on account of hypertrophy of the pericytes and perivascular connective tissue cells, sometimes surrounding the capillary in a ring. The lumen of these vessels was constricted and the pinocytotic activity of the endothiocytes reduced (Fig. 2e).

Ultrastructural study of the myocytes in areas of subsarcolemmal invaginations revealed separation and partial lysis of the myofibrils. Numerous lipid inclusions were found in other muscle fibers beneath the sarcolemma and in the thickness of the fiber.

The changes in the skeletal muscle of the experimental animals revealed histologically, histochemically, and electron-microscopically, when related to the duration of AD, thus indicate that changes in vessels of the microcirculatory bed correspond to those typical of diabetic microangiopathies. They are manifested as increased vascular permeability, congestion, intravascular aggregation of erythrocytes, and perivascular and tissue edema. In long-standing diabetes, these changes are joined by thickening of the vascular walls due to widening of the basement membranes and their permeation by PAS-positive material, and hypertrophy of the pericytes and smooth-muscle and adventitial cells. Ofter these changes are accompanied by a decrease of vascular permeability. Changes described in the muscle fibers are observed only in the case of long-standing AD and they are most probably secondary, caused by disturbances of the microcirculation and of vascular permeability. Proliferation of adipose tissue resembles the deposition of fat in vacant spaces when lipid metabolism is disturbed in AD.

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COMPENSATORY AND REPAIR PROCESSES IN THE THYROID GLAND OF MONTH-OLD DESYMPATHIZED RATS

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It is well known that proliferative activity of the thyroid parenchyma is induced by hypothalamic influences through thyrotrophin (TSH), secreted by the adenohypophysis [4, 7, 9]. This pathway is not the only possible mode of action on mitotic activity of the thyroid epithelium, which is certainly under the control of other regulatory factors [1, 3, 5, 10]. Every year our ideas on the character of the course of thyroid gland (TG) regeneration in different functional states of the autonomic nervous system are widened. However, insufficient attention has been paid to the study of the rôle of the sympathetic nervous system,

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TABLE 1. Comparative Rates of Regeneration of TG in Normally Developing and Partially Desympathized Rats after Resection of Two-Thirds of the Gland (M ± m)

Parameter	Group of animals	Without recessation	Subtotal thyroidectomy, time before sacrifice of animals, days: 3	5	7	15
Height of thyrocytes, μ	Control	11,3±0,1 (100)	13,1±0,1* (115,7±1,1)	14,10±0,1* (123,7±1,1)	13,2±0,2* (117,0±1,7)	11,1±0,2 (97,8±1,5)
	Exptl.	8,9±0,2* (100)	12,2±0,1** (136,1±1,6***)	12,2±0,2** (136,3±2,2***)	12,0±0,2** (133,9±2,2***)	10,8±0,2** (121,2±1,9***)
SRI ($\cdot 10^{-1}$), μ^{-1}	Control	2,5±0,1 (100)	10,2±0,9* (401,6±34,2)	11,4±0,1* (447,6±43,7)	6,58±0,7* (259,1±26,4)	3,5±0,3* (139,4±11,8)
	Exptl.	1,7±0,4* (100)	5,7±0,6** (343,9±33,7)	5,31±0,54** (319,3±32,53***)	5,3±0,6** (318,1±36,1)	4,1±0,5** (244,6±30,1***)
MI, %	Control	13,9±1,0 (100)	34,0±1,6* (244,8±11,7)	36,0±1,4* (258,3±10,4)	31,0±1,4* (223,5±10,3)	24,6±1,5* (177,2±10,6)
	Exptl.	17,4±1,0* (100)	53,3±2,4** (306,2±13,6***)	58,2±3,0** (334,2±17,2***)	55,7±2,1** (319,7±11,8***)	35,4±2,1** 203,2±11,9
RI, %	Control	16,1±1,1 (100)	24,5±0,9* (152,5±5,8)	24,4±0,9* (151,8±5,8)	20,8±0,7* (129,6±4,7)	16,9±0,8 (105,5±5,3)
	Exptl.	24,3±1,0* (100)	42,1±1,7** (173,2±7,1)	34,8±1,2** (143,7±5,0)	31,3±1,0** (128,8±4,2)	25,0±1,1 (102,9±4,4)

Legend. Percentage of value for corresponding experimental group without resection given in parentheses. *$p < 0.05$ compared with control group without resection, **$p < 0.05$ compared with experimental group without resection, ***$p < 0.05$ compared with control group at corresponding times after resection.

phylogenetically older than the transhypophyseal system, in the regulation of regeneration of TG after partial thyroidectomy.

The aim of the present investigation was to study the rates of regeneration of TG at different times after resection of two-thirds of the gland in normally developing and partially desympathized rats.

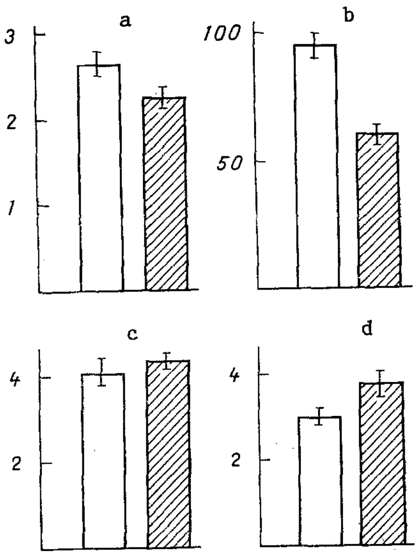
EXPERIMENTAL METHODS

Experiments were carried out on 100 noninbred male rats aged 1 month. For the first 14 days after birth the experimental animals received a solution of guanethidine (Isobarin, from Pliva, Yugoslovia) in a dose of 15 mg/kg by daily subcutaneous injection. Physiological saline was injected into the remaining rats. The animals were killed under superficial ether anesthesia 3, 5, 7, and 15 days after subtotal thyroidectomy. TG and the cranial cervical sympathetic ganglion (CCSG) were fixed in Bouin's and Carnoy's fluids and embedded in paraffin wax; serial sections were cut to a thickness of 4-5 μ and stained with hematoxylin and eosin (for TG) and with methylene blue (for CCSG). To verify the partial sympathectomy, the number of neurons with a clearly outlined nucleus was counted in every 5th section through CCSG. The results were aggregated and the value obtained was used as an indicator of the number of nerve cells in the ganglion.

Repair processes in TG after resection of two-thirds of the gland were evaluated quantitatively by studying the time course of the gravimetric parameters of the gland, the height of the thyroid epithelium, and the value of the stereologic resorption index (SRI). Proliferative activity was assessed as the ratio of the number of mitotically dividing cells to the total thyrocyte population (mitotic index – MI) and according to data of autoradiography with ^{3}H-thymidine (the radiologic index – RI). For the electron-microscopic investigation small fragments of the glands were fixed in glutaraldehyde, postfixed in OsO_4, and embedded in Epon-Araldite M. Ultrathin sections were stained with uranyl acetate and studied in the JEM-7A microscope. Serum levels of tri-iodothyronine (T_3) and thyroxine (T_4) and the TSH concentration in the pituitary gland were determined in all the experimental groups by means of commercial kits (Byk-Mallinckrodt, West Germany).

EXPERIMENTAL RESULTS

Adminsitration of guanethidine by the schedule mentioned above caused depopulation of nerve cells in the rat CCSG. The number of nerve cells in the experiment was 1025 ± 277 compared with 5648 ± 682 in the control ($p < 0.005$). An increase in the relative density of the connective-tissue component was observed in TG of the partially desympathized animals,



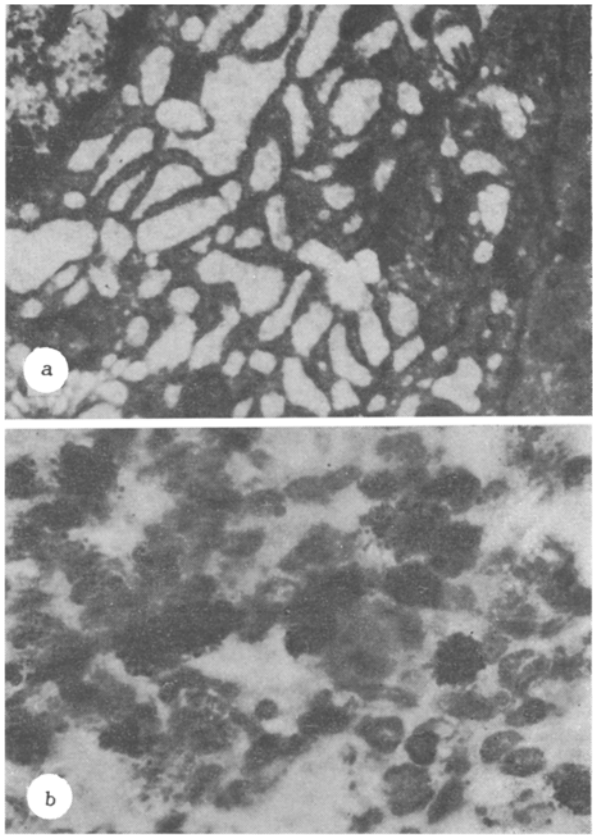


Fig. 1   Fig. 2

Fig. 1. Parameters of hormonal activity of TG and the adenohypophysis of normally developing and desympathized rats. a) T_3 (in nmoles/liter); b) T_4 (in nmoles/liter); C) TSH (in μg/liter); d) T_3/T_4 (in conventional units $\times 10^{-2}$). Unshaded columns) control; shaded) experiment.

Fig. 2. TG of desympathized animals on 3rd day after resection of two-thirds of the gland. a) Large concentration of DNA-synthesizing cells in follicle wall (magnification: ocular 10, objective 90; stained with Mayer's hematoxylin). b) Fragment of cytoplasm of a thyrocyte with dilated cisterns of endoplasmic reticulum and with accumulation of mitochondria (12,800×).

due to hyperemia of the gland, arising as the result of the reduced adrenergic innervation of the vessel walls. Morphometric analysis of the gland showed a marked decrease in SRI and in the average height of the thyroid epithelium compared with the control (Table 1). Histologically, edema of the stroma and individual swollen thyrocytes with signs of cloudy-swelling degeneration were found in the gland. The changes described were focal in character and did not extend to most of the cells, in which invagination of the nuclear membrane and dilatation of the cisterns of the endoplasmic reticulum were observed under the electron microscope.

The T_3 and T_4 levels in the blood serum of the experimental rats were lowered (Fig. 1a, b). Since the plasma TSH concentration of the desympathized animals did not differ significantly from the control (Fig. 1c), this suggests a change in the processes of interaction between the adenohypophysis and TG. Deiodination of T_4 was considerably intensified under these circumstances (Fig. 1d). We know that T_3 has activity 5-6 times greater than T_4, and that its turnover is 2 or 3 times faster [2]. Thus an increase in conversion of T_4 into T_3 after desympathization is a compensatory reaction, aimed at maintaining effective influences of thyroid hormones on target cells.

Resection of two-thirds of TG was followed in the initial postoperative period by restructuring of all the remaining parts of the gland, as shown by new follicle formation and activation of proliferative processes. MI and the number of DNA-synthesizing cells rose significantly as early as on the 3rd day after the operation (Table 1). Preparation of the

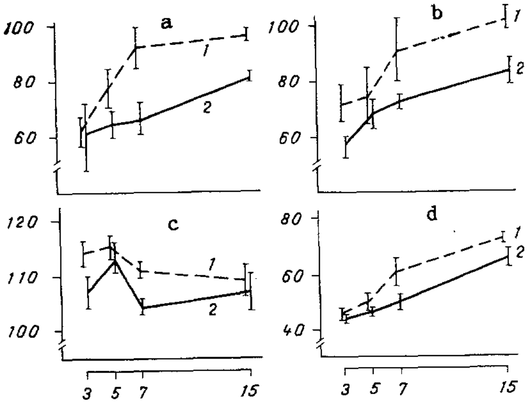


Fig. 3. Time course of regenerative changes in T_3 (a), T_4 (b), TSH (c), and gravimetric parameters of TG (d) of control and partially desympathized rats at different times after subtotal thyroidectomy. Abscissa, times of resection (in days); ordinate, percentage of parameter for corresponding experimental group without resection. Continuous line represents animals with intact sympathetic nervous system, broken line – desympathized rats.

cells to divide and cell proliferation were observed more clearly in the zone of resection, where "new" tissue was being formed. However, in the remaining part of the gland also, the number of DNA-synthesizing and dividing thyrocytes was increased. The marked reduction of density of colloid, and the increase in SRI and the mean height of the thyroid epithelium are evidence of the development of compensatory and repair processes in the gland.

After desympathization repair processes in TG after resection of two-thirds of the gland took place just as in normally developing rats, by regenerative hypertrophy. The number of DNA-synthesizing and mitotically dividing cells in the residual part of the denervated TG was significantly increased (Table 1; Fig. 2a). The thyroid epithelium was hypertrophied, the tubules of the endoplasmic reticulum dilated (Fig. 2b), and a large concentration of mitochondria and droplets of intracellular colloid was observed. Comparison of the serum T_3 and T_4 levels in the partially desympathized rats after resection of TG with the corresponding parameters in animals with an intact sympathetic nervous system showed an increase in the rate of rise of the concentration of thyroid hormones in the blood, especially seven and 15 days after thyroidectomy, preceded by desympathization (Fig. 3a, b). This latter effect may be due both to the stronger thyrotrophic activity of the pituitary (Fig. 3c) and to intensified cell proliferation followed by an increase in weight of the gland (Fig. 3d).

The study of the course of repair of TG after partial thyroidectomy in normally developing and desympathized rats showed that the changes observed followed a similar course. However, the degree of realization of the regenerative powers of the denervated TG was considerably higher. In the intact animals, the sympathetic nervous system thus has an inhibitory influence on proliferative activity of TG. With a marked degree of reduction of the sympathetic innervation of the gland, repair processes in TG take place much more rapidly.

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