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## RESPONSE OF THE THYROID GLAND TO EXPERIMENTAL PARTIAL AND TOTAL PANCREATECTOMY

R. I. Polyak and V. I. Zvyagintsev

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The terminal or central part of the pancreas was resected or the whole gland removed in dogs. At different times after the operation the morphological and functional state of the thyroid gland was studied by histological, histochemical, and morphometric methods. The changes discovered indicate that structural and functional transformations of the thyroid gland are determined primarily by the type of operation on the pancreas: Resection of the terminal portions causes temporary and slight changes in the thyroid gland, whereas after total pancreatectomy marked degenerative and atrophic changes develop in the glands, leading to a state of functional exhaustion.

KEY WORDS: thyroid gland; partial resection of the pancreas; pancreatectomy.

Functional connections between the thyroid gland and pancreas have frequently been described both clinically and experimentally, but most attention has been paid to the study of the response of the pancreas to hypo- and hyperproduction of thyroid hormones. The direction of adaptation of the thyroid gland and the extent of its reserves in states of partial or total pancreatic deprivation have not been specially studied. Yet such information would be interesting in connection with the study of the rationale of the use of hormones and drugs acting on the thyroid gland after partial and total pancreatectomy.

## EXPERIMENTAL METHOD

Experiments on 50 dogs were carried out by the method described previously [5]. In series I the terminal part of the pancreas was resected (15 dogs); in series II the central part of the pancreas was resected and the main efferent ducts ligated and divided (15 dogs), whereas in series III total pancreatectomy was performed (20 dogs). Between 3 days and 1 year after the operation the dogs were killed and the thyroid gland

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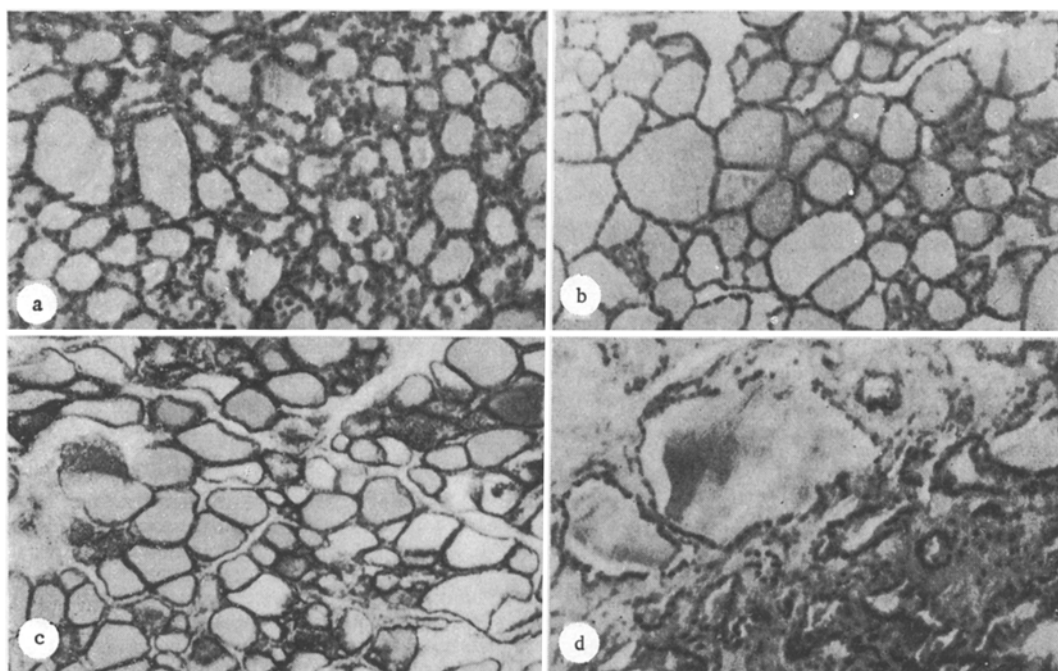


Fig. 1. Thyroid gland of dog: a) intact: equal numbers of small, medium-sized, and large follicles; b) after resection of terminal parts of pancreas: many large irregularly shaped follicles filled with thick colloid; c) after resection of central part of pancreas: large follicles predominate but their maximal diameter is reduced; desquamated thyrocytes present in lumen; connective-tissue septa widened; d) after pancreatectomy: small and medium-sized follicles predominate, some of them deformed, and separated by wide fibrous bands. Hematoxylin-eosin; a, b, c 56  $\times$ ; d 140  $\times$ .

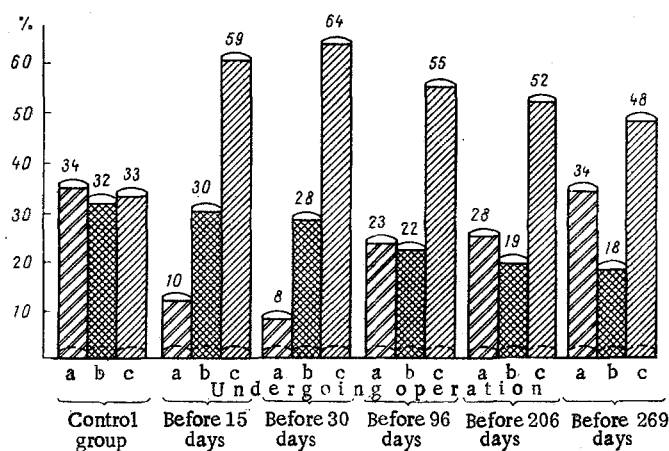


Fig. 2. Relative percentages of small (a), medium-sized (b), and large (c) follicles in thyroid gland of dog after resection of central part of pancreas.

TABLE 1. Morphological and Functional Indices of the Thyroid Gland in Dogs of Control Group and Totally Pancreatectomized Dogs

Group of animals	Time after pancreatectomy, days	Relative proportions of follicles, %			Mean value ( $M \pm m$ )				
		small	medium-sized	large	diameter of follicles, $\mu$	height of thyroid epithelium, $\mu$	BI	index of colloid accumulation	effective surface area of follicles, $\mu$
Control Pancreatectomized	—	34,4	32	33,6	95 $\pm$ 1,8	4,2 $\pm$ 0,1	23,0 $\pm$ 0,9	11,3 $\pm$ 0,4	98,6 $\pm$ 2,0
	to 5	6	32	62	126 $\pm$ 5,4	4,1 $\pm$ 0,07	31,2 $\pm$ 2,6	15,5 $\pm$ 2,3	130,7 $\pm$ 2,1
	to 15	10	40	50	114 $\pm$ 5,0	3,5 $\pm$ 0,08	33,1 $\pm$ 1,8	16,2 $\pm$ 0,9	117,5 $\pm$ 2,5
	to 24	32	34,5	33,5	94 $\pm$ 3,0	3,7 $\pm$ 0,1	25,6 $\pm$ 1,1	12,7 $\pm$ 0,5	98,0 $\pm$ 3,2
	to 33	58	30	12	77 $\pm$ 3,2	3,2 $\pm$ 0,07	24,0	12,0	80,2

measured, weighed, and studied histologically, histometrically, and histochemically. Attention was paid to the color and state of the colloid, its thickness, the presence of vacuolation of fissures, the state of the connective-tissue septa and blood vessels, and the distribution of follicles of large, medium, and small diameter. In 50 follicles of each preparation the diameter of the follicles and the height of the thyroid epithelium were measured in five fields of vision, and Braun's index (BI) [2], the index of colloid accumulation [1], and the effective surface area of the follicles were determined. Sections were stained with hematoxylin-eosin and by Van Gieson's method. The content of acid and alkaline phosphatases (by Gomori's method), RNA (by Brachet's method), DNA (by Feulgen's method), and neutral mucopolysaccharides (by McManus's method) was determined. The numerical results were subjected to statistical analysis.

## EXPERIMENTAL RESULTS

The results showed that structural and functional transformations of the thyroid gland are due primarily to the type of operation on the pancreas. For instance, after resection of the terminal parts of the pancreas follicles of large diameter predominate (47-56%) in the thyroid gland and are filled mainly with dense, intensely stained colloid, sometimes with fissures. In the center, however, follicles of small or medium size were present. There were few resorption vacuoles. BI increased, indicating some decrease in thyroid function. After 3 months the number of small and medium-sized follicles was increased and the colloid was stained more palely. Resorption vacuoles were present. The thyroid epithelium was on average a little higher (Fig. 1). The effective surface of the follicles, BI, and the index of colloid accumulation were similar to the values of these indices in intact dogs. Toward the end of the period of observation the number of follicles of different diameters became equal and the mean diameter of the follicles fell to 102-100  $\mu$ . The number of small follicles increased considerably as a result of the formation of new follicles. The colloid was mainly liquid, pale in color, with frequent vacuoles and many mitoses. The diameter of the nuclei and the height of the thyroid epithelium and BI were indistinguishable from those in the control. The response of the thyroid gland to resection of the terminal parts of the pancreas was thus phasic in character. After the operation function was depressed, but signs of stimulation of function soon appeared in those parts that had been in a state of relative rest; later the thyroid glands entered into the phase of recovery.

The response was different to resection of the central part of the pancreas accompanied by ligation and division of the main efferent ducts. The absolute weight of the thyroid gland decreased but the relative weight increased because of the decrease in body weight. During the first 2 days follicles of large diameter predominated (58-60%), and the mean diameter of the follicles was  $121 \pm 3.1 \mu$ . The colloid was mostly dense and it stained intensely. Resorption vacuoles were few in number. Low epithelium, in places cubical, but higher in others, was seen. There were few mitoses. The mean diameter of the nuclei and the height of the epithelium were reduced a little compared with the control group to  $3.4 \pm 0.3$  and  $4.0 \pm 0.4 \mu$ , respectively. BI was increased to  $30.9 \pm 3.8$ .

A gradual decrease in the mean diameter of the follicles then took place but large follicles still predominated. The index of colloid accumulation and the effective surface area of the follicles both decreased. A further reduction in size of the nucleus and in the height of the colloid epithelium continued. The epithelium was uniform and low. BI fell slowly but still remained fairly high at  $28.8 \pm 2.4$ . There were very few mitoses. Desquamation, degeneration, and necrobiosis of the epithelium were observed. Connective tissue proliferated, deforming the follicles, and seepage of colloid into the stroma could be seen. Later signs of atrophy were clearly manifested.

Total pancreatectomy without replacement therapy caused death of the animals in the course of 3-6 weeks. During the first days large follicles filled with dense colloid predominated (62%) in the thyroid gland (Table 1). The index of colloid accumulation was  $15.5 \pm 2.3$ , the effective surface area of the follicles was  $130.7 \pm 2.1 \mu$ , and BI was high at  $31.2 \pm 2.6$ . Later the majority of follicles were small, often deformed. The mean diameter of the follicles fell to  $77 \pm 3.2 \mu$ , the colloid accumulation index to 12.0, and the effective surface area of the follicles to  $80.2 \mu$ . The nucleus became much flatter and the height of the thyroid epithelium decreased. The mean diameter of the nuclei became  $2.8 \pm 0.07 \mu$  and the height of the thyroid epithelium  $3.2 \pm 0.07 \mu$ . BI was 24.0. Increased desquamation of the epithelium was observed in the glands and its nuclei became pyknotic. Seepage of colloid into the stroma and walls of blood vessels was well marked. Activity of alkaline and, in particular, acid phosphatases decreased, as also did the RNA content in the cytoplasm of the epithelium and in the nucleoli and also the DNA content in the nuclei of the follicular and interfollicular epithelium. Neutral mucopolysaccharides were detected in the colloid as considerable accumulation of PAS-positive material. Changes indicating functional exhaustion developed early in the thyroid gland.

Comparison of the effect of the different types of pancreatic resection on the structure of the thyroid glands shows that after resection of the central part structural changes in the thyroid gland increased, whereas after resection of the terminal parts a recovery phase began at different times in different dogs, and it coincided in time with the development of regenerative processes in the resected pancreas. Incomplete regeneration of the pancreas has been reported on several occasions previously [3, 4, 6]. It was emphasized [4] that the weight of the pancreas after resection was less than its weight in the control. However, this did not take account of the fact that the resections of the dog's pancreas were not equivalent as regards the conditions created after the operation for regeneration [5]. Removal of the central part of the pancreas led to atrophy and sclerosis of the residual areas. After resection of the terminal parts, when the main efferent ducts remained patent, the weight of the residual part of the pancreas, although not reaching its weight in the control, was nevertheless always appreciably greater than the mean weight calculated for that same part. This fact, together with the recovery of the internal and external secretory functions of the pancreas, indicates that under certain conditions (patency of the ducts) the pancreas quite clearly has adequate powers of regeneration. Restoration of pancreatic function and the increase in weight of the residual part of the organ were also accompanied by gradual return of the thyroid gland to its initial morphological and functional state.

The results are evidence that after partial or total pancreatectomy, if attempts are made to influence the functional state of the thyroid gland the type of operation and the time elapsing after the operation must be taken into account.

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