

possess incomparably greater affinity under physiological conditions for steroid hormones that are trophic for the particular organ; under these circumstances the "unconcern" of the cells for other steroids is determined by superposition of "insensitivity" of the saturable component to them and "blocking" of the unsaturable component of PM, for reasons pointed out above.

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#### EFFECT OF SYMPATHETIC IMPULSES ON PARAFOLLICULAR CELLS (C CELLS) OF THE THYROID GLAND

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UDC 612.441.014.2-06:612.89

KEY WORDS: thyroid gland; sympathetic innervation; C cells; serotonin.

The specific activator of the thyroid gland is the thyrotrophic hormone of the pituitary, but it is also dependent on direct nervous impulses travelling along efferent nerve fibers. Sympathetic impulses have an excitatory action on the thyroid gland; they stimulate the uptake of iodine by the gland, intrathyroid hormone production, and secretion of thyroid hormone [1-4]. Besides the follicular and interfollicular epithelium, the thyroid parenchyma also contains parafollicular or C cells, of neural origin, which produce the iodine-free protein hormone calcitonin. The fact that the C cells belong to the neuroendocrine (the "AFUD") system is confirmed by the presence of monoamines (especially serotonin) in them, and also by the ability of C cells to assimilate and decarboxylate monoamine precursors [7, 9-11]. The C cells are not dependent on the pituitary, removal of which is not reflected in their state. Accordingly the question arises whether sympathetic impulses take part in the regulation of functional activity of these cells, and the investigation described below was carried out to study this problem.

#### EXPERIMENTAL METHOD

Experiments were carried out on male rabbits weighing 1.5-1.8 kg, divided into three groups with seven or eight animals in each group. Group 1 (control) consisted of intact rabbits. In the experimental rabbits of group 2 the superior cervical sympathetic ganglia (the main source of the sympathetic innervation of the thyroid gland) was subjected to prolonged stimulation by application of a thin silver wire loop to the ganglion. Animals of group 3 underwent bilateral extirpation of these ganglia (cervical sympathectomy). The experiment lasted 10 days. At the end of that time the animals were autopsied and the thyroid glands removed and stained by Sawicki's method [12]. In parallel tests the serotonin concentration in thyroid gland homogenates was determined by Kulinskii and Kostyukovskaya's method [5]. Since an increase in the secretory activity of the glandular cells is accompanied by swelling of their cytoplasm and nucleus, on examination of thyroid gland sections stained by the above method outlines of the C cells were projected by means of a drawing apparatus on paper, so that their area of cross section could be measured with a planimeter and expressed in square microns.

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Khar'kov Research Institute of Endocrinology and Hormone Chemistry. (Presented by Academician of the Academy of Medical Sciences of the USSR L. T. Malaya.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 91, No. 6, pp. 725-727, June, 1981. Original article submitted November 27, 1980.

TABLE 1. Mean Area of Cross Section of C Cells and Serotonin Content in Rabbit Thyroid Gland ( $M \pm m$ )

Group of animals	Exptl. conditions	Area of cross section, $\mu^2$	Serotonin conc., $\mu\text{g/g}$
1	Control	$221,2 \pm 2,57$	$0,516 \pm 0,058$
2	Stimulation of superior cervical sympathetic ganglia	$266,7 \pm 2,29$ $P < 0,001$	$0,702 \pm 0,049$ $P < 0,02$
3	Extrapolation of superior cervical sympathetic ganglia	$202,3 \pm 1,71$ $P < 0,001$	$0,320 \pm 0,037$ $P < 0,01$

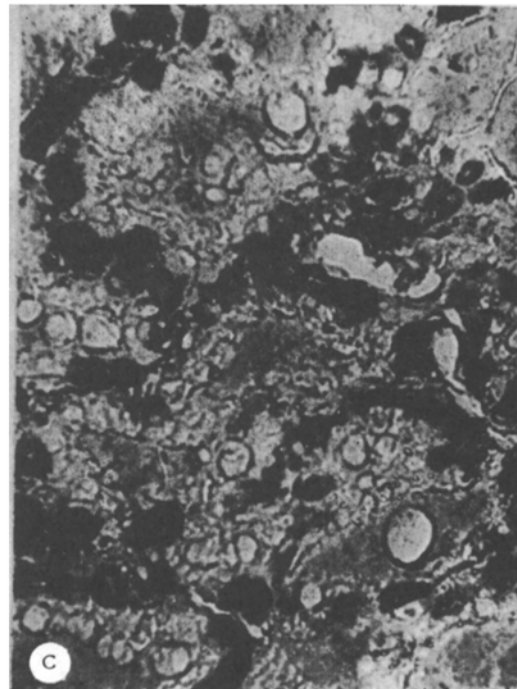
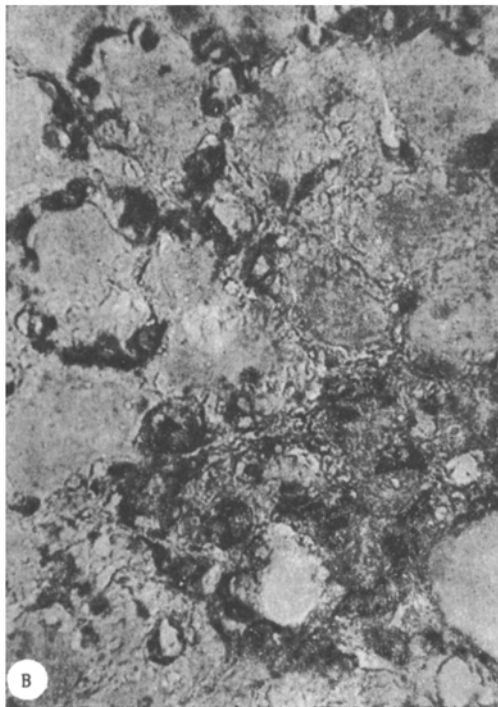
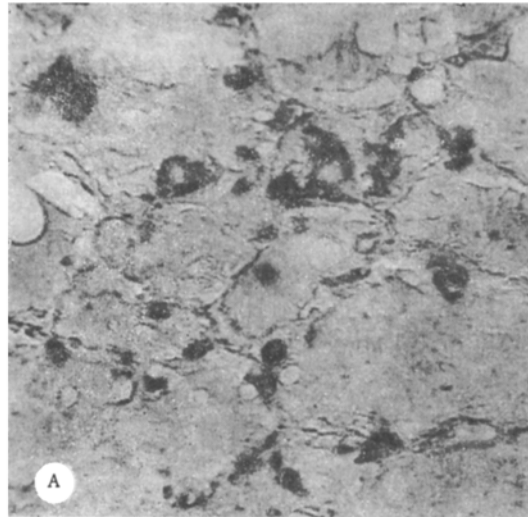


Fig. 1. C cells in thyroid gland. A) Control (intact rabbit), B) on 10th day after bilateral stimulation of superior cervical sympathetic ganglia, C) on 10th day after bilateral extirpation of superior cervical sympathetic ganglia. Stained by Sawicki's method,  $320\times$ .

## EXPERIMENTAL RESULTS

The C cells were concentrated mainly in the central zones of the thyroid parenchyma. In intact rabbits the C cells varied in size but most of them were comparatively small (Table 1), although occasionally larger ones were seen (Fig. 1A). Their cytoplasm was densely packed with secretory granules.

Upon stimulation of the superior cervical sympathetic ganglia the quantity and dimensions of the C cells increased (Fig. 1B). The nuclei of the C cells markedly swelled and the secretory granules in the cytoplasm were arranged more loosely than among the intact rabbits which indicates increased secretory activity by these cells. Indeed, the content of the serotonin secreted by the C cells in the thyroid was higher in comparison with its original value (Table 1).

After bilateral cervical sympathectomy the functional state of the C cells differed (Fig. 1C). The dense distribution of granules in the cytoplasm and the distinct decrease in size of these cells compared with the control (Table 1) point to weakening of their secretory activity, which was confirmed by a decrease in the serotonin concentration in the thyroid glands of the ganglionectomized rabbits.

It can be concluded from these results that sympathetic impulses affect C cells and that this effect is stimulating. As a result of the simultaneous stimulating effect of sympathetic impulses on functional activity both of the thyroid epithelium and of the neuroendocrine C cells, an increase in the specific secretion of iodine-containing thyroid hormone is accompanied by an increase in secretory activity of the C cells. That this relationship is a regular one is confirmed by the fact that if functional activity of the thyroid epithelium is weakened as a result of hyperthyroidization of experimental rabbits for 30 days, the mean area of cross-section of the C cells was only  $175.8 \pm 1.83 \mu^2$ , i.e., less than initially.

The parallel trend of changes in functional activity of the thyroid epithelium and C cells, which was so clearly expressed during stimulation or after extirpation of the superior cervical sympathetic ganglia, is repeated in other cases of thyroid gland activity. For instance, persistent hyperfunction of the thyroid gland in thyrotoxicosis is accompanied by an increase in the number of C cells in the thyroid parenchyma, especially compared with their number in "nontoxic goiters" (i.e., in euthyroid goiter [6]).

An increase in secretory activity of the C cells means an increase in the secretion of calcitonin and serotonin. However, calcitonin and serotonin accumulate in C cells in the same granules, and for that reason increased secretion of the former ought to be accompanied by equally increased secretion of the latter.

Serotonin itself is known to have a stimulating action on thyrocytes. A similar activating effect, accompanied by a marked increase in proliferation of the thyroid parenchyma, has been observed in response to the action of an increased quantity of exogenous calcitonin [8].

The parallel nature and simultaneous appearance of changes in secretory activity in the follicular epithelium and in the C cells suggest that the role of the latter in the thyroid gland is not only to produce calcitonin and serotonin, but also to potentiate the functional activity of the follicular epithelium, on which both calcitonin and serotonin exert a stimulating action.

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