The Effect of Changes in Antral pH on the Basal Release of Gastrin[1] (37293)

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Acidification of the gastric antrum reduces the secretion from denervated and innervated fundic pouches in response to various stimuli (1–4). With sensitive radioimmunoassay technics it is possible to directly measure serum concentrations of gastrin released from the antrum during periods of variation in antral acidity (5). In the present work we report direct evidence on the timing of gastrin release after application of solutions at varying pH to antral mucosa which was not otherwise stimulated. Gastrin concentrations in blood draining the gastric antrum were measured by radioimmunoassay.

Materials and Methods. Twelve adult mongrel dogs were divided into two groups of six. Each dog was fasted for 24 hr and anesthetized with pentobarbital sodium. At laparotomy the blood supply of the antrum was dissected to allow intermittent sampling of the antral venous outflow as described previously (6). The antrum was isolated from the fundus by means of a clamp placed across the antra-fundic junction. A double-lumen catheter for perfusion was placed via the duodenum into the antrum, and the pylorus was ligated around the catheter. During a 30 min basal period, the antral secretions were collected for determination of pH. Antral perfusion was then begun using solutions of 0.9% NaCl adjusted to pH values between 1.0 and 8.0. The rate of perfusion was 150 ml/hr; the inflow pressure was less than 2 cm H_2O and visible distension of the pouch did not occur. Antral venous blood samples for gastrin measurement were obtained twice in the basal state (—15 min and zero time) and at 15 min intervals throughout the experiments.

In six dogs (Group 1) continuous antral perfusion was begun at pH 7.0, and every 30 min the pH of the perfusate was lowered by 1 unit in order to make the antrum more acid. In the other six dogs (Group 2) the antrum was perfused for 30 min periods, first at pH 7.0, then serially at pH 3.0, 8.0, 1.0 and 7.0. Sections of antral mucosa were taken for histologic study at the end of each experiment.

The gastrin concentrations in the serum of the antral venous blood were measured by radioimmunoassay (5) and are expressed as the mean of the observed values with the corresponding standard error (±SE). Student's *t* test was used to determine statistical significance of the data.

Results. Irrigation of the antrum with solutions of varying acidity produced no histologic evidence of injury to antral mucosa.

Group 1 (Fig. 1.) The results of measurement of gastrin values in antral venous blood in the six dogs are shown in Fig. 1. The mean basal serum gastrin was 172 ± 23 pg/ml. The pH of the aspirated basal secretions from the antral pouch was between 3.5 and 5.0. Irrigation of the antrum with saline pH 7 increased the gastrin concentration to a peak of 390 ± 69 pg/ml ($p < 0.02$). Stepwise lowering of the pH of the antral perfusate resulted in progressive diminution in gastrin values. At pH 5 gastrin levels fell to 215 ± 61 pg/ml and at pH 3, to 120 ± 28 pg/ml. Perfusion at pH 2 and pH 1 resulted in gastrin levels significantly lower than basal levels (at pH 2 the gastrin value was 108 ± 21 pg/ml, and at pH 1 gastrin was 107 ± 24 pg/ml).

Group 2 (Fig. 2). Mean basal serum gastrin values in the venous outflow of the

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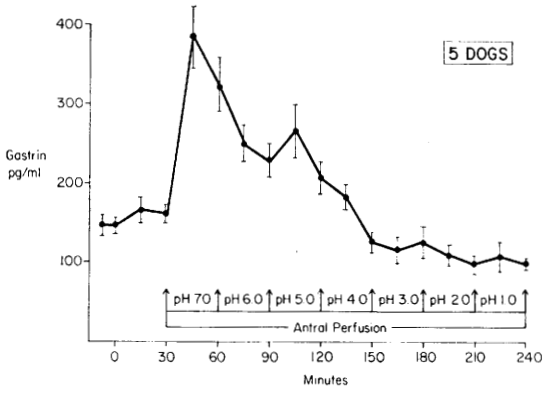

FIG. 1. Effect of a stepwise decrease in antral pH on gastrin concentrations in the antral venous outflow.

antrum in these six dogs was 88 ± 9 pg/ml (Fig. 2). The pH range of basal antral secretions was between pH 4 and 5 in all dogs. Perfusion of the antrum with saline pH 7 increased the antral venous gastrin to 225 ± 34 pg/ml ($p < 0.02$). When the pH of the antral perfusate was changed to pH 3, there was a significant decrease of gastrin levels to 104 ± 13 pg/ml ($p < 0.01$). Perfusion with saline pH 8 increased gastrin significantly to 254 ± 21 pg/ml and subsequent perfusion with saline pH 1 resulted in a fall in the antral venous gastrin concentration to 70 ± 6 pg/ml, a level significantly below basal ($p < 0.05$). When perfusion was then begun with saline pH 7, gastrin levels rose significantly again to 175 ± 13 pg/ml.

Discussion. Basal serum gastrin levels in antral vein blood show more variations from dog to dog than do peripheral blood levels (5) but antral vein concentrations for individual fasting dogs remain relatively constant. The reasons for the large differences in gastrin values from the antral vein of the two groups of dogs is not clear. Each assay has internal standards which rarely vary more than 10% from assay to assay. Variations between groups of dogs are not uncommon and we do not as yet have a satisfactory explanation. Coprophagia is not rare in fasting dogs, but the stomachs were inspected at operation and were empty. As far as can be determined, the gastrin levels represent basal values.

There has been considerable difference of opinion regarding the mechanism responsible for the suppression of gastric acid secretion after antral acidification (4, 7). The development of highly sensitive radioimmunoassay technics for measurement of physiologic levels of circulating gastrin has allowed direct study of antral gastrin release under varying conditions. We have shown that acidification of acetylcholine solution only partially blocks its stimulatory effect on gastrin release from the antrum (5), and vagal release of gastrin induced by electrical stimulation of the antral vagus is only partially suppressed by antral acidification (8).

It has long been a question whether simply raising antral pH would bring about the release of gastrin. The present studies show a very close relationship between the pH to which

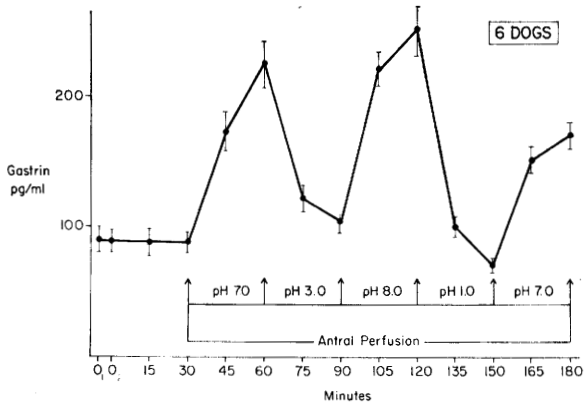

FIG. 2. Effect of antral pH changes on the gastrin concentration of the antral venous outflow.

the antral mucosa is exposed and the rate at which gastrin is released from the antrum into the circulation. Neutralization of the antrum results in significant increase of gastrin release compared to the resting state (pH 3.5–5). On the other hand, perfusion of the antrum with saline adjusted to pH 1 significantly lowers but does not totally suppress basal release of gastrin by the antrum. These studies have demonstrated by direct measurement that measurable and, probably, physiologically significant amounts of gastrin are released during basal periods. There is a very sensitive feedback mechanism between antral pH and gastrin release. Antral acidification results in a significant diminution of antral gastrin release.

Summary. Gastrin concentrations in the blood draining the gastric antrum were measured by radioimmunoassay during changes in the antral pH. Neutralization of the antrum (raising the basal ambient pH of 3.5–5 to 7 or 8) resulted in a significant increase of antral venous gastrin concentration. Acidification of the antrum significantly lowered, but did not abolish, the basal release of gastrin.

These studies demonstrated, by direct measurement of gastrin, the presence of a very sensitive feedback mechanism between antral pH and gastrin release, and that gastrin may be released by simply raising the basal antral pH to 7.

1. Woodward, E. R., Lyon, E. S., Landor, J., and Dragstedt, L. R., Gastroenterology **27**, 766 (1954).

2. Woodward, E. R., Robertson, C. R., Fried, W., and Schapiro, H., Gastroenterology **32**, 868 (1957).

3. Gillespie, I. E., and Grossman, M. I., Amer. J. Physiol. **203**, 557 (1962).

4. Thompson, J. C., *in* "Gastrin" (M. I. Grossman, ed.), p. 193. Univ. of California Press, Berkeley (1966).

5. Jackson, B. M., Reeder, D. D., and Thompson, J. C., Amer. J. Surg. **123**, 137 (1972).

6. Charters, A. C., Odell, W. D., Davidson, W. D., and Thompson, J. C., Surgery **66**, 1041 (1969).

7. Thompson, J. C., Annu. Rev. Med. **20**, 291 (1969).

8. Becker, H. D., Reeder, D. D., and Thompson, J. C., Clin. Res. **21**, 49 (1973).

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