EFFECT OF INSULIN AND GLUCOSE ON DEVELOPMENT OF GASTRIC ULCERS

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In rats subjected to an ulcerogenic procedure (Shay's operation), administration of insulin or glucose leads to the development of more severe ulceration of the gastric mucous membrane.

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Considering the role of insulin as a hormone regulating various aspects of carbohydrate, lipid, and protein metabolism, there is reason to suppose that it exerts a definite action on the nutrition of tissues and, in particular, on the gastric mucous membrane. The juice secreted by the gastric glands under the influence of insulin resembles the "vagus juice" and has a high hydrochloric acid concentration and high digestive power [1]. In some cases, injection of 10 units insulin into patients with histamine-resistant achlorhydria causes liberation of free hydrochloric acid in the gastric juice [4]. Since insulin stimulates gastric secretion, it must be supposed on a priori grounds that it activates the peptic factor, which is an important component in the mechanism of development of gastric ulcer.

The object of the present investigation was to study the effect of insulin and glucose on development of ulcers in the gastric mucous membrane.

EXPERIMENTAL METHOD

Albino rats weighing 120-140 g were used as experimental animals. Under ether anesthesia laparotomy was performed and the stomach removed together with the pancreas. Using ophthalmic forceps small pieces were pinched from the middle part and tail of the pancreas, until about 60-70% of the gland tissue had been removed. During the operation attempts were made to spare the dense network of blood vessels; the large ducts of the gland remained intact. Gastric ulcers were induced in the experimental animals 17-19 days after the operation, and also in intact animals (control group) by our modification [2] of Shay's method (ligation of the pylorus). The animals were sacrificed 24 h after ligation of the pylorus and the number of ulcers in the gastric mucous membrane was counted macroscopically, and their depth and size estimated. In other experiments, the animals were injected with protamine – zinc – insulin in a dose of 0.2-0.4 unit. In a series of experiments administration of insulin was followed by injection of glucose solution (5 ml, 3.6%) intraperitoneally once or twice daily before Shay's operation was performed. The experiments were carried out on 154 rats (in five series).

EXPERIMENTAL RESULTS

Partial resection of the pancreas had no effect on development of degenerative lesions in the gastric mucous membrane, as shown by the almost equal number of erosions and ulcers in the animals of the experimental and control groups (experiments of series I). Consequently, partial pancreatectomy, causing a decrease in insulin content (hypoinsulinism), had practically no effect on the resistance of the gastric mucous membrane. Since in the experiments of series I the insulin apparatus was not totally removable, the animals developed only a mild form of diabetes (blood sugar 113-114 mg%). Evidently, only some slight disturbance of carbohydrate metabolism (depression of glucose utilization) was present, and this was not reflected in the nutrition of the gastric mucous membrane.

After Shay's operation, preceded by injection of 0.2 unit insulin, only a slight increase in the number of ulcers was observed in the gastric mucous membrane (experiments of series II), whereas injection of

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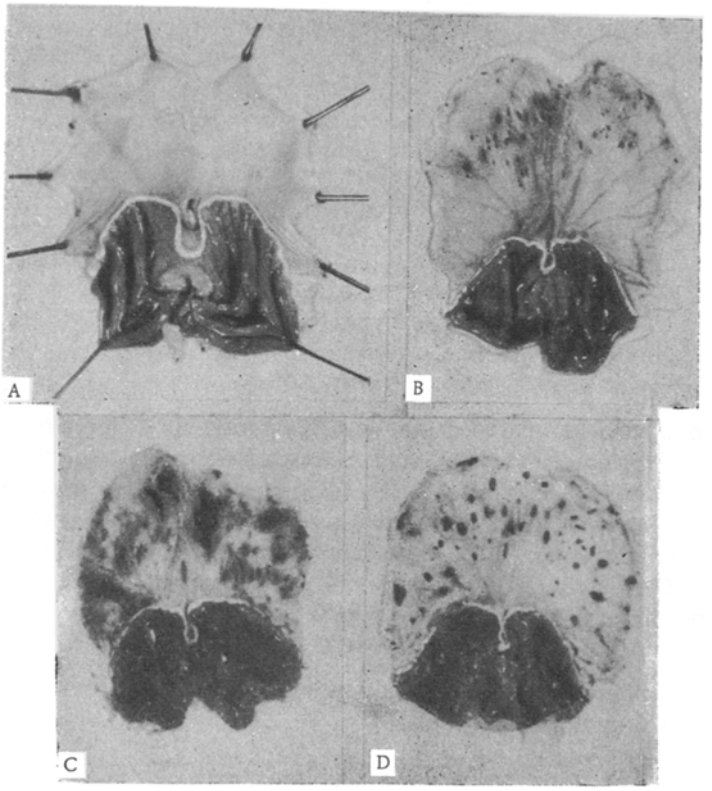

Fig. 1. Mucous membrane of the stomach. A) Normal; B) after ulcerogenic procedure; C) after injections of insulin in dose of 0.4 unit followed by ulcerogenic procedure; D) after injections of glucose (3.6%) followed by ulcerogenic procedure.

0.4 unit insulin (experiments of series III) over a period of three days before the ulcerogenic procedure led to a marked increase in the number of all types of lesions (especially large ulcers) in the gastric mucous membrane of the animals of the experimental group (see Fig. 1).

In the analysis of the results of the experiments of series III, it was important to determine to what degree the increase in number of ulcers following administration of insulin was due to the ensuing hypoglycemia. Accordingly, the experiments of series IV were carried out, in which the experimental animals received glucose as well as insulin (control animals received glucose only). In these experiments insulin also increased the number of ulcers. It may, therefore, be concluded that the hypoglycemia itself did not disturb nutrition of the mucous membrane, and this disturbance must in fact be attributed to changes in the energy metabolism in the tissues resulting from administration of insulin. The experiments of series V (in which one group of animals received glucose parenterally on the days preceding Shay's operation while the other group was subjected to the ulcerogenic procedure only) showed that injection of glucose also increases the sensitivity of the gastric mucous membrane to the ulcerogenic factor.

The results of the experiments of series IV and V can be explained on the assumption that one of the main functions of insulin is to stimulate the utilization (oxidation of glucose in the peripheral tissues, so that hyperinsulinism may lead to excessive "combustion" of glucose, thus disturbing the normal course of metabolic processes in the gastric mucous membrane. In addition, administration of glucose alone (experiments of series V) may itself aggravate this state, and may also, as has been shown [3], bring about a greater liberation of insulin because of an increase in the sugar concentration in the blood flowing through the pancreas. The possibility is not ruled out that the injected insulin, by activating the gastric secretory function, enhances the role of peptic factors increasing the degree of ulceration.

It was thus concluded from the results of the investigation that activation of carbohydrate metabolism under the influence of insulin has an adverse effect on nutrition of the gastric mucous membrane, whereas a deficiency of insulin (development of a mild form of diabetes) is not reflected in the development of degenerative changes in the gastric mucous membrane.

LITERATURE CITED

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