THE ROLE OF THE THYROID GLAND IN THE REGULATION OF CELL DIVISION

I. E. Epova

Dept. of Histology (Chief – Assistant Prof. I. A. Alov), Khabarovsk Medical Institute

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Cell division in the various tissues is controlled by the neurohumoral regulator system of the body. The thyroid gland plays an important part in this regulating system. I. A. Alov's experiments [1] with thyroid hormone injections and methylthiouracil blockading of the thyroid gland have shown that the thyroid hormone is a powerful stimulator of cell division. Other authors, on the basis of almost identical experiments, are inclined to consider the thyroid hormone as an antimitotic agent [6, 7, 8].

The purpose of this work was to clarify the importance of the thyroid gland in the regulation of cell division, by using other methods to stimulate and suppress its function.

EXPERIMENTAL METHODS AND RESULTS

In the first series of experiments, we studied mitotic activity change in various organs when the thyroid gland had been completely removed.

The experiments were done on white rats. The thyroid gland was removed bilaterally by the usual method. After the death of the animals, histological inspection of the operation region checked the completeness of the gland's extirpation. Mitotic activity was determined only in those animals in which the gland had been completely removed. In the control animals, the thyroid gland was exposed by operation, but not damaged or removed. The experimental and control animals were killed 10 hours after the operation, and mitotic intensity was determined in the epithelium of the cornea, intestine, tongue and skin. Mitotic intensity in the tissues was judged according to the amount of dividing cells in an area of 1,65 mm^2 and according to the coefficient of the phases (the relation of the two first mitotic phases to the two ensuing ones). The dividing cells were counted on four sections (10 microns) taken from one region, 100 microns apart. Mitotic activity in the cornea was determined on total preparations. The data was statistically processed by the Fisher-Styudent method.

Table 1 shows the results of the first series of experiments.

TABLE 1

Change in Mitotic Intensity After Extirpation of the Thyroid Gland

Animal group	No. of animals	Number of mitoses (M ± m) and coefficient of the phases (K)			
		Cornea	Intestine	Tongue	Skin
Control	6	99 ±6.5 K=3.2	399±15.0 K=4.2	40.3±4.5 K=2.4	36±1.5 K=4.3
Thyroid gland extirpation	7	60.0±6.9 K=3.6	315± 5.4 K=4.3	34.6±5.3 K=3.0	26±1.5 K=3.9

Thus, complete removal of the thyroid gland caused mitotic activity to decrease. Ten days after the extirpation of the gland, mitotic intensity had decreased $1\frac{1}{2}$ times in the epithelium of the cornea, intestine, tongue, and skin. This same relatively small decline in mitotic activity was also observed in experiments with 6-methylthiouracil blockade of the thyroid gland [1, 2]. Evidently, the other mechanisms regulating cell division can partly compensate for the exclusion of the thyroid gland.

In a second series of experiments, we studied mitotic activity change in the same organs with a hyperfunctioning thyroid gland.

White mice were injected with a thyrotropic hormone. To prepare the thyrotropic hormone, acetonizing powder was extracted from the anterior lobe of the hypophisis of large horned cattle by a 0.1 N solution of $NaHCO_3$ for a period of 24 hours in the cold. For a period of 8 days, the mice were injected subcutaneously with 0.3 ml of the extract twice daily (a dose equivalent to 10 ml of the acetonizing powder of the hypophisis per 100 g of weight). The control animals were injected with a corresponding amount of a physiological solution. After the death of the mice, the thyroid gland was examined histologically.

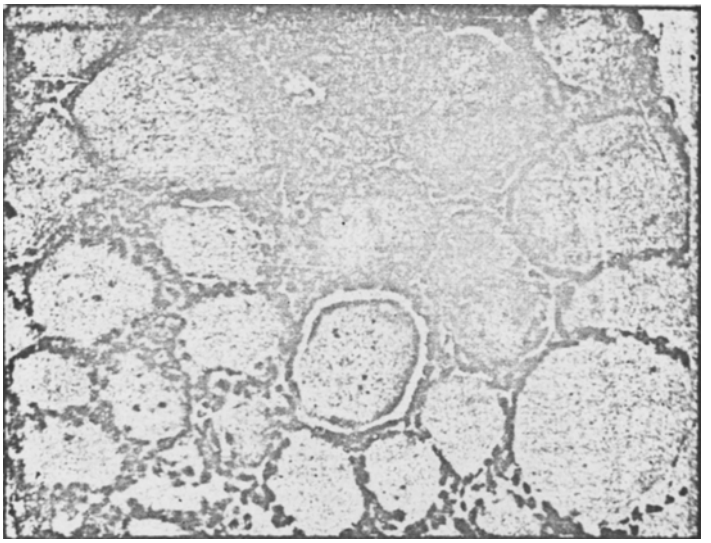

Fig. 1. White mouse thyroid gland under conditions of normal maintenance of the animal.

A repeat injection of the thyrotropic hormone given the white mice caused activation of the thyroid gland. The gland increased in size and incurred hyperemia; the follicular epithelium became cylindrical in form; the central follicles grew smaller and partially emptied; the colloid became vacuolized, and epithelial proliferation was observed (Fig. 1, 2). At the same time that the functional activity of the thyroid gland increased, change of mitotic activity occurred in the experimental organs (Table 2).

Mitotic intensity increased $2\frac{1}{2}$ times in the epithelium of the cornea and tongue, $1\frac{1}{2}$ times in the epithelium of the intestine, and $2\text{-}2\frac{1}{2}$ times in individual experiments.

The results of the experiments show that the thyrotropic hormone is a stimulator of cell division in the body. Thyrotropic hormone activation of the thyroid gland caused mitotic activity in the different organs to appreciably increase. The removal of the thyroid gland is attended by a decrease in mitotic activity.

Several authors [3, 4, 5] have shown that one of the activators of the thyroid gland is the process of daily illumination. Accessory illumination of the animals also caused mitotic activity to increase [6]. Comparing these facts, we decided that the mitotic stimulation effected by light is probably realized through the thyroid

TABLE 2

Change in Mitotic Intensity When the Thyroid Gland is Activated by the Thyrotropic Hormone

Animal group	Number of animals	Number of mitoses (M ± m) and coefficient of the phase (K)		
		Cornea	Intestine	Tongue
Control	8	92.3±7.9; $K=1.0$	324±15; $K=1.5$	23±1.7; $K=1.6$
Thyrotropic hormone	15	192.8±8.5; $K=1.1$	491±23.9; $K=1.0$	63.8±3.8; $K=1.0$

gland. We conducted a third series of experiments to study the role of the thyroid gland in the activation of cell division under conditions of accessory illumination of the animals.

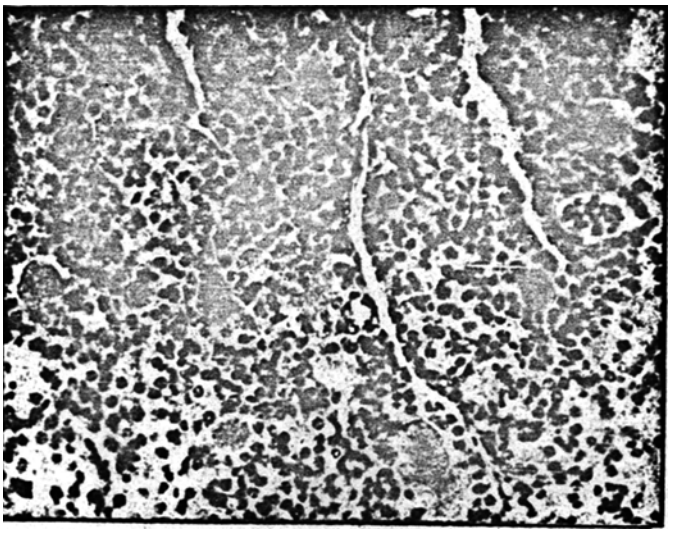

Fig. 2. Thyroid gland of a white mouse after the thyrotropic hormone injection.

The first group of experiments in this series studied mitotic activity change under conditions of accessory illumination. The experiments were conducted in March and April on white mice. The experimental animals were kept in glass jars and given accessory illumination daily for 10 days for 5-6 hours, beginning at 7 p.m. (electric 60 w bulb at a distance of 2 meters). The control group of mice were kept in cells, without accessory illumination.

The results of the experiments are given in Table 3.

As is evident from Table 3, with accessory illumination mitotic intensity increased $2^1/_2$ times in the epithelium of the cornea; in the epithelium of the tongue, there was no essential change. Changes in the structure of the thyroid gland attesting to its increased activity were simultaneously observed. In the thyroid glands of the majority of mice, increase in the height of the follicular epithelium, vacuolization of the colloid, and, in some experiments, the almost complete disappearance of the colloid were observed (Fig. 3). The degree of change in the thyroid gland varied in different animals; in all cases it was considerably lower than when the gland was activated with the thyrotropic hormone.

TABLE 3

Change in Mitotic Intensity due to Accessory Illumination

Animal group	Number of animals	Number of mitoses (M ± m) and coefficient of the phases (K)		
		Cornea	Intestine	Tongue
Control	13	60.9± 9.7; $K=1.1$	291±15.5; $K=0.9$	46± 8.1; $K=1.0$
Illumination	13	161±13.3; $K=1.2$	428±19.2; $K=0.8$	42± 7.3; $K=1.4$
Control + 6-methyl-thiouracil	18	95.2±13.8; $K=1.3$	302.5±16.9; $K=1.0$	18.9±14.5; $K=1.0$
Illumination + methyl-thiouracil	9	85±11; $K=0.9$	278±11.8; $K=0.9$	15± 3.2; $K=1.1$

These observations allow the hypothesis that mitotic activity change in accessory illumination is associated with the activation of the thyroid gland by light. To verify this hypothesis, a second group of experiments was conducted in this series.

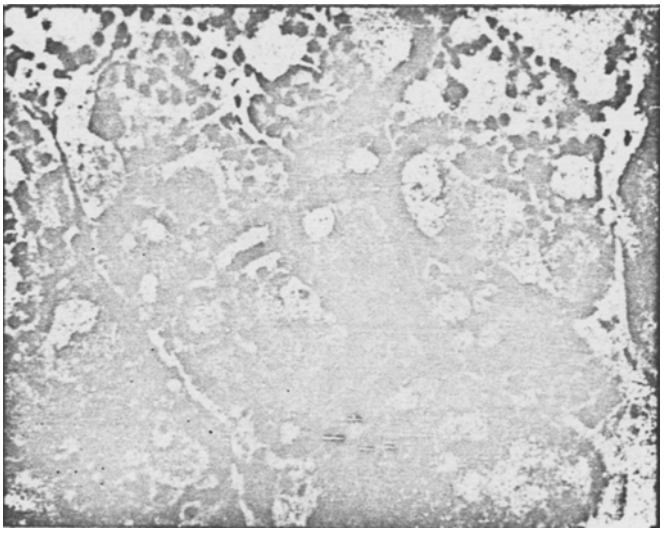

Fig. 3. Thyroid gland of a white mouse after accessory illumination.

The conditions of maintenance and accessory illumination for the experimental and control animals were the same as in the first group of experiments. Five days before the beginning of the experiment, we began to add 6-methylthiouracil, which causes hypofunction of the thyroid gland, to the food of the experimental and control animals (5 mg a day per animal). Methylthiouracil administration was continued during the accessory illumination period, and, in this way, the experimental and control animals received this preparation for a period of 15 days.

The 6-methylthiouracil administration caused a typical goiter-forming reaction (hypertrophy of the gland, increase in epithelial height, proliferation, emptying of separate follicles).

Mitotic activity change in the epithelium of the cornea, intestine and tongue showed that, when the thyroid

gland was blockaded by 6-methylthiouracil, accessory illumination of the animals did not stimulate mitotic activity (Table 3). Moreover, in those mice which had been subjected to accessory illumination, there was even a slight (statistically unreliable) decrease in the intensity of cell division. Therefore, one must also note that the mice which had received 6-methylthiouracil did not endure accessory illumination as well as the normal animals in the first group of the experiments.

The results of this experimental series imply that the increase in mitotic activity which occurs in accessory illumination is accomplished through the thyroid gland. Activation by light of the thyroid gland causes the intensity of cell division to increase, as do the other methods of intensifying the gland's function.

Thus, the experiments described show that the thyroid gland plays an important role in the regulation of cell division in the body.

The thyrotropic hormone is a powerful stimulator of cell division, and the activation of cell multiplication by different environmental factors (in our experiments, light) is, in a series of cases, done through the thyroid gland.

SUMMARY

Experiments carried out on white rats have shown that the complete extirpation of the thyroid gland decreases mitotic activity in different tissues. Injection of thyrotropic hormone increased thyroid gland and mitotic activity. The latter is also increased in the case of accessory illumination of animals. This reaction proceeds by means of the thyroid gland activation; after the blockade of thyroid gland with methylthiouracil, accessory illumination of mice does not bring about an increase of cell division in the tissues.

LITERATURE CITED

[1] I. A. Alov, Byull. Eksptl. Biol. i Med, 1955, Vol. 40, No. 12, pp. 47-50.

[2] A. A. Voitkevich, Bull. acad. sci. USSR, Ser. biol., 1945, No. 4, pp. 385-395.

[3] A. A. Voitkevich, Fiziol. Zhur. SSSR, 1948, Vol. 34, No. 6, p. 722.

[4] B. I. Noyikov and L. Favorova, Doklady Akad. Nauk SSSR, 1947, Vol. 58, No. 4, pp. 701-704.

[5] L. A. Utkin, Byull. Eksptl. Biol. i Med. 1953, Vol. 36, No. 7, issue 1, pp. 36-40.

[6] G. K. Smelser, Anat. Rec., 1947, Vol. 97, No. 3, pp. 369-370.

[7] G. K. Smelser and V. Ozanis, J. Cellular Comp. Physiol., 1954, Vol. 43, No. 1, pp. 107-117.

[8] K. Stein, S. Quinby, and A. Moellen, Anat. Rec., 1947, Vol. 99, pp. 249-264.