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MORPHOLOGICAL AND FUNCTIONAL CHANGES IN THE PANCREAS AFTER EXPERIMENTAL REPAIR OF THE INJURED WALL OF THE CERVICAL PART OF THE ESOPHAGUS

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There are isolated reports in the literature on the character of disturbances of carbohydrate metabolism after operations on the thoracic part of the esophagus [2]. It has been shown [3], for instance, that resection of the esophagus in its thoracic part causes trophic disturbances of the acinar parenchyma and insular apparatus in the pancreas, accompanied by infiltration of the stroma by polymorphonuclear leukocytes and lymphocytes. This may be connected with injury to small branches of the vagus nerve during the operation, for we know that the paraventricular-vagal mechanism plays an important role in regulation of the endocrine function of the pancreas [1].

The aim of this investigation was to study carbohydrate metabolism and the morphological structure of the pancreas following injury and subsequent repair of a subtotal defect of the wall of the cervical part of the esophagus.

EXPERIMENTAL METHOD

The blood sugar level and the morphological structure of the pancreatic insular apparatus were investigated in experiments on 40 young and middle-aged mongrel dogs. After resection of two-thirds of the circumference of the esophagus for a length of 4-5 cm the operation was concluded by replacement of the subtotal defect in the wall of the cervical part of the esophagus by means of artificial prostheses. The blood sugar concentration was studied by the glucose oxidase method using the "Ames Dextrostix" express system. Glucose loading was at the rate of 1.75 g glucose/kg body weight. Material for histological investigation was taken strictly from definite areas of the tail and body of the pancreas, and the pieces were fixed in 12% neutral formalin solution and embedded in paraffin wax. Sections 5-7 μ thick were stained with hematoxylin and eosin and with aldehyde-fuchsine by the Gabe–Dyban method. The number of islets was counted morphometrically in 100 fields of vision. The investigation was carried out before the operation and on the 3rd, 7th, 14th, 21st, 30th, 40th, 60th, 120th, and 180th days thereafter. Three intact dogs on which access to the cervical part of the esophagus was

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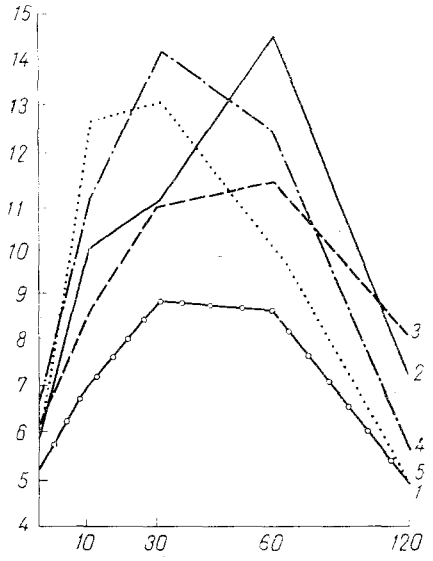

Fig. 1. Blood sugar curves in postoperative period. Abscissa, time (in min); ordinate, blood sugar level (in mmoles/liter). 1) Control; 2-5) 3rd, 7th, 14th, and 21st days respectively.

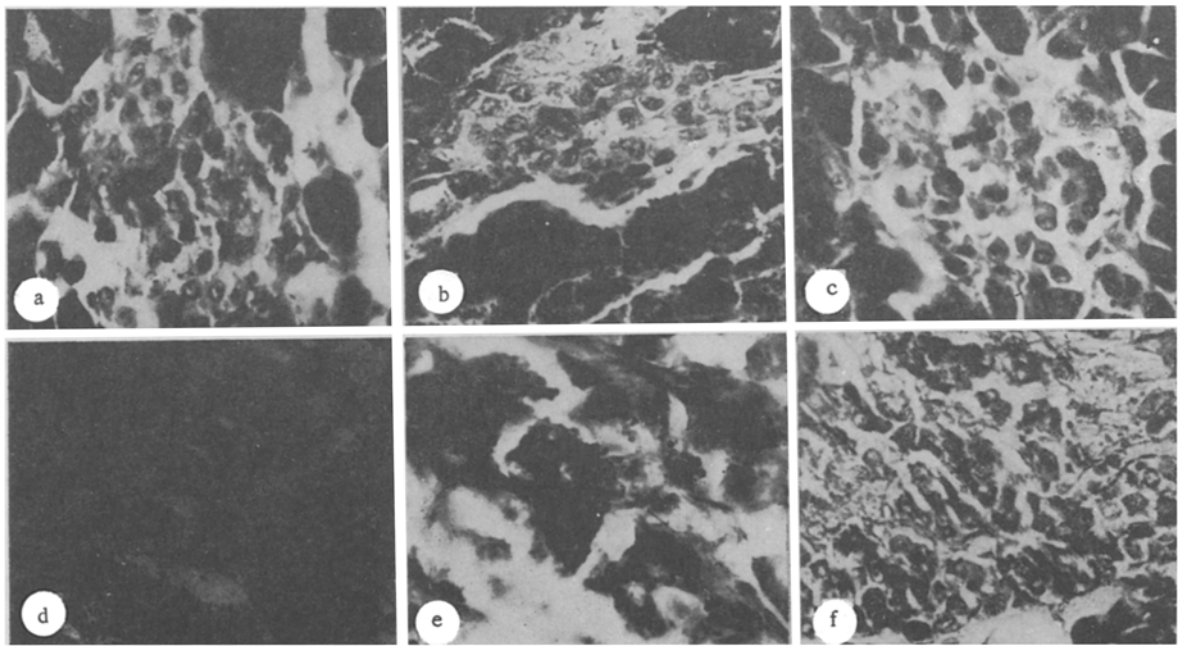

Fig. 2. Histological and histochemical changes in islets of Langerhans after experimental repair of injured wall of cervical part of esophagus. a) 3rd day after operation: focal necrosis and dystrophy of cells. 280 ×; b) 14th day after operation: focal necrosis and reduction in number of islet cells. 280 ×; c) 21st day after operation: necrosis of individual cells, most of them unchanged. 280 ×; d) 60th day after operation: focal necrosis of islets and acinar parenchyma. 630 ×; e) 180th day after operation: clearly outlined aldehyde-fuchsinophilic granules in cytoplasm of β-cells. 630 ×; f) Control (14th day), β-cells predominate in islets, many aldehyde-fuchsinophilic granules. 280 ×; a-c) stained with hematoxylin and eosin; d-f) stained with aldehyde-fuchsine by Gabe—Dyban method.

TABLE 1. Morphometric Characteristics of Insular Apparatus in Postoperative Period

Time of observation, days	Number of cases	$M \pm m$	σ	P
Control	4	61,25±1,74	3,49	
3-rd	3	45,0±1,73	3,0	<0,01
7-th	3	45,6±2,33	4,0	<0,02
14-th	5	29,2±2,39	5,35	<0,001
21-st	3	43.33±3,37	5,85	<0,05
30-th	4	39,5±1,89	3,78	<0,001
40-"	3	38,0±1,52	2,64	<0,01
60-"	3	52,6±1,05	1,82	<0,02
120-"	3	62,0±7,74	13,42	>0,5
180-"	3	64,33±5,69	9,86	>0,5

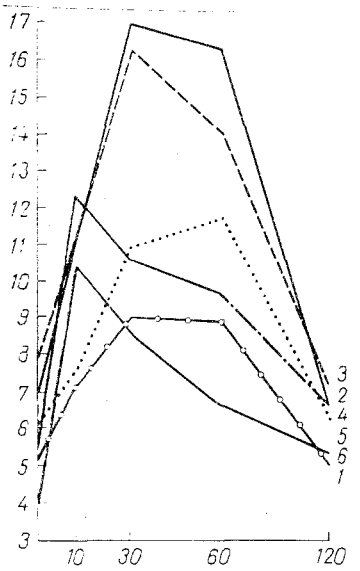

Fig. 3. Blood sugar curves in postoperative period. 1) Control, 2-6) 30th, 40th, 60th, 120th, and 180th days respectively. Remainder of legend as to Fig. 1.

obtained, after which the wound was sutured in layers, served as the control. In the postoperative period the experimental animals were kept on parenteral feeding, changing after the 8th day to tube feeding, and after the 45th-50th day to ordinary feeding. The numerical results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

The experiments showed that the blood sugar curve in the postoperative period was diabetic in character (Fig. 1). On the 3rd day after the operation the fasting blood sugar level was 6.18 ± 0.43 mmole/liter (5.13 ± 0.12 mmole/liter in the control, $P < 0.02$), and after loading the curve became "two-humped," the second peak being higher than the first. The maximal rise of the blood sugar curve occurred at the 60th minute (14.51 ± 1.40 mmole/liter, compared with 8.79 ± 0.60 mmoles/liter in the control, $P < 0.001$), and this was followed by a fall to 7.07 ± 0.41 mmoles/liter at the 120th minute (4.9 ± 0.25 mmoles/liter in the control, $P < 0.001$). The blood sugar level and the character of the blood sugar curve under these circumstances agreed with changes in the morphological structure of the insular apparatus. A rise of the blood sugar was linked with focal necrosis and degeneration of the islet cells (Fig. 2a) and also with a decrease in the total number of islet cells. Staining with aldehyde-fuchsine by the Gabe–Dyban method showed that the changes described above mainly affected β-cells. On the 7th day the blood sugar curve became protracted and flattened out: the initial blood sugar concentration was 6.17 ± 0.16 mmole/liter ($P < 0.001$), rising after 30 min to 11.02 ± 0.65 mmoles/liter ($P < 0.001$) and after 60 min to 11.42 ± 0.57 mmoles/liter ($P <$

0.001), and falling after 120 min to 7.9 ± 0.63 mmoles/liter ($P < 0.001$). Histological examination during this period revealed pycnosis and lysis of the β-cell nuclei. By the 14th day the curve became high and protracted: the initial blood sugar level was 6.72 ± 0.16 mmole/liter ($P < 0.001$), rising after 30 min to 14.15 ± 1.49 mmole/liter ($P < 0.001$), and falling after 120 min to 5.52 ± 0.19 mmole/liter ($P < 0.01$). Many islet cells were shrunken and necrotic, and their number was considerably reduced (Fig. 2b). On the 21st day the blood sugar curves showed a maximal rise of the blood sugar level after 30 min (12.94 ± 0.39 mmole/liter, $P < 0.001$). Later it fell gradually, and by the 60th minute it was 9.97 ± 0.27 mmole/liter ($P < 0.001$), and after 120 min it had not regained its initial value (4.9 ± 0.25 mmole/liter, $P > 0.5$). At this time after the operation many cells of the insular apparatus had a normal histological structure, but some of them were shrunken and necrotic (Fig. 2c). On the 30th and 40th days (Fig. 3) a high and protracted type of blood sugar curve was still found, with the maximal increase in the blood sugar concentration at the 30th minute, to 16.99 ± 0.23 and 16.25 ± 0.50 mmole/liter ($P < 0.001$) respectively. After 60 min it still remained high (16.25 ± 0.50 and 13.79 ± 0.67 mmole/liter, $P < 0.001$) and had not regained its initial level after 120 min. Signs of degeneration, with vacuolation and shrinking of the nuclei were still present as before in the β-cells, and half of the β-cells had lost their granules. By the 60th day the fasting blood sugar had almost regained the normal value (5.55 ± 0.10 mmole/liter, $P < 0.001$). The character of the curve was irritative, with the maximal rise of the blood sugar level after 10 min to 12.26 ± 0.55 mmole/liter ($P < 0.001$) followed by a fall after 60 min to 9.55 ± 0.29 mmole/liter ($P < 0.02$) and after 120 min to 6.54 ± 0.44 mmole/liter ($P < 0.001$), although it still remained higher than initially. On the 120th day hyperglycemia was still present, with an initial blood sugar level of 6.10 ± 0.24 mmole/liter ($P < 0.001$) and a maximal increase after 60 min to 11.57 ± 0.90 mmole/liter ($P < 0.01$). The blood sugar still remained high after 120 min (6.10 ± 0.24 mmole/liter, ($P < 0.001$). After 60 and 120 days, histological and histochemical investigations revealed focal changes, of unequal severity. Extensive areas of total necrosis of the islets together with the acinar parenchyma were observed (Fig. 2d). In other areas the number of islets was reduced (52.6), their outlines remained intact, and in occasional β-cells aldehyde-fuchsinophilic granules were clearly visible. However, individual β-cells showed dystrophic changes: pycnosis, vacuolation, and necrosis. On the 120th day the dystrophic changes in the islet cells were more marked than on the 60th day. By the 180th day the dystrophic changes were much reduced and the islets were congested with blood, the β-cells were large, and the insulin granules in them were clearly outlined (Fig. 2e, f). The blood sugar curve was irritative in character, with a low initial sugar level (3.82 ± 0.25 mmole/liter, $P < 0.001$), a maximal rise after 10 min (10.41 ± 0.83 mmole/liter, $P < 0.001$), a sharp fall until the 30th minute (8.42 ± 0.14 mmole/liter, $P < 0.01$), and a further fall to the 60th minute (6.51 ± 0.27 mmole/liter, $P < 0.001$) and the 120th minute (5.19 ± 0.069 mmole/liter, $P < 0.001$).

Morphometric investigation (Table 1) revealed a gradual decrease in the number of islets from the 3rd day (45.0) to the 14th day (29.2), followed by an increase until the 21st day (43.33). On the 40th day their number fell again (38.0) and then rose gradually until the 60th day (52.6). By the 180th day this parameter was a little higher than initially, at 64.33.

It can thus be concluded that after injury to the wall of the cervical part of the esophagus followed by repair of the subtotal defect considerable disturbances of carbohydrate metabolism are observed. The diabetic character of the blood sugar curves, as the morphological investigations showed, is due to dystrophic changes in the insular apparatus and to a decrease in the number of islets, which leads to reduction of the endogenous reserves of insulin and disturbance of its secretion. The results are evidence of the important role of the paraventricular-vagal pathway in regulation of endocrine function.

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