COMPENSATORY HYPERTROPHY OF THE THYROID GLAND

R. A. Gibadulin

Laboratory of Growth and Development (Head – Professor L. D. Liozner),
Institute of Experimental Biology (Director – Professor I. N. Maiskii), AMN SSSR, Moscow
(Presented by Active Member AMN SSSR N. N. Zhukov-Verezhnikov)
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There has been very little experimental study done on the question of compensatory hypertrophy of the thyroid.

Halsted [6] carried out a large series of experiments on dogs, and showed that after removal of from two-fifths to an entire lobe of the thyroid gland, compensatory hypertrophy of the other lobe essentially began after 2 months. In a later work [7], however, he obtained other results. Loeb [9], using guinea pigs, established that compensatory hypertrophy is manifested to a very weak degree, even at long periods of time after the operation (2-4 months). M.P. Gorbunova [3] noted compensatory phenomena in the remaining lobe after removing one lobe and simultaneously transplanting it in the same animal, following the method of Lazrenko.

None of these authors studied the quantitative changes associated with compensatory hypertrophy. Other authors [5, 11, 12] that have studied compensatory hypertrophy have investigated it in still less detail.

Alteration in the functioning of the remaining portion of the thyroid gland during compensatory hypertrophy has been studied in two works. Logothetopoulos and Doniach [8] removed one lobe of the gland in rats weighing 250 to 350 g, and observed a small degree of hypertrophy of the remaining lobe (71%) 55 days after the operation. The level of radioactive iodine uptake was restored to normal in the course of 10 days. Knigge [7] did not observe significant compensatory hypertrophy in cats, following removal of one lobe of the thyroid. Restoration of function (according to a series of tests) was noted 12-32 weeks after the operation.

In view of the current state of the question, and taking into account the marked reactivity of the thyroid that was demonstrated in a number of works [1,2], we decided to carry out special experiments with the purpose of studying compensatory hypertrophy of the thyroid gland in greater detail.

EXPERIMENTAL METHOD

Two series of experiments were set up, on 102 male white rats, whose average weight at the beginning of the experiment was equal to 225 g. The animals were maintained on standard briquetted food in unlimited quantity. Material was taken for histological treatment at 4-71 days after the operation, using 5 rats in the control and an average of 7 rats for the experimental group.

The entire right lobe was removed under ether narcosis, and weighed on a torsion balance. The operation was performed without the use of iodine. In the control animals, an incision was made in the stratified muscles, and the thyroid gland was exposed. With rare exceptions, the wounds healed without suppuration. When the animals were sacrificed, the remaining left lobe was extracted, weighed, fixed in a 10% solution of formalin and Bouin's solution, and imbedded in paraffin, and serial sections were prepared, 6-7μ in thickness. The sections were stained with hematoxylin-eosin, and isolated sections – with azan according to Heidenhain. In addition to a general survey of the histological preparations, we determined the percent relationship of the epithelium, colloid, and stroma of the gland, according to the method of Uotila and Tala [12, 13]. Besides this, we measured the area of individual follicles, located along a line connecting opposite poles of the long axis of the gland.

EXPERIMENTAL RESULTS

During the experiment, both the control and the experimental animals gained weight.

The dynamics of the weight elevation in the hypertrophied left lobe of the thyroid are presented in the table.

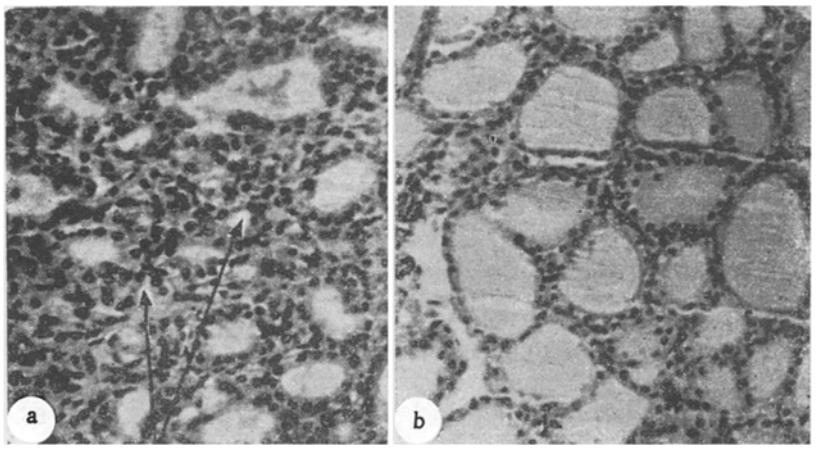

Fig. 1. Newly formed microfollicles in the left lobe of the thyroid gland, undergoing compensatory hypertrophy, on the 4th day after removal of the right lobe of the organ (a). Thyroid gland from a control animal (b). Magnification 225 ×.

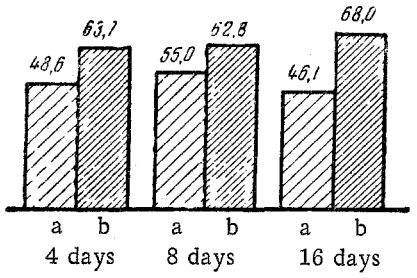

Fig. 2. Relative area occupied by the epithelium in the control (a) and in the experimental group (b) (in percent).

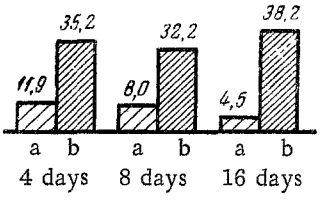

Fig. 3. Percent ratio of the microfollicles to all the follicles in the control (a) and in the experimental group (b).

It is apparent from the table that as early as the 4th day after the operation the weight of the hypertrophied left lobe was equal to 71.5% of the weight of the entire organ in the control animals. A similar ratio was retained on the 8th, 12th, and 16th day, and a repeat run (8th and 16th day) led to the same results as were seen in the first series of experiments. Subsequently, the weight of the left lobe again rose.

After only 4 days, the remaining left lobe differed significantly from the control in its structure. Gigantic follicles were sometimes encountered, which were never seen in the control. Obviously, colloid was accumulated in them. Small follicles predominated in the center of the gland, with tall epithelium and large nuclei. In places, most frequently in the central zone, there were sections with densely packed epithelial cells. Among them it was possible to differentiate isolated, slightly contoured, microfollicles. An increase was observed in the height of the epithelium, and in follicles of intermediate size, the walls were thicker (Fig. 1). Mitoses were frequent, and were observed both in the follicular and interfollicular epithelium.

On the 8th day, these changes were manifested more sharply. Hypertrophy of the follicular epithelium was observed in all the large follicles. On the 12th-16th day, the picture was changed very little from that previously described. Small follicles also predominated. In certain follicles, the epithelium was very tall, and their lumina looked like slits, testifying to the great functional intensity. The colloid in the majority of follicles was markedly thin, and stained a sky-blue with azan. Mitoses were encountered less frequently.

The follicular epithelium was hypertrophic up to the 71st day after the operation, but to a lesser degree than at the earlier intervals. The presence of a greater number of microfollicles in the experimental group than in the control continued throughout the course of the entire experiment. Beginning with the 31st-35th day after the operation, thickening of the colloid was noted in a large number of the follicles, and it was seen to stain an orange color with azan.

We undertook an attempt to study the quantitative changes in the structure of the gland. For this purpose, we determined the area occupied by the epithelium, colloid, and stroma. Determination of the percent relationship of the epithelium to the remaining tissue showed that the area it occupied was increased (Fig. 2).

Weight Changes in the Hypertrophied Lobe of the Thyroid Gland

Interval following beginning of experiment (days)		Average weight of entire gland in the control animals (mg)	Average weight of hypertrophied left lobe (mg)	Ratio of weight of hypertrophied left lobe to weight of entire organ in control animals (in %)
first series	second series			
4	–	20	14.3	71.5
8	–	19.7	14.3	72.6
–	8	22.9	13.9	60.6
12	–	24.2	17.9	74.0
16	–	23.8	17.4	73.2
–	16	21.3	15.1	70.9
–	21	26.7	22.9	85.8
–	31	21.4	18.5	86.4
–	35	23.3	18.9	81.4
–	71	23.6	20.2	85.6

The relative area, occupied by the epithelium, was significantly greater in the experimental group than it was in the control. The difference was definitely significant statistically. The increase in area occupied by epithelium occurs both as a result of its multiplication and secondary to the increase in height of the follicular epithelium.

One of the most essential elements characterizing compensatory hypertrophy is the great intensity with which new follicles are formed, i.e., new structural units. They originate via different pathways: by means of division (fragmentation) of large follicles into 2 or 3 independent structures; by budding, whereby a microfollicle forms in the wall of a relatively large follicle, and then separates from it; by the formation of microfollicles from the interfollicular tissue, with subsequent accumulation of colloid. As a result, the gland acquires a microfollicular type of structure.

As we know, the formation of new follicles in the thyroid occurs in intact animals too, and is closely dependent upon the functional state of the organ and external conditions. However, in a lobe undergoing compensatory hypertrophy, the intensity with which new follicles are formed exceeds that seen in an intact gland by several times.

For a quantitative characterization of microfollicle formation, we determined the percent relationship of the microfollicles (up to 1000μ^2) to the number of follicles of all measurements (Fig. 3). The difference between the experimental and control groups was statistically significant.

As can be seen in Fig. 3, the number of microfollicles in the experimental group exceeded the number in the control animals by several times. Apparently, the difference in the number of microfollicles in the control on the 4th, 8th, and 16th days reflected, to a certain degree, the effect of the operative trauma on the functional state and, correspondingly, on the structure, of the thyroid gland. This influence was demonstrated clearly in the work of I. A. Éskin and Yu. B. Skebel'skaya [4].

From the experiments described, it would follow that removal of one lobe of the thyroid in white rats causes compensatory hypertrophy in the absolute majority of the animals. Compensatory hypertrophy is reflected by an increase in the weight of the remaining lobe which, by the 21st day, attains approximately 85% of the weight of the entire organ in the control animals. In the early stages, mitotic division of the follicular and interfollicular epithelium is intensified, with subsequent differentiation of new follicles. At later intervals, multiplication of the epithelium becomes less intense. In the remaining lobe, the height of the epithelium increases, and the metabolic processes between the follicular epithelium and the colloid become more active. The increase in the amount of epithelial tissue and the height of the epithelium leads to a shift in the relationship of the colloid and epithelium in favor of the epithelium; the area occupied by the latter increases.

Compensatory hypertrophy is also characterized by more intense formation of new follicles, which originate via different pathways and lead to a marked increase in the amount of functioning tissue and a reorganization of the gland's structure into a microfollicular type.

SUMMARY

The right lobe of the thyroid gland was removed in male rats, weighing 225 g; 8-16 days after the operation the weight of the remaining left lobe constituted 70%, and in 21-31 days, about 86% of that of the whole gland of

the control animals. The area, occupied by the epithelium, increased from 55 to 68% as compared to the colloid and stroma. The amount of microfollicles increased from 11.9 to 32-38%. The height of the follicular epithelium and the number of mitoses increased in the remaining lobe of 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.
