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Comparative Morphometric and Information Analysis of the Changes in Different Parts of the Pancreas Following Ligation

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The compensatory-adaptive changes in the guinea pig exocrine and endocrine pancreas following ligation are studied using morphometric and information methods. Objective criteria for evaluating organ changes are elaborated. The specific features of regeneration in exocrine and endocrine parts of the organ are described.

Key Words: *pancreas; ligation; regeneration*

The regeneration processes taking place in different parts of the pancreas in pathological states have their own specific features, so that the results of regeneration are functionally different [1-3]. For this reason, the rising frequency of insulin-dependent (type I) diabetes and of acute and chronic pancreatitis morbidity makes it imperative to seek new ways of stimulating reparative and compensatory processes in this organ. This applies especially to the endocrine part of the gland, since its function cannot be fulfilled adequately by extrapancreatic mechanisms, in contrast to the exocrine part [1,3].

The goal of this study was to examine regeneration processes in intact and atrophied parts of guinea pig pancreas following ligation that blocked the outflow from two-thirds of the organ.

MATERIALS AND METHODS

The experiment was carried out on 44 guinea pigs (8 intact controls and 6 experimental groups of 6 animals each group). Ligation of the spleen-adjacent part (60-63% of the total organ) was performed under ether anesthesia. Animals were sacrificed under ether 7, 14, 21, 30, 60, and 105 days following the operation. The material was examined using a complex of histological, histochemical, morphometric, and information analysis [2].

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RESULTS

In the healthy endocrine part of the guinea pig pancreas the spleen-adjacent segment ("tail") demonstrates more structural diversity than the duodenal segment ("head"), a feature which is reflected by the information indexes (Table 1). This is due to the localization of giant islets and solitary B cells almost exclusively in the tail.

Following gland ligation, which necessarily induces atrophy of the exocrine part in the distal compartments, specific features of regeneration of acinous and islet tissue can be observed.

The compensation of exocrine function is realized by "remote regeneration", particularly, on account of the intact part of the gland. An increase in acinus size is noted here, associated with acinous cell hypertrophy. Mitoses of acinocytes

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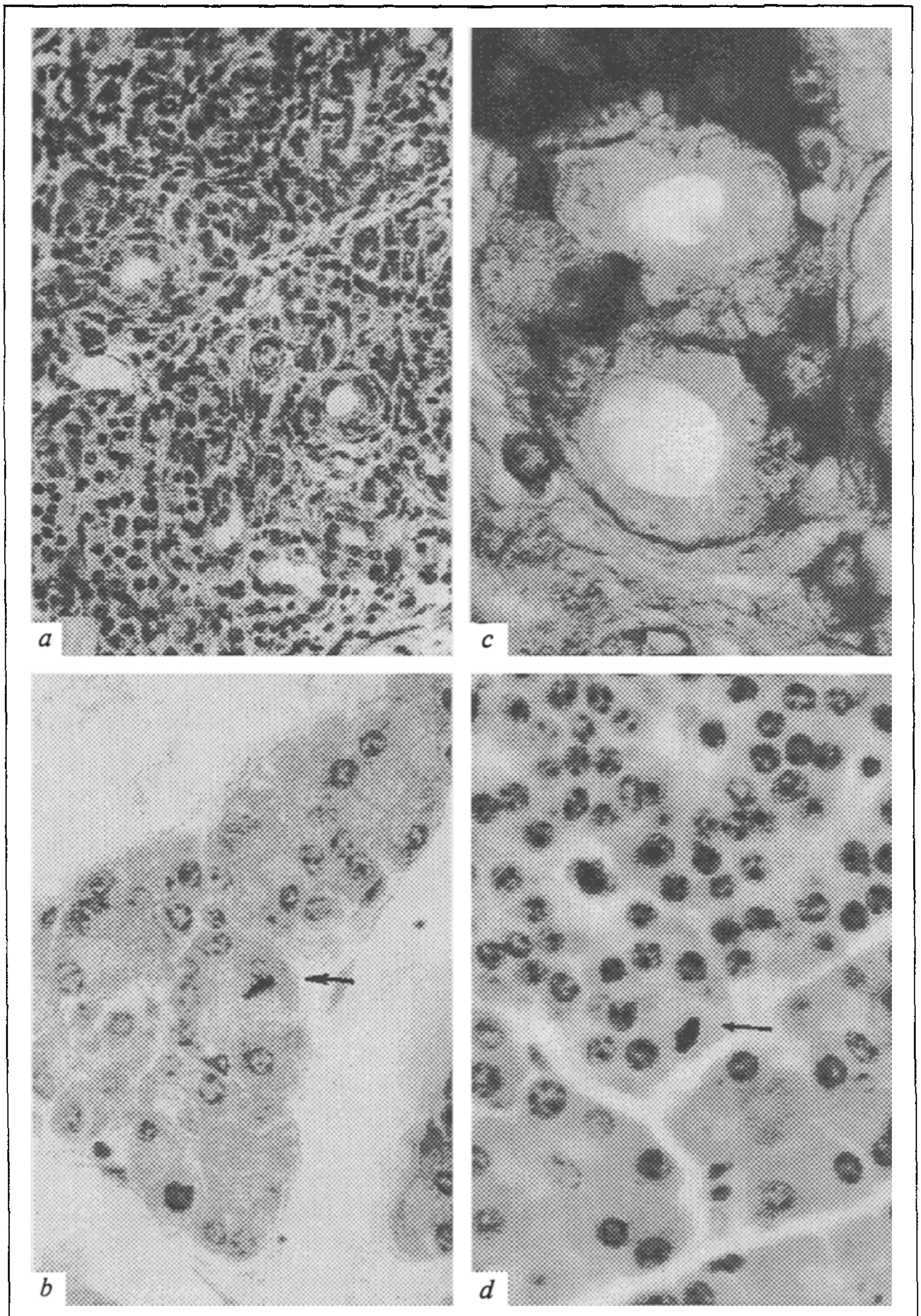

Fig. 1. Histological picture of ligated (*a*, *c*) and remaining (*b*, *d*) parts of the guinea pig pancreas. *a*) formation of acino–ductal structures and development of connective tissue replacing the atrophied acini; staining with iron hematoxylin, ×144; *b*) mitosis (arrow indicates metaphase) in acinous cell of remaining pancreatic part, 14th day of experiment; staining with hematoxylin–eosin, ×270; *c*) development of B cells within epithelium of intercalary ducts; staining with aldehyde–fuchsin–orange, ×630; *d*) mitosis (arrow indicates metaphase) of islet cell in remaining part, 21st day of experiment; staining with hematoxylin–eosin, ×630.

(Fig. 1, *b*) are rare and do not play a significant role. By the 14th day hypertrophy of acini in the remaining part of the gland attains a reliable level ($p<0.02$) and persists during the progressive atrophy and lipomatosis in the ligated part of the gland (Table 2). At this time a marked hypertrophy and hyperplasia of the mucous glands of the large ducts in the remaining part of the gland are

TABLE 1. Information Indexes of Endocrine Part of Guinea Pig Pancreas after Ligation

Day of experiment	Absolute entropy	Relative entropy, %	Excess, %	Information index of effect
Control	1.4264 / 1.1975	61.4 / 58.8	38.6 / 41.2	– / –
7	1.6272 / 1.5270	70.1 / 76.4	29.9 / 23.6	−0.1408 / −0.2752
14	1.7882 / 1.3599	77.0 / 68.0	23.0 / 32.0	−0.2536 / −0.1356
21	1.7966 / 1.4866	77.3 / 74.3	22.7 / 25.7	−0.2591 / −0.2414
30	1.7958 / 1.4318	77.3 / 71.6	22.7 / 28.4	−0.2590 / −0.1957
60	1.7404 / 1.3831	74.9 / 69.2	25.1 / 30.8	−0.2201 / −0.1530
105	1.5614 / 1.3872	67.2 / 69.4	32.8 / 30.6	−0.0946 / −0.1584

Note. Numerator reflects the ligated part of the gland; denominator reflects the volume of the intact part.

seen, the result of glandulocyte hypertrophy and proliferation.

The changes in the islets of the ligated and remaining part of the pancreas are markedly different. An increase in the level of structural diversity (the values of absolute and relative entropy and the information index of effect) in the islet tissue of the ligated part is connected with the appearance of multiple solitary B cells and the formation of small islets via secondary differentiation of the epithelium of the acino-ductal structures (Fig. 1, *c*). The latter develop from the atrophied acini and through the proliferation of intercalary parts of the ducts. The rate of increase of solitary B cell number is maximal from the 14th to the 21st day (by 2.0-2.2%). It is during this period that the mitotic activity of acino-ductal epitheliocytes also reaches its maximum (20-23‰) and 34-36э‰, respectively).

Starting from the 21st-30th day the rate of increase in the endocrine tissue volume slackens. This may be primarily related to the changes in the forming conective tissue. Thus, by the 21st day the processes of fibrillogenesis come to predominate. Mature fibroblasts represent 77.0% of cells, and the density of cell arrangement decreases to 912.5±109.5 per mm^2, as compared to 1160.7±91.2 per mm^2 on the 14th day.

The intact part of the pancreas is characterized by hypertrophy and proliferation of insulocytes (Fig. 1, *d*). The maximum increment of endocrinocyte mitotic activity is recorded on the 21st day (mitotic index equal to 3.5‰, normal level about 0.01‰). The increase of the B/A cell ratio to 4.09 (the normal ratio is 3.62) points to the predominant differentiation of B insulocytes. The tempo of increase in the number of small (by 8.3%), large (by 6.0%), and giant (by 5%) islets in the intact part of the pancreas also peaks on the 21st day. At this same time in the exocrine tissue frequent solitary B cells appear. This may be evidence of the involvement of new compensatory mechanisms of endocrine gland function, namely acino-insular transformation.

Thus, the compensatory-adaptive changes in exocrine and endocrine tissue of ligated and intact

TABLE 2. Morphometric Parameters of Exocrine Pancreas after Ligation

Day of experiment	Diameter of acini, μ	Diameter of gland ducts, μ	Volume of gland ducts, %
Control	27.9±1.2	28.1±1.9	2.2
7	28.8±1.5	29.9±2.6	2.14
14	31.7±2.1	33.2±3.3	3.4
21	32.6±2.7	28.7±2.7	6.2
30	32.7±3.1	30.2±2.9	6.7
60	32.6±2.9	30.9±3.0	6.8
105	32.3±3.3	32.1±3.1	7.9

parts of the pancreas proceed synchronously and preferentially involve the endocrine elements. The specific features of the process in the exocrine part are hypertrophy of acini and hypertrophy and hyperplasia of the mucous glands of the large ducts.

The compensation of endocrine function in the ligated part of the pancreas is realized through secondary differentiation of the epithelium of the acino-ductal structures and is limited by the peculiarities of the forming connective tissue. In the intact part of the pancreas the prevailing processes are hypertrophy, insulocyte proliferation with preferential B cell differentiation, and, later, acino-insular transformation.

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Morphogenesis of a Canalicular-Hypertensive Model of Pancreatitis

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A rat model of acute pancreatitis is presented. Its conformity to the pancreatic changes during human pancreatitis is shown. The morphology of experimental pancreatitis development in rats is studied.

Key Words: *experimental pancreatitis; model*

The pathogenesis and morphogenesis of acute and chronic pancreatitis continue to attract attention, and experimental models have recently been elaborated [1-5]. The conformity of the experimental results to the human situation depends on the model used. Cold-induced pancreatic damage [1] does not take account of the biliopancreatic reflux and intraductal hypertension which cause the development of acute pancreatitis in 48.4% cases [2]. Ligation of the commom bile duct [4] or intraduodenal administration of harmful agents [3] is unable to model the selective and primary nature of pancreatic damage and its extent cannot be varied.

The goal of the present study was to design a hypertensive model of pancreatitis in albino rats with primary pancreatic disorders at the regulatable level and analyze its pathomorphology.

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MATERIALS AND METHODS

The experiments were carried out on 70 albino rats. Ten animals made up the control group, while 60 rats served for experimental modeling of pancreatitis according to the method elaborated by us earlier (Proposal № 1076-93).

The model is based on the specific topography of the pancreatic ducts in the rat. The common duct of the gastric and splenic segments empties into the common bile duct 9-10 mm distal to the junction of the hepatic (lobe) ducts. The main duct of the duodenal segment empties into the common bile duct 7-8 mm proximal to the hepato-pancreatic ampulla (Fig. 1). The pancreatic

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