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The character of excretion of neutral red after various types of vagal denervation of the stomach and during insulin stimulation of gastric secretion was studied in acute experiments on 24 dogs. Differences in the functions of branches of the vagus nerves distributed in the stomach wall were discovered.

Classical anatomical data indicating the presence of widely anastomosing nervous plexuses, viz., subserous, intermuscular, and submucous [1], have given rise to the idea that impulses along all branches of the vagus nerve can affect the whole mucous membrane. This view has been confirmed by clinical observations of difficulty or even impossibility of obtaining total vagal denervation of the stomach. However, many observations on patients show that blocking the parasympathetic innervation of the stomach causes a marked decrease in acid gastric secretion, with healing of gastric and duodenal ulcers. Preservation of the integrity of the stomach as an organ under these circumstances makes vagotomy a more sparing operation than resection of the stomach and gastrectomy.

However, the increasing use of vagotomy in the treatment of peptic ulcer has been delayed by a number of unsolved problems. The more important of these are as follows. 1) At what level must the vagus nerve be divided, and what type of vagotomy is preferable (total or selective)? 2) What is the reason for differences in the effects of incomplete vagotomy? 3) Is it possible to make absolutely sure during the operation that the vagotomy will be sufficiently complete and effective? The experimental and clinical solution of all these problems is clearly impossible without precise knowledge of the anatomy and physiology of the parasympathetic innervation of the stomach.

The present investigation was carried out to study the parasympathetic innervation of the stomach.

EXPERIMENTAL METHOD

The experimental animals were 24 dogs of both sexes and different ages, weighing from 2 to 15 kg, deprived of food for 20-24 h before the experiment. Under general anesthesia (morphine, thiopental sodium) laparotomy was performed through an upper midline incision. The vagus nerve was divided at different levels depending on the aim of the experiment, and different degrees of denervation of the stomach were achieved. Depending on the level and type of vagotomy, the experiments were subdivided as follows: division of the left vagal nerve trunk, 6 cases (Nos. 3-8); division of the right vagal nerve trunk, 5 cases (Nos. 9-13); selective gastric vagotomy with preservation of one gastric terminal, 6 cases (Nos. 14-19), selective gastric vagotomy with preservation of two adjacent terminals, 5 cases (Nos. 20-24). Two animals in which the vagus nerve was not divided served as the control (cases Nos. 1 and 2).

After division of the branches of the vagus nerve, the stomach was brought up into the wound as far as possible and opened along the greater curvature in order to preserve the nerve branches running along the lesser curvature, and to interfere as little as possible with the blood supply to the organ. Bleeding vessels were tied, and the stomach was straightened out with holding forceps. The mucous membrane was

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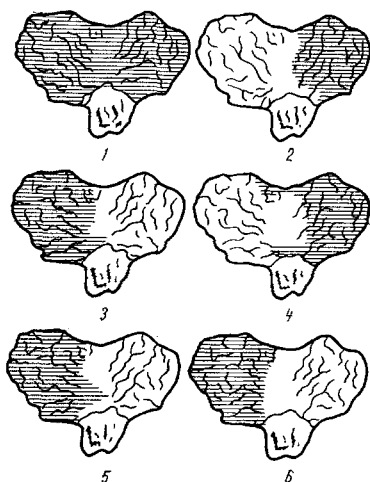


Fig. 1. Dog's stomach: primary secretory response in control and after division of main trunk of vagus nerve. Explanation in text.

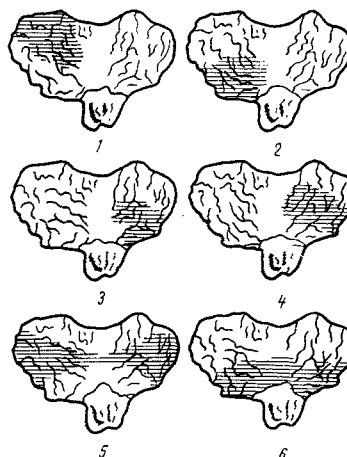


Fig. 2. Dog's stomach: primary secretory response after vagotomy with one and two terminal gastric branches left intact. Explanation in text.

carefully freed from contents. To stimulate the gastric glands along the vagus nerves, insulin was injected into the animal in a dose of 1.5 units/kg body weight, the dose normally used to study the vagal phase of gastric secretion in dogs [2]. At the same time, 10-20 ml (depending on the weight of the animal) of 2% neutral red solution was injected. Insulin stimulation was preferred to electrical because of the extensive use of insulin in clinical practice, and also because after insulin stimulation, unlike electrical, spontaneous gastric secretion is absent, even in cases of incomplete vagotomy.

To determine the secretory zones of the gastric mucosa, the method of chromoscopy was used. Innervated areas of the mucosa were determined visually by examining the excretion of neutral red, for the dye is eliminated in the period of secretory activity of the gastric glands [2-4].

Every 5-7 min, filter paper was applied to the mucous membrane, and to prevent the dye from spreading, the sheets were at once dried over the flame of a burner. By this method the beginning of excretion of the dye could be determined precisely and the borders of the secretory zones accurately recorded. An idea was obtained of the true zone of gastric mucosa secreting the dye, and its area could be measured. The concentration of dye eliminated could be estimated reasonably accurately from the intensity of staining of the paper. In some experiments, using universal indicator paper, the pH of the medium was measured in different parts of the gastric mucosa. The duration of the investigation did not exceed 3 h. The time when elimination of dye began (the primary secretory response) and the time of the generalized response were recorded. The first of these times reflected the direct vagal secretion, the second the beginning of the hormonal (humoral) phase of gastric secretion.

EXPERIMENTAL RESULTS

In 2 dogs (cases Nos. 1 and 2) in which for control purposes and also to examine the time and character of elimination of the dye, the vagus nerve was not divided, the remainder of the experiment took place as described above. In these experiments the duration of the latent period was 13 and 17 min, and at the end of this time elimination of the dye was observed by the mucosa of the body and fundus of the stomach. The intensity of elimination of the dye was later in the region of the body and less in the mucosa of the fundus of the stomach. During secretion, some increase in the degree of hyperemia of the mucous membrane was observed, and this was particularly marked in the period of maximum elimination of the dye. The results are shown in Fig. 1:1. The diagram represents the stomach opened along the greater curvature. The shaded areas show the zones of primary secretion.

After division of the trunk of the left vagus nerve (cases Nos. 3-8) the mucous membrane of the anterior stomach wall did not excrete the dye, but secretion by the innervated part of the mucous membrane was at a reasonably high level. The primary secretory response in these cases was recorded after

12-18 min (Fig. 1: 2, 4). After division of the right trunk of the vagus nerve (cases Nos. 9-13), neutral red appeared in response to insulin hypoglycemia on the anterior wall of the stomach (Fig. 1: 3, 5, 6). In these experiments it was clear that the mucous membrane of the fundus of the stomach secreted dye less intensively than the mucous membrane of the body. In all experiments in which the vagus nerve trunks were divided, 25-64 min from the beginning of injection of the dye it began to be eliminated in the denervated areas of the mucous membrane of both the fundus and body of the stomach (generalized secretory response). No dye was eliminated from the antrum. No appreciable parallel could be detected between the onset of the primary and generalized secretory responses. The mean difference between the recorded times was 30 min. In some experiments the time interval between the beginning of primary secretory response and the generalized response varied within wide limits (8 min in experiment No. 9; 47 min in experiment No. 4).

It is interesting to note that 1 mg atropine produced the same complete blocking of vagal impulse activity as surgical vagotomy. This was shown conclusively by experiment No. 11: a combination of division of the posterior trunk of the vagus nerve with injection of atropine was followed by absence of elimination of dye from the whole gastric mucosa, at least during 3 h of observation.

A highly distinctive secretory response was obtained in experiments in which most of the gastric terminals of the parasympathetic nerve were divided and only one of the branches leading to the various parts of the stomach wall was left intact. The diagrams illustrating the results of these observations (Fig. 2: 1-4) show clearly that, despite some superposition of the secretory zones excreting the dye, each branch is virtually a terminal. Stimulation of only the superior (proximal) branch of the anterior vagus (case No. 15) induced secretion in a limited area of the anterior wall of the gastric mucosa (Fig. 2: 1). If all branches were divided except the middle terminal of the anterior (case No. 17) or posterior (case No. 16) vagus, the area of elimination of dye was confined to the central part of the body of the stomach on the anterior or posterior wall respectively (Fig. 2: 4). Preservation of the distal branches of the vagus (cases Nos. 14 and 18, Fig. 2: 2, 3) was followed by recording of secretion of dye only in the distal parts of the mucosa of the body of the stomach, immediately adjacent to the antrum. The time of appearance of the primary secretory response in this series of experiments varied within wide limits, from 11.5 to 43 min. The shortest latent period was observed in case No. 15, when partial denervation of the stomach was carried out 46 days before the acute experiment. In this case elimination of the dye took place more intensively than in experiments Nos. 14, 16-18. The ratio between the area of the primary secretory zone and the total area of the gastric mucosa in cases Nos. 14, 15, and 18 was 1:12.4, 1:11.6, and 1:8.7 respectively (mean 1:10.9). Considering that the number of visible terminals running from each trunk to the stomach wall is between 7 and 12, the ratios fully confirm that the branches are indeed terminal in nature both anatomically and functionally. In no case in this series of experiments was a generalized secretory response obtained. Like the primary secretory response, it was absent in case No. 19 in which one branch of the anterior division of the vagus nerve running directly to the pylorus was left intact.

The secretory profile in experiments in which two adjacent terminals of the vagus nerve running to opposite surfaces of the gastric mucosa were stimulated (cases Nos. 20-24) showed a distinctive result. In cases Nos. 20 and 23 in which adjacent branches running to the central part of the body of the stomach were preserved, a primary secretory response was recorded in relatively localized adjacent areas of the gastric mucosa in the middle parts of the body (Fig. 2: 5). In cases Nos. 21 and 22 a primary secretory response was found in adjacent areas of the mucous membrane of the distal part of the stomach body (Fig. 2: 6). Characteristically, a generalized secretory response was found in cases in which the mucous membrane of the distal parts of the stomach remained innervated. The latent period of the primary secretory response in cases Nos. 20, 21, 22, and 24 corresponded in general to that found in the preceding series of experiments.

These experiments showed that the distribution of the terminal gastric branches of the vagus nerves is segmental in character. After vagotomy the secretory response of the mucous membrane depends on the degree of denervation of the stomach. Inadequate vagotomy is the result of preservation of individual branches running to the antral portion of the stomach.

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