

REGENERATION OF THE THYROID GLAND IN WHITE
RATS AND THE CHANGE OF HEIGHT OF THE THYROID
EPITHELIUM OF THE REGENERATING WOUNDED SURFACE
IN EXPERIMENTAL HYPO- AND HYPERTHYROIDISM

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Information concerning hormonal influences on regenerative processes in the thyroid gland are contradictory. Many authors consider that in experimental hypothyroidism produced by the action of 6-methylthiouracil (6-MTU), the regenerative power of the thyroid is lost or considerably reduced [2-4, 11, 12]. On the other hand, it has been suggested that there is no difference in the proliferation of the thyroid parenchyma after resection of the intact thyroid gland, even during experimental hypothyroidism [5]. Some authors [6, 7, 9, 10] maintain that the thyroid hormone is a powerful stimulator of regeneration in the thyroid gland and in organs and tissues in general, whereas others are inclined to consider it as exerting an antimitotic influence [13, 14, 15].

Furthermore, sufficient work has not been done on the functional condition of the thyroid epithelium of a regenerating surface, and no data are available about changes concerning its height during regeneration. Only A. A. Voitkevich [2] has pointed out that in the thyroid gland, during hypofunction, the function of such glandular islets either coincides with the functional phase of the follicles of the main mass of the gland, or else is somewhat enhanced.

In the present work we have studied the regenerative processes and changes in the height of the thyroid epithelium of white rats on the 1st, 2nd, 3rd, 5th, 15th, and 30th day after bilateral resection of one third of the gland under the following conditions: 1) injection of an excess of thyroidin, 2) blockade of the thyroid gland with 6-MTU, 3) alternating action of 6-MTU and thyroidin — here the possibility of a change within a short space of time in the nature of the differentiation of the secretory cells of the hypophysis brought about by the first preparation was excluded by injection of the second preparation into the control animals also [1, 5].

EXPERIMENTAL METHODS

The experiments were carried out by a method identical with the one we used previously [8]. We studied the microscopical structure of the gland in the region of the damage inflicted at operation, and in its undamaged part. In these same zones we determined the height of the epithelium (from 100 measurements per zone).

EXPERIMENTAL RESULTS

In the thyroid glands of the controls between the 1st and 30th day after the operation signs of stimulation developed. The cells of the follicular epithelium hypertrophied and increased in height, and there was a hydrolysis and vacuolization of the colloid. At this stage the follicles sometimes lost their rounded form. From the first day after the operation in the wounded surface of the gland there was a reactive inflammation which terminated on the fifth day. At this time cords of follicular epithelium were formed which differentiated into microfollicles. All over the gland new microfollicles were formed from the interfollicular islets and the follicular epithelium.

The height of the follicular epithelium in the undamaged part of the gland increased gradually from the first to the fifth day, and stayed at this height until the 30th day of the experiment.

In the region of the damage there was a variation in the height of the epithelium and from the 1st to 15th day after the operation it was significantly higher than in the undamaged region, and by the 30th day it was the same height all over the gland (see Table; Fig. 1, first row).

Height of Thyroid Epithelium in the Region of the Damage Inflicted at Operation and in the Undamaged Part

Conditions of experiment	Index	Days after operation					
		1st	2nd	3rd	5th	15th	30th
Control	M_1	12,13	13,47	11,66	13,82	12,34	13,52
	M_2	9,18	12,24	12,83	13,85	14,10	14,16
	t	4,04	2,23	1,46	0,04	2,59	1,25
	P	<0,02	<0,1	<0,3	>0,9	<0,05	<0,3
6-MTU before and after operation	M_1	14,10	15,46	15,89	11,80	12,09	14,72
	M_2	14,56	16,07	16,27	14,65	14,71	14,97
	t	0,92	1,22	0,76	4,45	4,76	0,91
	P	<0,4	<0,3	<0,5	<0,02	<0,01	<0,4
6-MTU before operation	M_1	14,54	15,41	14,42	10,74	10,43	13,26
	M_2	15,70	15,94	15,36	14,13	11,09	13,58
	t	2,18	1,01	1,14	3,94	1,10	0,42
	P	>0,05	<0,4	<0,4	<0,02	<0,4	<0,7
Thyroidin before and after operation	M_1	9,51	9,38	10,15	12,18	11,22	11,16
	M_2	5,94	6,73	6,08	12,21	7,62	10,82
	t	5,85	2,78	6,36	0,02	4,04	0,33
	P	<0,01	<0,05	<0,01	>0,9	<0,02	<0,8
Thyroidin before operation	M_1	8,98	9,55	9,33	11,14	11,41	13,38
	M_2	5,77	5,31	5,99	7,43	12,91	13,39
	t	6,42	12,91	5,56	6,18	2,0	0,01
	P	<0,01	<0,01	<0,01	<0,01	<0,2	>0,9
6-MTU and thyroidin before and after operation	M_1	11,06	10,43	9,75	14,17	12,38	14,11
	M_2	6,74	6,34	6,22	11,71	3,58	11,37
	t	11,67	11,05	11,38	4,26	7,17	4,28
	P	<0,01	<0,01	<0,01	<0,02	<0,01	<0,02
6-MTU and thyroidin before operation	M_1	9,92	10,79	10,54	10,77	13,54	13,37
	M_2	6,62	7,87	7,54	9,40	11,22	11,47
	t	41,25	4,78	6,25	1,69	3,74	3,96
	P	<0,01	<0,01	<0,01	<0,2	=0,02	<0,01

Note: M_1 — height of thyroid epithelium in the damaged region; M_2 — height of thyroid epithelium in the undamaged part of the gland (in microns).

In the second experiment (with experimental hypothyroidism), the glands were in a condition of marked stimulation. The cells of the follicular epithelium were large and tall. The colloid in the follicles had been completely absorbed, and in some of them there still remained a small amount of pale blue frothy colloid. The follicles were uneven in shape, crenated, and in parts their opposite walls were in contact. In the damaged surface and extending to a small depth in the underlying part of the gland there was a zone of reactive inflammatory changes. Here the degenerative changes of the follicular epithelium were more apparent than they were in the controls, and there were hemorrhages into their cavities. The processes of formation of new glandular epithelium in the damaged surface area began only on the 5th day after the operation, and were very weakly shown. However, the cessation of the action of 6-MTU after the operation facilitated the regeneration of the gland from the wounded surface. Also, regenerative hypertrophy occurred in the main mass of the gland [8].

For the first three days after the operation the height of the epithelium was uniform throughout the gland. Between the 5th and 15th days, in the region of the operational damage the height of the epithelium was significantly lower than it was in the main part of the gland (see Table; Fig. 1, second row). After the operation the action of 6-MTU ceased, but the height of the follicular epithelium gradually fell throughout the whole gland until the 15th day. Both before and after the operation the rate of change of the height of the epithelium in the zone that was damaged was the same when under the influence of 6-MTV (see Table; Fig. 2, second row).

In the third experiment with experimental hyperthyroidism, atrophy occurred in the thyroid gland. The follicles were stretched and filled with a dark blue or red colloid. The cells of the follicular epithelium were flattened and shallow. In the operated region there was a well-marked reactive inflammatory process which terminated on

the fifth day after the operation. At this time, strong epithelial cords were formed in the wounded surface, and developed into microfollicles. In the main mass of gland no regenerative processes were observed. The epithelium of the newly-formed follicles was higher than that of the undamaged region where, for the first three days after the operation, it was shallow (see Table; Fig. 1, third row). However, on account of the increasing functional stimulus, from the fifth day onwards the height of the epithelium increased. In the damaged region, during the first three days and on the 15th day after the operation the epithelium was taller than elsewhere. By the 30th day it was uniform throughout the whole gland. If however after the operation the action of thyroidin ceased, then for the first five days there was a marked difference in the height of the follicular epithelium between the undamaged and the operated regions: in the former it was shallow, and in the latter tall. By the 15-30th day after the operation no difference in height between the epithelium of the different parts of the gland could be seen, and it resembled the epithelium of the control animals at the corresponding time (see Table; Fig. 2, third row).

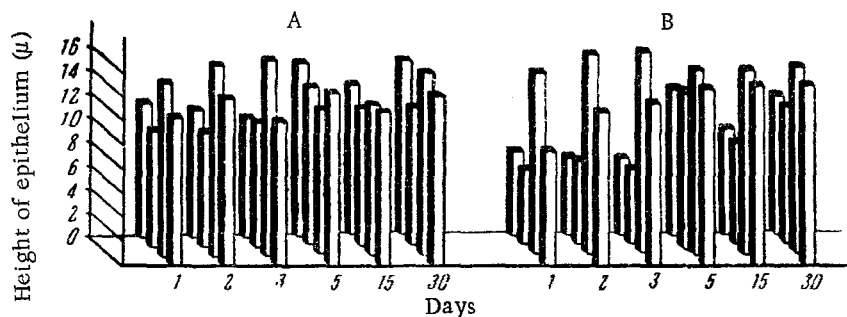


Fig. 1. Change in height of the thyroid epithelium in experimental hypo- and hyperthyroidism in the damaged and undamaged parts of the gland (action of the preparations was tested before and after operation). First series – control; second series – in hypothyroidism; third series – in hyperthyroidism; fourth series – with alternating action of 6-MTU and thyroidin. A – Damaged zone. B – Central part of the gland.

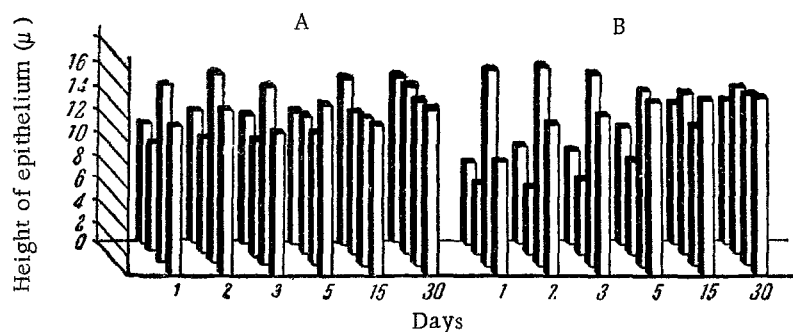


Fig. 2. Change of height of thyroid epithelium in experimental hypo- and hyperthyroidism in the zone damaged at operation and in the undamaged part of the gland (the preparations acted only before the operation). Indications as in Fig. 1.

In the fourth experiment, the animals received alternately 6-MTU and thyroidin. The 6-MTU was given first. In these animals the thyroid gland was in a condition of moderate functional excitation. The follicles were rounded or unevenly rounded in shape, and contained pale or dark blue colloid. There was some vacuolization at the periphery, and some resorption of colloid. The epithelium was cubical or low-cubical. The hyperemia in the gland was better shown than in the control group. The reactive inflammation at the wounded surface ceased at the fifth day after the operation. At this time cords of follicular epithelium were formed here, and they differentiated into microfollicles. In the main mass of the gland, there was a mild proliferation of parenchyma. The newly-formed

thyroid epithelium was higher and its protoplasm paler than that of the undamaged region. In some of the cells drops of a blue substance, the precursor of colloid appeared. In the first three days after the operation, in the main mass of the gland the follicular epithelium was shallow. From the 5th to the 30th day, its height increased considerably. In the damaged region of the gland, throughout the whole of the experiment the follicular epithelium was taller than in the main part (see Table; Fig. 1, fourth row). The same height changes in the follicular epithelium were observed when the preparations acted before the operation (see Table; Fig. 2, fourth row).

The results obtained indicate that in experimental hypothyroidism, regeneration from the wounded surface of the thyroid is suppressed, but that the lack of thyroid hormone is no obstacle to the development of regenerative hypertrophy. Also, during experimental hyperthyroidism, regeneration of the wounded surface takes place normally, but an excess of thyroid hormone has a depressing effect on the proliferation of thyroid parenchyma in the main mass of the gland.

When thyroid function is blocked with 6-MTU between the 5th and 15th day after the operation, in the damaged region the follicular epithelium is more shallow than it is in the main part, but when there is an excess of thyroidin in the body during the development in this region of a reactive inflammatory process the follicular epithelium is higher than in the undamaged region.

We must suppose that during the inflammatory reaction and regenerative phase the height of the thyroid epithelium regenerating in the damaged area does not depend on the thyrotropic activity of the hypophysis, but the difference in height between the follicular epithelium of the main part of the thyroid and the regenerating epithelium of the damaged area is due to the fact that they are at different phases of their secretory cycle.

SUMMARY

The concentration of thyroid hormone and the condition of the thyroid gland play an important part in the regeneration of the gland after excision of one-third of both lobes. The epithelium regenerating at the wound surface is lower in experimental hypothyroidism and higher in hyperthyroidism than it is in the uninjured portion. Evidently, variations in height are due to differences in the phase of the secretory cycle.

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