REGENERATIVE AND COMPENSATORY PHENOMENA IN THE PANCREAS AFTER ITS RESECTION

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The special course of regenerative processes in the pancreas and the inconstancy of its regenerative reactions have been reported in the literature [1-11].

The object of this investigation was to determine the influence of the character of the operation on the regenerative processes in the pancreas.

EXPERIMENTAL METHOD

The investigation was conducted on 63 dogs from which certain portions of the pancreas were removed in aseptic conditions. Different methods were used for dealing with the stump of the gland, with the object of excluding or retaining the external secretion.

After the operation the functional state of the incretory apparatus and of the exocrine part of the gland was studied. For this purpose, the blood sugar concentration was estimated in a fasting state and after double loading with glucose, the amylase and sugar in the urine were determined and the presence of neutral fat and undigested muscle fibers in the stools was sought. At the end of the period of observation, the microstructure of the part of the pancreas remaining after resection was investigated. Preparations were stained with hematoxylin-eosin and by Van Gieson's method.

Depending on the type of resection, the operations performed were distributed among the following groups (Fig. 1): 1) resection of the terminal portion of the pancreas (16 cases); 2) removal of the central portion, analogous to the head of the human pancreas, with ligation and division of the efferent ducts (12 cases); 3) resection of the central and one terminal portion (9 cases); 4) removal of the gland with preservation of the part near the duct (12 cases); 5) resection of the gland and subsequent suture of the stump into the jejunum (14 cases).

EXPERIMENTAL RESULTS

Analysis of the results obtained showed that in all the animals immediately after the operation the blood sugar level rose to 160-200 mg% as a result of the operation trauma. From the 3rd-4th day the blood sugar level fell to 120-140 mg%. Later, in the animals undergoing resection of the pancreas, the fasting blood indices were within normal limits.

Meanwhile, the results of the experiments with double sugar loading (2 g glucose/kg body weight) showed that after resection of the pancreas, the sugar curve did not always follows its original course. Whereas on the day before

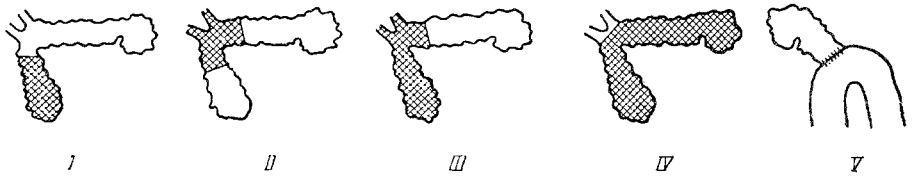

Fig. 1. Scheme of different types of resection of the pancreas. I—Resection of the terminal part of the gland, II—resection of the central part (body) of the gland, III—resection of the terminal part and body of the gland; IV—resection of the gland with preservation of a small part around the duct, V—resection of the gland with suture of the terminal portion into the lumen of the jejunum.

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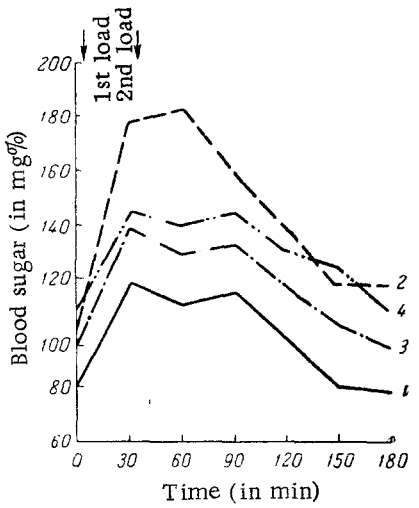

Fig. 2. Results of double glucose loading test before and after resection of the pancreas. Along the axis of ordinates—blood sugar (in mg%), along the axis of abscissas—time (in min); 1 before operation, 2-4) on the 4th, 20th, and 150th days respectively after operation.

the operation the blood sugar concentration of the animal after the first administration of glucose was 118 mg% and after the second it fell to 110 mg%, the same test repeated on the dogs after resection of large areas of the pancreas (up to $^2/_3$ of the organ) was accompanied by changes differing from those observed before the operation. On the 4th, 20th, and 150th days, 30 min after the first load, the blood sugar reached 178, 142, and 140 mg% respectively. Although in the later stages after the operation, the rise of the curves was less marked, they remained high, and the decrease in the blood sugar level took place very slowly. In the last test (2.5 h after the first load), the blood sugar was 100-120 mg%, i.e., 40-20 mg more than before the operation (Fig. 2). In general, the blood sugar curves obtained in the postoperative period differed from the background pattern by their higher rise, which was increased after the second dose of glucose, and their slower fall. These results demonstrate the functional insufficiency of the insular apparatus when presented with increased demands (glucose loading, high carbohydrate diet). However, as the time after the operation increased, the blood sugar curves returned to their initial pattern, reflecting the compensatory and regenerative powers of the islet-cell tissue of the residual portion of the gland. Removal of the various parts of the pancreas caused different effects on the regenerative changes and compensatory powers of the residual part of the organ. After resection of the terminal portions of the pancreas, as before the operation, the pancreatic juice flowed into the duodenum because the principal efferent ducts remained intact. However, removal of the central portion, like resection of the head of the human pancreas, led to mechanical closure of the efferent ducts of the pancreas, to an increase in the pressure of the secretion accumulating in them, and to various detrimental effects associated with this.

Ligation of the efferent ducts, and also division of the large and small ducts in different directions led to the development of immediate postoperative complications (pancreatic necrosis, peritonitis), and these later adversely affected the regeneration of the organ, so that in the study of the compensatory and regenerative reactions of this unique organ, the operations artificially combined under the heading of "resection of the pancreas" cannot be regarded as analogous.

Investigation of the external secretion of the pancreas after resection showed that removal of the terminal portion of the organ was not accompanied by disturbance of the processes of absorption and assimilation of lipids and proteins. After such operations little or no neutral fat (staining with Sudan III) or undigested muscle fibers were found in the stool.

In the animals undergoing resection of the central part of the gland with ligation and division of the principal ducts, and also removal of the central portion and one of the terminal portion of the pancreas, the stools showed marked changes. Throughout the period of observation, many drops of neutral fat and many undigested muscle fibers were excreted with the stools. The degree of the observed disturbances varied (in 18 of 21 animals +++ for lipids, and ++ for muscle fibers), i.e., despite the fact that large areas of pancreatic tissue remained behind in the dogs, the changes in the stools indicated disturbances of the digestion and absorption of proteins and lipids.

In the dogs in which the stump of the gland was sutured into the lumen of the jejunum in the early period proteins and lipids taken with the diet were badly assimilated. The external appearance of the stools was considerably changed. Whereas, before the operation the stools were formed and dark colored, and on investigation usually no neutral fat and few or no undigested muscle fibers could be found, after the operation the appearance was different. The stools became pale, liquid, and copious. Investigation of the stools during the first months and later revealed many undigested muscle fibers and large quantities of droplets of fat, mainly large.

After two months the stools became more formed, and from liquid their consistency changed to porridge-like. The number of undigested muscle fibers fell considerably, and in occasional fields of vision badly digested fibers with persistent cross-striation could still be seen. For a long period small scattered droplets of neutral fat could be seen. However, unlike the animals of the preceding group, these dogs gained weight and their condition was similar

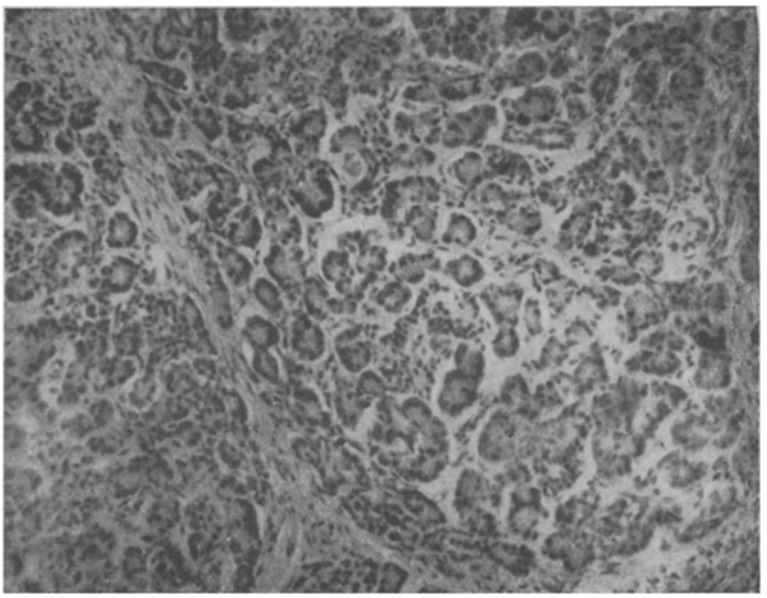

Fig. 3. Pancreas of a dog after resection and formation of a pancreatico-jejunostomy. Increase in thickness of the interlobular connective-tissue septa. Hematoxylin-eosin. Objective 20, ocular 9.

to what it had been before the operation. Hence, general observations on the animals and the results of function tests suggest the existence of compensatory and regenerative processes in dogs undergoing resection of the pancreas followed by suture of the terminal portion into the lumen of the jejunum.

Conclusive evidence on this point was obtained by microscopic investigation of the portion of the pancreas remaining after resection. These results showed that removal of the terminal portions of the gland, while retaining the patency of the efferent ducts, was accompanied by proliferation of the connective tissue mainly in the zone of resection of the gland. No appreciable atrophy of the parenchymatous elements could be found in the residual part of the organ.

The least favorable as regards outcome was subtotal resection of the pancreas. After the almost complete removal of the pancreas, leaving behind small areas near the ducts, in three cases the development of fatty necrosis was observed, and this caused the animals' death. Suppurative inflammation of the surrounding cellular tissue was observed in the lobules of the pancreas remaining near the efferent ducts. On the surface small foci of fatty necrosis were found, alternating with foci of suppurative inflammation. Areas of fatty necrosis were also seen in the substance of the glandular tissue. In the surviving animals cyst-like cavities were found in the region of the foci of destruction.

Removal of the central portion of the gland, or of the central portion together with a terminal portion, was accompanied by the development of atrophic changes and proliferation of the connective tissue in the residual portion of the pancreas. Fibrous connective tissue extended in broad bands between the lobules of the glands, and in some places surrounded them in a ring. With an increase in the period of observation the atrophic changes became more marked and the amount of connective tissue increased. From 3 to 7 months after resection of the central portion some areas of the pancreas became surrounded by a thick connective-tissue capsule. Because of proliferation of the connective tissue the walls of the blood vessels became thicker. In these experiments, no restoration of the function of the gland took place, and on microscopic examination the acinar cells showed no signs of regeneration.

When communication between the pancreas and the intestinal lumen was preserved by formation of a pancreatico-jejunostomy, the proliferation of the connective tissue in the part of the gland near the anastomosis was less marked, and the atrophy of the parenchyma of the gland was very slight. In some preparations an efferent duct with a wide, free lumen lined with cubical epithelium could be seen among the parenchyma subdivided into lobules.

In the experiment in which the stump of the gland was peritonized with omentum and, consequently, isolated from the lumen of the bowel, the results obtained were different from those described in the animals with pancreatico-jejunostomy even when the extent of the resection was the same. From 2 to 3 months after the operation,

marked atrophy of the acinar tissue and intensive proliferation of the connective tissue between the lobules and on the surface of the terminal portion of the gland were found in the pancreas of the dogs of group 1. At the same time, and also much later, in the animals of group 2, only very slight thickening of the interlobular connective tissue septa was observed, and instead of atrophy, a marked increase in the size of the acini was seen (Fig. 3).

It may be concluded from these results that anastomosis of the residual portion of the gland with the lumen of the digestive canal facilitates the development of the compensatory powers of the pancreas.

The part of the organ isolated from the bowel was converted into a cicatrized formation in which it was difficult to distinguish the dissociated and atrophied glandular elements, and the external secretory function gradually disappeared. The creation of conditions for drainage of the pancreatic juice was thus of great importance to the regeneration of the pancreas and compensation of the functions disturbed by resection of the organ.

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