EFFECT OF HYDROCORTISONE ON THE THYROID DURING STIMULATION OF ITS FUNCTION

A. A. Voitkevich and L. K. Leonova

UDC 612.44.014.46:615.361.453

The question of the physiological interaction between the hormones of the adenohypophysis has recently become topical in connection with the discovery of the biochemical relationship existing between certain pituitary hormones and of their common neurosecretory regulation. The functional relationships between the thyroid and adrenal glands and the interference in the biosynthesis of the adrenocortico tropic and the thyrotropic hormones in the secretory cells of the pituitary are therefore of considerable interest [1].

The action of the glucocorticoids on the structure and function of the thyroid gland has been demonstrated [3-5, 8], and the absorption and organic fixation of radioactive iodine have been shown to be depressed in the thyroid epithelium by the action of corticosteroids [8]. Conversely, adrenalectomy stimulates iodine metabolism and the synthesis of the thyroid hormones.

The object of the present investigation was to study the effect of adrenal hormone on the thyroid gland in a state of increased functional activity.

EXPERIMENTAL METHOD

Experiments were carried out on 25 female rats weighing from 125 to 161 g, distributed into 5 series. The animals of the control series received no treatment. The remaining animals received daily injections of hydrocortisone (2.5 mg) or were given 6-methylthiouracil (6-MTU) by mouth (3 mg). These preparations were given for 10 days in the following combinations: 6-MTU for 5 days, followed by hydrocortisone; hydrocortisone for 5 days, followed by 6-MTU for 10 days.

At the end of the experiment both lobes of the thyroid were studied histologically. One lobe was fixed in Carnoy's fluid and the other in an alkaline alcoholic solution of formalin, and the peroxidase activity was then determined by the peroxidase reaction. The cell nuclei of these preparations were stained with a 0.5% aqueous solution of methyl green. After removal of the paraffin wax, some of the histological sections were stained with hematoxylin-eosin, and others were stained for ribonucleoproteins by Brachet's reaction and for tyrosine by Geyer's modification [7]; instead of the 7-amino-1-naphthol-5-sulfonic acid recommended, 2,2-dioxy-(1-1-azo)napthalene-4-sulfonic acid was used.

EXPERIMENTAL RESULTS

The histological findings reflecting thyroid function revealed a decrease in the activity of the gland under the influence of hydrocortisone. The results of the study of the histological sections showed that the reaction of inhibition was strongest in the thyroid follicles lying at the periphery of the organ. In the central zone of each lobe the follicles contained comparatively little colloid and the epithelial cells varied from high-cubical to prismatic.

The histochemical changes relevant to the investigation were more marked in the follicles in the central zone of each lobe of the thyroid. The histochemical reaction for peroxidase, an enzyme concerned in the synthesis of both thyroid hormones, was very clear and distinct. In the functionally stimulated thyroid cells the α-naphthol reaction revealed small peroxidase granules predominantly in the apical parts of the cytoplasm; the granules were sometimes joined together into chains or merged into droplets. The enzyme was present in the stimulated follicles in the peripheral zone of the vacuolated colloid. In the case of very strong stimulation of the function of the thyroid epithelial cells, the reaction for peroxidase took on a more diffuse character, frequently expressed by the appearance of dust-like stippling, but without any clear escape of granules into the colloid material.

Laboratory of Experimental Endocrinology, Academy of Medical Sciences of the USSR, at Voronezh Medical Institute. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 63, No. 5, pp. 87-90, May, 1967. Original article submitted May 10, 1965.

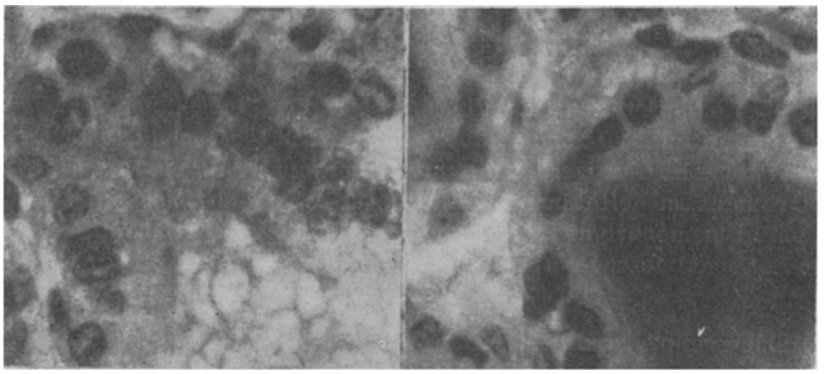

Fig. 1 Fig. 2

Fig. 1. Thyroid gland of a rat receiving 6-MTU for 10 days. Prismatic epithelium, vacuolation of colloid. Reaction for tyrosine with counterstanding of nuclei with hematoxylin. 1200 ×.
Fig. 2. Thyroid gland of a rat receiving 6-MTU for 5 days against a background of administration of hydrocortisone (10 days). High epithelium, vacuolation of colloid absent. Reaction for tyrosine with counterstanding of nuclei with hematoxylin. 1200 ×.

Brachet's reaction for ribonucleoproteins was positive and clear in the thyroid epithelium and, in particular, in the colloid of the follicles of the control animals. The reaction of the gland cells for tyrosine showed a similar picture: tiny lilac-pink granules were uniformly distributed in the cytoplasm. During activation of the thyroid with 6-MTU the content of ribonucleoproteins and tyrosine in the cytoplasm of the secretory cells rose appreciably, while that in the colloid fell.

When various combinations of hydrocortisone with 6-MTU were given, no marked difference was observed between the histological picture and the histochemical reactions depending on the order of their administration. In the various combinations hydrocortisone had an inhibitory effect on the phase of excitation of the secretory cells brought about by 6-MTU.

The prolonged administration of hydrocortisone (10 days), associated with a correspondingly severe depression of the adenocorticotrophic function of the pituitary, was accompanied by a more marked reaction of the thyroid glands to 6-MTU (Figs. 1 and 2).

The epithelial cells were still prismatic, but the vacuolation of the colloid was much reduced and the desquamation of the epithelial cells into the lumen of the follicle was also less marked, particularly in the peripheral zone of the thyroids of the animals treated with the two preparations in turn. The administration of hydrocortisone, for instance, interfered with the activity of the proteolytic enzymes, and thereby prevented the liquefaction and resorption of the colloid. This was particularly evident after the combined action of hydrocortisone (10 days) and 6-MTU (5 days). Activation of the thyrotrophic function of the anterior lobe of the pituitary in these conditions, although causing considerable excitation of the cells of the thyroid epithelium and also a typical hyperemia, nevertheless clearly depressed the resorption of the colloid deposited in the follicles. There is also reason to suppose that in these conditions the accumulation of new colloid material was prolonged. The content of ribonucleoproteins and, in particular, of tyrosine in the cytoplasm of the secretory cells was higher than normally.

However, the thyroid of these animals differed in the character of distribution of these constituents from the gland in the animals receiving 6-MTU alone. In relation to the peroxidase activity in the thyroid cells of the thyroid gland, however, no significant difference was found between the two series of rats compared.

It may be concluded from these experiments that hydrocortisone has a blocking action on the process of resorption of colloid, thereby inhibiting the outflow of hormone into the blood. The results are in agreement with experimental findings and clinical observations according to which the corticosteroid hormones lower the intensity of the absorption of radioactive iodine and the level of the secretory processes in the thyroid gland [6. 9]. The possibility is not ruled out that the corticosteroid hormones weaken the action of

antithyroid agents on hormone synthesis in the secretory cells of the thyroid gland. According to the histochemical evidence, the combined effect of hydrocortisone and 6-MTU brought the secretory cells closer to the normal state than the antithyroid factor alone. In these experimental conditions, of course, the functional relationships embodied in the processes of formation of the trophic hormones in the anterior lobe of the pituitary were important. Reports have been published that the steroid hormones inhibit the secretion of the thyrotrophic hormone in the pituitary [6]. It may be supposed that the inhibition of the adrenocorticortrophic function of the pituitary by hydrocortisone does not depress but, on the contraty, stimulates to some extent the thyrotrophic activity of the pituitary, which can also be stimulated by administration of the antithyroid agent.

LITERATURE CITED

1. A. A. Voitkevich, Probl. Éndokrinol., No. 3, 89 (1964).
2. E. A. Kolli, Byull. Éksp. Biol., No. 7, 27 (1953).
3. Yu. B. Skebek'skaya, Probl. Éndokrinol., No. 5, 15 (1958).
4. Ya. Kh. Tarakulov, Biochemistry of the Hormones of the Thyroid Gland in Normal Conditions and in Thyroid Pathology [in Russian], Tashkent (1962).
5. G. Chimello, A. Cantone, and V. Ricotti, Boll. Soc. Ital. Biol. Sperim., 23, 1187 (1962).
6. D. S. Frederickson, P. H. Forshman, and G. V. Thorn, Journ. Clin. Endocr., 12, 541 (1952).
7. G. Geyer, Acta Histochem., 13, 355 (1962).
8. S. Kovacs and M. Vertes, Endocrinologie, Bd 43, S. 105-9 (1962).
9. F. Thorcild and R. Vagn, Acta Endocrin., 42, 1 (1963).