

# EFFECT OF PARTIAL PANCREATECTOMY ON TONUS OF THE VAGUS NERVE CENTER OF DOGS IN CHRONIC EXPERIMENTS

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It has been shown [3-6] that the preliminary (several days before the experiment) removal of part of the pancreas and ligation of its ducts in warm-blooded animals causes certain disturbances of the parasympathetic innervation of the heart. These disturbances consist of a lowering of the excitability of the vagus nerves, a decrease in the negative inotropic effects, weakening of the negative chronotropic and dromotropic effects, shortening of the period of vagal arrest of the heart, and some degree of depression of its automatism.

Particularly marked changes are observed in the vagal tone. On the 6th-10th day after the operation, bilateral vagotomy is not accompanied by the usual increase in frequency of the cardiac contractions and in some cases leads to a paradoxical slowing of the heart [3]. The changes described were demonstrated entirely in acute experimental conditions and were explained by disturbance of the acetylcholine metabolism in the pancreatectomized animals.

In the present investigation the tonus of the vagus nerves was studied after partial pancreatectomy in chronic experimental conditions.

## EXPERIMENTAL METHOD

Experiments were carried out on 18 dogs and the electrocardiogram (ECG) was recorded in lead 2. The tonus of the vagus nerves was estimated from the difference in heart rate before and after subcutaneous injection of 1 ml of a 0.1% solution of atropine, and the adequacy of the dose used was judged from the absence of effect of further injection of the preparation. In some experiments, before the tonus of the vagus nerves was determined, morphine (2 ml of a 1% solution) or acetylcholine (2 ml of a 1 : 10,000 solution) was injected. The investigations were carried out repeatedly every 2 or 3 days, both before the operation and during the 2-4 weeks after removal of approximately half the pancreas and ligation of its ducts.

## EXPERIMENTAL RESULTS

Before the operation the initial frequency of the cardiac contractions varied in the different dogs from 80 to 140 beats/min (mean 99). After injection of atropine the heart rate rose to 160-260 beats/min (mean 182). The heart rate was thus increased on the average by 84% after injection of atropine.

From the 3rd to 4th day after pancreatectomy the heart rate rose slightly from its initial level. In some cases this increase was progressive and reached its maximum on the 7th-9th day. Subsequently, the heart rate fell, but usually remained a little higher than its preoperative level. In the first 10 days after the operation, the initial heart rate varied in the different experiments from 106 to 156 beats/min, with a mean value of 125 beats/min. Simultaneously with the increase in the heart rate, its rhythm became more regular on account of the diminution or disappearances of the respiratory arrhythmia.

Injection of atropine against this background in every case caused an increase in the heart rate, although in both its relative and absolute values the increase was much less than before the operation. After injection of atropine the heart rate varied in this period from 142 to 170, with a mean value of 158 beats/min, i.e., it rose by only 26% of its initial value. Later, parallel with slowing of the heart rate, the degree of

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increase in frequency of the cardiac contractions increased, and the difference between the heart rate before and after injection of atropine increased successively and approached its values before the operation. Hence, the preliminary operative disturbance of pancreatic function, as in the acute experiment, caused an increase in the initial heart rate, a marked decrease of vagal tonus, and some decrease in the frequency of the automatic rhythm observed after blocking the parasympathetic innervation.

Although the changes observed in the acute and chronic experiments were consistent in principle, the results of the latter experiments showed certain distinguishing features. These included the higher initial frequency of the cardiac contractions both before and after the operation, the comparatively smaller increase in the heart rate after blocking the vagus nerves, especially in the animals not undergoing pancreatectomy, and the somewhat smaller change in the tonus after the operation, and also the earlier appearance of the changes and their longer duration. Although in individual cases after the operation changes in the activity of the heart on atropinization were almost completely absent, the paradoxical slowing of the heart rate sometimes observed after vagotomy was not found in the chronic experiments. An important factor determining the differences between the results of the acute and chronic experiments was evidently the use of morphine as basal anesthetic, for it causes a marked increase in the tonus of the vagus nerve centers. For this reason in experiments on 4 dogs, before atropine was given, morphine solution was injected, causing a decrease in the heart rate of the intact dogs by 15-50 beats/min. Injection of morphine on the first days after the operation caused little or no change in the heart rate, and only later, as the vagal tonus was restored, did the morphine again begin to exhibit its usual action. Hence, under the influence of morphine, the initial heart rate was reduced, especially before the operation, and the difference between the tonus of the vagus nerves before and after the operation increased considerably and came close to the values obtained in the acute experiments.

Because of reports of disturbance of the acetylcholine metabolism after partial pancreatectomy in warm-blooded animals [1, 7], in an attempt to restore this metabolism to normal, pharmacological acetylcholine was injected into two pancreatectomized dogs. The acetylcholine was injected intravenously, daily from the 3rd day after the operation, including on the day of the experiment 1 h before the investigation. These experiments showed that this injection completely prevented the change in tonus of the vagus nerves in the pancreatectomized animals. The initial heart rate after the operation was not increased, but actually lowered below normal. Atropinization caused a marked increase in the heart rate, essentially indistinguishable from its value before the operation. The action of the injection acetylcholine did not quickly pass away, but was present even 24 h after its injection in the form of persistence of a fairly high tonus of the vagus nerves. This result may be of definite practical importance in connection with the problem of management of the postoperative period following surgical operations on the pancreas.

So far as the changes in the character and shape of the ECG after partial pancreatectomy are concerned, these were very similar to those observed in the acute experiments [3]. These changes consisted of slight shortening of the P — Q interval, lengthening of the QRST segment, a decrease in the amplitude of the principal waves of the ECG, and reduplication of the P and R waves.

The results obtained thus indicate the presence of significant disturbances of the tonus of the vagus nerve centers and the electrical activity of the heart after operations on the pancreas.

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