THE ROLE OF THE PANCREAS IN THE COMPLEX REFLEX REGULATION OF CARBOHYDRATE METABOLISM

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In previous work [3, 4, 6] we showed that the act of eating exerts a complex reflex influence on the process of carbohydrate metabolism. The present work is devoted to the question of the role of the pancreas in the complex reflex regulation of carbohydrate metabolism in connection with food intake.

E. and L. Hedon [13] found that 2½ hours after total pancreatectomy an increase begins in the blood sugar content. N. S. Veller, P. M. Charnaya and B. M. Rodkina [1, 2] performed this operation on dogs and obtained diabetic hyperglycemia 4-7 hours after the animals awoke from anesthesia. These authors have shown that, against a background of depression of the central nervous system with amytal narcosis, diabetic hyperglycemia is detected in dogs 12-30 hours after depancreatization, arising only against a background of the restoration of the function of the central nervous system.

The examinations cited were performed in such a way that an irreversible disturbance to the organism as a whole ensued, due to extirpation of the pancreas; this is their chief drawback.

In critical experiments on dogs and cats Grafe and Meythaller [12] and also T. Kosako [14] established that the injection of glucose solutions into the femoral and portal veins produces severe hyperglycemia, while injection into an artery of the pancreas produced only negligible hyperglycemia, and at times even hypoglycemia. By using the angiostomic method and inserting a cannula into the pancreatico-duodenal vein, N. P. Kotchnewa and E. C. London [7-11] established a small reduction in the sugar content of the blood flowing from the pancreas. In the opinion of these authors the pancreas secretes its hormone periodically in response to an excess of sugar in the blood, while epinephrine enters the blood continuously. To all appearances the incretion of insulin on an empty stomach does not occur.

EXPERIMENTAL METHODS AND RESULTS

We employed a new method in order to decide the question of the role of the pancreas in the regulation of carbohydrate metabolism in the organism as a whole, namely the temporary exclusion of the pancreas from the general blood stream. For this end, the pancreatico-duodenal vein was placed in a specially constructed cannula [5]; by turning the screw of the cannula, we temporarily stopped the entrance into the general blood stream of blood flowing from the pancreas.

Critical experiments were performed on cats. Blood samples were taken simultaneously from a vein of the pancreas and from the peripheral blood. Their sugar content was determined both during normal blood circulation and after exclusion of the blood of the pancreas from the general blood stream.

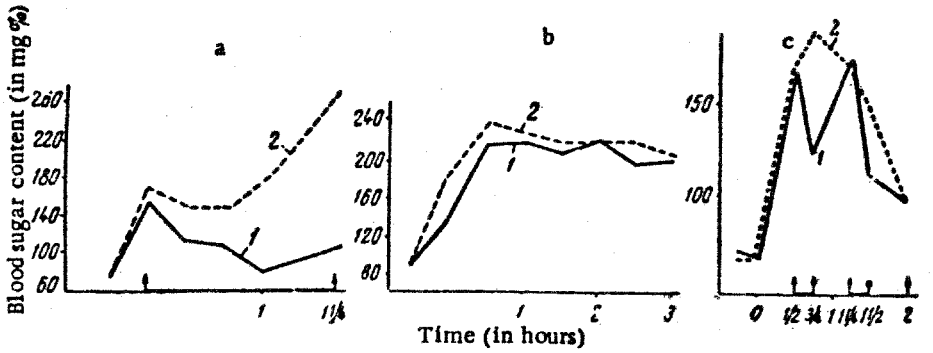

Fig. 1. Blood sugar content.
a) during exclusion of the pancreas from the general blood stream; b) during normal blood circulation in the pancreas; c) during short-term exclusion of the pancreas from the general blood stream and its subsequent inclusion; 1) blood sugar content of the pancreatic vein; 2) the same in the general blood stream; ↑↑)Flow of blood halted.

The results of the first series of experiments, which were performed on 6 cats (Fig. 1,a), showed that after exclusion of the pancreas from the general blood stream the sugar content of the peripheral blood increased, while that of the blood of the pancreatic vein decreased.

In the second series of experiments, performed on 3 cats, an examination was made of the sugar content of the blood flowing from the pancreas and that of the peripheral blood during undisturbed blood circulation through the pancreas and during partial exclusion of the pancreas from the general circulation. Under these circumstances there occurred a simultaneous and almost identical increase in the sugar content of the blood of the pancreatic vein and of the general blood stream (Fig. 1, b).

Thus it is apparent from the experiments that under the normal conditions of existence of an organism the pancreas is just that organ in which there takes place a considerable absorption of sugar from the circulating blood. Our data differ from the results of the experiments of E. C. London and N. P. Kotchnewa [10] who noted only a negligible absorption of sugar from the blood by the pancreas.

In order to make more precise the question as to how reversible are the changes which arise in the regulation of blood sugar content, experiments were conducted, the purpose of which consisted in clarifying the period necessary for restoration of normal sugar content in the blood of the pancreatic vein and in the peripheral blood after temporary exclusion of the pancreas from the general circulation.

In experiments performed on 6 cats the pancreas was excluded from the general blood stream for 15 minutes, and then blood circulation was restored once again in the pancreas for 30 minutes. Exclusion of the pancreas from the general blood stream produced in only 15 minutes a considerable reduction in the sugar content of the blood of the pancreatic vein and, simultaneously, an increase in the sugar content of the peripheral blood. When the pancreas was subsequently re-included in the general blood stream, within 30 minutes the sugar content of the blood of the pancreas and that of the general blood stream once again became almost identical (Fig. 1, c).

The data put forward indicate a direct relationship between sugar content, both that of the general blood stream and that of the blood flowing from the pancreas, and the conditions of blood circulation in the pancreas itself; they permit one to assume that uninterrupted circulation of blood through the pancreas is necessary for the maintenance of the normal blood sugar level and for the proper course of the process of utilization of sugar by tissues. During the circulation of blood through the pancreas there occurs a very intensive absorption by it of sugar from the circulating blood, considerably exceeding the absorption by the other organs over the same interval of time.

These facts oblige one to presume that the incretion of insulin by the pancreas is accomplished without interruption, and not periodically, and that the hyperglycemia which is observed after the exclusion of the pancreas develops in the first few minutes, and not after several hours, as some researchers have hitherto considered [1, 2].

In the second part of our work we studied the role of the pancreas in the complex reflex regulation of carbohydrate metabolism in connection with the intake of food.

Experiments were conducted on an esophagostomized dog, well adapted to laboratory treatment. A cannula was applied to the pancreatic vein. In order to conduct experiments with actual and simulated feeding during partial exclusion of the pancreas from the general blood stream, the cannula was screwed on before the juncture of the pancreatic with the duodenal vein. First control experiments were conducted without the intake of food; then a study was made of the influence of simulated feeding with 500 ml of a 10% glucose solution on the course of carbohydrate metabolism during normal blood circulation in the pancreas and after its exclusion from the general blood stream. After a definite interval of time the screw of the cannula was loosened and normal blood circulation restored in the pancreas.

In these experiments the sugar and lactic acid content of the peripheral blood was studied.

The control experiments showed that the blood sugar content throughout the entire experiment (5 hours), both during normal blood circulation in the pancreas and during its partial exclusion from the general blood stream, decreased about equally. The lactic acid content of the blood decreased during the partial exclusion of pancreas from the general blood stream; after the restoration of blood circulation in the pancreas it returned to its earlier level or even somewhat exceeded it.

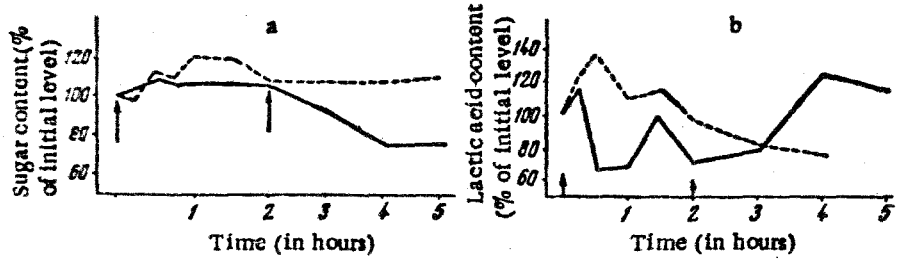

Fig. 2. The influence of simulated feeding with glucose.
a) blood sugar content; b) lactic acid content; 1) during normal blood circulation in the pancreas; 2) during partial exclusion of the pancreas from the blood circulation. The arrows indicate the beginning and end of the exclusion of the pancreas from the general blood stream.

Simulated feeding with glucose during partial exclusion of the pancreas from the general blood stream initially produced a hyperglycemic effect, as it did during normal blood circulation. After the pancreas was re-incorporated in the general blood stream, however, a significant and prolonged reduction in blood sugar content was observed (Fig. 2, a). The lactic acid content of the blood decreased after simulated feeding with the glucose solution during exclusion of the pancreas, while in the experiment without disturbance to the flow of blood from the pancreas it increased for an extended period of time (Fig. 2, b). The mechanism of this phenomenon is still not clear and further research is required.

Analysis of the data obtained after simulated feeding with the glucose solution during various conditions of blood circulation in the pancreas permits one to assume the presence of a connection between the changes in carbohydrate metabolism and the disturbance to the circulation of blood in the pancreas. Partial exclusion of

the pancreas results, after simulated feeding with glucose solution, in a reduction of the reflex phase of hyperglycemia and hypolactacidemia; the subsequent incorporation of the pancreas into the general blood stream results in hyperlactacidemia and a reduction in blood sugar content due to the excess of insulin, which during exclusion of the pancreas temporarily did not leave it to enter the circulating blood.

On the basis of our experiments the conclusion can be drawn that the effect of a rise in blood sugar after simulated feeding with glucose is accomplished with the participation of the pancreas. During partial exclusion of the pancreas from the general blood stream, the act of simulated feeding of an animal produces in it a decrease in the hyperglycemic and lactacidemic effect.

The results of the present work attest to the important role of the pancreas in the regulation of the sugar and lactic acid content of the blood and in the process of their utilization by tissues.

SUMMARY

The effect of temporary exclusion of the pancreas from the general blood circulation on the blood sugar content in the vanae pancreaticae and in peripheral blood was studied.

In critical experiments carried out on 15 cats it has been stated that the cessation of the blood flow from the pancreas brings about an increase in sugar content in the peripheral blood and its decrease in the blood of the vanae pancreaticae. In the case of free blood circulation through the pancreas, sugar content increased almost to an equal degree in both peripheral blood and vanae pancreaticae.

In series experiments on esophagostomized dogs it has been shown that, when the pancreas is excluded from the general blood circulation, simulated feeding with glucose brings about hyperglycemia and hyperlactacidemia.

These results reveal the important role of pancreas in the complex reflex regulation of carbohydrate metabolism.

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