Gastroduodenal motor gradients in the dog after pyloroplasty

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Ormsbee, Herbert S. III, and Paul Bass. Gastroduodenal motor gradients in the dog after pyloroplasty. Am. J. Physiol. 230:2: 389-397. 1976. — Circular muscle contractile activity of the antrum and duodenum and gastric emptying of a liquid test meal were investigated in unanesthetized dogs in which the gastroduodenal junction (GDJ) was altered (Heineke-Mikulicz pyloroplasty). After pyloroplasty, antralization (antral-like contractions occurring in the first portion of the duodenum) was observed during the digestive state. Antralization replaced the normal periods of inhibition that separate periods of duodenal contractions during the interdigestive burst. Bethanechol (0.1 mg/kg sc) and metoclopramide (2.0 mg/kg iv) were capable of stimulating interdigestive contractile activity in the altered GDJ. Pentagastrin (1.0 µg/min iv) produced a differential stimulation on the antrum without appreciably affecting duodenal contractile activity. Pyloroplasty also enhanced the emptying of a 300-ml curate-fat liquid test meal. An intact hypomuscular segment between the antrum and duodenum is important for normal coordinated contractile activity between the antrum and the duodenum and for the normal gastric emptying of liquids.

METHODS

Motor activity. Eight healthy mixed-breed dogs of either sex (9.5-16.5 kg) were used in the study of motor activity. Four of the dogs were in a control group and four were in a group that received Heineke-Mikulicz pyloroplasty. The motor activity of the gastroduodenal area was monitored in all dogs under various challenges. Between experiments the dogs were maintained on solid laboratory chow and water ad libitum in a constant-temperature environment with a 12-h light-dark cycle.

Surgical procedures were performed by the same individual (HSO) with sterile surgical technique and pentobarbital anesthesia (35 mg/kg iv). Heineke-Mikulicz pyloroplasties were performed with a midline abdominal incision. A 5-cm longitudinal incision was made that extended 3 cm on the antrum and 2 cm on the duodenum. The mucosa and muscle layers were closed transversely with one layer of suture and a second transverse suture layer approximated the serosa. The pyloroplasty was inspected at surgery to assure that the GDJ was not obstructed. This was confirmed at the time of autopsy by passing a finger through the junction.

Each control dog and each dog in the pyloroplasty group was implanted with a group of five extraluminal strain gage force transducers. The construction and method of implantation of these transducers have been described (3). The force transducers were connected to a Cannon plug that was surgically implanted subcutane-
Motor activity was recorded for 45 min. This test meal was instilled orally by a gastric tube and consisted of 200 g of canned dog food (Vets dog food, Perk and one liquid meal and three drugs. The solid meal had to be aspirated from the stomach with one or two 50-g weights to the larger amplitude contractions and then the sum is determined for the four force ranges. The motility index (MI) for these experiments is represented by the formula,

\[ MI = (N_1 \times 1) + (N_2 \times 2) + (N_3 \times 4) + (N_4 \times 8) \]

where \( N \) equals the number of contractions within the particular force range. Since the number of contractions occurring during an experiment is readily available from the formula for the motility index, a parameter called the frequency of contraction was also available for analysis. For any experimental challenge, antral data from all dogs were subjected to an analysis of variance by a completely random design with unequal

![FIG. 1. Positions of extraluminal force transducers used to monitor contractile activity. Position 1 was on body of stomach, positions 2 and 3 were on antrum, positions 4 and 5 were on duodenum.](image-url)
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replication (due to failure of some transducers). A similar analysis of variance was used for all the data from the duodenum. In some instances data collected from two positions on one organ in either the control or the pyloroplasty conditions were analyzed by a paired t test (20). The number of total degrees of freedom (df) used in any analysis was determined by testing the difference between the variance about the mean for all experiments in all dogs and the variances about the means for individual dogs. This was done with the conventional F test (20). If F was significant (meaning the variance about the grand mean was greater than the variances about individual means) then df = N – 1, where N was the number of dogs. If F was not significant then total df = N – 1, where N was the number of experiments (usually 2 experiments per dog). Whenever total df was calculated by the former method, the F value determined in the analysis of variance was considered to be a conservative estimate of real F. Whether the F values from the analyses of variance were significant or not, the differences among means were tested by a Bayesian multiple comparison test with a K ratio of 100:1, which corresponds to the conventional 0.05 level of significance (22).

Gastric emptying. Seven healthy mixed-breed dogs (9.5–15.0 kg) were used in this study. (The first 3 dogs were used in the motor study described above, and the remaining 4 dogs were surgically prepared for a different study.) All animals were conditioned to the laboratory environment and to the passage of a gastric tube (French no. 20) through a bite block before the beginning of studies on gastric emptying. The index of gastric emptying in these experiments was the volume of a 300-ml citrate-fat liquid test meal remaining in the stomach after 45 min. This time period was chosen since it is approximately the t 1 for the citrate-fat test meal previously determined in normal dogs (24).

The citrate-fat liquid test meal consisted of 300 ml of trisodium citrate (19.6 g/liter) with 10 mM oleic acid suspended by 0.5% Tween 80. The test meal also contained 40 mg/liter phenolsulfonphthalein as a nonabsorbable marker to determine gastric volumes by a colorimetric method. The osmolarity of this test meal was 225 mosM measured by freezing-point depression.

After at least an 18-h fast, the dog was placed in a stand in the laboratory and a tube was passed through a bite block into the stomach. One or two 50-ml rinses of distilled water were administered and aspirated through the tube to remove any residual food particles and secretions. The room-temperature citrate-fat test meal was then instilled and the tube was withdrawn. After 45 min the tube was reinserted, the stomach aspirated, and one 50-ml rinse administered and aspirated.

The optimal density of phenolsulfonphthalein was measured in the original test meal, in the meal aspirated, and in the final rinse solution. The volume of test meal remaining in the stomach was calculated by the method employed previously in this laboratory (24).

In this study each animal served as its own control. The mean volume remaining in the stomach with its standard error was determined for at least three experiments before and three experiments after Heineke-Mik-ulicz pyloroplasty. These two means were then compared in each animal by the Student t test. The means (grand mean) for all control experiments and all experiments after pyloroplasty were compared with a paired t test.

RESULTS

Interdigestive state. The basal and burst patterns on the antrum and duodenum were present in all dogs (Fig. 2). Control records demonstrated periods of interdigestive inhibition coordinated with the contractions of greater amplitude from the antrum. This particular pattern was disrupted after pyloroplasty. Typical periods of inhibition in the duodenal cap were replaced by contractions more antral than duodenal in character (Fig. 2, middle and bottom panels; position 4). Farther down the duodenum, the typical burst pattern with periods of inhibited activity was apparent. The alteration observed in the duodenal cap was called antralization of the duodenum. Antralization of the duodenum was observed in the preburst and the burst periods of the interdigestive state.

The analysis of variance for the motility index on the antrum showed that during a burst period there was a significant difference in motor activity within the antrum (Fig. 3). In all animals position 3, the terminal antrum, had a greater motility index than position 2, the oral portion of the antrum. During the same period no differences were found for either position monitored on the duodenum in either group of dogs.

Digestive state. In our laboratory, digestive state activity is defined as the type of contractile activity observed after feeding the dog 200 g of canned dog food. This is characterized by a continuous pattern of low-amplitude contractile activity on the antrum, compared with the amplitudes of contractions during an interdigestive burst, and by intermittent activity on the duodenum.

Three differences were observed between the digestive state activities of control and pyloroplasty dogs. First, antralization of the duodenum was apparent in dogs with pyloroplasty shortly after feeding. This pattern continued for the duration of the experiment. Second, in the group of animals with pyloroplasty, antral position 3 had a significantly greater (Bayesian multiple comparison test) motility index than position 2 (Fig. 4). Although this trend was apparent for the control dogs, it was not statistically significant. The third difference was observed on the duodenum, where motility index values at position 5 were significantly greater in pyloroplasty dogs than in control dogs. The difference in motility index values on the duodenum was due to a significantly greater number of contractions during the 1st h postprandial at position 5 after pyloroplasty (229 ± 37 vs. 61 ± 15).

Citrate-fat test meal. The citrate-fat test meal stimulated duodenal circular muscle contractility in control dogs and in those with pyloroplasty. There appeared to be no stimulation of the antrum with this test meal in control dogs, but some stimulation was apparent on the terminal antrum in the pyloroplasty group of dogs (Fig.
When these data were subjected to analysis of variance, no significant differences were found for the antrum or for the duodenum.

**Drugs.** All dogs showed a similar response to pentagastrin infusion (Fig. 6). Pentagastrin stimulated the antrum to a frequency of approximately 6 contractions/min. (After bethanechol or food the antral contractions were approximately 4.5/min.) The faster rate of contraction on the antrum was accompanied by few contractions on the duodenum (Fig. 6, positions 4 and 5). In all dogs the amplitude of contraction at position 3, the terminal antrum, was greater than that at position 2, the orad portion of the antrum.

The paired *t* test performed on the differences in the antral motility indices for the control dogs demonstrated...
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strated a significant difference ($P < 0.05$) between positions 2 and 3 (Fig. 7). This suggests that pentagastrin can stimulate differentially the antral smooth muscle

![Graph showing motility index ± SE for digestive state. Letters and numbers are as described in Fig. 3 (60-min analysis).](image)

**Fig. 4.** Motility index ± SE for digestive state. Letters and numbers are as described in Fig. 3 (60-min analysis).

with a greater effect on the most terminal portion of that organ. When the paired $t$ test was performed on the data from the dogs with pyloroplasty, a highly significant difference ($P < 0.01$) was found between the motility indices for the two antral positions (Fig. 7). An analysis of variance for the data from the duodenum showed no significant differences.

Bethanechol in either group stimulated circular muscle contractile activity of the antrum and duodenum. The analysis of variance of the motility index data demonstrated no significant differences on the antrum or duodenum for the 30-min period of analysis.

During a basal period, metoclopramide stimulated the body, antrum, and duodenum to a variable extent in all dogs. Analyses of variance performed for the antral and duodenal motility indices showed no significant differences within either organ or between the control and pyloroplasty groups of dogs. In contrast, in the digestive state, each antral position in the control dogs had a significantly greater motility index than the antral positions in the pyloroplasty group of dogs (Fig. 8). No significant differences were found on the duodenum in the digestive state between the two groups of dogs. Metoclopramide enhances antral contractility in control dogs. This effect, which was not observed in dogs with pyloroplasty, establishes a large gradient of motor activity from the antrum to the duodenum.

*Gastric emptying of citrate-fat meal.* The results for

![Graph showing gastric emptying of citrate-fat meal.](image)

**Fig. 5.** Examples of circular muscle contractile activity for citrate-fat liquid test meal. *Upper panel:* pattern from control dog; *lower panel:* pattern from dog with pyloroplasty. In each case 300 ml of citrate-fat meal was instilled into stomach between arrows. Positions, force bars, and time bar are as described in Fig. 2.
the seven dogs studied before and after pyloroplasty are presented in Table 1. Dogs 1, 2, and 3, the dogs also used in the motor study, showed no significant change in the amount of citrate-fat meal remaining in their stomachs after 45 min. Of the four additional dogs studied, three demonstrated a significant decrease in the amount of citrate-fat meal remaining in their stomachs during the test period after pyloroplasty. When the mean values from all dogs were compared before and after surgery, the difference was significant ($P < 0.02$). In all animals the means were smaller (indicating more emptying) after pyloroplasty. Hence, pyloroplasty alone tends to enhance the gastric emptying of the citrate-fat test meal.

**DISCUSSION**

Contractile activity in the stomach and small bowel follows an underlying pattern of electrical activity. This electrical activity consists of the basic electric rhythm (BER) and its superimposed spike potentials. Whenever contractions occur, they are preceded by spike potentials that characteristically appear on one portion of the BER waveform. In the stomach the BER originates...
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The composite result demonstrated that pyloroplasty enhanced the emptying of the citrate-fat meal. It is presumed that the juxtaposition of antral and duodenal musculature at the pyloroplasty suture line creates less of a separation between the two organs than in the normal dogs. This alteration of the normal G1J allows a greater response of the terminal antrum to fat, steepening the gradient and enhancing the emptying of the citrate-fat liquid test meal.

Qualitatively and quantitatively the smooth muscle stimulation after bethanechol was the same in dogs with or without pyloroplasty. Thus, pyloroplasty does not affect the antral or the duodenal cholinergic receptors; the anatomical alteration at the G1J does not affect the interaction of bethanechol with the cholinergic receptors in the smooth muscle. This same conclusion was drawn previously after a study of vagotomy and pyloroplasty procedures (19).

The present study of the responses to metoclopramide confirms the results of Jacoby and Brodie (12). In the interdigestive state metoclopramide stimulated both antral and duodenal circular muscle contractile activity. Control dogs and dogs with pyloroplasty showed a variable response to the drug in the interdigestive state. In man, the motor response to metoclopramide appears to depend on the pattern of contractile activity existing when the drug is administered (14). Since in the present experiments the drug was injected in a basal period, the preexisting contractile pattern may not be as important in determining the response to metoclopramide in the dog.

In the digestive state metoclopramide enhanced the contractile activity of the antrum and duodenum. In dogs, implanted with mercury-column strain gages, metoclopramide stimulates propulsive antral motor activity, eliminating an initial phase of retropulsive mixing activity (15). The data from the present study provide some support for Kelly’s hypothesis. Metoclopramide produced a striking effect on the gradient of antral-duodenal activity in the digestive state in control animals. The motor activity was much greater in the antrum than in the duodenum. This type of contractile pattern may be responsible for increased propulsion and the characteristically observed enhanced emptying with metoclopramide. Unlike control dogs, the dogs with pyloroplasty had significantly less antral motor activity after metoclopramide. The steep antral-duodenal gradient observed in the control animals was lacking in the pyloroplasty group. Whether or not metoclopramide enhances emptying after pyloroplasty remains to be determined.

Doozois and Kelly (7) and Cooke and associates (6) have demonstrated delayed emptying of liquid test meals in dogs intravenously infused with pentagastrin. This may partly be explained by the ability of pentagastrin to decrease gastric body pressure (26). Cooke et al. (6) further showed that pentagastrin increased the motility index on the antrum of dogs, indicating an increase

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**Table 1. Gastric emptying of citrate-fat test meal before and after Heineke-Mikulicz pyloroplasty**

<table>
<thead>
<tr>
<th>Dog</th>
<th>V_n Prepyloroplasty</th>
<th>V_n Postpyloroplasty</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>206.6 ± 9.3</td>
<td>197.2 ± 3.0</td>
<td>NS*</td>
</tr>
<tr>
<td>2</td>
<td>164.9 ± 1.2</td>
<td>151.1 ± 10.2</td>
<td>NS</td>
</tr>
<tr>
<td>3</td>
<td>205.9 ± 4.8</td>
<td>189.6 ± 3.5</td>
<td>NS</td>
</tr>
<tr>
<td>4</td>
<td>189.3 ± 11.5</td>
<td>124.8 ± 6.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>5</td>
<td>159.6 ± 4.0</td>
<td>133.8 ± 5.0</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>6</td>
<td>194.1 ± 9.9</td>
<td>177.5 ± 1.2</td>
<td>NS</td>
</tr>
<tr>
<td>7</td>
<td>189.1 ± 5.5</td>
<td>141.9 ± 13.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Grand mean</td>
<td>187.1 ± 7.0</td>
<td>160.0 ± 11.1</td>
<td>&lt;0.02</td>
</tr>
</tbody>
</table>

Values are means ± SE for amount remaining in stomach after 45 min either before (prepyloroplasty) or after (postpyloroplasty) surgery. At least 3 experiments contributed to each value. n = 7, df = 6. * NS, not significantly different. + Paired t test was performed with means from dogs before and after pyloroplasty.
in the frequency and amplitude of contractions. These facts appear to contradict the hypothesis that antral-duodenal gradients explain stomach emptying. Cooke et al. (6) did not present data for duodenal contractile activity, so an analysis of the gradient could not be made. The present results with infusions of pentagastrin demonstrate a pattern of antral circular muscle contractile activity that may be responsible for the delayed emptying with pentagastrin. A differential stimulation of the antrum was recorded in the present experiments from the two extraluminal force transducers implanted on that organ (Cooke et al. analyzed records from only one antral force transducer). Pentagastrin consistently produced a greater amplitude response from the terminal antrum than from the orad portion of the antrum. This difference was significant in both groups of dogs. Pentagastrin did not appear to stimulate the duodenum at either of the positions monitored in either type of dog preparation. Thus, when pentagastrin is administered in the interdigestive state it produces a differential stimulation of the antrum and a steep antral-duodenal gradient of motor activity.

The following hypothesis is offered to explain the ability of pentagastrin to delay emptying. The delayed emptying of liquids observed in conjunction with pentagastrin administration is due to an increase in the retropulsive properties of the antral musculature. The increased frequency of antral contractions and the greater amplitude of contractions in the terminal antrum set the stage for increased resistance to flow into the small bowel as well as increased retropulsion of antral contents. The decreased pressure in the gastric body due to pentagastrin (26) would also favor retropulsion. This does not negate the theory of antral-duodenal motor gradients being responsible for gastric emptying but simply adds a corollary. In addition to the antral-duodenal motor gradients shown for liquid test meals, antral motor gradients are also involved in regulating gastric emptying of liquids. It is well documented that antral motor gradients at the terminal antral contraction described by Carlson et al. (5), result in the regulated emptying of solid food by causing retropulsion. We therefore conclude that under certain circumstances (e.g., pentagastrin administration) the emptying of liquids may be regulated by an antral gradient of motor activity.

The Heineke-Mikulicz pyloroplasty procedure brings the antral and duodenal smooth muscle layers into juxtaposition. Thus, on the anterior surface of the gastroduodenal segment, the natural separation of the circular layer and the diminution of the longitudinal layer are altered. The present experiments demonstrate that this surgical alteration of the GDJ can affect both gastric emptying characteristics and physiologically or pharmacologically induced motor activity of this segment. In contrast to the work of Ludwick et al. (16), the present results show that Heineke-Mikulicz pyloroplasty is not obstructive to the emptying of liquids, but enhances the emptying of the citrate-fat liquid test meal. This result indicates that the normal anatomical relationship of the GDJ has some importance in the coordination of the gastric emptying of liquids. After pyloroplasty, motor gradients present during the emptying of a solid meal were different from those in control dogs. An intact GDJ thus appears to have importance in the type of motor patterns present during the emptying of solid and liquid meals.

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