Gastroduodenal motor gradients in the dog after pyloroplasty

HERBERT S. ORMSBEE III AND PAUL BASS
School of Pharmacy, Center for Health Sciences, Madison, Wisconsin 53706

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 citrate-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 normal gastric emptying of liquids.

The human gastroduodenal junction (GDJ) has been characterized histologically by a complete separation in the circular smooth muscle layer with only a small amount of longitudinal smooth muscle crossing from antrum to duodenum (10). In vivo electrophysiological studies in the dog support a similar type of anatomical description. The canine GDJ is a zone of attenuated electric activity separating the characteristic electric pattern of the antrum from that of the duodenum (2, 8). During the digestive state, a correlation exists between the antral basic electric rhythm (HER) and spike potentials of the duodenum (1, 18). This electric pattern apparently governs the coordinated contractile activity that regulates gastric emptying. The antral-duodenal contractile patterns vary according to the type of solid or liquid meal present in the stomach (18, 25). The mechanism responsible for the motor or electric coordination between the antrum and duodenum has not been determined.

Various gastroduodenal surgical procedures, called pyloroplasties, involve enlarging the opening between the antrum and duodenum. Pyloroplasties alter the normal anatomical relationship between the muscle of the antrum and duodenum at the GDJ. One of these surgical alterations, called a Finney pyloroplasty, has been shown to alter antral-duodenal motor coordination and to impair gastric emptying of liquids and solids (16, 17). This evidence suggests that gastric emptying is affected when the mechanical activities of the antrum and duodenum are no longer separated by the hypomuscular GDJ.

The present study was undertaken to evaluate further the role of the hypomuscular segment in affecting the motor coordination between the antrum and duodenum. Heineke-Mikulicz pyloroplasty, a less radical surgical procedure than Finney pyloroplasty, was used to alter the normal relationship between the antrum and duodenum. Both circular muscle contractile activity and gastric emptying of a liquid test meal were investigated to evaluate motor relationships in control dogs and dogs with pyloroplasty.

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 Tween 80 in a solution of trisodium citrate. The liquid meal was a 300-ml citrate-fat mixture (kindly supplied by Robins Research Laboratories, Richmond, Va.), which initiated digestive activity. The liquid meal was a 10 mM suspension of oleic acid and 0.5% fat, which can affect duodenal receptors and slow emptying (11), was still operative after pyloroplasty.

The first of the three pharmacological challenges was bethanechol chloride (0.1 mg/kg sc). Bethanechol is a cholinergic agonist that was used to study the effect of pyloroplasty on the cholinergic response of the antrum and duodenum. The second drug, pentagastrin (Peptavlon, kindly supplied by Ayerst Laboratories, New York City) was infused into a forelimb vein at a rate of 1 μg/min for 20–30 min. Pentagastrin is known to stimulate antral contractile activity (6) and was used to further evaluate the antral-duodenal relationship in the two groups of dogs. The third drug, metoclopramide HCl (kindly supplied by Robins Research Laboratories, Richmond, Va.), 2 mg/kg iv, was administered during a basal period in the interdigestive state and 30 min after the animal was fed 200 g of canned dog food. Although this drug has been claimed to enhance stomach emptying (12, 13) its mechanism of action has not been proven.

The circular muscle contractile activity from the five positions in each dog was recorded on an eight-channel Beckman type R411 Dynograph recorder. Data from two replicates of all of the challenges described above was collected wherever possible for each dog. The records were evaluated manually.

The time of analysis differed from challenge to challenge, but was the same length in each dog for each individual challenge. The interdigestive burst period was analyzed for 10 min of peak activity and the basal period was analyzed for 1 h. Activity from the digestive state was analyzed for 1 h and the citrate-fat test meal was analyzed for the time period used in the gastric-emptying study, 45 min. Contractile activity after bethanechol and pentagastrin administration was analyzed for periods up to 30 min; activity after metoclopramide was analyzed for 1 h in either the digestive or interdigestive state.

Data collected from all transducers except on the body of the stomach were subjected to quantitative analysis. A motility index was calculated for transducers on the antrum and duodenum as previously described (4, 19, 21). Briefly, the numbers of contractions within four set force ranges are multiplied by a factor giving more weight to the larger amplitude contractions and then the sum is determined for the four force ranges. The force ranges used were 5–10 g, 10–20 g, 20–40 g, and 40–80 g. The lower range was selected as the one that would include the smallest amplitude contractions that could be discriminated from baseline artifact or respiration. 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
GASTRODUODENAL CONTRACTILE ACTIVITY

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 $t_{1/2}$ 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-Mikulicz 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 duodenal 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. Antralization of the duodenum was observed in the preburst and the burst periods of the interdigestive state.

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. 2).
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...
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 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](http://ajplegacy.physiology.org/)

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

**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.
FIG. 6. Examples of circular muscle contractile activity during an infusion of pentagastrin (1.0 μg/min iv). Note differential stimulatory effect within antrum. Upper panel: from control dog; lower panel: from dog with pyloroplasty. Positions, force bars, and time bar are as described in Fig. 2.

FIG. 7. Motility index ± SE for pentagastrin (1.0 μg/min iv) response. Letters and numbers are as described in Fig. 3 (20-min analysis).

FIG. 8. Motility index ± SE for metoclopramide (2.0 mg/kg iv) response in digestive state. Letters and numbers are as described in Fig. 3 (60-min analysis).

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 wave form. In the stomach the BER originates from...
GASTRODUODENAL CONTRACTILE ACTIVITY

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

<table>
<thead>
<tr>
<th>Dog</th>
<th>Vr Prepyloroplasty</th>
<th>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>183.6 ± 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.

from a pacemaker area along the greater curvature in the orad corpus (23). In the duodenum a pacemaking area exists within the 1st cm of the duodenal cap (9). This latter pacemaker area is incised during the pyloroplasty procedure and reoriented in juxtaposition with the midantrum. Such a manipulation of the duodenal pacemaker might affect the electrical patterns of the gastroduodenal junctional area and the consequent motor activity.

In the present experiments Heineke-Mikulicz pyloroplasty altered normal patterns in circular muscle contractile activity from the duodenal cap in both the interdigestive and digestive states. Antralization of the duodenum occurred in the burst period, during preburst activity and in the digestive state. Duodenal inhibition during the burst period was replaced with antralization. Thus, the alteration of the normal anatomical relationship at the GDJ due to pyloroplasty impairs a physiological response during both the interdigestive and digestive states. The present experiments provide data on the type of contractile activity present during the emptying of solid food. The possible effects of antralization of the duodenum and of the changes in digestive state contractile patterns after pyloroplasty on the emptying of solid food remain to be studied.

The citrate-fat meal stimulated duodenal contractile activity in both control dogs and dogs with pyloroplasty but had little effect on antral contractile activity. This is the typical response to a citrate-fat meal as described by others (25). Basically, this test meal promotes a shallow gradient of motor activity from antrum to duodenum. This is in contrast to the steep gradient of activity found with the citrate test meal. A shallow antral-duodenal gradient results in relatively delayed emptying of the citrate-fat test meal. Although the emptying of the test meal was not significantly enhanced in the three dogs studied for motor activity and emptying, their motility index values showed a tendency for the terminal antrum to have greater activity than that for the control dogs. This pattern of contractile activity would steepen the antral-duodenal gradient and thereby hasten the emptying of the test meal. This may be the reason why in three of four additional dogs in which only gastric emptying studies were performed the emptying of the citrate-fat test meal was significantly enhanced. 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 GDM 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 GDJ 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 in the emptying of the citrate-fat test meal.
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 planted 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 oral 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 retro-pulsive 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, 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 gastro-duodenal 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.

We gratefully acknowledge the excellent technical assistance of Mr. Bruce Steinhagen.

Present address of H. S. Ormsbee III: Dept. of Surgery, University of Maryland School of Medicine, Baltimore, Md. 21201.

Received for publication 27 January 1975.

REFERENCES


