

## MORPHOLOGY AND PATHOMORPHOLOGY

# Morphometric Analysis of the Pancreas Regenerating after Resection

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Regeneration of exo- and endocrine compartments of guinea pig and rat pancreas after partial resection is studied. The key role of  $\beta$ -cell hypertrophy and acinoinsular transformation in the compensation of endocrine function and typical regenerative modification in the exocrine pancreas are demonstrated.

**Key Words:** *pancreas; resection; regeneration*

Development of surgical treatment of chronic pancreatitis and of organ-sparing operations for benign tumors of the pancreas [2] prompts further studies of the mechanisms responsible for the compensation of pancreatic function. Although regeneration of the exocrine pancreas was studied in sufficient detail [1,4,5], the problem of  $\beta$ -cell recovery was not solved. Our aim was to study regeneration of the pancreatic islets after partial resection of the organ in comparison with our previous data obtained in experiments with ligation of the pancreatic duct [3].

### MATERIALS AND METHODS

Regenerative changes occurring in the pancreas were studied in 46 guinea pigs and 18 albino rats of both sexes after resection of two thirds of the distal part of the pancreas. The animals were sacrificed 1, 5, 10, 20, 30, 60, and 90 days after surgery. Both surgery and sacrifice were performed under ether anesthesia. Pieces of the pancreas were fixed in formalin, Rouget, Bouin, and Carnoy solutions and embedded in paraffin. Sections were stained with hematoxylin and eosin, iron hematoxylin, Mallory phosphotungs-

tic acid hematoxylin, aldehyde fuchsin, and Fenaf stain. Some pieces of rat pancreas were fixed with osmium tetroxide and embedded in Epon-Araldite. Semithin sections were stained with toluidine blue. Ultrastructure of rat pancreas was studied by transmission electron microscopy under a UEMB-100K electron microscope. Ultrathin sections were cut in an LKB-8800 ultratome and contrasted with uranyl acetate and lead citrate by the method of Reynolds. Morphometric data on the guinea pig pancreas were analyzed by the variation statistics methods using Student's *t* test and elements of the information theory [3].

### RESULTS

Changes in the exocrine pancreas after resection were typical in both species and occurred at the same interval as after ligation of the pancreatic ducts [3]. Some specific changes were observed in pancreatic islets. Acinal hypertrophy and more intense staining of homogeneous and zymogenous zones of the exocrine pancreas after resection reflected impaired secretion. Hyperplasia of the goblet cells and the glands of the large ducts similar to that occurring after ligation of pancreatic ducts was observed in guinea pigs. After resection, an increase in mitotic activity of ductal epithelium was recorded earlier

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TABLE 1. Morphometric Parameters of the Endocrine Part of Guinea Pig Pancreas after Resection ( $M \pm m$ )

Time of examination	% of initial weight	Number of islets per 10 mm <sup>2</sup>	Mean number of cells per islet	B/A coefficient
Control	-	16.5±0.5	44.5±3.0	3.68
Day 1	41.2±3.9	18.0±2.0*	40.5±3.0*	3.76
Day 5	46.7±4.0	22.0±1.5	52.0±4.5	3.95
Day 10	59.5±2.2	24.5±2.5	58.0±5.0	4.04
Day 20	73.4±4.1	29.0±3.0	73.5±5.5	4.36
Day 30	78.1±3.0	31.5±2.0	68.5±5.5	4.25
Day 60	79.8±3.2	28.0±2.0	58.5±7.5	4.07
Day 90	74.7±2.5	26.5±2.5	55.5±7.2	3.88

Note. All differences reliable ( $p < 0.05$ ) except those with the asterisk.

(on days 2-5) than after ligation (day 7). This may be due to instantaneous loss of a considerable volume of the organ, while progressive degradation of two thirds of pancreatic parenchyma as a result of atrophy requires at least 7 days in the ligation model [3].

After resection, the weight of the pancreas was not restored either in rats or guinea pigs. In guinea pigs, maximum regeneration was observed on days 60-90 postoperation (Table 1). There was no outgrowth of pancreatic tissue from the resection zone. Morphometric and information parameters of the islets indicate that peak compensatory changes occur between days 20 and 30 (Table 2), which is similar to the corresponding period in the ligation model [3]. However, the contribution of  $\beta$ -cell mitoses in this process is insignificant. The maximum mitotic index recorded on day 20 is 0.16% (0.01% in the control). Acinoinsular transformation was the major regenerative change in the endocrine pancreas after resection. It was particularly pronounced in the acinous tissue adjacent to large and giant islets. This process was studied by light microscopy both in rats and guinea pigs and by electron microscopy in rats (Fig. 1). It should be noted that giant islets were not seen in the proximal part of the pancreas in control guinea pigs. The relative count

of giant islets ( $3.8 \pm 0.1\%$ ) and that of large islets ( $13.7 \pm 1.2\%$  vs.  $3.6 \pm 0.3\%$  in the control) reached the maximum on day 30 after resection. A parallel decrease in the relative count of small islets ( $30.5 \pm 3.5\%$  vs.  $53.5 \pm 2.0\%$  in the control) was observed, while the number of medium-sized cells remained stable. Such a "recalibration" of the islets is related to the acinoinsular transformation. In the early period, the formation of type B acinoislet cells predominates, as evidenced by the ratio between  $\beta$  and  $\alpha$  cells in the islets (the B/A coefficient). Electron microscopy revealed polymorphism of the mitochondria and rough endoplasmic reticulum and the presence of zymogen and one type of endocrine granules in the cytoplasm.

Taken together with the published data [1,2], our findings indicate that regeneration of the exocrine pancreas is due predominantly to hypertrophy of the acinocytes and to hypertrophy and hyperplasia of ductal epithelium. The absence of tissue outgrowth from the resection zone is associated with the absence of an adequate connective-tissue carcass [1]. Hypertrophy of remaining  $\beta$  cells and the acinoinsular transformation are the main mechanisms of islet regeneration after resection. This transformation can be regarded as the mechanism responsible

TABLE 2. Information Parameters of the Endocrine Part of Guinea Pig Pancreas after Resection

Time of examination	Absolute entropy	Relative entropy, %	Excess, %	Information index of the effect
Control	1.4264	61.4	38.6	-
Day 1	1.1960	59.8	40.2	+0.0012
Day 5	1.4878	74.4	25.6	-0.2424
Day 10	1.6481	82.4	17.6	-0.3763
Day 20	1.6879	84.4	15.6	-0.4095
Day 30	1.7711	88.5	11.5	-0.4800
Day 60	1.7277	86.4	13.6	-0.4428
Day 90	1.7121	85.6	14.4	-0.4297

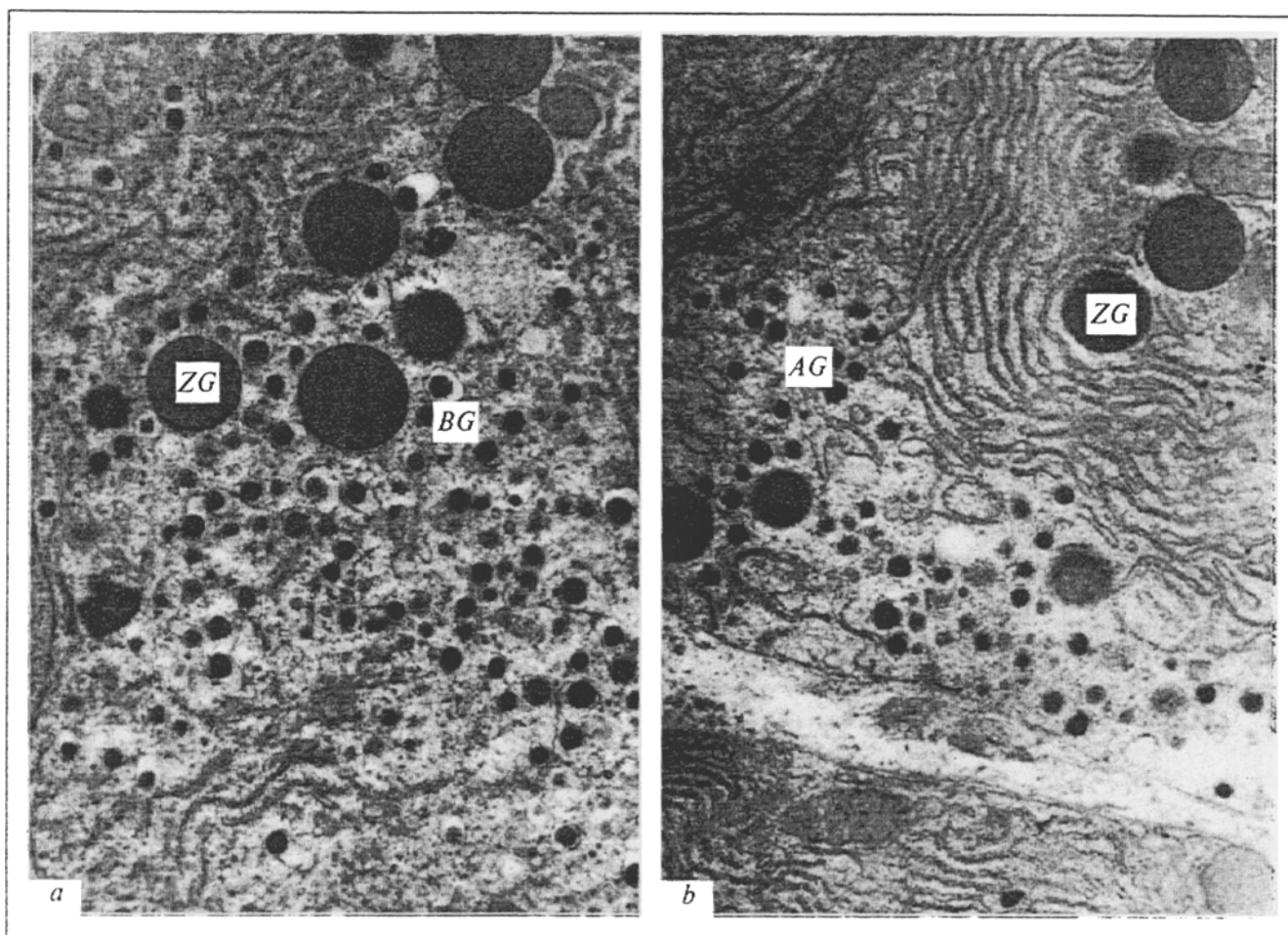


Fig. 1. Acinoinsular cells, type B (a) and A (b) in the remaining portion of rat pancreas on day 30 after resection. ZG: zymogen granules; BG: B granules; AG: A granules. Electron micrographs.  $\times 8000$ .

for urgent compensation of endocrine function of the pancreas.

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