

# REVEALING AN EFFECT EXERTED BY SYMPATHETIC IMPULSES ON THE THYROID

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The absence of any definite and maintained effect on the thyroid from the nervous apparatus has been the reason for the widespread view that efferent nervous impulses entering this organ produce no secretory effect, and have only a vasomotor influence [13]. It is usually supposed that the regulation of thyroid function is brought about exclusively by humoral means through action of the thyrotropic hormone of the hypophysis. However the abundant and varied innervation of the thyroid compels us to be cautious in categorically denying the possibility of a direct influence of nervous impulses on thyroid function. Although certain observations show that sympathetic impulses are not without effect on the response of the thyroid to 6-methylthiouracil, in particular as the uptake by it of radio-active iodine [4] or the regeneration of thyroid parenchyma [6, 9], or the ability to alter its sensitivity to thyrotropic hormone [8] concerned; nevertheless disturbance of functional activity or thyroid structure evoked by transection or stimulation of the appropriate sympathetic or parasympathetic nerves has a very slight and variable influence on the normal intact animal. At the same time the isolated thyroid parenchyma responds by a marked increase in the uptake of oxygen to the addition of a sympathomimetic substance adrenalin to the incubation medium, whereas acetylcholine (a parasympathetic mediator) under the same circumstances greatly reduces the respiration rate of isolated thyroid parenchyma, even under conditions when the thyroid gland had previously been stimulated by thyrotropic hormone [3].

Thus the mediators of the nervous system may exert a very definite and direct action on the thyroid in vitro. Because no effect is manifest in vivo we must suppose that the nervous influence is in some way masked by a more powerful action exerted on the thyroid gland by the thyrotropic hormone. If this is so, then if the influence of the thyrotropic hormone were reduced, the influence of nervous impulses should become sufficiently manifest even in the intact animal.

We studied the effect of removal and stimulation of these various cervical sympathetic ganglia, which form the main source of sympathetic innervation to the thyroid on the uptake of radio-active iodine under conditions under which the production of thyrotropic hormone is reduced. This latter effect was produced by means of aminasin [1, 7, 10, 12, 14].

## EXPERIMENTAL METHOD

The experiments were carried out on male rabbits weighing 2.5-3 kg. The superior cervical sympathetic ganglia were removed at one operation, or these ganglia were stimulated by application of a single turn of a spiral of thin silver wire of diameter 0.2-0.3 mm. Ten days after the operation the experimental rabbits received an injection of 1  $\mu$ Ci of  $KI^{131}$  without carrier. A count of the radioactivity of the thyroid was made 2, 4, 6, 8, 12, 24, 30, 48, 72, 96, and 120 h after the injection by means of a Geiger-Müller AAM-4 tube, which was set up at an accurately measured distance from the rabbits neck and used in conjunction with a P-II counting system. The results obtained were expressed as a percentage of the dose injected.

Aminasin was given by mouth in a dosage of 25 mg/kg daily, starting at the day of the operation. A post mortem examination was made after the radiation measurements had been completed. The thyroid glands were fixed in Zenker formalin. The glands were embedded in celloidin-paraffin. Sections were cut and stained in azan,

Effects of (1) Removal and (2) Stimulation of the Superior Cervical Sympathetic Ganglia on (1) the Height of the Cells of the Follicular Epithelium of the Thyroid Gland and (2) on the Hypophyseal Content of Thyrotropic Hormone

Conditions of experiments	Height of cells of the thyroid epithelium (in $\mu$ )	Mean height of cells of the thyroid epithelium of control rabbits		Height of cells of the thyroid epithelium of guinea pig recipients (in $\mu$ )	Mean height of the cells of the thyroid epithelium of guinea pig recipients	
		$\mu$	% of original value		$\mu$	% of original value
Normal rabbit	8.151 $\pm$ 0.010 8.005 $\pm$ 0.020	8.08 $\pm$ 0.015	100	8.11 $\pm$ 0.090 8.995 $\pm$ 0.085	8.55 $\pm$ 0.090	100
Removal of superior cervical ganglia	7.589 $\pm$ 0.060 8.301 $\pm$ 0.050	7.99 $\pm$ 0.05	98.9	10.980 $\pm$ 0.090 10.920 $\pm$ 0.090	10.65 $\pm$ 0.09	124.8
Stimulation of the superior cervical ganglia	6.861 $\pm$ 0.050 7.049 $\pm$ 0.050	6.95 $\pm$ 0.05	86	7.190 $\pm$ 0.027 6.980 $\pm$ 0.028	7.08 $\pm$ 0.028	82.8
Aminasin	8.281 $\pm$ 0.050 8.432 $\pm$ 0.040	8.35 $\pm$ 0.04		6.862 $\pm$ 0.050 6.709 $\pm$ 0.050	6.78 $\pm$ 0.05	89.5
Aminasin + removal of the superior cervical sympathetic ganglia	8.508 $\pm$ 0.050 8.138 $\pm$ 0.060	8.32 $\pm$ 0.06	102.9	7.161 $\pm$ 0.060 7.078 $\pm$ 0.050	7.118 $\pm$ 0.06	93.9
Aminasin + stimulation of the superior cervical sympathetic ganglia	8.289 $\pm$ 0.030 8.010 $\pm$ 0.050 7.298 $\pm$ 0.050	7.86 $\pm$ 0.04	97	5.434 $\pm$ 0.060 6.566 $\pm$ 0.060	6.0 $\pm$ 0.06	79.1

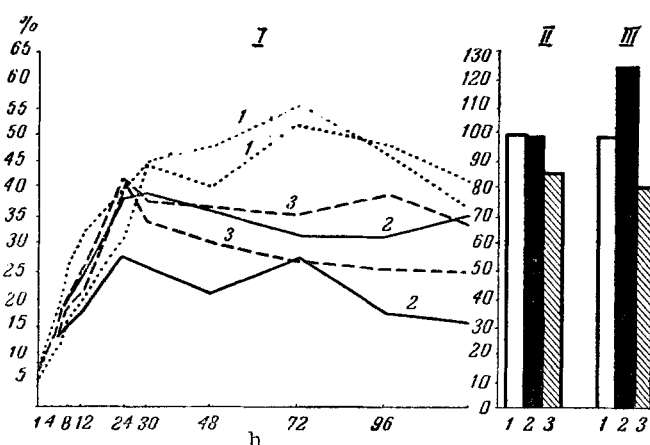


Fig. 1. Effect of removal or stimulation of the superior cervical sympathetic ganglia from normal rabbits. 1) Curves of uptake of  $I^{131}$  by the thyroid gland; II) mean height of cells of the follicular epithelium of the thyroid gland; III) amount of thyrotropic hormone in hypophysis (mean height of cells of thyroid epithelium of recipients receiving the hypophyses under test); 1) intact rabbits; 2) effect of ganglionectomy; 3) effect of stimulation of the superior cervical ganglia.

intact animals, whereas there was a marked reduction in height in animals in which these ganglia were stimulated (see table, and Fig. 1). These changes in the height of the thyroid cells may be explained on the grounds that sympathetic impulses exert a depressive influence on the thyrotropic function of the hypophyses [3, 5]. Actually, in cases where the superior cervical sympathetic ganglia were extirpated the amount of thyrotropic hormone in the hypophysis increased, and when the ganglia were stimulated it fell (see Fig. 1). Thus both the reduction in the reaction of the cells of the follicular epithelium which would have been expected to follow sympathectomy, and

and the height of the cells of the follicular epithelium was measured by means of an ocular micrometer; 250-300 measurements were made in each case, and the results obtained were studied biometrically. The hypophyses of these rabbits were dried in acetone, ground to a powder, and tested on guinea pigs by the method of Barnett [11]. Their thyroid hormone content was inferred from the increase in the mean height of thyroid cells of recipients which received the hypophyses under test.

#### EXPERIMENTAL RESULTS

As can be seen from Fig. 1, in the control rabbits, (i. e., in those which received no aminasin) the curves of the  $I^{131}$  uptake of the thyroid remain within the original range despite the stimuli applied to the superior cervical sympathetic ganglia; any change may be attributed to individual variation.

The mean height of the cells of the follicular epithelium in the sympathectomized rabbits remained practically the same as in the intact animals,

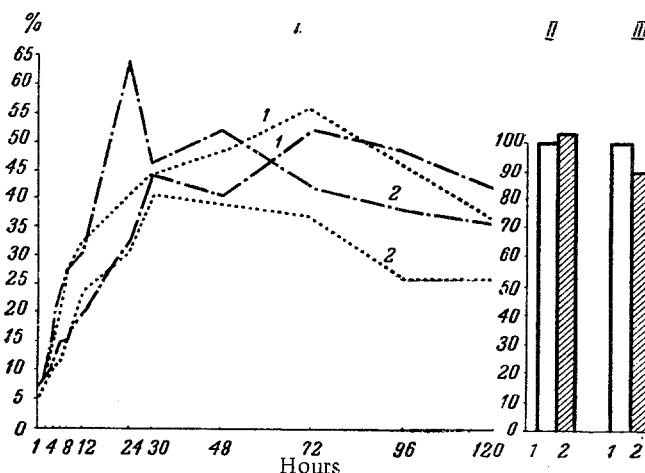


Fig. 2. Influence of aminasin on the thyroid gland and on thyrotropic function of the hypophysis while sympathetic innervation remained intact. Intact rabbits (dotted line); effect of aminasin (line under dot).

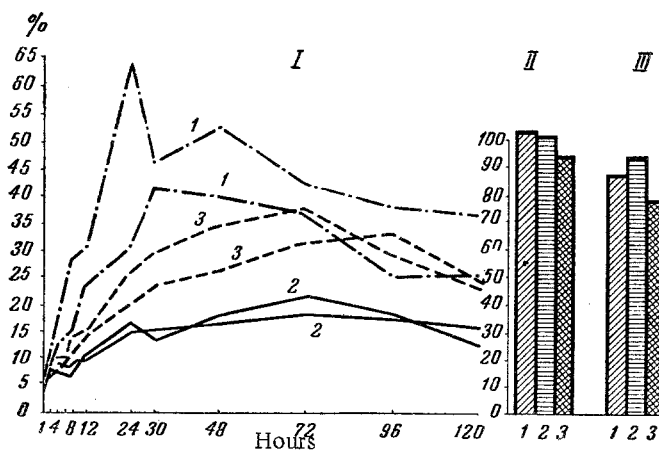


Fig. 3. Effect of extirpation or stimulation of the superior cervical ganglia under conditions when hypophyseal thyrotropic function was reduced by aminasin. 1) Effect of aminasin when the sympathetic innervation was intact; 2) effect of ganglionectomy when the thyrotropic hypophyseal function was reduced by aminasin; 3) effect of stimulation of the superior cervical ganglia under the same conditions. Other indications as in Fig. 1.

the anticipated possible increase in this reaction after stimulation of the ganglia were eliminated, and the changes were reversed under the influence of thyrotropic hormone.

If the influence of the sympathetic impulses entering the thyroid had been purely vasomotor the reaction of the cells of the follicular epithelium and the rate of uptake of  $I^{131}$  by the thyroid parenchyma would both have been influenced in the same direction. The difference in the two responses was therefore evidence against this hypothesis.

The use of aminasin in cases where the superior cervical sympathetic ganglia remained intact was associated with a small but definite reduction of thyrotropic function (see table, and Fig. 2). However, not only was the height of the follicular epithelium not reduced, but it actually increased somewhat (see Fig. 2). The rate of uptake of  $I^{131}$  by the thyroid gland remained within normal limits [except for the fact that the maximum was reached somewhat earlier (see Fig. 2)]. The divergence between the responses of the thyroid cells and the intensity of thyrotropic function of the hypophysis indicated that under these conditions when the influence on the thyroid gland of the thyrotropic hormone is attenuated certain other factors become manifest.

The influence of sympathetic influences on the adenohipophysis during the action of aminasin is in the same direction as in the case of normal animals [10]. Extirpation of the superior cervical ganglia is associated with some increase of hypophyseal thyrotropic hormone (above the control value), but stimulation of the ganglia leads to a subsequent reduction in the amount of this hormone (see table, and Fig. 3), although the extent of the shift in this case was somewhat less than in the controls. The reaction of the cells of the follicular epithelium is also of the kind found in normal animals; extirpation of the cervical ganglia led to no marked change in the height of these cells, and stimulation led to a slight reduction in their height (see Fig. 3). However the influence of sympathetic impulses on the uptake of  $I^{131}$  by the thyroid during the action of aminasin was more marked. In this case the curves for the uptake of  $I^{131}$  in the ganglionectomized rabbits lay definitely below the curves plotted for rabbits in which the superior cervical ganglia were stimulated (see Fig. 3).

Thus a comparatively small reduction in the influence of the thyrotropic hormone on the thyroid gland, brought about by the influence of aminasin, was sufficient to manifest the influence exerted on the thyroid by sympathetic impulses.

Under these conditons the difference in the uptake of  $I^{131}$  by the thyroid in ganglionectomy as contrasted with stimulation of the superior cervical ganglia shows that the influence of the sympathetic impulses amounts to more than simply a vasomotor effect. Hence it follows that the normal regulation of the thyroid is not brought about exclusively by the thyrotropic hormone but is the result of the interaction of the influence of this humoral agent and the influence of nervous impulses reaching the thyroid parenchyma along the nerve fibers supplying the gland.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. Some or all of this periodical literature may well be available in English translation. A complete list of the cover-to-cover English translations appears at the back of this issue.

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