REGENERATION OF THE THYROID IN HYPOPHYSECTOMIZED RATS

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Extirpation of the hypophysis is accompanied by significant morphological changes in the thyroid tissue, as described by several writers [1, 4, 7, 8]. Because of the current importance of the problem of the regeneration of thyroid tissue, the experimental study of this problem in hypophysectomized animals is of particular interest. We have studied the regeneration of the thyroid in 60 male albino rats weighing between 85 and 125 g, after removal of the hypophysis.

EXPERIMENTAL METHOD

Three groups of rats were used in the experiments. Hypophysectomy was performed on the animals of the first group, those of the second group remained intact, and in the rats of the third group (controls) the skull was trephined (but without interference to the hypophysis). Half the right lobe of the thyroid was resected in all the rats, at the same time as hypophysectomy was performed. The hypophysis was removed by the paratracheal vacuum method as modified by Bagramyan and Sakhatskaya [2]. After the operation the rats were kept in heated cages at 28-30°. The animals were sacrificed 5, 10, 15, 18, 20, and 30 days after the operation. After extraction, the thyroids were weighed on torsion scales and then fixed in 10% formalin or Bouin's fluid, and embedded in paraffin wax. Sections were stained with hematoxylin-eosin, and with azocarmine by Heidenhain's method; polysaccharides were detected by the PAS reaction. The hormones in the thyroid glands were estimated by biological tests on tadpoles of tailless amphibians (Rana esculenta) by Voitkevich's method [3], with a parallel histological control.

EXPERIMENTAL RESULTS

After hyposectomy, the thyroids of the rats underwent marked atrophy. In the control animals the thyroid consisted of follicles of different sizes, mainly average. The wall of the follicles was formed of cubical epithelium. The colloid in most follicles was intensively vacuolated and gave a strong PAS-positive reaction. The liquid colloid contained in the follicles stained pale blue with azan, and the coagulated colloid stained red.

In the hypophysectomized animals the thyroids were anemic and reduced in size and weight. The follicles in the residual part of the gland and in the opposite lobe were distended by the accumulation and delayed elimination of colloid; as a result they were greatly increased in size. The thyroid epithelium was flattened. The cell nuclei were compact, flat, and intensively stained. Individual follicles had ruptured and were replaced by connective tissue. The colloid was strongly oxyphilic, dense, and dark red in color when stained with azan, and showed a stronger PAS positive reaction than in the controls.

The thyroid hormones were estimated on the eighteenth day after operation by implantation of pieces of the gland (1 mg) into the abdominal cavity of tadpoles. The results of these tests showed that the mean biological activity (difference between rate of resorption of larval organs expressed as a percentage of control values) of the regenerating lobe of the gland in the control animals was 60.9% and in the hypophysectomized animals it was slightly lower—43.3%.

Regeneration of the thyroid tissue was studied in the animals of all the experimental groups in relation to the times at which the material was taken. Regeneration was studied in the residual part of the gland, especially in the region of injury.

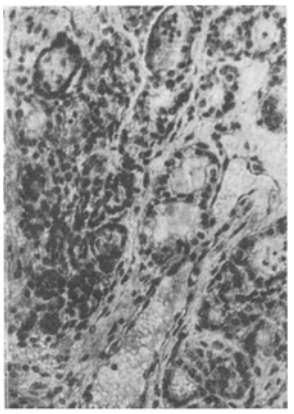

Fig. 1. Intensive formation of new follicles 10 days after partial thyroidectomy in a control animal. 240x.

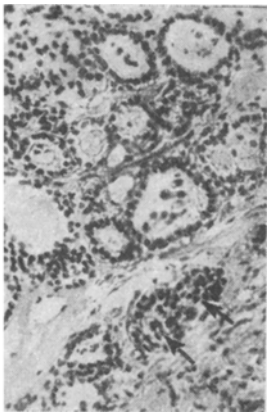

Fig. 2. Solitary follicles in the course of formation in the zone of injury 10 days after hypophysectomy and simultaneous partial thyroidectomy. 240x.

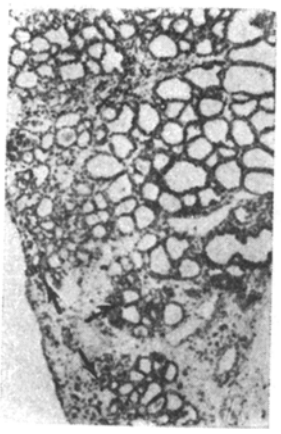

Fig. 3. New thyroid tissue in the zone of injury (indicated by arrow) 20 days after partial thyroidectomy in a control animal. 72x.

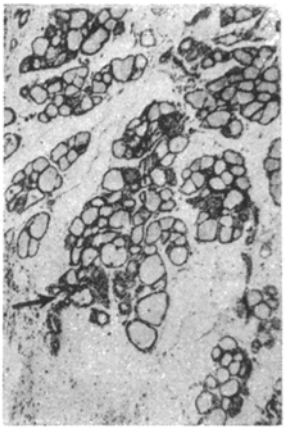

Fig. 4. Solitary new follicles in the zone of injury 20 days after hypophysectomy and simultaneous partial thyroidectomy. 72x.

In the control rats 5 days after resection of the thyroid the region of injury was observed to be invaded by epithelial cells, which began to be grouped into small follicles. The thyroid cells formed into follicles had large nuclei, poor in chromatin, and a weakly oxyphilic cytoplasm. Migration of epithelial cells took place from the injured follicles and interfollicular islets. The movement of thyroid cells into the region of injury was favored by the stream of migrating mesenchymal cells, which set the epithelial cells in motion. The connective-tissue cells also supplied the new thyroid tissue with nutriment. Besides fibroblasts, the young connective tissue of the zone of injury contained numerous histiocytes, lymphocytes, and cells with granules of hemosiderin. In the area of the gland next to the zone of injury dilated blood vessels were observed. In the zone of injury and at a distance from the wound surface, solitary mitoses were observed among the thyroid cells.

In the hypophysectomized animals the region of injury was invaded by a few epithelial cells. In the areas of the gland next to the wound surface atrophic changes were observed. In the residual part of the gland and in the zone of injury no cells undergoing mitotic division were encountered.

In the control animals on the tenth day after the operation intensive formation of new follicles was observed in the zone of injury (Fig. 1). The young developing follicles already contained cavities filled with a weakly oxy-

philic colloid, giving a PAS-positive reaction. At this period mitoses were observed in the residual part of the gland and the zone of injury among the ordinary thyroid cells. In parts of the gland remote from the wound surface small follicles were found, formed by cells of the interfollicular islets. By the tenth day the signs of inflammation had subsided, the leukocytes were fewer in number, but the blood vessels remained dilated.

At the same period, in the hypophysectomized animals the residual part of the gland showed marked atrophic changes. No mitoses were observed among the thyroid cells in the gland. Microfollicles were observed very rarely. In the region of injury the regenerative processes were severely retarded: only a few thyroid cells and developing follicles could be seen (Fig. 2).

On the twentieth day after the operation the region of the defect in the control animals was filled with new follicles and connective tissue, rich in collagen fibers (Fig. 3). The young follicles were distinguishable from the old by their small size and their less oxyphilic, vacuolated colloid. In the residual part of the gland small follicles were present along with those of medium size. By the twentieth day the formation of thyroid tissue was incomplete: in the region of injury small developing follicles could still be seen.

On the thirtieth day follicle formation was largely complete in the zone of injury. The newly formed follicles were larger in size and filled with oxyphilic colloid. The gland was surrounded by a connective-tissue capsule.

On the twentieth and thirtieth days after operation the residual part of the gland in the hypophysectomized animals showed severe strophic changes. It consisted of large follicles filled with dense, oxyphilic colloid. The thyroid epithelium was greatly flattened. The regenerative processes were severely depressed. In the zone of injury solitary new follicles were observed (Fig. 4).

In the rats in which only the skull was trephined (without removal of the hypophysis), the course of the regenerative processes in the thyroid tissue was mainly the same as in the controls. The trauma itself had no significant effect on the course of regeneration in the thyroid.

The experimental results showed that hypophysectomy leads to changes in the structure and function of the thyroid; markedly atrophy of the gland and destruction of the follicles were observed. The colloid present in the distended follicles was imperfect, for it possessed weak hormonal activity, as shown by biological tests on tadpoles. The thyroid was in a state of marked hypofunction. This is also confirmed by the well known experiments using radioactive iodine as indicator [5, 6].

The thyroid, when the seat of structural and functional changes, possesses weak powers of regeneration. In hypophysectomized rats the degree of regeneration of the thyroid tissue is insignificant. Further experiments on hypophysectomized animals followed by compensation with different hormones will help to elucidate which of the hormones of the anterior lobe of the hypophysis (ACTH or TCH) is responsible for regenerative processes in the thyroid gland.

SUMMARY

Following a simultaneous excision of the hypophysis and half of the right lobe of the thyroid a study was made of regeneration of the gland in 60 young male rats. The thyroid was investigated 5, 10, 15, 18, 20 and 30 days after the operation. A marked atrophy of the residual part of the thyroid was seen in the hypophysectomized animals. Colloid contained in the dilated follicles possessed relatively weak hormonal activity in biological tests on tadpoles. In conditions of hypophysectomy processes of regeneration in the area of injury show marked inhibition and only individual follicles are formed anew.

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