Canine gastric pacemaker

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to determine the site of origin of the canine gastric pacemaker potential (PP). In six dogs, longitudinal (orad-to-caudal) gastric
bisection was performed, the greater (GC) and lesser curvature (LC) halves were reunited, and electrodes were implanted on
each half. After recovery, gastric electric activity was recorded intermittently in the conscious fasted dogs for 3 months. The orad
one-fourth of the stomach along the GC was then resected, and the dogs were restudied. After bisection, the PP of the GC arose
in the orad corpus, had a regular rhythm and a mean frequency of 5.2 cycles/min, and was propagated caudally. In contrast, the
PP of the LC at first arose from multiple sites and had an irregular rhythm and a slower mean frequency of 3.2 cycles/min. However,
the frequency of the PP of the LC gradually increased and, by 14
days after bisection, the PP of the LC was coupled to that of the
GC. Resection of the orad corpus along the GC decreased the
frequency of the PP of the LC gradually increased and, by 14
days after bisection, the PP of the LC was coupled to that of the
GC. Resection of the orad corpus along the GC decreased the
PP frequency in the remaining stomach about 1 cycle/min, but
did not alter electric coupling between the halves or PP propaga-
tion. The data indicate that the dominant site of origin of the
gastric PP is in the GC half of the orad corpus.

Prior studies have shown that gastric peristalsis originates
somewhere in the orad end of the stomach, but the exact
site is not known. Some workers have suggested a location
along the lesser curvature near the esophagogastic junction
(1, 8, 10), whereas others have stated that the site of
origin varies (3).

Workers in our laboratory and others have shown that
gastric contractions (peristalsis) are coupled with the
gastric pacemaker potential (PP) and that these contrac-
tions occur when action potentials are recorded with the
cycles of the PP (4, 6, 12). The PP, like peristalsis, has been
found to originate somewhere in the orad end of the corpus
and then to be propagated aborally to the pylorus (6, 12).
Some observations indicate that the PP originates at the
cardia (1), whereas other experiments point to a location
near the greater curvature (9, 13, 15, 18). The purpose of
these experiments was to define more exactly the site of
origin of the gastric PP in healthy, conscious dogs. We
wondered at first if the origin was from a band of tissue
surrounding the stomach at the orad end of the corpus. A
preliminary report of this work has been given (11).

Methods

Six healthy, mongrel, female dogs, 10–14 kg, were studied.
Electric activity was recorded by monopolar silver-wire
electrodes, similar to those used in this laboratory in the
past (12). The tips of the electrodes, which had been elec-
trolytically coated with silver chloride, projected 2 mm from
one surface of flat, two-layered Teflon disks. The electrode
passed through one layer of the disk and was connected
between the layers to a Teflon-insulated copper lead, 12
inches long. The entire disk, except for the tip of the
electrode, was sealed with epoxy resin. Three holes were
drilled in the disk, and sutures were passed through them
to attach the disk to the viscera. The insulated lead from each
disk was connected to a pin of a 9-pin tube socket mounted
with dental impression material (Acrolite) in a cylindrical
metal cannula. The cannula had an inner flange and an
outer flange. Four holes in the inner flange were used to
suture it to the abdominal wall.

With sterile operating technique during anesthesia with
sodium pentobarbital given intravenously, a longitudinal
orad-to-caudal gastric bisection was performed in each
dog from the apex of the fundus to and through the pylorus,
completely separating the stomach into greater and lesser
curvature halves (Fig. 1). The halves were immediately
sutured, and four electrodes were implanted serially on the
anterior serosal surface of the distal portion of each half,
midway between the incision and each curvature at ap-
proximately 1.5-cm intervals (Fig. 1). The most caudal
electrodes were approximately 1 cm orad to the gastro-
duodenal junction.

The metal cannula containing the nine-pin tube socket
was brought to the surface through a small incision in the
right anterior abdominal wall in the midclavicular line.

Electric recordings were begun the day after operation
and were made one or more times a week for 3 months
thereafter. The dogs were fasted for at least 18 hr before
each recording session. They were trained to rest quietly in
slings in the standing position during the sessions. Insulated
wire leads were attached to the pins in the cannula and
connected to an eight-channel, rectilinear pen recorder
(Brush Mark 200). Alternating-current amplifiers with a
time constant of 1 sec were used. Differences in potential
between the visceral electrodes and an indifferent electrode
placed subcutaneously in the right hind limb of the dog
were recorded at each session. The electric apparatus was
capable of recording frequencies greater than 100 cycles/
sec.

The recordings are analyzed as follows. The configuration,
amplitude, and rhythm of the PP were noted at each
recording site on each recording occasion, and a compari-
sion was made between the tracings from the various elec-
trodes.

The frequency of the PP was determined by counting the
number of its cycles during 6 min of recording, calculating the mean, and expressing the result in cycles per minute. The onset of the initial positive deflection of the triphasic complex of the PP from the isoelectric line was taken as the start of the cycle of the PP.

A second type of analysis of PP frequency was made on one randomly selected recording obtained from each dog before the 9th and one after the 14th postoperative day (before and after coupling). Individual cycles of the PP were identified at each electrode site during a 6-min sequence of electric recording, and, when possible, they were followed or tracked from electrode 1 through electrodes 2, 3, and 4, and from electrode 1' through electrodes 2', 3', and 4'. The duration of each of the individual cycles at each recording site varied only slightly. For example, the duration of different cycles at a single electrode site were also the same, except in one dog (Table 2).

The pattern of fasting electric activity in the wall of the stomach was studied as before for an additional 3 months, beginning the day after the second operation. The electrodes of dog 2 began “shorting out” 3 months after the first operation. Therefore, the original electrodes were excised in this dog, and a new set was applied in corresponding sites on the posterior wall of the stomach. Two weeks after the new electrodes were in place, fasting recordings were started and were continued one or more times a week for an additional 10 weeks. The orad one-fourth of the stomach was then resected, and the observations were continued.

RESULTS

One of the dogs died 6 days after the first operation. The remaining five dogs ate poorly the first few days after the bisection and vomited occasionally. After the first week, however, the dogs had good appetites, ate well, and did not vomit. They were healthy and maintained their weight throughout the observations. Their general well-being was not affected by the presence of the electric apparatus.

After gastric bisection, the PP was detected by all the electrodes on the greater curvature half of the stomach (Fig. 2). Usually, the PP had a consistent triphasic configuration, a uniform amplitude at each recording site, and a regular rhythm (Fig. 2). Its frequency was about 5 cycles/min and was the same at each recording site along the greater curvature (Table 1, Fig. 3).

Individual cycles of the PP were tracked easily from electrode 1' through electrodes 2', 3', and 4' in the greater curvature half. The direction of propagation of the PP was determined by recording bipolely between two monopolar electrodes in each gastric half, the configuration and consistency of the diphasic responses indicating oral or caudal propagation (12).

A second operation was performed on each animal 3-6 months after the gastric bisection, the purpose of which was to excise the pacemaking region. The proximal half of the stomach was again bisected through both anterior and posterior walls by incising the now well-healed incision site of the previous bisection. The orad one-fourth of the stomach on the greater curvature side was then removed. The defect created in the stomach by the excision was closed by approximating the corresponding points on the anterior and posterior walls of the stomach.

The electrodes of dog 3 began “shorting out” 3 months after the first operation. Therefore, the original electrodes were excised in this dog, and a new set was applied in corresponding sites on the posterior wall of the stomach. Two weeks after the new electrodes were in place, fasting recordings were started and were continued one or more times a week for an additional 10 weeks. The orad one-fourth of the stomach was then resected, and the observations were continued.

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TABLE 1. Effect of gastric bisection on frequency of gastric pacesetter potential (PP) in fasting dog

<table>
<thead>
<tr>
<th>Dog</th>
<th>Day After Operation</th>
<th>Mean Frequency of PP, t cycles/min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lesser curvature electrodes</td>
<td>Greater curvature electrodes (1' through 4')</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>2.2</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>4.0</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>4.5</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>3.2</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>3.2</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td></td>
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<td>3.2</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>Grand mean</td>
<td>3.2</td>
</tr>
</tbody>
</table>

* Data from 2 representative days between the 1st and 8th postoperative day are shown for each dog. † During 6 min of recording. ‡ Frequencies were the same at electrodes 1' through 4', except for dog 1 on 3rd day, when the frequency at electrode 1' was 5.5.

TABLE 2. Effect of gastric bisection on duration of individual cycles of gastric pacesetter potential (PP) in fasting dog

<table>
<thead>
<tr>
<th>Dog</th>
<th>Day After Operation</th>
<th>Mean Duration of Cycles of PP, † sec</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lesser curvature electrodes</td>
<td>Greater curvature electrodes (1' through 4')</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>12.1±0.3</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>12.8±0.6</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>22.2</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>14.8</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>15.7±0.23</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>20.0</td>
</tr>
<tr>
<td>Overall mean</td>
<td>17.5</td>
<td>22.0</td>
</tr>
</tbody>
</table>

* During 6-min intervals. † All values except those shown ranged from 1.0 to 1.6. ‡ Values were same at electrodes 1' through 4', except for dog 4, when mean duration ± se at electrode 3 was 10.7 ± 0.3 and at electrode 4' was 10.6 ± 0.3. se was between 0.1 and 0.2 for all other means. Values of greater curvature half differed significantly from those of lesser curvature half (P < 0.01, Student t test). § Significantly different (P < 0.05, Student t test) from electrode 1.

In dog 4 the mean duration of the cycles differed at sites 3' and 4' by 0.1 sec, an insignificant difference.

The configuration of the electric complexes obtained by recording bipolarly from the monopolar electrodes of the greater curvature half identified caudal propagation of the PP cycles (Fig. 4).

Occasional periods of irregular electric rhythm were detected from the electrodes of the greater curvature half in three of the six dogs. However, on most days, even in these dogs, and on all occasions in the other three dogs, the electric activity was in the regular pattern of the undisturbed stomach. Thus, all of the features of the pattern of the elec-

FIG. 2. Regular pattern of electric activity of greater curvature half of stomach 5 days after gastric bisection. Pacesetter potential has a consistent triphasic configuration, a uniform amplitude at each recording site, and a regular rhythm. Frequency of pacesetter potential is same at each recording site. Small "spikes" superimposed on tracings in Figs. 2 and 4-8 are electrocardiograms.

FIG. 3. Effect of gastric bisection on frequency of pacesetter potential on lesser curvature half of stomach at electrode 3 and on greater curvature half of stomach at electrode 3' in six dogs (for electrode positions, see Fig. 1). Each point is mean value during 6 min of recording on that day.
tric activity in the greater curvature half of the bisected stomach generally were normal.

In contrast, the PP of the lesser curvature half of the stomach did not have a fixed site of origin in the first 6 days after operation. During this time, the configuration and amplitude of the PP varied from cycle to cycle at the same recording site (Fig. 5), and the rhythm of the PP was often irregular. The PPs of different frequencies were recorded from the lesser curvature half, and these were always slower than the PP frequency of the greater curvature half (Table 1, Fig. 3).

It was difficult or impossible to track a cycle of the PP from electrode 1 through electrodes 2, 3, and 4 in the recordings from the lesser curvature half during the first 6 days after bisection. The duration of an individual cycle detected by an electrode differed greatly from the duration of the cycle detected by the next adjacent aborad electrode. The duration of different cycles at a single recording site also varied greatly. The standard errors of the mean duration of the cycles at each of the electrode sites were large, much larger than those of the greater curvature half (Table 2).

These large standard errors did not, however, display the wide range of variability as adequately as the individual tracking results. In dog 4 on the 5th day after bisection, when the mean duration of the PP cycles at different electrodes on the lesser curvature half varied by only 0.7 sec (the least of any dog), the majority of the duration measurements made in sequence from electrode 1 through 4 differed by 0.5–1 sec, clearly indicating in these instances the PP rhythms were uncoupled. In the remainder of the sequences in this dog that day, some coupling may have been present. For example, in 4 of 26 sequences, the duration of the PP at each of the four electrode sites differed by only 0.1 sec, and in these instances the PPs were likely coupled. In other words, in this dog for brief periods a dominant pacemaker was present in the lesser curvature half. Dominant pacemakers in the lesser curvature half also appeared and disappeared in the other dogs, but their appearance was always temporary.
Regardless of the presence of a dominant pacemaker, the mean durations of the cycles from the lesser curvature half were significantly greater than those of the greater curvature half (Table 2).

Recordings made simultaneously from the two halves showed that the PP of the lesser curvature half was not coupled to that of the greater curvature half in any dog during the first 6 days after bisection (Fig. 6).

The frequencies of the PP of the lesser curvature half gradually increased after bisection, and in every dog by 14 days the frequencies of the two halves were the same (Fig. 3) and their rhythms were synchronized or coupled (Fig. 7). The coupled rhythm was usually regular, although periods of irregularity occurred occasionally (Fig. 8).

After coupling, individual cycles could be easily tracked from electrode 1 through electrodes 2, 3, and 4 and from electrode 1' through electrodes 2', 3', and 4'. The duration of a specific cycle was then the same, or almost the same, at electrodes 1 and 1' and also at all aborad electrode sites as it was sequentially detected. The durations of different cycles varied only slightly. The standard errors of the mean durations over the 6 min were less than 0.5 sec at all electrode sites in all dogs. The mean durations over the 6 min at all sites in each dog in both the lesser curvature and greater curvature halves were either identical or did not differ significantly.

After coupling, bipolar recordings showed that the cycles of the lesser curvature half were consistently propagated aborally, like those of the greater curvature half.

![Lesser Curve](image)

![Greater Curve](image)

**TABLE 3. Effect of resection of orad fourth of stomach along greater curvature on frequency of gastric pacemaker potential (PP) in fasting dog**

<table>
<thead>
<tr>
<th>Dog</th>
<th>Mean Frequency of PP, cycles/min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before resection†</td>
</tr>
<tr>
<td>1</td>
<td>4.9</td>
</tr>
<tr>
<td>2</td>
<td>5.1</td>
</tr>
<tr>
<td>3</td>
<td>5.1</td>
</tr>
<tr>
<td>4</td>
<td>5.2</td>
</tr>
<tr>
<td>5</td>
<td>5.1</td>
</tr>
<tr>
<td>Grand mean</td>
<td>5.1</td>
</tr>
</tbody>
</table>

* Mean of 10 weekly values; SE < 0.1 for all values. † And after recovery from gastric bisection; also, after implantation of second set of electrodes in dog 3 (see text). ‡ All values differed significantly from those before resection (P < 0.01, Student t test).

Resection of the orad one-fourth of the stomach along the greater curvature decreased the frequency of the PP in the wall of the remaining part of the stomach in both the lesser and greater curvature halves by about 1 cycle/min in every dog, and the decrease persisted throughout the 3 months of observation after the second operation (Table 3). The electric rhythms of the greater and lesser curvature halves, however, remained coupled. The resection resulted in no significant change in the velocity of PP propagation in either the greater or the lesser curvature half of the stomach and did not alter the caudad direction of propagation.

**DISCUSSION**

Our data confirm the earlier finding in acute experiments by Weber, Kohatsu, and Nelsen (18) and others that normally the dominant gastric pacemaker in the dog is located...
in the greater curvature half of the orad corpus and not in the region of the esophago-gastric junction.

The electric pattern in the greater curvature half of the stomach after bisection was the same as that of dogs with intact stomachs (6, 12), but the operation uncoupled the electric activity of the lesser curvature half from that of the greater curvature half. The lesser curvature half was no longer driven by a dominant pacemaker, and a reduced PP frequency, periods of irregular rhythm, and multiple pacemaker sites resulted. Clearly, the gastric PP does not arise from a band of tissue surrounding the orad stomach, but from a site in the greater curvature half of the stomach close to the junction of its middle and orad thirds. The fibers that are responsible for its origin and spread from this site have not been identified.

The absence of electric coupling between the two halves of the stomach after bisection was temporary. Recovery occurred 6–14 days after bisection. In this experiment, the re-establishment of coupling in the stomach after longitudinal bisection contrasts with the findings after transverse transection of Sugawara (17) and Shiratori et al. (16) in the stomach and Bunker, Johnson, and Nelsen (2) and of Code and Szurszewski (5) in all the small bowel of dogs. All groups noted uncoupling of the PP of the transected, though re-united, gut with a decrease in PP frequency distal to the transection which persisted for at least 2 months in the experiments of Sugawara (17) and lasted throughout the “several weeks” that the dogs were studied after operation in the experiments of Bunker et al. (2) and for 3 months of study by Code and Szurszewski (5). Transverse section of the gut interrupted the longitudinal fibers, which are known to conduct the PP, at least in the small bowel. Our bisection of the stomach presumably maintained continuity of the longitudinal fibers; however, it must have temporarily disturbed these or other fibers concerned with gastric PP propagation to the lesser curvature half. The mechanism by which propagation is re-established to the lesser curvature half of the stomach 6–14 days after longitudinal bisection is unknown.

A new pacemaker emerged when the pacemaking site along the greater curvature of the orad corpus was resected. It initiated PPs, which were aborally propagated, just as the normal pacemaker did, but its frequency was slower by about 1 cycle/min. This was not as great a reduction in frequency as that produced by others after transection of the stomach in the antrum, when the frequency of the PP was reduced caudad to the cut by about 2 cycles/min (16–18). These findings are compatible with the concept of a gradient in the rate of generation of the natural or intrinsic PP in the smooth muscle cells of the wall of the stomach. The cells of fastest natural frequency are located in the greater curvature half of the orad corpus of the stomach and those of slowest natural frequency in the distal antrum, the gradient arrangement being somewhat similar to that described in the small intestine (5, 7, 11).

It appears that the smooth muscle cells of the orad corpus along the greater curvature entrain those of the lesser curvature and the distal stomach because they produced the gastric PP of fastest frequency. The smooth muscle cells of the lesser curvature and distal stomach have slower intrinsic PP frequencies, but can accept and be driven by the faster orad pacemaker. The frequency of the PP is the same in all parts of the intact stomach of healthy dogs (6, 12) because of this entrainment, and in this study it was the same in all regions of the stomach not separated from the pacemaker by bisection. When the pacemaker with the fastest frequency is resected, the group of cells with the next fastest intrinsic frequency assumes the pacemaking function.

The results indicate that the direction of propagation of the PP is determined by the position or site of the group of cells having the fastest frequency. The fastest cycling group of cells drive the others. The direction of propagation of the PP is then from the cells with the fastest intrinsic frequency to those with slower intrinsic frequencies. If there is no dominant pacemaker, propagation may be either orad or caudad.

The smooth muscle cells of the fundus of the stomach must possess different electric properties from those of the corpus and antrum, because the PP is not transmitted into the fundus (12). The smooth muscle cells of the corpus and antrum, when separated from a faster pacemaker, will propagate PPs in orad and caudad directions, but those of the fundus do not accept or propagate the corporal PP at all. The basis of the blockade is unknown.

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REFERENCES


