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Effect of Gastrin on Electrical Activity of Antrum and Duodenum of Dogs (40481)

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The stimulatory action of gastrin on antral electrical activity is well known (1). In previous studies, however, doses of gastrin used to increase antral motor activity were high compared to those required for stimulation of gastric acid secretion which has been regarded as the primary physiological action of gastrin (2). Accordingly, in the present study we tested gastrin within the range of doses used to establish response curves for gastric acid secretion (3).

The experiments were done in fasted dogs. Since electrical and motor activity of the gut in the fasted state exhibits cyclic activity (4, 5), the period of motor quiescence, phase I of the interdigestive myoelectrical complex, was chosen as the test period to avoid confusion between spontaneous and gastrin-induced activity. During phase I pacesetter potentials show few or no action potentials.

Methods and procedures. Using sterile surgical technique and inhalation anesthesia (methoxyflurane), monopolar silver–silver chloride wire electrodes were sewn to the serosal surface of the gastric antrum and duodenum of four healthy mongrel female dogs. The silver wire of the electrodes protruded 0.5–1 mm into the tissue from an acrylic disc in which the wire was mounted. The electrodes and their connections to a multipinned socket, mounted in a stainless steel cannula, were similar to those used in previous studies (6). The antral electrodes were placed 1, 3, and 5 to 7 cm orad to the pylorus and the duodenal electrodes were 5 and 10 cm distal to the pylorus. The cannula carrying the leads was brought to the surface through the left mammary line and fixed to the sheath of the rectus muscle by stainless steel sutures.

Following recovery from the surgical procedure, the animals were trained to lie quietly on the side or to stand partially supported in a nylon mesh sling. Electrical recordings were obtained by connecting each electrode to a channel of a Brush Mark 200 direct-writing pen recorder, using a time constant of one second and an indifferent electrode placed beneath the skin or attached to the flange of the metal cannula in the abdominal wall.

Tests were done when the dogs had been fasted for 24 hr. Cycles of the interdigestive myoelectric complex were always observed (4). In the dogs used in the present study, the mean ± SE interval between phase III of the complex was 94.5 ± 3.3 min (n = 12) and mean ± SE duration of phase I, the period of few or no action potentials, was 48.6 ± 2.7 min (n = 12).

Synthetic unsulfated human little gastrin (G17-I, Imperial Chemical Industries Pharmaceuticals) was dissolved in 0.1 M NH_4OH and then diluted in physiological saline solution before being infused via a leg vein at a uniform rate of 32 ml h^{-1} using a syringe pump. The infusion of gastrin was started 10 minutes after onset of phase I of the interdigestive myoelectric complex and continued for 30 min. Each dose of gastrin was given on a different day in random order and each dose was tested twice in each dog. The doses used ranged from 12.5 to 200 pmol kg^{-1} h^{-1}.

During the last 5 min of each 30-min test period, at which time electrical activity had reached a steady plateau, the pacesetter potential frequency and the percentage incidence of pacesetter potentials with action potentials were determined. In control experiments, a saline infusion was given and the same determinations made during the same 5-min period. Recordings from the same electrode were used for both control and test measurements.

In three of the four dogs, duodenal electrical recordings were sufficiently free of artifact to be readily analyzed for pacesetter potential frequency and for incidence of action potentials.

Results. As the dose of gastrin was increased, pacesetter potential frequency increased in both the antrum and the duodenum (Fig. 1). The values in the figures are for that electrode in each animal which gave

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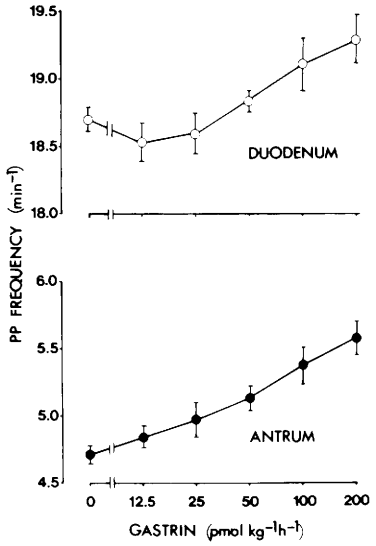

FIG. 1. Effect of graded doses of gastrin on pacesetter potential frequency in the antrum (8 tests, 4 dogs) and duodenum (6 tests, 3 dogs). Each dose was given on a separate day. In this and subsequent figures, vertical bars denote SE of mean.

the clearest record, but similar electrical responses were seen in all electrodes. With the highest dose used, 200 pmol kg^{-1} h^{-1}, antral pacesetter potential frequency increased by 0.9 min^{-1} from a basal value of 4.6 min^{-1} and duodenal pacesetter potential frequency increased by 0.6 min^{-1} from a basal value of 18.7 min^{-1}. The smallest dose producing a significant ($p < 0.05$) increase above basal was 25 pmol kg^{-1} h^{-1} for the antrum and 50 pmol kg^{-1} h^{-1} for the duodenum.

To study the effect of a very high dose of gastrin, 400 pmol kg^{-1} was infused during 1 min in 3 dogs (Fig. 2). Antral pacesetter potential frequency increased for 2–5 min to a mean peak ± SE of 7.34 ± 0.12 min^{-1} (n = 11) and then rapidly declined. Throughout the response each antral pacesetter potential carried action potentials. While this antral electrical response was occurring, duodenal electrical activity diminished to the point that neither pacesetter potentials nor action potentials could be identified. This strong inhibitory action usually ceased within 10 minutes.

Action potentials. As the dose of gastrin was increased, the incidence of pacesetter potentials with action potentials increased in both the antrum and the duodenum (Fig. 3), reaching 84% in the antrum and 39% in the duodenum with the highest dose tested, 200 pmol kg^{-1} h^{-1}.

Discussion. The results show that gastrin produced dose related increases in the incidence of antral action potentials. The threshold dose for this effect was similar to the threshold dose for gastric acid secretion, about 25 pmol kg^{-1} h^{-1} (3). In other studies we (7) have shown that doses of gastrin in the same range as those used in the present study stimulate motor activity in antral pouches in dogs.

Gastrin also produced dose related increases in antral pacesetter potential frequency with a threshold similar to that for

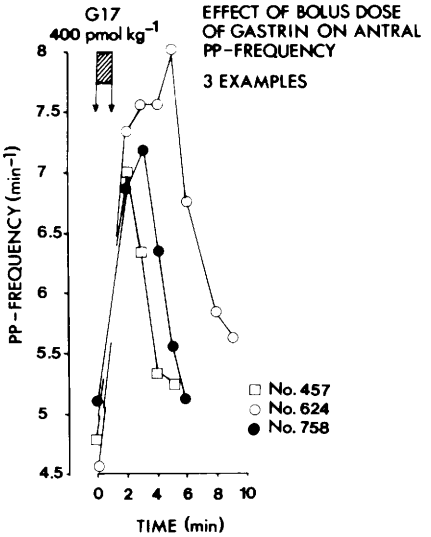

FIG. 2. Effect of a large dose of gastrin on antral pacesetter potential frequency in 1 test in each of 3 dogs.

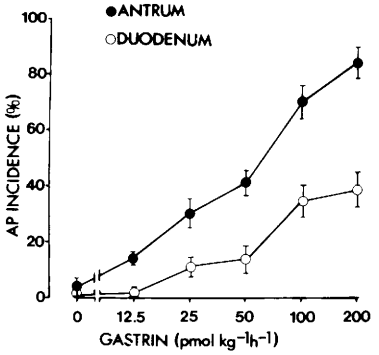

FIG. 3. Effect of graded doses of gastrin on incidence of action potentials on pacesetter potentials in the antrum (8 tests, 4 dogs) and duodenum (6 tests, 3 dogs). Each dose was given on a separate day.

the effect on action potentials. With a dose of gastrin that produces near maximal acid secretion (3), 200 pmol kg^{-1} h^{-1}, the frequency increased to 5.2 min^{-1} from a basal level of 4.6 min^{-1}. With a very large dose of gastrin, 400 pmol kg^{-1} given as an intravenous bolus in 1 min, a much higher frequency was achieved, 7.3 min^{-1}, a value within the range of the highest frequencies that have been achieved by electrical pacing, 6 to 8.8 min^{-1} (8). With doses up to and including 200 pmol kg^{-1} h^{-1}, the changes observed were sustained during the entire 30 min of observation, but with the 400 pmol kg^{-1} dose given in 1 min, the changes were not sustained.

The amount of gastrin released by a meal is enough to stimulate gastric acid secretion (9) and therefore should be enough to stimulate antral electrical activity. After eating, the incidence of antral action potentials on pacesetter potentials appears to depend on the nature of the meal, being least, 0 to 50%, with fat (10); greatest, 100%, with milk or saline (3); and intermediate, about 70%, with a mixed meal. Gastrin could contribute to this increased incidence of action potentials after eating but is unlikely to be the sole or major factor because a meal of saline which releases little or no gastrin markedly increases the incidence of action potentials. After eating, the pacesetter potential frequency decreases (10) whereas gastrin causes it to increase, so we must assume that the factors acting to decrease frequency after a meal predominate.

Duodenal electrical activity was also affected by gastrin. Both incidence of duodenal action potentials and duodenal pacesetter potential frequency increased with increasing doses of gastrin.

Summary. In dogs with electrodes chronically implanted on the stomach and duodenum, graded doses of intravenously infused synthetic human unsulfated little gastrin (G17-I) produced, in both the stomach and duodenum, graded increases in a) frequency of pacesetter potential, and b) incidence of pacesetter potentials with action potentials. The threshold doses of gastrin for these effects were about 25 pmol kg^{-1} h^{-1} in the stomach and about 50 pmol kg^{-1} h^{-1} in the duodenum. These doses of gastrin are similar to the threshold dose for gastric acid secretion.

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