REFERENCES

1. N. I. Dmitrieva, Arkh. Anat., No. 1, 106 (1978).
2. N. I. Dmitrieva and V. G. Kassil', Arkh. Anat., No. 9, 84 (1982).
3. L. D. Devenport and I. A. Devenport, Physiol. Psychol., **10**, No. 4, 399 (1982).
4. M. A. Warren and K. S. Bedi, J. Comp. Neurol., **210**, 59 (1982).

STRUCTURE AND FUNCTION OF THE THYROID GLAND AFTER THYMECTOMY

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The opinion has frequently been expressed in the literature that the thymus has a pathogenetic role in the development of diseases of the thyroid gland [1, 4]. At the beginning of this century satisfactory results of treatment of Basedow's disease by thymectomy were described [11]. However, experimental data on the effect of thymectomy on thyroid function are sporadic, in some cases the experiments were conducted by methods that are difficult to compare, and on animals of different species and age, besides which the times elapsing after the operation differed. These investigations confirm the view that it is unacceptable to describe interaction between the thymus and thyroid gland in terms of an "increase" and "decrease," for the processes concerned run a phasic course [2, 7, 9].

The aim of this investigation was to detect structural and functional changes in the thyroid gland after thymectomy on mature rats and to examine their time course.

EXPERIMENTAL METHOD

Experiments were carried out on 110 noninbred male albino rats weighing 120-130 g. Thymectomy was performed by the usual method [10]. The radical nature of the operation was confirmed visually and histologically. Intact animals and rats undergoing a mock operation served as the control. The mock operation included all the steps of thymectomy except the last stage, namely removal of the thymus. The animals for investigation were killed by decapitation in the winter period, at the same time of day, and 1, 2, 3, 6, and 12 months after thymectomy. Total concentrations of thyroxine (T_4) and tri-iodothyronine (T_3) in the blood serum were determined by the use of kits from "Byk-Mallinckrodt" (Germany) and kits of USSR/CIS origin for radioimmunoassay (Institute of Bioorganic Chemistry, Academy of Sciences of the Belorussian SSR – now Belarus' – Minsk). For morphologic investigation the thyroid gland was fixed in a 12% solution of neutral formalin and in Carnoy's fluid. Dewaxed sections were stained

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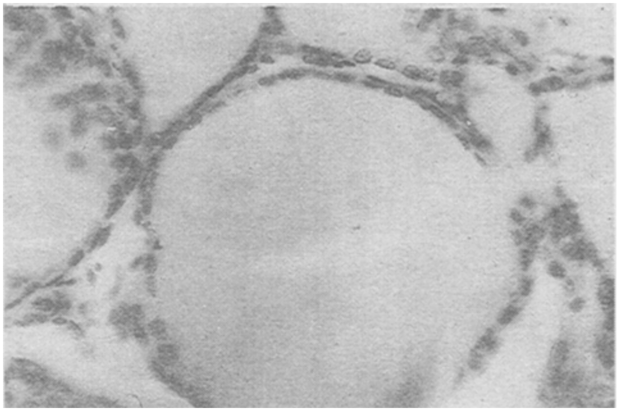

Fig. 1. Thyroid gland of mature rats 2 months after thymectomy. Enlarged follicle containing homogeneous colloid, thyrocytes flattened. Hematoxylineosin, 500×.

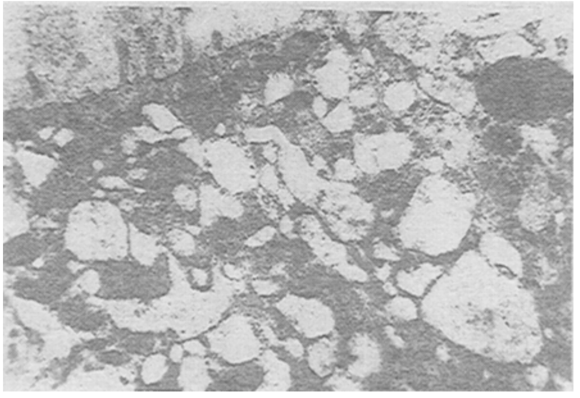

Fig. 2. Thyroid gland 2 months after thymectomy. Concentrations of colloid in cytoplasm of thyrocyte. 11,300×.

with Ehrlich's hematoxylin and eosin, RNA was revealed by Brachet's method and DNA by Feulgen's method. The total protein content in structural components of the tissues was studied by Danielli's method in Shubich's modification [5]. Neutral glycosaminoglycans were studied by the PAS reaction. The height of the thyrocytes and the minor and major diameters of the follicles were determined in survey preparations by means of an MOV-1 × 15 micrometer attached to the BIOLAM-R2 light microscope. The volume of the follicles was calculated by the equation $V = (\sqrt{Dd})^3$, where V is the volume, D the major diameter, and d the minor diameter of the follicle [4]. The results were subjected to parametric statistical analysis by computer and also by the nonparametric Wilcoxon–Mann–Whitney test. Thyrocytes were studied electron-microscopically 2, 6, and 12 months after thymectomy. The electron-microscopic investigation was conducted by traditional methods [6].

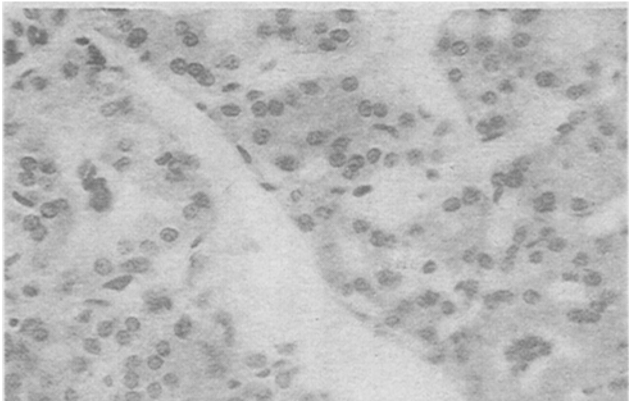

Fig. 3. Thyroid gland 12 months after thymectomy. Necrobiotically changed thyrocytes in lumen of a follicle. Hematoxylin and eosin, 400×.

EXPERIMENTAL RESULTS

Signs of weakening of morphological and functional activity of the thyroid gland begin to develop with effect from the first month after the operation, and increase to the second and third months. This is shown by a progressive increase in volume of the follicles (Table 1), by accumulation of colloid in their lumen, a decrease in height of the thyrocytes (Fig. 1), a fall in the level of protein synthesis and in the total protein content of the cytoplasm of the thyrocytes and islet cells, and also a decrease in the content of neutral glycosaminoglycans in the cytoplasm of the thyrocytes and their accumulation in the colloid. Masses of DNA were distributed uniformly in the karyoplasm of the thyrocytes, except in pycnotically changed, homogeneously stained nuclei, and those with peripheral condensation of DNA. On electron-microscopic study 2 months after the operation secretory granules of different sizes and large inclusions with uniformly granular contents, corresponding in density to colloid, could be detected in the cytoplasm of the flattened thyrocytes (Fig. 2). Cisterns of the Golgi complex (GC) were collapsed, and very few vesicles were present. Condensation of chromatin was observed in the nucleus, and was more marked around the nucleolus and beneath the membrane.

Starting with the first month of observation and for a period of 6 months, a significant fall in the serum thyroid hormone (T_3 and T_4) levels was observed in the thymectomized animals (Table 2). It can be tentatively suggested that depression of thyroid function, which we observed during the first 6 months after the operation, was due to the insufficient thyrotrophic function of the pituitary gland.

A tendency toward recovery of thyroid gland morphology and function was seen 6 and 12 months after thymectomy, after depression of its function, although complete compensation of the existing disturbances did not arise. The volume of the follicles was close to the control value, and the thyrocytes were cubical or high cubical in shape. Desquamated necrobiotically changed thyrocytes were discovered in the lumen of some follicles more often than in the control (Fig. 3). Concentrations of RNA, total proteins, and neutral glycosaminoglycans in the thyrocytes and islet cells remained low, although higher than at previous times of observation. On electron-microscopic investigation after 6 and 12 months a few microvilli were found on the apical parts of the thyrocytes. The apical parts of most thyrocytes were saturated with secretory granules of different sizes. The volume of the cisterns of the endoplasmic reticulum was reduced. GC was poorly developed. In some thyrocytes the mitochondria were swollen, with widened intracristal spaces. The changes described above were more marked 12 months after the operation.

TABLE 1. Volume of Follicles and Height of Thyrocytes of Thyroid Gland of Mature Rats at Different Times after Thymectomy

Iime after thymeccomy (months)	Volume of follicles (in μm^3)		Height of thyrocytes (in μm)	
	control (intact animals)	experiment	control (intact animals)	experiment
1	41 045±1278	81 564±3050*	9,99±0,010	6,64±0,17*
2	43 270±1085	127 375±3074*	8,1±0,05	4,59±0,008*
3	45 000±1068	119 854±2041*	8,41±0,077	5,63±0,03*
6	56 375±1124	52 654±1238 $p<0{,}005$	7,2±0,04	5,4±0,06*
12	57 772±1100	58 838±1027 $p>0{,}05$	7,11±0,04 $p<0{,}001$	5,73±0,09*

TABLE 2. Time Course of Serum Total Thyroxine and Total Tri-iodothyronine Levels of Mature Male Rats after Thymectomy

Experimental groups of animals	Thyroxien (in μg/100 ml) Time after thymectomy (months)					Tri-iodothyronine (in ng/100 ml) Time after thymectomy (months)				
	1	2	3	6	12	1	2	3	6	12
Intact – I	5,0±0,7	3,4±0,3	3,5±0,2	4,3±0,4	3,6±0,3	85±5	75±6	82±4	79±16	85±16
(n)	(6)	(5)	(7)	(9)	(5)	(13)	(6)	(7)	(6)	(5)
Undergoing mock operation – TE	5,5±0,7	3,7±0,4	—	—	—	88±6	77±8	—	—	—
(n)	110	108				103	102			
Thymectomized – TE	5,1±0,4	3,1±0,2	3,1±0,4	4,6±0,9	4,9±0,6	80±4	64±8	74±3	62±8	112±26
(n)	(6)	(5)	(7)	(6)	(5)	(6)	(6)	(8)	(5)	(6)
Per cent of MO (on I)	92	83*	88	106	142*	90*	83*	90*	78*	132*

Legend: n) number of animals in group; *p ≤ 0.05.

The increase in thyroid function toward the end of a year after thymectomy was confirmed by a significant rise of the serum T_3 and T_4 levels in thymectomized rats (Table 2).

Our investigations thus demonstrated the important regulatory role of the thymus. A thymus hormone deficiency in the circulating blood stream after thymectomy evidently modifies secretion of thyrotrophin releasing hormone in the hypothalamus through a feedback mechanism [8], and also the thyroid-stimulating function of the adenohypophysis, which may perhaps lead to marked depression of thyroid function. In our view, stimulation of thyroid function observed 12 months after thymectomy is not central in genesis, but is the result of activation of autoimmune processes in the absence of the thymus.

REFERENCES

1. A. V. Epishin, I. N. Dekailo, and N. A. Epishina, Klin. Med., No. 3, 27 (1986).
2. V. I. Kuznik, N. V. Vasil'ev, and N. N. Tsybikov, Immunogenesis, Homeostasis, and Nonspecific Resistance of the Organism [in Russian], Moscow (1989).
3. S. G. Maine-Avgustinovich, L. V. Gerbil'skii, and V. I. Arkhipenko, Arkh. Anat., No. 6, 106 (1979).
4. O. K. Khmel'nitskii and V. A. Brezhneva, Arkh. Patol., No. 1, 9 (1991).
5. M. G. Shubich, Arkh. Patol., No. 12, 68 (1963).
6. B. Weakley, Electron Microscopy for Beginners [Russian translation], Moscow (1975).
7. J. Comsa, E. Phillipp, and U. Leonardt, Israel J. Med. Sci., **13**, 354 (1977).

8. N. R. Hall, I. P. McGillis, B. L. Spangelo, et al., Neural Modulation of Immunity, ed. by R. Guillemin et al., New York (1985), pp. 169-193.
9. W. Pierpaoli and H. Besedowsky, Clin. Exp. Immunol., **20**, 323 (1975).
10. D. B. S. Racelis, Z. Zisbrod, and H. Schanzer, Mount Sinai J. Med., **47**, No. 3, 289 (1980).
11. S. Taylor, Lancet, **2**, 865 (1964).

ANNIVERSARY G. N. KRYZHANOVSKII (ON HIS 70TH BIRTHDAY)

November 11, 1992 is Georgii Nikolaevich Kryzhanovskii's 70th birthday.

For more than 45 Years G. N. Kryzhanovskii has devoted himself to science, serving at the Institute of General Pathology and Pathophysiology of the Russian Academy of Medical Sciences where he has held posts ranging from Graduate Student to Director of the Institute. G. N. Kryzhanovskii's researches have followed two main directions: general pathology and pathophysiology of the nervous system. As a general pathologist, G. N. Kryzhanovskii has established a number of principles governing activity of biological systems under normal and pathological conditions: the structural and functional discreteness (quantization) of biological processes, the intermittent activity

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