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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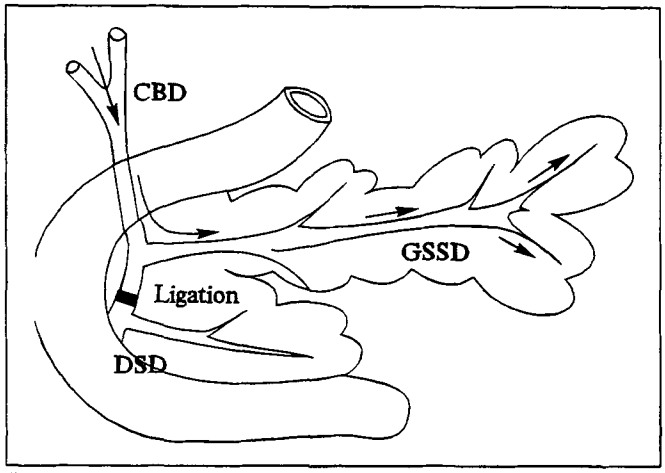

Fig. 1. Topography of pancreatic ducts in the rat and technique of pancreatitis modeling; arrow indicates the direction of spread of the preparation injected. *CBD*: common bile duct; *DSD*: duodenal segment duct; *GSSD*: duct of gastric and splenic segments.

damage is achieved by administration of 1% potassium permanganate [5] into the ducts via puncture of the common bile duct at the site of its origin. Temporary ligation of the common bile duct proximal to the inflow of the duodenal duct causes a selective reflux, ductal hypertension, and alterations in the acino-ductal junctions within the duct system of the gastric and splenic segments (70-75% of the pancreatic tissue). The volume of damage in the pancreatic tissue can be monitored by changing the degree of ligation. On average, each animal received 0.1 ml of solution per 100 g body weight.

Animals were sacrificed by ether anesthesia 3, 6, and 12 hour and 1, 3, 7, 14, 21, and 30 days after the start of the experiment. Paraffin sections of the pancreas were stained with hematoxylin-eosin, after Brachet, with toluidine blue, cresyl violet acetate, or by means of Schiff reaction.

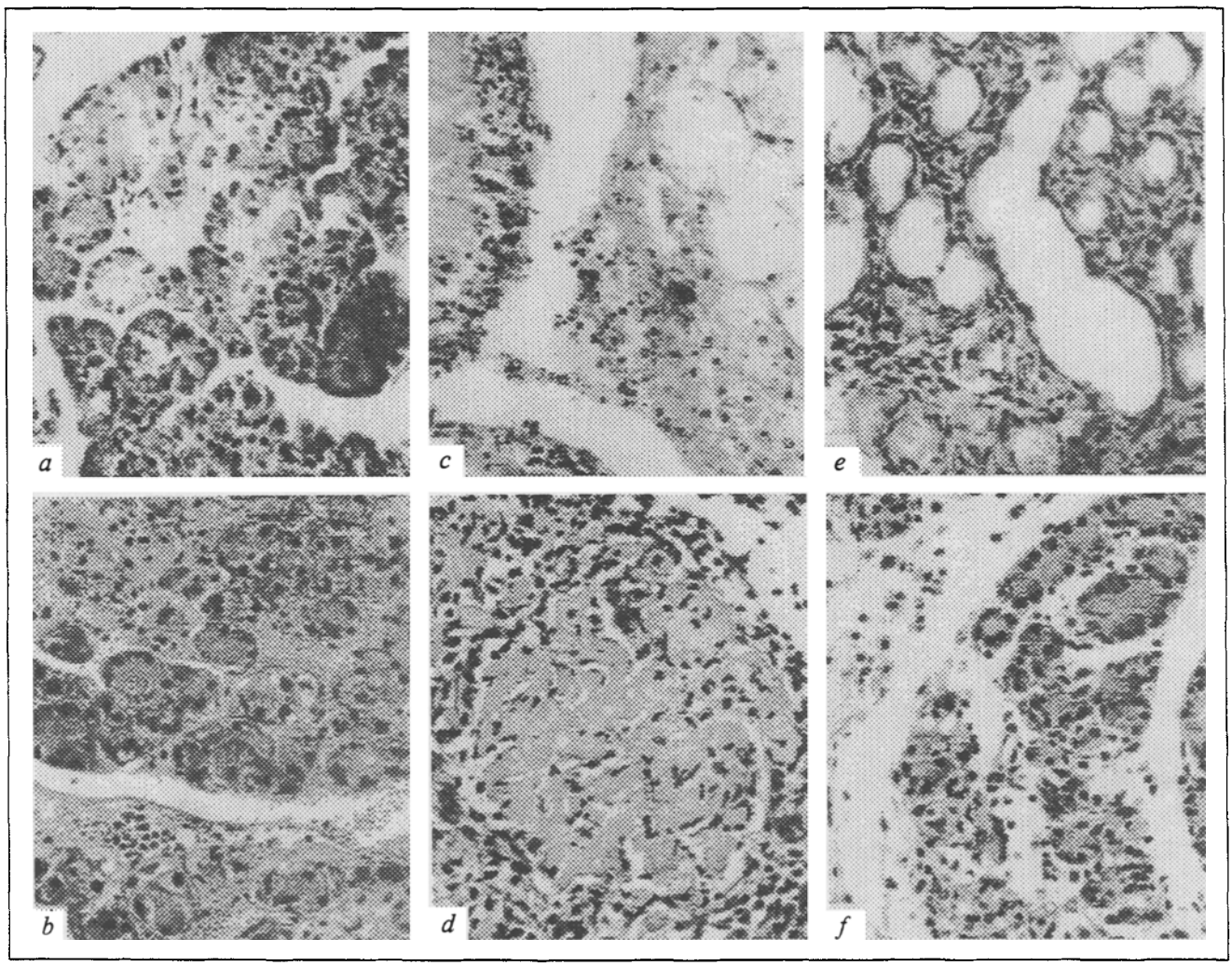

Fig. 2. Morphology of experimental hypertensive pancreatitis in the rat. *a*) intracellular edema, vacuolizing dystrophy, and necrosis of acinous cells; 1st day; *b*) hemorrhagic necrosis of pancreas; 3rd day; *c*) lipoid necrosis and inflammatory infiltration; 3rd day; *d*) islet necrosis; 7th day; *e*) multiple microcysts; 21st day; *f*) dystrophy and necrosis of duodenal segment acini; 30th day. Hematoxylin–eosin. ×144.

Activity of serum amylase was recorded after Caraway, serum lipase after Tietz, and blood sugar was recorded by the orthotoluidine method.

RESULTS

Three hours after injection a marked hyperemia and "hyaloid edema" of the gland are observed. The borders of acinous cells are indistinguishable, and the cytoplasm is diffusely weakly basophilic, apparently manifesting disorganization of the elements of the granular endoplasmic reticulum. A large amount of zymogen is accumulated in some acinocytes, due to the blockage of secretion extrusion. Amylase activity increases 15-25-fold (700-780 U) by the 6th hour of the experiment.

The end of the first day sees an increase in the intracellular edema. The acinus diameter is markedly ($p<0.001$) enlarged (32.0±1.3 μ as opposed to the normal 23.1±0.08 μ). The majority of acinous cells undergo vacuolar dystrophy. The necrosis of exocrine tissue spreads. Clasmatosis within acinocytes is observed (Fig. 2, *a*). The ducts are enlarged and filled with necrotized and desquamated epithelium. Hemorrhagic phenomena are already noted. However, leukocyte infiltration is absent.

The 3rd-7th days are marked by progression of hemorrhagic and development of lipolytic (lipoid) necrosis. An inflammatory cellular infiltrate (Fig. 2, *b*, *c*) is formed. The necrosis begins to spread to the islets (Fig. 2, *d*).

This causes the blood sugar level to rise slightly and then to be maintained at the upper level of the norm (5.12-5.60 mmol/liter). The lipase activity shows a more than twofold increase.

From the 14th to the 30th day in the necrotized gastric and splenic segments against the background of marked lymphoid, macrophage, and mast cell infiltration there is a proliferation of fibrous connective tissue and multiple microcysts form, lined with squamous epithelium (Fig. 2, *e*).

In the duodenal segment up to the 30th day the alterations are of the edematous pancreatitis type. After one month (Fig. 2, *f*) necrosis of acini is often seen against the background of lymphoid infiltration. These features may be evidence, first, of the recurrent nature of the process. Second, the necrosis-associated lymphoid infiltration may reflect its immune basis.

Thus, in our model of acute pancreatitis in rats, intraductal hypertension goes along with enzymolysis of pancreatic tissues, which causes hemorrhagic and then lipoid pancreonecrosis. By the 21st-30th day the process assumes a chronic recurrent course. The model makes it possible to formulate the main principles of patho- and morphogenesis of acute pancreatitis followed by chronic pancreatitis [3], is highly reproducible, and is optimal for experiments on rats.

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