Human Gastric Pacesetter Potential

Site of Origin, Spread, and Response to Gastric Transection and Proximal Gastric Vagotomy

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A cyclic change in electrical potential, the pacesetter potential (slow wave or control potential), is present in the wall of the distal stomach of man [*1–3*]. The cycles, which are omnipresent, have a regular rhythm and a frequency of about 3/min [*4–9*]. They are thought to arise from a pacemaker located somewhere in the proximal stomach and to spread aborally from the pacemaker through the distal stomach to the pylorus, phasing the onset of action potentials and peristaltic contractions as they go [*10*]. However, the exact location of the gastric pacemaker and the pattern of spread of the pacesetter potentials are unknown.

The primary aim of this study was to determine the exact site of origin of the human gastric pacesetter potential—the location of the gastric pacemaker—and to define the pattern of spread of the pacesetter potential from the pacemaker to the distal stomach. A secondary aim was to determine the effect of gastric transection and proximal gastric vagotomy on the pattern of the pacesetter potential.

Methods

Patients Studied. Twenty-six patients (16 males, 10 females) were studied while they were undergoing celiotomy. (Informed consent was obtained for this purpose.) Their ages ranged from nineteen to eighty-two years. Eight patients had no known gastric disease; four of these patients were undergoing operation for gallstones, two for pancreatic disease, and two for chronic ulcerative colitis. Eighteen patients had diseases of the stomach, including three with gastric ulcer, three with gastric cancer, and twelve with duodenal ulcer.

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The patients were starved of food and water for at least 8 hours before operation. Atropine sulfate and meperidine HCl (Demerol) were given 1 to 2 hours preoperatively, and anesthesia was induced with sodium thiopental (Pentothal Sodium) and maintained with enflurane (Ethrane), nitrous oxide, and intermittent doses of curare or succinylcholine. A midline abdominal incision was made, the stomach exposed, and the gastric electrical activity immediately recorded.

Recording Technic. Gastric electrical activity was recorded with sterile, stainless steel needle electrodes, 0.3 mm in diameter and 1.2 cm long. The shafts of the electrodes were insulated with vinyl paint, but 1 to 2 mm of their tips was exposed.

The electrodes were inserted through the serosa into the tunica muscularis of the anterior gastric wall. Bipolar recordings from two electrodes positioned 2 to 3 mm apart were made in most patients to minimize interference from electrical "noise," the electrocardiogram, or respiration. However, monopolar recordings were sometimes used, with the indifferent electrode placed in the anterior abdominal wall.

Recordings were made from the gastric fundus, cardia, corpus, and antrum. Four to six sites were monitored simultaneously. Electrodes were positioned 1 to 3 cm apart along both a longitudinal and a transverse axis of the stomach in the corpus, but only along a longitudinal axis in the antrum. The distances between recording sites and from recording sites to the cardia and pylorus were carefully measured.

The electrodes were connected by insulated copper leads to high impedance, alternating current amplifiers with a time constant of 1 second and a sensitivity of 1 mV/cm. Optical coupling was used in the amplifiers to minimize electrical hazards to the patient. The output of the amplifiers led to direct-writing pen recorders (Gould-Brush, Mark 260) used at paper speeds of 1 or 2 mm/sec. The apparatus was capable of recording frequencies up to 100 Hz.

Gastric Transection. Gastric electrical activity was measured both before and after complete transverse transection of the gastric wall in four patients; one of these required distal gastric resection for gastric cancer and three required it for peptic ulcer.

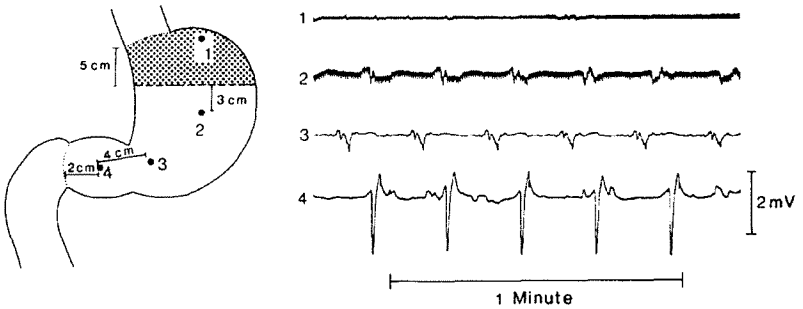

Figure 1. Pacesetter potentials are found in mid and distal corpus and in antrum of human stomach but not in fundus and proximal corpus.

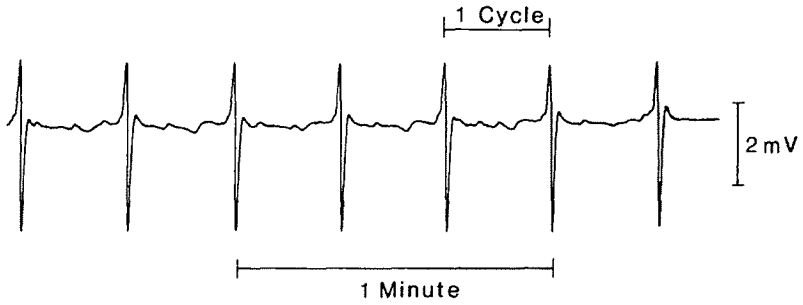

Figure 2. Cycles of pacesetter potential consist of a triphasic complex followed by an isopotential segment. Their rhythm is regular and their frequency is about 3/min.

Our hypothesis was that if the transection was made at a level proximal to the site of the gastric pacemaker, no change in the frequency of the pacesetter potential in the distal stomach would be noted. But if the transection was distal to the pacemaker, the frequency of the pacesetter potential in the distal stomach would be slowed, while that in the proximal stomach would be unchanged. The data would thus help to localize the site of the pacemaker in man, just as it has in dogs [*11–14*].

The distal stomach was mobilized, and the proximal or midcorpus was transected at sites varying from 5 to 14 cm distal to the cardia, as dictated by the disease being treated, but the attachment of the distal stomach to the pylorus and duodenum was left intact. Electrical recordings were then obtained simultaneously from the proximal and distal segments of the transected stomach, after which the resection of the distal stomach was completed.

Proximal Gastric Vagotomy. Gastric electrical activity was measured both before and after proximal gastric vagotomy in eleven patients to assess the role of the vagi in regulating the gastric pacemaker and the pattern of spread of pacesetter potentials from it. The entire fundus and corpus of the stomach were vagally denervated, while the vagal nerves to the distal 7 cm of the antrum were left intact.

Analysis of Recordings. The sites of occurrence, configuration, and rhythm of the pacesetter potentials were noted at all recording sites. The amplitude of the largest deflection of the pacesetter potential from the baseline of a typical cycle was measured at each recording site. The mean frequency of the pacesetter potential in cycles/minute was determined over 3 to 5 minute intervals, and the frequency at different sites was compared.

The direction of propagation of the cycles was determined by identifying specific cycles based on slight variations in cycle length and then tracing the direction of propagation of those cycles as they were sequentially detected by electrodes positioned at adjacent locations.

The mean velocity of propagation of five consecutive cycles was determined, based on the distance measured between electrodes and the seconds required for propagation between electrodes.

The patterns of electrical activity in patients without gastric disease were compared with those in patients with gastric ulcer, gastric cancer, or duodenal ulcer. Changes in the frequency, velocity, and direction of propagation of the pacesetter potential produced by gastric transection or proximal gastric vagotomy were also sought.

Differences were analyzed with the use of the Student t test for unpaired data when comparing data between patients and for paired data when comparing data from the same patients.

Results

Satisfactory electrical recordings were obtained from all but two patients. The recordings in these two patients had so much electrical "noise" that they could not be accurately assessed, and so they were discarded.

Electrical Pattern of Intact Stomach. Pacesetter potentials were consistently found in the mid and distal corpus and the antrum of the intact stomach. However, pacesetter potentials were never found orad to a transverse axis 5 cm distal to the cardia—that is, in the fundus, cardia, or proximal corpus of the stomach. (Figure 1.)

The cycles of the pacesetter potential usually consisted of an initial triphasic complex followed by

TABLE I Amplitude, Frequency, and Velocity of Human Gastric Pacesetter Potential

Patients	Mean (SE) Amplitude (mV)			Mean (SE) Frequency (cycles/min)†			Mean (SE) Velocity (cm/s)		
	Corpus	Proximal Antrum	Distal Antrum*	Corpus	Proximal Antrum	Distal Antrum	Corpus	Proximal Antrum	Distal Antrum*
No gastric disease	0.6 (0.2) n = 6	0.4 (0.1) n = 6	1.4 (0.5) n = 6	3.3 (0.3) n = 6	3.1 (0.0) n = 5	3.2 (0.1) n = 6	0.5 (0.1) n = 3	0.3 (0.1) n = 3	0.6 (0.0) n = 3
Gastric ulcer	0.4 (0.2) n = 3	0.2 (0.1) n = 3	0.6 (0.2) n = 3	3.1 (0.5) n = 3	3.1 (0.3) n = 3	3.1 (0.3) n = 3	0.4 (0.1) n = 2	0.3 (0.1) n = 2	0.6 (0.2) n = 2
Gastric cancer‡	0.8 n = 1	0.4 (0.1) n = 2	1.0 (0.3) n = 2	3.5 n = 1	3.3 (0.3) n = 2	3.3 (0.4) n = 2	0.1 n = 1	0.2 n = 1	0.4 (0.0) n = 2
Duodenal ulcer									
Before PGV	0.4 (0.1) n = 9	0.5 (0.1) n = 8	1.2 (0.3) n = 7	3.1 (0.1) n = 8	3.1 (0.3) n = 9	3.0 (0.3) n = 10	0.4 (0.1) n = 4	0.3 (0.1) n = 6	0.6 (0.1) n = 7
After PGV	0.6 (0.3) n = 5	0.4 (0.1) n = 9	1.1 (0.3) n = 11	3.0 (0.3) n = 5	3.3 (0.3) n = 10	3.2 (0.3) n = 11	0.3 (0.0) n = 3	0.4 (0.1) n = 10	1.0 (0.2) n = 10

Note: PGV = proximal gastric vagotomy.
* Overall mean in distal antrum differs from overall means in corpus and proximal antrum; $p < 0.01$, Student t test.
† Means do not differ; $p > 0.05$, Student t test.
‡ Patient with antral dysrhythmia excluded.

a second isopotential period. (Figure 2.) The amplitude of the largest deflection of the initial complex was greater in the distal antrum than in the proximal antrum and the corpus. (Table I.)

The rhythm of the cycles was generally regular, but small variations in cycle length were found on some occasions in most patients. The frequency of the cycles was identical, or nearly so, in all parts of the stomach from which the pacesetter potential could be recorded. (Table I.) The overall mean frequency of the cycles was 3.2/min, and the frequency varied little between patients, with one exception. The exception was a patient with adenocarcinoma of the antrum, where the antral pacesetter potential had an irregular rhythm and a rapid frequency of 6 to 8 cycles/min. (Figure 3.)

The direction of propagation, determined by following a single cycle as it was detected sequentially by serially placed electrodes, was consistently aborad along the longitudinal axis of the stomach in both the corpus and the antrum. (Figure 4.) However, the direction of propagation along a transverse axis in the midcorpus was always from the greater curve toward the lesser curve in seven of nine patients tested (Figure 5), and it was intermittently so in the two others.

The overall mean velocity of aborad propagation of the pacesetter potential was 0.3 cm/sec in the corpus and proximal antrum, but it increased to 0.6 cm/sec in the distal antrum. (Table I.)

The pattern of electrical activity in patients with gastric diseases did not differ from that present in patients without such diseases (Table I), with the exception of the patient with antral cancer described above.

Action potentials, the electrical activity that occurs with the pacesetter potential when contractions are present, were not detected in any patient.

Effect of Transection. In three of four patients, the frequency of the pacesetter potential decreased by 0.8 to 1.8 cycles/min in the stomach distal to a site of transection of the corpus, whereas it remained unchanged in the segment proximal to the transection. (Figure 6.) The fourth patient, who had an obstructing duodenal ulcer associated with a greatly dilated stomach, did not show a change in the frequency of the pacesetter potential after transection in either the proximal or the distal segment.

Effect of Vagotomy. Proximal gastric vagotomy did not consistently alter the amplitude, rhythm, frequency, direction, or velocity of propagation of the pacesetter potentials. (Table I.)

Comments

Our investigation shows that the human gastric pacemaker is located in the midcorpus along the greater curve 5 to 7 cm aborad to the cardia. Pacesetter potentials were found at all sites distal to this area but not proximal to it. The cycles were propagated from the pacemaking area across the stomach to the lesser curve and also distally to the pylorus.

The findings with gastric transection provide further evidence for the midcorporal site of the gastric pacemaker and also support the concept of a gradient of intrinsic frequency of generation of pacesetter potentials in the human stomach. The pacemaker generates the cycles of the pacesetter potential at the fastest frequency, with distal areas beating more slowly when they are separated from the pacemaker. The pacemaker entrains the distal segments in the intact stomach and drives up their frequency to its own frequency.

The pattern of gastric electrical activity in man is remarkably similar to that found in dogs [*11–15*], except that the frequency of the human cycles is 3/min, whereas that of the dog is 5/min.

Ectopic pacemakers that generate pacesetter potentials irregularly and at rapid frequencies can appear in patients with gastric cancer, as exemplified

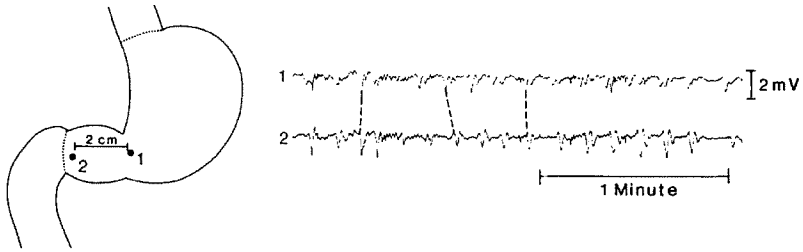

Figure 3. Antral pacesetter potentials with an irregular rhythm and a rapid frequency of 6 to 8 cycles/min in a patient with antral adenocarcinoma.

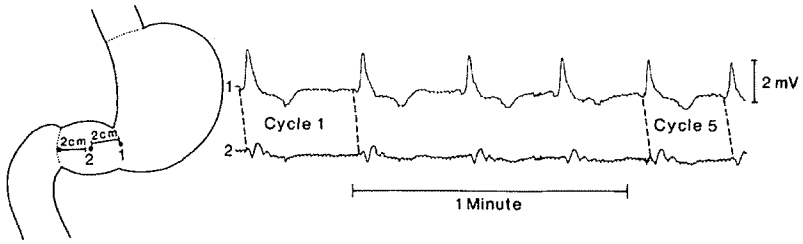

Figure 4. Cycles of antral pacesetter potential, identified by their length, are consistently propagated aborally.

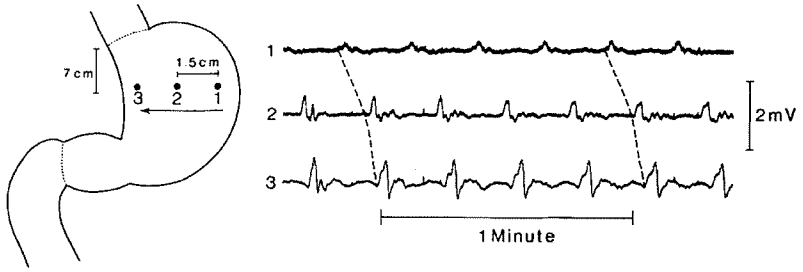

Figure 5. Cycles of midcorporal pacesetter potential are propagated from greater curve to lesser curve.

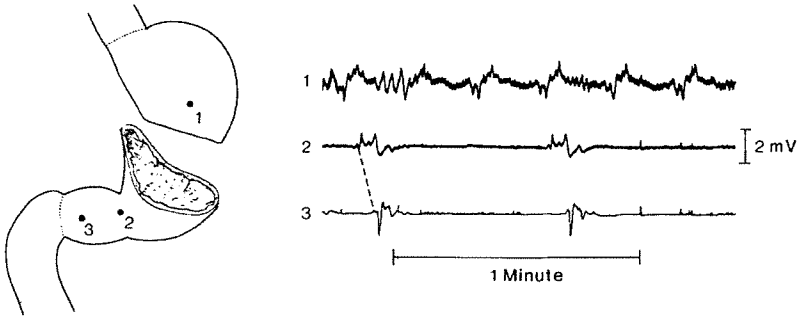

Figure 6. Cycles of pacesetter potential have a frequency of 3/min proximal to a transection 14 cm from cardia but only 1/min distal to transection.

by one of our patients and as shown by other investigators [2,3,7]. The altered electrical patterns produced by such an ectopic pacemaker could result in altered motor patterns, perhaps accounting for the impaired gastric emptying sometimes present in such patients. However, because gastric arrhythmias are not consistently found in patients with gastric cancer, monitoring the pattern of gastric electrical activity is unlikely to be useful as a clinical diagnostic test for cancer.

Our results confirm those of Stoddard et al [16,17], who found that proximal gastric vagotomy did not greatly alter the pattern of pacesetter potentials in the distal stomach. These data provide further evidence that the generation and propagation of pacesetter potentials are myogenic phenomena.

Summary

Gastric electrical activity was recorded from twenty-six patients at celiotomy. The human gastric pacemaker was localized to an area in the midcorpus along the greater curve. Pacesetter potentials were generated regularly by the pacemaker at a mean frequency of 3.2 cycles/min and were propagated circumferentially and aborally from the pacemaker,

increasing in amplitude and velocity as they approached the pylorus. The pattern of pacesetter potentials in patients with gastric ulcer, gastric cancer, and duodenal ulcer was similar to that of patients without such diseases. Complete transection of the gastric corpus isolated the distal stomach from the natural pacemaker and resulted in the appearance of a new pacemaker in the distal stomach with a slower frequency. The fact that proximal gastric vagotomy did not greatly alter the frequency of generation or the pattern of propagation of the pacesetter potential provided further evidence that both are myogenic phenomena.

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Discussion

Robert E. Condon (Milwaukee, WI): This is a potentially very important observation made by the authors. I am impressed with how rugged the gastric pacemaker is and how little anesthesia, an operation, and other things seem to do with it. The important issue is whether or not spike potentials are superimposed on these pacesetter waves, and whether or not the spike potentials are associated with muscular contraction. If the authors have such data, I would be very interested in hearing it. Particularly, I would be interested to know whether or not the percentage of times in which spike potentials were superimposed on slow waves was changed by vagotomy.

Keith A. Kelly: Of what importance are these physiologic observations to a surgeon? The importance is that the gastric pacesetter potential has a key role in gastric motility. It sets the pace of gastric peristalsis and thereby controls the rate of gastric emptying of solids. These facts are of special interest today because we and others have been able recently to pace the gastric pacesetter potential of dogs. We can pace the stomach much in the same way that one can pace the heart. Thus, in the future we may be able to treat abnormalities in human gastric peristalsis caused by disease or operation by gastric pacing.

President Longmire: I am sure that all of us have had the experience of performing gastroenterostomies in patients with cancer as well as other conditions and finding how poorly some of these will empty when there is no mechanical explanation. Possibly some of this obstruction is caused by interference with the normal motility of the stomach as indicated in this particular study.

Ronald A. Hinder (closing): In reply to Doctor Condon, the electrical counterpart of muscle contraction of the stomach is the action potential (or spike potential) which is in turn phased by the pacesetter potential. In our studies, carried out at the time of celiotomy, we were never able to record action potentials and never observed contractions of the stomach. We, therefore, cannot comment on the effect of proximal gastric vagotomy on postoperative gastric motility other than to say that when contractions occur their frequency is probably unchanged after proximal gastric vagotomy.