily; ten other rats were kept under the same conditions but did not receive thyroid (control). In the second experiment, thyrotoxicosis was induced in ten male rats of the same weight by administration of triiodothyronine (the French preparation "Trithyron," containing 25 μg hormone per tablet) by gastric tube in a dose of 5 μg per animal daily for the first 14 days, and thereafter in a dose of 10 μg daily. In both experiments the preparations were given for 28 days. The animals were weighed every week. At the end of the experiment, under ether anesthesia, blood was taken from the chambers of the heart and centrifuged for 30 min to obtain the serum, in which the calcium concentration was determined in mg/100 ml serum by a colorimetric chelation method using fluorexon as indicator.

Laboratory of Pharmacology, Department of Research into the Technology of Endocrine Preparations of VNIIA, and Department of Pathological Anatomy, M. F. Vladimirskii Moscow Regional Clinical Research Institute. Institute of Human Morphology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 71, No. 2, pp. 111-113, February, 1971. Original article submitted July 8, 1970.

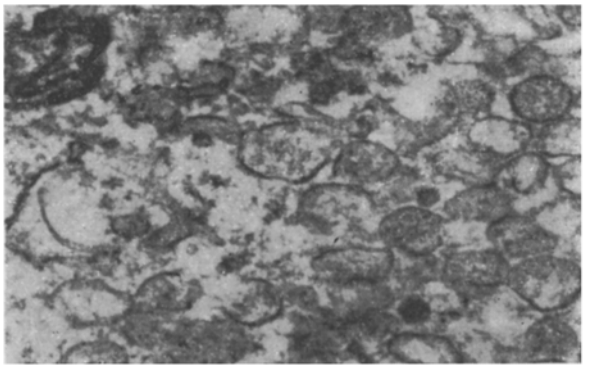

Fig. 1.

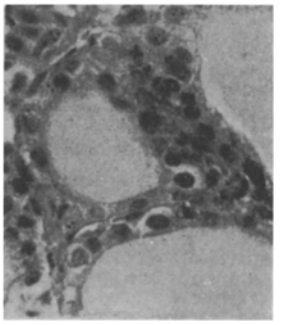

Fig. 2

Fig. 1. Area of cytoplasm of thyroid parafollicular cell. Thyrocalcitonin granules, 65,000 ×.

Fig. 2. Changes in thyroid gland of rat. Pale parafollicular cell in interfollicular islet. Hematoxylin-eosin, 250 ×.

The thyroid glands and long bone taken from the animals sacrificed at the end of the experiment were studied under the light and electron microscopes. The following methods of histological investigation were used: the reactions of Brachet and Feulgen, Shabadash's PAS reaction, toluidine blue, picrofuchsin-fuchselin, and Best's reaction. For the electron-microscopic investigation, small pieces of thyroid gland were fixed by Palade's method with osmium tetroxide and embedded in Araldite. Ultrathin sections were shadow-cast with uranyl acetate and lead citrate.

EXPERIMENTAL RESULTS

During the first 1-2 weeks of administration of thyroid or triiodothyronine, the increase in body weight of the experimental animals was considerably retarded compared with the controls. Later, however, the difference in weight gradually disappeared and by the end of the experiment the experimental and control animals were equal in weight. No statistically significant increase in the serum calcium level was observed in animals receiving thyroid hormones. In animals of all groups it varied from 8 to 10 mg%.

Histological investigation of the thyroid showed that in animals receiving thyroid or triiodothyronine the follicular epithelium was flattened, the lumen of the follicles was dilated, and some of them were loaded with colloid.

Electron-microscopic investigation revealed numerous free-lying ribosomes and polysomes in the cytoplasm of the narrow follicular cells. Elements of the granular endoplasmic reticulum were few in number and they appeared as narrow canals. Few mitochondria could be seen in the cytoplasm of these cells. Follicular epithelial cells which had lost their limiting membranes were apparent. The nuclei of these cells were irregular in outline and contained conglomerations of chromatin. Vacuolated granular endoplasmic reticula and swollen mitochondria were present in the cytoplasm.

The parafollicular pale cells contained numerous circular granules, surrounded by a membrane, in their cytoplasm (Fig. 1). The diameter of the granules was 1500-2500 Å. The material in the granules was weakly osmiophilic and delicate in structure. In some granules the matrix was strongly osmiophilic and electron-dense. Unlike the parafollicular cells observed in experimental thyroiditis [1], the cytoplasm of the pale cells in animals receiving an excess of thyroid hormones contained many more granules with an osmiophilic matrix.

At the same time, small foci of proliferation of thyroid gland tissue appeared. The follicular cells of these foci were enlarged, and they exhibited amitotic and mitotic division and the formation of interfollicular islets. These islets differentiated into microfollicles and foci of pale parafollicular cells were formed. These were large in size (8-12 μ in diameter), and occurred in groups of 1-3 cells, not in contact with colloid (Fig. 2). They contained little RNA, DNA, PAS-positive material, or acid mucopolysaccharides. The pale cells were rich in enzymes: dehydrogenase and α-glycerophosphatase [10]. Thyrocalcitonin was present in the microsomal fraction of these cells [4].

Changes developing in the bone tissue as a result of prolonged administration of thyroid or triiodothyronine to the animals were focal in character. They consisted of marked congestion of the blood vessels of the intertrabecular stroma, a mosaic pattern of the trabecular structures, a decrease in the number of osteocytes in the trabeculae, and fragmentation and indentation of the edges of individual trabeculae. The trabeculae were weakly impregnated with lime.

The discovery that changes in the follicular system of the thyroid gland in animals receiving relatively large doses of thyroid hormones for long periods were accompanied by the appearance of large numbers of pale parafollicular cells and by corresponding changes in the skeletal system suggests that these two processes are linked. In experimental thyrotoxicosis it can be assumed that bone metabolism is increased, and that pale-cell hyperplasia develops in the tissues of the thyroid gland, leading to an increase in the production of thyrocalcitonin, which fixes calcium in the bone tissue.

LITERATURE CITED

1. V. F. Koldalenko, Vestn. Akad. Med. Nauk SSSR, No. 1, 61 (1968).
2. P. Adams et al., Quart. J. Med., 36, 1 (1967).
3. J. Aub et al., J. Clin. Invest., 7, 97 (1929).
4. C. Cooper and A. Tashjian, Endorinology, 79, 819 (1966).
5. M. Croizet et al., Bordeaux Med., 1, 2027 (1968).
6. R. Gittes and G. Irvin, Science, 148, 1737 (1965).
7. P. Hirsch et al., Sciences, 146, 412 (1964).
8. P. Hirsch and P. Munson, Endocrinology, 79, 655 (1966).
9. M. Logan et al., Am. J. Physiol., 135, 419 (1942).
10. A. Pearse, Proc. Roy. Soc. B, 164, 478 (1966).
11. J. Puppel et al., Surg. Gynec. Obstet., 81, 243 (1945).
12. F. von Recklinghausen, in: Rudolf Virchow Festschrift, Berlin (1891), p. 1.