FORMS OF DEVELOPMENT OF REGENERATION IN THE THYROID GLAND OF ALBINO RATS

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Many internal organs of mammals have been shown to be capable of regenerating in different ways, notably by regeneration from the wound surface and by regeneration hypertrophy [7].

The processes of histogenesis in the residue of the thyroid gland after experimental resection have been studied in considerable detail [2,5,8]. It is not yet clear, however, what are the possible forms and ways of development of regeneration, and by what factors it may be influenced. For instance, in addition to the view that regeneration of the thyroid may take place by a compensatory outgrowth from the wound surface [2], the opinion is held that only slight regeneration takes place in the region of the operation wound, and that regeneration hypertrophy takes place in the residual parenchyma [4]. It has thus been demonstrated that regeneration of the thyroid may take the form of either a typical regeneration or a regeneration hypertrophy, expressed by a profound reconstruction of the parenchyma of the gland.

The object of our research was to discover the significance of different functional states of the thyroid gland in determining which form of regeneration – regeneration hypertrophy or regeneration from the site of injury – takes precedence in the thyroid gland of albino rats, and to study the influence of the thyroid hormone on this process.

EXPERIMENTAL METHOD

Experiments were conducted on 88 young male rats weighing 100-200 g. A bilateral resection of one-third of the thyroid was performed on all the animals, which were divided into four series. The animals of the control series were subjected to the operation only. A state of hypothyroidism was induced in the animals of the second series by administration of 6-methylthiouracil (10 mg/100 g body weight/day), and hyperthyroidism in the animals of the third series by administration of thyroidin (10 mg/100 g body weight); the animals of the fourth series received 6-methylthiouracil and thyroidin (10 mg/10 g body weight each) alternately, each preparation being given for 4 days. Each series of animals except the control was divided into two groups: the animals of the first group received the preparations for 10 days before and 30 days after the operation, and the animals of the second group only for 10 days before the operation.

The operation was performed at the same time of day in sterile conditions and under general anesthesia with 10% hexanastab (hexobarbital soluble) solution, injected intramuscularly in a dose of 0.3-0.4 ml. After the operation the animals were sacrificed at the same time of day on the following and the 2nd, 3rd, 5th, 15th, and 30th days. The thyroids were fixed in Bouin's fluid. Sections were cut to a thickness of 6-7μ and stained with azan and iron hematoxylin.

We studied the microscopic structure and development of the regenerating thyroid in the region of the operation wound and in the uninjured part. The degree of regeneration present in these zones was estimated by counting the mitoses in the cells of the gland (3000 cells in each zone). The results of the counts in each series were treated by statistical methods.

EXPERIMENTAL RESULTS

A systematic examination of histological preparations of the thyroid glands after the operation on the animals of the control group showed the presence of regeneration both at the wound surface and throughout the parenchyma of the gland. This was demonstrated by the appearance of mitotic division among the parenchymatous cells both in the

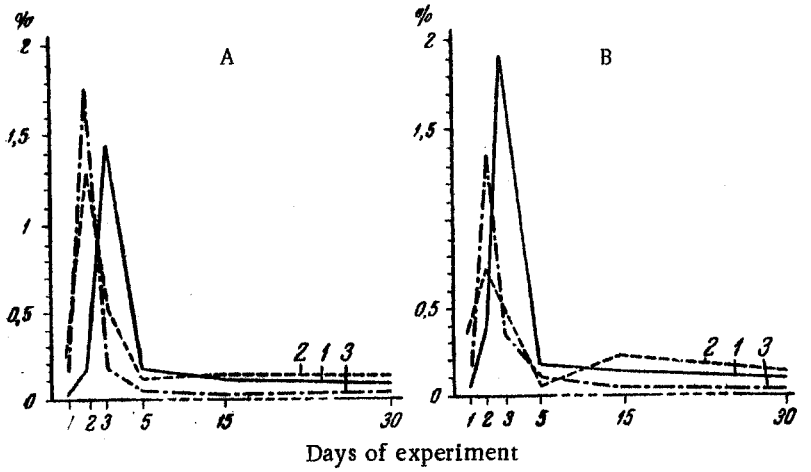

Fig. 1. Change in the mitotic activity of the follicular epithelium of the thyroid gland in the animals of the second series. A) Zone in the center of the uninjured part of the thyroid; B) zone of the operation wound in the gland. 1) Control; 2) 6-methylthiouracil before and after operation; 3) 6-methylthiouracil before operation.

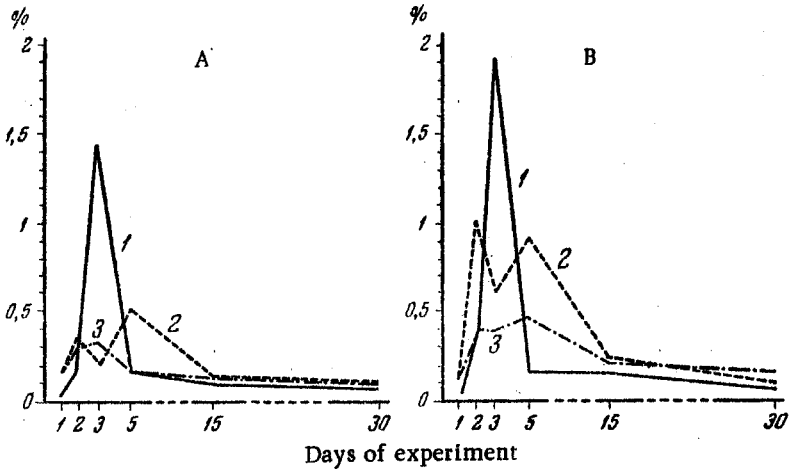

Fig. 2. Change in the mitotic activity of the follicular epithelium of the thyroid in the animals of the third series. A, B) As in Fig. 1. 1) Control; 2) thyroidin before and after operation; 3) thyroidin before operation.

zone of the operation wound and in the center of the uninjured part of the thyroid. The maximal number of mitoses in both zones was observed on the 3rd day after operation (Fig. 1). On the 5th day the mitotic activity fell sharply almost to the initial level, and it remained on practically the same level thereafter until the end of the experiment. The difference between the levels of mitotic activity of the glandular cells in the area of the operation wound and in the uninjured area of the thyroid was not statistically significant.

It must be pointed out that the increase in mitotic activity in the parenchymatous cells in both zones coincided in time with the development of reactive inflammation in the injured part of the gland. This observation confirmed I. A. Alov's suggestion [1] that the protein products of incomplete tissue destruction after injury to an organ stimulate cell division.

Hence, in the normally functioning thyroid, in response to bilateral resection of one-third of the gland, both regeneration hypertrophy and regeneration from the site of injury developed to an equal degree.

A different picture was observed during regeneration of the thyroid in a state of functional strain. Regeneration from the wound surface at the site of resection was very slight in degree, and the reactive inflammation was more

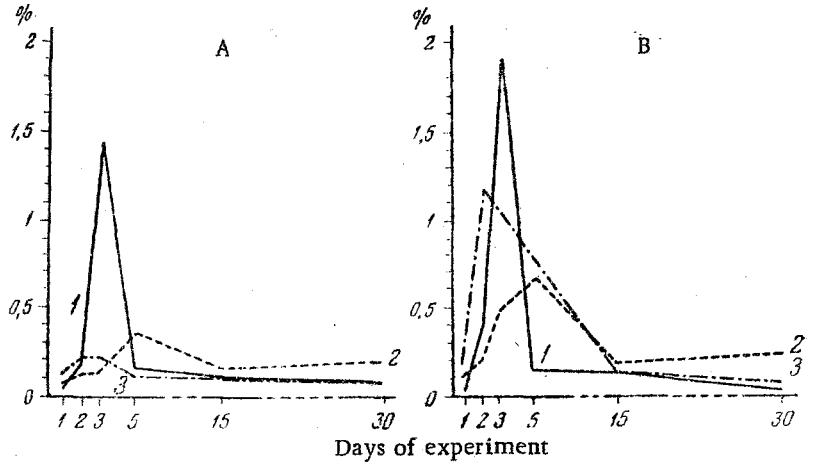

Fig. 3. Change in the mitotic activity of the follicular epithelium of the thyroid in the animals of the fourth series. A, B) As in Fig. 1. 1) Control; 2) 6-methylthiouracil and thyroidin before and after operation; 3) 6-methylthiouracil and thyroidin before operation.

protracted in its course. The maximum of mitotic activity both in the center of the uninjured part of the gland and in the region of the operation trauma took place on the second day after the operation (see Fig. 1). If administration of 6-methylthiouracil was discontinued after the operation, the same mitotic activity was observed in the center of the thyroid as when the drug was given before and after the operation; however, in the region of the wound surface of the gland the mitotic activity was higher on the second day than when administration of 6-methylthiouracil was continued. Although discontinuing the administration of 6-methylthiouracil favored the development of regeneration from the wound surface, the process of regeneration as a whole was far less advanced in this series than in the control animals.

Consequently, if the thyroid gland was in a state of functional stress, its mitotic activity in the region of the operation wound was less intensive than in the normally functioning gland before the operation, and this was shown by the practical absence of inflammation in this region. The process of regeneration in the functionally strained thyroid thus predominantly followed the pattern of regeneration hypertrophy, for in the uninjured part its mitotic activity was high, and the formation of new follicles was observed.

Regeneration of the thyroid gland in a state of hypofunction as a result of the action of exogenous thyroidin, and showing considerable atrophic changes, took place as follows in response to the removal of one-third of each lobe. Whereas in the region of the operation wound of the gland increased mitotic activity was observed from the 2nd to the 5th day after operation, the activity in the uninjured part of the thyroid was significantly lower (Fig. 2).

Discontinuing the administration of thyroidin to the animals after the operation not only did not lead to an increase in the mitotic activity of the glandular cells, but was accompanied by a decrease in activity both in the region of the wound surface and in the uninjured part of the thyroid.

Hence, regeneration of the glandular tissue of the thyroid when in a state of hypofunction, when the animal was saturated by administration of exogenous thyroidin, took place mainly by regeneration from the wound surface.

In animals receiving alternately 6-methylthiouracil and thyroidin, the thyroid (judging from the morphological evidence) was in a state of moderate functional excitation. Administration of the drugs before and after the operation was accompanied by an insignificant increase in mitotic activity in the uninjured part of the gland until the 5th day after operation (Fig. 3). In the region of the operation wound a greater increase in mitotic activity was observed, reaching its maximum on the 5th day after operation. If the alternate administration of the drugs was limited to the preoperative period, a very slight increase in mitotic activity was also observed in the center of the gland, but in the region of the operation wound it reached a maximum on the second day and then fell to the 15th day after operation (see Fig. 3).

The following conclusions may be drawn from the facts we have described. The thyroid hormone, which in general stimulates regeneration in injured organs and tissues [6, 9, 10], also stimulates regeneration in the region of the operation wound in the thyroid when the function of the gland is suppressed by exogenous thyroidin. Excess of

thyroidin, however, causing atrophic changes in the thyroid, does not promote regeneration hypertrophy in the uninjured part of the gland. It was evidently this fact which led certain researchers [11, 12, 13] to consider that thyroid hormone is an antimitotic factor. A hypothyroid state (caused by administration of 6-methylthiouracil) in association with functional stress of the thyroid affected regeneration in such a way that in the part of the gland not functioning (the region of reactive inflammation) there was no reperative regeneration. At the same time, however, it is evident that thyroid hormone was not necessary for the process of regeneration hypertrophy to take place in these same conditions in the uninjured part of the thyroid gland.

It may thus be postulated that the character of the response of the thyroid to injury, i.e., the development of one or other mode of regeneration, is determined both by the presence of thyroid hormone in the body and by whether or not the part of the gland in which regeneration is taking place is functioning, or whether it is the seat of reactive inflammatory changes as a result of the injury.

Thyroidin deficiency leads to marked inhibition and retardation of inflammatory processes at the site of the operation wound, but does not prevent the development of regeneration hypertrophy in the whole mass of the thyroid gland. Excess of exogenous thyroidin in the body, which suppresses the function of the thyroid gland itself, does not prevent the development of regeneration processes from the wound surface, but it does depress the development of regeneration hypertrophy in the bulk of the gland.

If injury to the thyroid is not accompanied by a change in the thyroidin concentration in the body, both regeneration hypertrophy and regeneration from the wound surface may take place.

SUMMARY

Regenerative processes in the thyroid gland of albino male rats pursue mainly the course of regenerative hypertrophy following resection of one-third of both lobes and methylthiouracil administration; regeneration of the resected area is but insignificant. This may be assessed by the topography of mitoses and the intensity of mitotic activity. In the thyroid gland of the thyroidin-treated rats a regeneration set in at the site of injury, since here a high mitotic activity of the gland was present. Regenerative hypertrophy was practically absent in its uninjured portion.

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