ORIGINAL ARTICLE

Gastric Myoelectric Activity in Patients with End-Stage Liver Disease

S. D. Caras, R. C. Dickson, Z. Lin, M. B. Ishitani, S. H. Caldwell & J. D. Z. Chen
University of Virginia Health Sciences Center, Dept. of Internal Medicine, Division of Gastroenterology, and Dept. of Surgery, Charlottesville, Virginia, USA

Caras SD, Dickson RC, Lin Z, Ishitani MB, Caldwell SH, Chen JDZ. Gastric myoelectric activity in patients with end-stage liver disease. Scand J Gastroenterol 1999;34:883–888.

Background: Abnormalities of gastrointestinal motility and transit time have been reported in association with end-stage liver disease. Motility abnormalities could be routinely studied if a simple noninvasive test were available. The electrogastrogram is a cutaneous measure of gastric myoelectric activity and correlates well with serosal recordings of gastric myoelectric activity. The aim of this study was to evaluate gastric myoelectric activity in patients with end-stage liver disease. **Methods:** Fourteen patients with end-stage liver disease had gastric myoelectric activity measured with the electrogastrogram. An electrogastrogram was considered abnormal when normal gastric slow waves were seen less than 70% of the time or there was no increase in the electrogastrogram amplitude after a meal. **Results:** Abnormal electrogastrograms were present in 8 of 14 (57%) end-stage liver disease patients. **Conclusions:** Abnormal gastric myoelectric activity is common in end-stage liver disease.

Key words: Electrogastrography; gastric motility; gastric slow waves; liver disease; stomach

Jiande Chen, Ph.D., Gastroenterology Division, University of Texas Medical Branch, Galveston, TX 77555-0764 (fax: +1 409 7473084)

Patients with end-stage liver disease (ESLD) have several complications, including ascites, encephalopathy, and bleeding secondary to portal hypertension. Frequently, these patients report upper intestinal symptoms including anorexia, bloating, nausea, and dyspepsia (1, 2). Some of these symptoms may be related to gastritis or peptic ulcer disease, but recent human and animal data have suggested there may be impairment in small-bowel motility and increased intestinal transit time associated with ESLD (3–5). A decrease in gastric emptying has also been shown in patients with chronic liver disease (6, 7). However, gastric myoelectric activity in patients with ESLD has never been studied. A simple, safe, noninvasive test would enable further investigation of these questions.

Slow-wave and spike activity are the two types of myoelectric activity observed in the stomach. The slow wave is present continuously and is characterized by regular, recurring changes in potential. It is believed that the slow wave originates in a region near the junction of the proximal one-third and distal two-thirds of the gastric body along the greater curvature.

The gastric slow wave determines the maximal frequency and propagation of the gastric contractions. The normal frequency of the slow wave is about 3 cycles per minute (cpm). Spike activity is directly responsible for antral contractions. The antral muscles contract when slow waves are superimposed with spike potentials (8).

Electrogastrography is a noninvasive technique for recording gastric myoelectric activity. With proper data analysis, an abnormal electrogastrogram (EGG) has been shown to correlate with upper intestinal symptoms and gastric dysmotility. Previous studies have shown that the EGG is a reliable measurement of gastric myoelectric activity compared with serosal recordings (8–12). There are no data on the use of EGG in patients with ESLD. The aim of this study was to evaluate gastric myoelectric activity in patients with ESLD.

Subjects and Methods

Subjects

Patients seen in an outpatient clinic for liver transplantation evaluation between March 1993 and August 1994 were considered for the study. Patients were excluded if there was a history of active alcohol use, diabetes, current viral illness, or previous gastric surgery. Fourteen patients with ESLD met the criteria and agreed to participate (7 women, 7 men; age, 20–63 years; mean, 45 years). The characteristics of these patients are shown in Table I. Pretransplant medications frequently used by our subjects included propranolol, lactulose, ranitidine, spironolactone, furosemide, and multivitamins at the time of the study. None of these medications caused any noticeable dyspeptic symptoms. No patient was taking any promotility agent or macrolide antibiotic at the time of the EGG measurement. Two patients were taking

Table I. Patient characteristics

Etiology of liver disease	
Hepatitis C	5
Hepatitis B	2
Ethanol	1
Autoimmune	2
Cryptogenic	1
Ethanol/viral	2
Hypervitaminosis A	1
Child class (Modified Child–Pugh classification)	
Class A	3
Class B	5
Class C	6
Ascites	
Absent or mild	7
Moderate or severe	7
Varices	
None	6
Grade I (no. treated)	2 (0)
Grade II	3 (1)
Grade III	3 (2)

calcium channel blockers for hypertension. One patient was taking loperamide for diarrhea. Only one patient had a history of gastric ulcer in this study. Ten healthy volunteers (five men, five women; age, 24–48 years) participated in the study as controls. None of these subjects had a history or symptoms of gastrointestinal disease or took medication the week before and during the study.

Dyspeptic symptoms were recorded, including nausea, vomiting, bloating, and abdominal pain.

Nausea was graded from 0 to 5 (0, <1/week; 1, 1–2/week; 2, 3–4/week; 3, 1–2/day; 4, 3–4/day; 5, constant), vomiting, bloating, and abdominal pain from 0 to 4 (0, <1/week; 1, 1–2/week; 2, 3–4/week; 3, 1–2/day; 4, >2/day).

Electrogastrographic measurements

Gastric myoelectric activity in each subject was measured using surface electrogastrography. Before the electrodes were attached to the abdominal surface, the skin was shaved (if necessary) and cleaned with sandy skin-prep paste (Omni Prep, Weaver & Co., Aurora, Colo., USA) to reduce the impedance. Three Ag/AgCl EKG electrodes (DNM, Dayton, Ohio, USA) were placed on the abdominal skin as shown in Fig. 1. Two epigastric electrodes were connected to yield a bipolar EGG signal. The other electrode was used as a reference. The EGG signal was measured with an ambulatory EGG recording unit (Digitrapper EGG, Synectics Medical Inc., Irving, Tex., USA). When this ambulatory unit was used, the EGG signal was amplified, simultaneously digitized, and stored on a digital chip. The cutoff frequencies for the low-pass and high-pass filters were 18 cpm and 1 cpm, respectively. The EGG signal was digitized at a rate of one sample per second (1 Hz). The subjects were in a supine position and were requested not to talk and to remain as still as possible during the recording, to prevent motion artefacts. After the study the EGG unit was connected to a 486 personal computer, and data were downloaded to the PC. A typical normal EGG recording is shown in Fig. 2 (top panel).

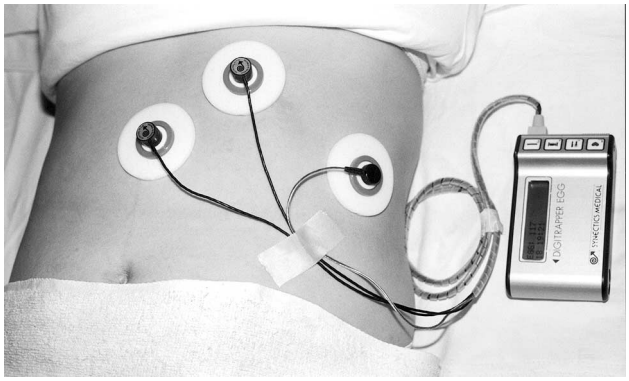

Fig. 1. Position of abdominal electrodes. The recorder is shown on the right.

Study protocol

The subjects fasted for at least 6 h before the study. The EGG recording was made for 30 min in the fasting state and 60 min immediately after ingestion of a 500-kcal turkey sandwich solid test meal.

The protocol was approved by the Human Investigation Committee at the University of Virginia. Signed consents to participate in the study were obtained.

Data analysis

Quantitative and statistical analysis of the EGG data was performed to investigate the effects of ESLD on the frequency, amplitude, and regularity of the EGG in the fasting and fed state. Variables computed from the EGG included the dominant frequency, peak power, and percentage of normal gastric slow waves. Visual analysis of this waveform is not possible, and spectral analysis was therefore used to compute the power of the EGG signal as a function of its frequency components.

The dominant frequency of the EGG. The dominant frequency was defined as the frequency at which the EGG power spectrum has its maximum peak power. The dominant frequency usually falls in the range of 0.5 to 9.0 cycles per minute (cpm) but was considered abnormal if it was not between 2 and 4 cpm. Tachygastria was defined as a dominant frequency greater than 4 cpm. Bradygastria was defined as a dominant frequency less than 2 cpm. The dominant frequency and the corresponding power were computed with each EGG tracing, using the smoothed power spectral analysis method (13).

Power of the dominant frequency and relative power. The power at the dominant frequency in the power spectrum is the EGG peak power. Relative power was defined as the difference in peak power (in decibels) at the dominant frequency between the fasting and fed states. The power (p) on the abscissa was expressed in decibels (dB) in accordance

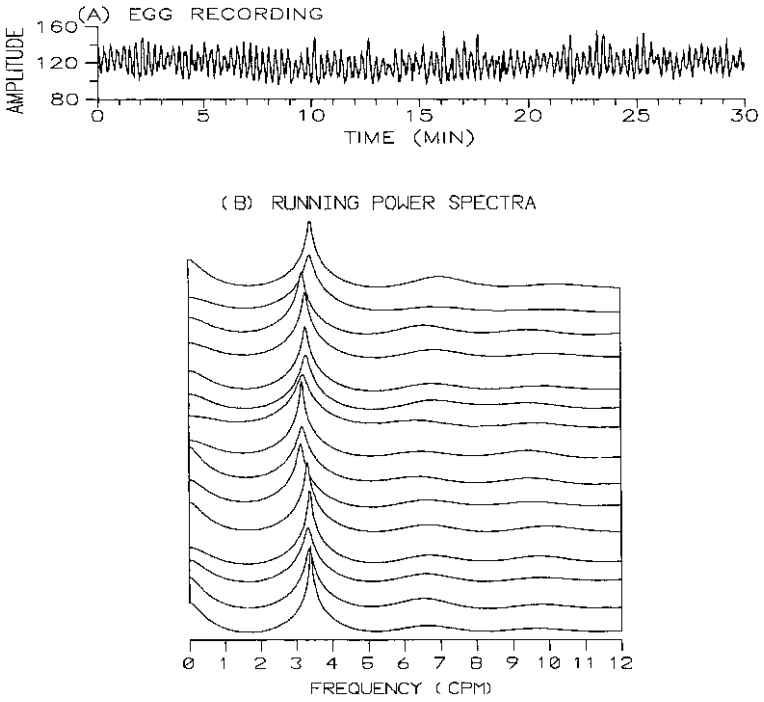

Fig. 2. The original recording and the running spectra of a normal electrogastrogram (EGG). Each spectrum was done every 2 min for a total of 30 min. The first 2-min spectrum is near the x-axis. Subsequent spectra move away from the x-axis. The percentage of normal slow waves is 100%, since all the individual spectra have dominant frequencies in the normal range.

with the following relationship: p (dB) = 10 $\log_{10}(A^2)$, where A was the amplitude of the signal.

Percentage of normal slow waves. The running spectra were computed by using the adaptive spectral analysis method (14). Each EGG recording was divided into blocks of 2 min without overlap. The power spectrum of each 2-min EGG was calculated and considered normal when the peak power was within the range of 2–4 cpm. The percentage of normal waves (PNW) was defined as the number of 2-min blocks with peak power at 2–4 cpm (NNW) divided by the total number of the 2-min blocks (TW); that is, PNW = NNW/TW.

Definition of abnormal EGG. An abnormal EGG has previously been defined as a recording with the percentage of normal slow waves less than 70% in either the fasting or fed state, or a decrease in power at the dominant frequency after the test meal (13).

Statistical analysis. The paired student *t* test was used to investigate the effect of the test meal on the EGG variables, and chi-square analysis was applied to investigate the difference between the patients and the healthy controls. All values were represented with mean ± standard deviation. Statistical significance was assigned for *P* values of <0.05.

Results

Regular gastric slow waves were recorded for all healthy controls, with a dominant frequency of 2.88 ± 0.22 cpm and a percentage of normal slow waves of $92.4\% \pm 7.4\%$ in the fasting state. After the test meal the dominant frequency was significantly increased to 3.07 ± 0.17 cpm ($P < 0.03$). A similar postprandial increase in the power of the dominant frequency was observed (6.96 ± 4.08 dB; $P < 0.003$). The percentage of normal slow waves remained unchanged after the meal ($94.0 \pm 5.9\%$; $P > 0.05$). No abnormal EGG was found in any of the healthy controls; that is, the percentage of normal gastric slow waves in either the fasting or the fed state was greater than 70%, and there was an increase in the power of the dominant frequency after the meal. Abnormalities in the EGG were, however, found in 8 of the 14 (57%) patients with ESLD ($P < 0.004$, in comparison with the controls). Five patients showed abnormal gastric slow waves in either the fasting or the fed state ($P < 0.04$, in comparison with the controls). Fig. 2 presents a normal EGG study, and Fig. 3 an abnormal EGG recording. Three patients had a postprandial decrease in the power of the dominant frequency (see Fig. 4 for an example). In contrast to the healthy controls, the dominant frequency of the EGG in the patients did not show a significant postprandial increase (2.99 ± 0.38 versus 3.02 ± 0.24; $P > 0.05$). In comparison with the healthy controls, the patients showed a decreased (but not statistically significantly) percentage of normal slow waves in both fasting ($81.9\% \pm 21.6\%$; $P = 0.06$) and fed ($86.1\% \pm 21.4\%$; $P = 0.1$) states. The average postprandial increase in the power of the

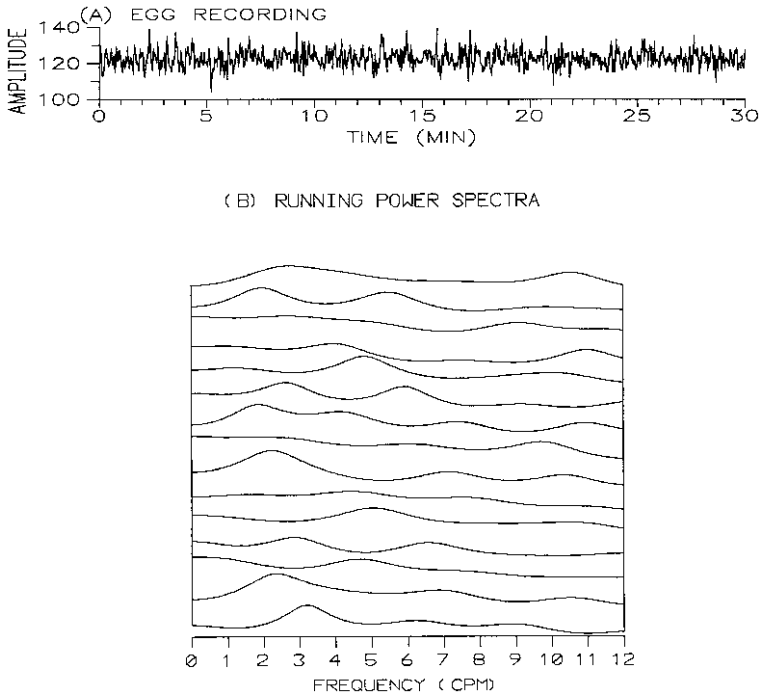

Fig. 3. The electrogastrogram (EGG) and the running spectra from a patient with a contained arrhythmia. Note the irregularity of the EGG recording compared with Fig. 2. This results in a running power spectra in which there is no consistent dominant frequency. From this spectra we can conclude that the gastric myoelectric activity is disorganized.

dominant frequency in the patient group was also lower (but not statistically significantly) than that in the healthy controls (5.21 ± 4.98 dB versus 6.96 ± 4.08 dB; $P = 0.3$).

The presence of altered gastric myoelectric activity did not correlate with the severity of liver disease, as EGG abnormalities were found in one of three patients with class-A cirrhosis, four of five with class-B, and three of six with class-C. There was no correlation with clinically significant ascites. EGG abnormalities were found in three of seven patients with absent or minimal ascites and in five of seven patients with moderate to severe ascites ($P = 0.34$). A relative decrease in power was found in two of seven patients who had absent to minimal ascites, and in one of seven patients with significant ascites. There was no significant correlation between EGG findings and albumin levels. Abnormal EGGs were found in five of eight patients with albumin greater than 2.8 and in three of six patients with albumin less than 2.8 ($P = 0.45$).

None of the healthy controls reported any symptoms of dyspepsia. However, most of the patients reported at least one of the symptoms. The mean total symptom score in the 14 patients was 5.75 ± 1.28. However, no correlation was found between the abnormality of any of the EGG variables and any of the dyspeptic symptoms or the total symptom score.

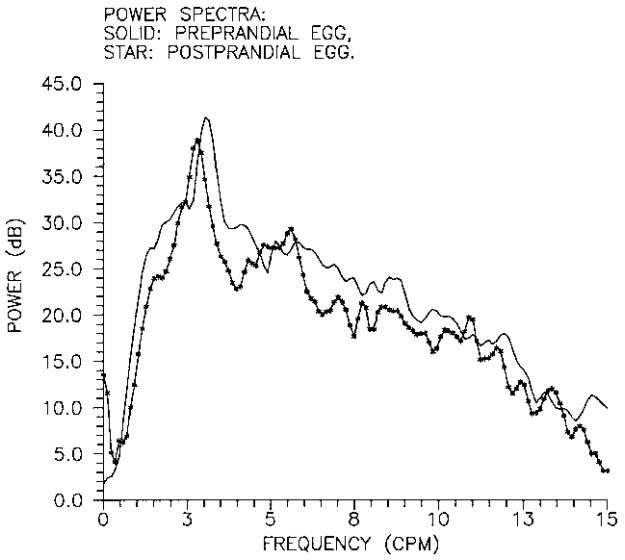

Fig. 4. The power spectra from a fasting and fed electrogastrogram. Note that the dominant power in the fed state is smaller than in the fasting state. This result is abnormal. The small frequency shift between fed and fasting EGGs is normal and is of no consequence.

Discussion

The EGG is a noninvasive measurement of gastric myoelectric activity. This method has previously been validated in our laboratory (11) and in others (8, 10, 15). Normal ranges of the dominant frequency, the percentage normal slow waves, and the relative power have been consistent between our laboratory (16, 17) and other investigators (18, 19).

In this preliminary study abnormalities in gastric myoelectric activity were shown in 57% of patients using both pre- and postprandial EGG studies. This is in marked contrast to the finding of normal EGGs in all asymptomatic healthy controls studied but similar to EGG findings in diabetics with gastroparesis (20, 21). The high percentage of the ESLD patients with abnormal gastric myoelectric activity correlates well with results of solid and liquid gastric emptying studies in the same patient population (6, 7).

Whereas both gastric myoelectric abnormalities and dyspeptic symptoms were observed in the ESLD patients, no correlation was noted between these two measurements. Numerous previous studies have reported a higher prevalence of gastric myoelectric abnormalities in patients with gastrointestinal symptoms (22–27). Reports on the correlation between gastric myoelectric abnormalities and dyspeptic symptoms have been conflicting. In a well-designed study investigating vection-induced motion sickness, Stern et al. (26) found that gastric dysrhythmia was a cause of motion sickness symptoms. Some other studies in patients with gastroparesis or functional dyspepsia, however, failed to show a significant correlation between gastric myoelectric abnormalities and symptoms (24). Similar controversial findings have also been reported in the literature between gastric manometry and symptoms or gastric emptying and symptoms. The disassociation between dyspeptic symptoms and gastric myoelectric abnormalities observed in this preliminary study might be attributed to the relative small size of the samples. This may also suggest that electrogastrography is not sensitive in distinguishing specific gastrointestinal symptoms in patients with ESLD. More studies are required for further investigation.

A potential cause of an abnormal EGG in these patients could be the presence of ascites, since power at the dominant frequency may be partially dependent on the distance between the skin electrodes and the stomach. However, relative power represents a ratio between the fasting and the fed state and thus should not be affected. In our study clinically significant ascites did not account for an increase in patients with abnormalities in relative power or an increased number of abnormal EGGs overall. These data suggest that the presence of ascites does not prevent adequate assessment of relative power with the EGG.

The mechanism of gastrointestinal motility disorders in ESLD is unclear. Mucosal edema secondary to hypoalbuminemia and portal hypertension could potentially affect motility. However, we found no relationship between the presence of EGG abnormalities and albumin, ascites, or Child–Pugh scores in our patients. These findings support gastric emptying data obtained on patients with liver disease. Autonomic dysfunction has also been proposed as a possible cause of gastrointestinal motility disorders, since there is a high prevalence of autonomic nervous system dysfunction in ESLD. However, Isobe et al. (7) found no correlation between abnormal gastric emptying in patients with ESLD and the R–R interval of the electrocardiogram. However, the lack of other measurements of autonomic dysfunction may limit their conclusion.

In summary, we have shown that there is a higher than expected rate of abnormal gastric myoelectric activity in patients with ESLD. Further investigation into the etiology of abnormal motility in these patients could provide insight into the mechanisms both of the dysmotility and of the hyperdynamic state associated with ESLD.

References

1. Sherlock S. Hepatic cirrosis. In: Diseases of the liver and biliary system. 8th ed. Oxford: Blackwell Scientific Publications; 1989. p. 410–24.
2. Mendenhall CL, Anderson S, Weesner RE, Goldberg SJ, Crolic KA. Protein calorie malnutrition associated with alcoholic hepatitis. Am J Med 1984;76:211–22.
3. Really JAG, Quigley EMM, Forst CF, Rikkers LF. Small intestinal transit in the portal hypertensive rat. Gastroenterology 1991;100:670–3.
4. Chesta J, Defilippi C, Defilippi CA. Abnormalities in proximal small bowel motility in patients with cirrhosis. Hepatology 1993;17:828–32.
5. Van Theil DH, Fagiuoli S, Wright HI, Chen MC, Gavaler JJ. Gastrointestinal transit in cirrhotic patients: effect of hepatic encephalopathy and its treatment. Hepatology 1994;19:67–71.
6. Galati JS, Holderman KP, Dalrymple GV, Harrison KA, Quigley EMM. Delayed gastric emptying of both liquid and sold components of a meal in chronic liver disease. Am J Gastroenterol 1994;89:708–11.
7. Isobe H, Sakai H, Masaki S, Sakamoto S, Narata H. Delayed gastric emptying in patients with liver cirrhosis. Dig Dis Sci 1994;39:983–7.
8. Smout AJPM, van der Schee EJ, Gashius JL. What is measured in electrogastrography? Dig Dis Sci 1980;25:179–87.
9. Abell TL, Malagelada JR. Glucagon-evoked gastric dysrhythmias in humans shown by an improved electrogastrographic technique. Gastroenterology 1985;88:1932–40.
10. Familoni BO, Bowes KL, Kingma YJ, Cote KR. Can transcutaneous recordings detect gastric electrical abnormalities? Gut 1991;32:141–6.
11. Chen JDZ, Schirmer BD, McCallum RW. Serosal and cutaneous recordings of gastric myoelectrical activities in patients with gastroparesis. Am J Physiol 1994;266:G90–8.
12. Pugh RMH, Murray LIM, Dawson JL, Pielsini ML, Williams R. Transection of the oesophagus for bleeding oesophageal varices. Br J Surg 1973;60:636–49.
13. Chen JDZ, McCallum RW. Clinical application of electrogastrography. Am J Gastroenterol 1993;88:1324–36.
14. Chen JDZ, Stewart WR, McCallum RW. Spectral analysis of episodic rhythm variations in the cutaneous electrogastrogram. IEEE Trans Biomed Eng 1993;40:128–34.
15. Stern RM, Koch KL, Stewart WR, Vasey MW. Electrogastrography: current issues in validation and methodology. Psychophysiology 1987;24:55–64.
16. Chen JDZ, Richards R, McCallum RW. Frequency components of the electrogastrogram and their correlation with gastrointestinal motility. Med Biol Eng Comput 1993;31:60–7.
17. Chen JDZ, McCallum RW. Frequency components of the electrogastrogram and their correlation with gastrointestinal motility. Med Biol Eng Comput 1993;31:60–7.
18. Koch KL, Stern RM. EGG data acquisition and analysis—the Penn State experience. In: Electrogastrography: principles and applications. New York: Raven Press; 1994.
19. Smout AJPM, Jebbink HJA, Samson M. Acquisition and analysis of electrogastrographic data—the Dutch experience. In: Electrogastrography: principles and applications. New York: Raven Press; 1994.

20. Chen JDZ, McCallum RW. Gastric slow wave abnormalities in patients with gastroparesis. Am J Gastroenterol 1992;87:477.
21. Abell TL, Camilleri M, Hench VS, et al. Gastric electromechanical function and gastric emptying in diabetic gastroparesis. Eur J Gastroenterol Hepatol 1993;3:163–7.
22. Cucchiara S, Riezzo G, Minella R, Vallone G, Vallone PF, Giorgio I, et al. Electrogastrography in nonulcer dyspepsia. Arch Dis Child 1992;67:613–7.
23. Geldof H, van der Schee EJ, Van Blankenstein M, Grashius JL. Electrogastrographic study of gastric myoelectrical activity in patients with unexplained nausea and vomiting. Gut 1986;26: 799–808.
24. Koch KL, Stern RM, Stewart WR, Vasey MW. Gastric emptying and gastric myoelectrical activity in patients with diabetic gastroparesis: effect of long-term domperidone treatment. Am J Gastroenterol 1989;84:1069–75.
25. Rothstein RD, Alavi A, Reynolds JC. Electrogastrography in patients with gastroparesis and effect of long-time cisapride. Dig Dis Sci 1993;38:1518–24.
26. Stern RM, Kenneth LK, Leibowitz HW, Lindblad IM, Shupert CL, Stewart WR. Tachygastria and motion sickness. Aviat Space Environ Med 1985;56:1074–7.
27. Hasler WL, Soudah HC, Dulai G, Owyang C. Mediation of hyperglycemia-evoked gastric slow wave dysrhythmias by endogenous prostaglandin. Gastroenterology 1995;108:727–36.

Received 11 January 1999
Accepted 18 May 1999