

# Electrogastrography as a diagnostic tool for delayed gastric emptying in functional dyspepsia and irritable bowel syndrome

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**Abstract** Several pathophysiological mechanisms have been proposed in functional gastrointestinal (GI) disorders, e.g. altered GI motility and sensitivity. The aim of this study was to investigate gastric electrical activity (GEA) in patients with functional dyspepsia (FD) or irritable bowel syndrome (IBS) compared with healthy controls (HC), and to assess if abdominal symptoms and delayed gastric emptying are associated with alterations in GEA, as determined by electrogastrography (EGG). Forty patients with FD, IBS or both were compared with 22 HC. EGG was performed before and after a standard meal. Frequencies and amplitudes pre- and post-prandially were analysed. Furthermore, gastric emptying and symptom scores were assessed. Eight of 40 patients (20%; three FD, three IBS, two FD and IBS) had delayed gastric emptying. Disturbed gastric emptying and lack of a postprandial increase in the EGG amplitude were significantly correlated ( $r = 0.8$ ;  $P < 0.005$ ). No differences between controls and patients were observed in the distribution of EGG frequencies. Treatment with the prokinetically active macrolide erythromycin improved gastric emptying, GEA and symptoms

( $n = 4$ ). The data suggest that EGG could be useful as a diagnostic tool in patients with FD and IBS to identify a subgroup of patients with delayed gastric emptying.

**Keywords** electrogastrography, functional dyspepsia, gastrointestinal motility, irritable bowel syndrome, macrolide.

## INTRODUCTION

Functional gastrointestinal disorders (FGID), in particular functional dyspepsia (FD) and irritable bowel syndrome (IBS), are frequently diagnosed in patients referred to gastroenterologists or specialized outpatient clinics. The pathogenesis of FD remains unclear; nevertheless, it has been proposed that FD and IBS might have a common pathophysiological basis, e.g. visceral hyperalgesia.<sup>1,2</sup> However, the alteration of gastrointestinal (GI) function causing symptoms in a particular patient mostly remains unclear, and the diagnosis is made solely by the individual complaints plus exclusion of obvious organic diseases and structural alterations. Several pathophysiological mechanisms have been proposed to underlying FD; among others alterations of GI motility and sensitivity.<sup>3–6</sup> However, in patients with FD such alterations are not investigated in clinical routine. It is controversial, whether alterations of gastric electrical activity (GEA) could be of clinical relevance at least in some patients with FD. Some studies report an increased degree of tachygastria,<sup>7</sup> others decreased postprandial power activity, as assessed by electrogastrography (EGG).<sup>8</sup> However, it is unclear, if such alterations are specific

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for FD, and if such disturbances are associated with altered GI function, in particular gastric motility, that might cause symptoms.

The aims of the study were to investigate whether patients with FD have alterations of GEA compared with healthy controls (HC), and whether these alterations can also be observed in patients with other FGID, in particular IBS. Furthermore, it was investigated whether such alterations in GEA are associated with disturbed gastric emptying, and whether they correlate with symptoms of FD and IBS. Additionally, we studied if alterations of GEA and emptying could be successfully treated by drug therapy with the macrolide erythromycin.

## MATERIALS AND METHODS

### Subjects

Adult patients who fulfilled Rome-II criteria for FD, IBS, or both were enrolled. Forty patients (nine men and 31 women, age 18–79, mean 38 years) suffering from FD ( $n = 16$ ), IBS ( $n = 13$ ), or coexisting FD and IBS ( $n = 11$ ), were referred to the outpatient clinic for diagnostic workings. Patients with pathological findings in colonoscopy, gastroscopy, laboratory values or other diagnostic tests explaining the symptoms, or patients having other systemic diseases were excluded from the study.

The 22 HC (10 males, 12 females, age 20–68, mean 33 years) who were included in the study had no history of GI disorders, except appendectomy, and took no regular medication. Patients and volunteers gave informed consent prior to the investigations. The studies were designed as follows.

### Assessment of symptoms

A validated symptom questionnaire had to be completed to quantify the average daily severity of dyspeptic and IBS symptoms during the previous 7 days, which was assessed on visual analogue scales (VAS) from 0 to 10 for each item.<sup>9</sup> The patients were asked for the following *dyspeptic symptoms*: indigestion, early satiety, upper abdominal pain, nausea, vomiting and fullness; and *IBS symptoms*: non-epigastric abdominal pain, bloating, sensation of incomplete evacuation after defecation, constipation and/or diarrhoea, mucus stools, influence of defecation on pain. These symptoms are considered to be quite characteristic in FD and IBS, respectively.<sup>10</sup> A maximal value of 60 points could be scored for dyspeptic and IBS symptoms, respectively. Furthermore, dyspeptic symptoms were

also assessed immediately before and 1 h after the ingestion of a meal at the gastric emptying test.

### Electrogastrography

The GEA was measured by means of EGG, as described earlier.<sup>7,8,11,12</sup> In brief, three electrodes were used: one placed half way between the umbilicus and xiphoid on the ventral midline. The second electrode was located 6 cm apart on the left side 1 cm below the lowest rib; and the third one (reference electrode) was placed in a way so that it formed an equilateral triangle together with the other two electrodes. The subjects were positioned comfortably in a supine position and requested to remain as still as possible to reduce motion artefacts. After an overnight fasting period of 10 h the EGG was recorded for a period of 60 min. Patients were given a 500 kcal standard test meal consisting of 40 g of toast, 90 g of melting cheese, 30 g of cornflakes, 200 mL orange juice, 250 mL tea (86.3 g of carbohydrates, 9.2 g protein, 13.3 g fat). The postprandial period was recorded for another 60 min. The EGG signal was recorded using a specially designed digital recorder (Digitrapper-EGG; Medtronic, Stockholm, Sweden), which included a one-channel EGG preamplifier, a band-pass analogue filter, an analogue-to-digital (8-bit precision) converter, and 96 kbytes of memory. The filter had a 1.8–16.0 cpm pass-band with a roll-off of 6 dB octave<sup>-1</sup>. The EGG signal was sampled at a rate of 4 Hz. The raw signal was examined visually to detect obvious motion artefacts. The data was analysed using specially designed software (Gastrosoft version 6.30; Irving, TX, USA). The results were expressed as percentage rates of normogastria, i.e. two to four cycles per minute (cpm), tachygastria (>4 cpm), bradygastria (<2 cpm), for both fasting and fed period. The amplitude of the dominant frequency of GEA was determined and presented as power of this activity. The power of the dominant frequency was measured both before and after the test meal, and the postprandial/fasting (P/F) EGG power ratio calculated.

### Gastric emptying test

To detect delayed gastric emptying, a radiopaque marker test was carried out, as described by Feldmann, simultaneously with the EGG recording.<sup>13,14</sup> Together with the above-mentioned standard test meal patients were given a gelatin capsule containing 10 cubic radiopaque test markers, 8 mm of length (Distribution: Gastroenterology Unit, Department of Internal Medicine, Kantonspital Basel, Switzerland). A plain

abdominal film was taken after 6 h to detect the position of the markers. During this time period no further food intake (except of tea without sugar or water during the last 5 h of the test) was allowed. If necessary, the exact position of test markers was detected radioscopically after a barium meal. A persistence of one or more markers in the stomach was considered abnormal. In HC the gastric emptying test was not performed to limit exposure to radiation.

**Drug treatment**

Four patients with delayed gastric emptying were treated with the prokinetically acting drug erythromycin orally.<sup>15,16</sup> After taking the drug at the dose of 250 mg t.i.d. for at least 4 days, assessment of symptoms, EGG and gastric emptying test were repeated as described above. In one patient, where this dose of the drug did not improve symptoms and gastric emptying, the dose was increased to 500 mg erythromycin t.i.d. and the investigations repeated again.

**Data analysis**

The data was analysed using Student's *t*-test and Mann-Whitney *U*-test, according to data distribution, and is presented as mean values ± SEM. Fisher's exact test was applied to check for independence within the cross-table. Coefficients of correlation were calculated according to Pearson and Spearman. Significance was accepted for *P* < 0.05.

**RESULTS**

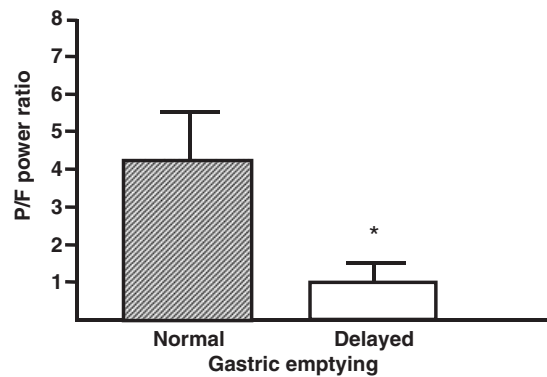
**Electrogastrography**

After visual analysis of the raw data and removal of artefacts, at least 98% of the EGG recording was analysed. The mean dominant EGG frequency at fasting and postprandially, and the P/F EGG power ratio showed no significant difference between the various groups (Table 1). However, comparison of P/F power ratio of patients with a pathological gastric emptying test to those with a normal gastric emptying test revealed a significantly diminished P/F EGG power ratio at delayed gastric emptying (Fig. 1). In comparison with the preprandial EGG amplitude, seven of eight patients with a pathological gastric emptying test had no increase in the postprandial EGG amplitude (Table 2). In contrast, 30 of 32 patients with a normal gastric emptying test showed a postprandial increase in the EGG amplitude (Spearman rho 0.8; *P* < 0.005).

**Table 1** Dominant frequency and P/F power ratio in the electrogastrography of patient groups and healthy volunteers

	Dominant frequency		P/F power ratio
	Fasting	Postprandial	
Functional dyspepsia (FD)	3.05 ± 0.34	3.12 ± 0.18	5.3 ± 4.2
Irritable bowel syndrome (IBS)	3.06 ± 0.29	3.12 ± 0.27	2.2 ± 2.7
FD + IBS	3.05 ± 0.23	3.12 ± 0.25	2.5 ± 2.7
All patients	3.05 ± 0.23	3.12 ± 0.23	3.5 ± 3.6
Healthy controls	2.90 ± 0.35	3.00 ± 0.35	3.3 ± 3.7

Results are expressed as mean ± SEM.



**Figure 1** Postprandial/fasting (P/F) power ratio in functional dyspepsia or/and irritable bowel syndrome patients with a normal (*n* = 32) or a pathological (*n* = 8) gastric emptying test. Mean values ± SEM. \*Indicates significant difference at *P* < 0.05.

**Table 2** Contingency table of gastric emptying and postprandial increase in electrogastrography (EGG) amplitude

		Gastric emptying	
		Normal	Delayed
Postprandial increase in EGG amplitude	Yes	30	1
	No	2	7

In this study, a sensitivity of 0.87 and a specificity of 0.94 can be calculated for the lack of a postprandial increase in EGG amplitude to predict a pathological gastric emptying test in the patient group. The positive predictive value is 0.78 and the negative predictive value is 0.97.

No differences in the percentages of time in the normal (2–4 cpm) range or dysrhythmia ranges were observed between the various patient groups or

**Table 3** Frequency distribution in the electrogastrography of patients with normal or delayed gastric emptying

Percentage of time	2–4 cpm		Bradygastria		Tachygastria	
	Fasting	Postprandial	Fasting	Postprandial	Fasting	Postprandial
Patients with normal gastric emptying	77 ± 15	86 ± 14	16 ± 26	13 ± 15	7 ± 8	4 ± 5
Patients with delayed gastric emptying	78 ± 18	78 ± 19	13 ± 12	13 ± 15	8 ± 8	6 ± 8

Data are given as mean values ± SEM.

between patients and HC in the fasting as well as postprandial period (data not shown). No differences in fasted or postprandial frequency distribution were observed between patients with normal gastric emptying and delayed gastric emptying (Table 3). No correlation between the individual symptom score and frequency distribution in the EGG was present among the various subgroups. The degree of present symptoms did not correlate with the EGG frequency data either.

## Symptoms

*Average daily dyspeptic and IBS symptoms* Dyspeptic and IBS symptoms were assessed by using a questionnaire at the time of study entry, i.e. at least 7 days before the test procedures of EGG and gastric emptying. The three patient groups scored significantly higher in dyspeptic and IBS complaints compared with the control group (Table 4). Patients with symptoms of FD + IBS had the highest scores for dyspeptic and IBS symptoms compared with the two other patient groups (Table 4). However, this difference was only significant for dyspeptic complaints. No disproportionately frequent symptoms could be discovered within one of the three subgroups. Vomiting was rarely reported in all groups. Bloating sensation was mentioned most frequently and with the highest intensity in all patient groups.

**Table 4** Average daily dyspeptic and irritable bowel syndrome (IBS) symptoms in the last 7 days in patients and healthy controls (HC)

	Average daily dyspeptic symptoms (VAS score)	Average daily IBS symptoms (VAS score)
Functional dyspepsia (FD)	17 ± 9	20 ± 13
IBS	15 ± 8	28 ± 9
FD + IBS	25 ± 11**	32 ± 14
HC	1 ± 3*	2 ± 2*

Data are given as mean values ± SEM. \*Significant difference compared with patient groups ( $P < 0.05$ ). \*\*Significant difference compared with other patient groups ( $P < 0.05$ ).

**Table 5** Score of dyspeptic symptoms before and after standard test meal in patients and healthy controls (HC)

	Fasted score of dyspeptic symptoms	Fed score of dyspeptic symptoms
Functional dyspepsia (FD)	7 ± 7	14 ± 9**
Irritable bowel syndrome (IBS)	4 ± 4	11 ± 8**
FD + IBS	10 ± 10	15 ± 12**
HC	0 ± 0*	1 ± 2*

Data are given as mean values ± SEM. \*Significant difference between healthy controls and all patient groups ( $P < 0.05$ ).

\*\*Significant difference between fasted and fed score of dyspeptic symptoms within the same group ( $P < 0.05$ ).

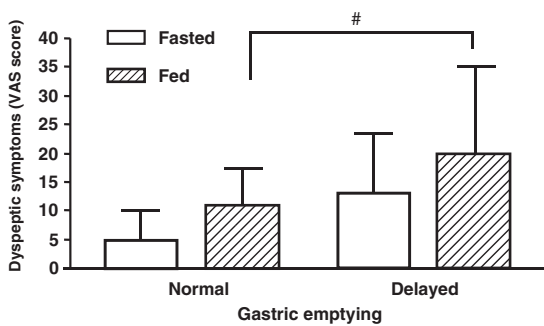
*Dyspeptic symptoms at test meal* This assessment of dyspeptic symptoms by questionnaire was performed directly before and after the test meal. The fasted and fed scores of dyspeptic symptoms were significantly higher in all patient groups compared with the HC (Table 5). In all patient groups the fed score of dyspeptic symptoms was significantly higher than the fasted score (Table 5).

## Gastric emptying

In about 20% of the patients a barium contrast solution was necessary to determine the exact position of the marker. In eight of the 40 patients (20%) a pathological gastric emptying test was found: 6 h after the standard test meal in four patients 10 markers were detected in the stomach by X-ray, in two patients nine markers, in one patient eight markers, and in another patient three markers. In other patients the markers could not be detected in the stomach.

Three patients with delayed gastric emptying were from the FD group, and another three from the IBS group. The other two patients with prolonged gastric emptying had both FD- and IBS-like abdominal complaints.

The patients with a pathological gastric emptying test had higher scores of dyspeptic symptoms at the fasted and fed state when compared with patients with



**Figure 2** Score of dyspeptic symptoms before and after a standard test meal in functional dyspepsia or/and irritable bowel syndrome patients with a normal ( $n = 32$ ) or a pathological ( $n = 8$ ) gastric emptying test. Data are given as mean values  $\pm$  SEM. Significant difference between normal and delayed gastric emptying ( $P < 0.05$ ).

normal gastric emptying. Whereby, only the postprandial score was significantly higher (Fig. 2).

### Erythromycin

Four of eight patients with a pathological gastric emptying test were treated with erythromycin. Two of the other four patients who could have been treated with erythromycin rejected this medication. In two other patients the tests could not be carried out because of time limits on the patient's part. After treatment with  $3 \times 250$  mg erythromycin for 6–10 days the protocol was carried out again on the four patients. Three patients showed normalization of the gastric emptying test. In the fourth patient the medication was raised to  $3 \times 500$  mg erythromycin a day. Thereafter, the same positive effect on gastric emptying was observed.

The score of average daily dyspeptic symptoms in the four patients who underwent a 1-week observation period at treatment with erythromycin ( $17 \pm 6$ ) was lower than before treatment ( $31 \pm 8$ ). The score of average daily IBS symptoms was also reduced by erythromycin treatment from  $34 \pm 10$  to  $21 \pm 8$ . The patient treated with the higher dose of erythromycin reached symptom scores comparable with those of the controls after a 1-week treatment with the compound.

The changes in EGG frequency distribution before and after treatment were diverse. One patient with high percentage of tachygastria during the fasting period had a normal distribution of frequencies after treatment. Another patient with initially normal distribution of frequencies displayed a higher portion of bradygastria in the postprandial phase, which was just slightly above the norm.

All patients showed a P/F EGG power ratio of  $>1$  after drug treatment. One patient showed no change of the P/F EGG power ratio after drug treatment with  $3 \times 250$  mg erythromycin compared with before drug treatment. After the erythromycin dose was raised to  $3 \times 500$  mg, a clear increase in the postprandial EGG amplitude was observed along with a P/F power ratio greater than one.

### DISCUSSION

The present study demonstrates that EGG is capable of detecting a subgroup of patients presenting with FD, IBS, or both entities of FGID with disturbed gastric motility. Only few studies have evaluated the correlation between postprandial amplitude rise in EGG and gastric emptying. A close relationship between altered GEA, a lack of postprandial rise in EGG amplitude, and delayed gastric emptying, as assessed by scintigraphy, was observed in 48 patients with nausea and vomiting of unknown cause.<sup>11</sup> The present results are in agreement with this observation and both studies suggest that a diminished postprandial amplitude in EGG is a reliable indicator of gastric motility disorders, even with the physiological mechanisms of postprandial rise in EGG amplitude not being clarified to date.<sup>12,17,18</sup> In the present study the distribution of frequencies in EGG was not useful in detecting differences among the groups of patients and controls investigated. No correlation was observed between EGG frequency and investigated groups, patient subgroups, symptoms or gastric emptying test. These results should be a matter of discussion keeping in mind that equivocal results are reported in the literature. Jebbink observed differences in frequency fractions between 30 diabetic patients with dyspepsia and 18 HC.<sup>19</sup> Chen observed frequency distribution abnormalities in 20 of 27 patients with dyspepsia when compared with healthy individuals.<sup>20</sup> As different methods have been applied in various investigations there is only limited comparability given. More standardized experiments will have to be performed to further evaluate the significance of differences in EGG frequency fractions as a possible factor taking influence on the genesis of symptoms in patients with FD or IBS. In this respect, a mapping of gastric surface potentials seems necessary to clarify the importance of electrode location.<sup>21</sup>

As regards EGG, standardization in performing EGG recordings is needed.<sup>22,23</sup> In addition, multiple-channel EGG introduces the possibility to study the propagation and coupling of slow waves in the stomach, and this technical progress may be helpful in the diagnosis of gastric dysfunction.<sup>24</sup>

The present observation that a diminished P/F power ratio can be observed in a subgroup of patients with FD and IBS is in accordance with the data of Leahy *et al.*<sup>7</sup> EGG was shown to be useful to define a subgroup of patients with FD and electrical rhythm disturbance. Leahy concluded that in IBS the electrogastrogram was abnormal only if concurrent dyspepsia was present. However, no gastric emptying test or pharmacotherapy was performed in that study. In addition, in the present study, all patients with IBS also reported at least some dyspeptic symptoms when investigated by a questionnaire. Therefore, the present data reveal a close association between an altered GEA, delayed gastric emptying and abdominal symptoms in a subgroup of patients with FD or IBS.

The radiopaque markers used in the gastric emptying test were 8 mm. In a study by Smith and Feldman<sup>14</sup> no significant difference in emptying was detected between 2 and 10 mm markers. In the study reported by Smith and Feldmann<sup>14</sup> all markers left the stomach after 6 h in 50 of 53 healthy subjects. Therefore, a delayed gastric emptying was presumed when one or more markers persisted in the stomach after 6 h. It was assumed that the supine position during the first hour after indigestion of the test meal would not influence the outcome of the gastric emptying test, which was measured over a total of 6 h. In another study by Feldman,<sup>13</sup> healthy subjects and diabetic patients underwent gastric emptying tests. In three of six diabetic patients with a normal gastric emptying as assessed by scintigraphy, test markers could still be detected in the stomach after 6 h. Thus, the gastric emptying test using radiopaque markers is assumed to be more sensitive in detecting altered gastric emptying similar to scintigraphy.

Therefore, the highly significant correlation in the present study between delayed gastric emptying and a missing postprandial rise in amplitude of the EGG seems to be of diagnostic and therapeutic relevance. The lack of a postprandial increase in EGG amplitude predicted a pathological gastric emptying test with a sensitivity of 0.87 and a specificity of 0.94. In addition, erythromycin raised the P/F power ratio in the current study, besides relieving upper abdominal complaints. It is reasonable to treat patients with delayed gastric emptying with a prokinetic drug, such as erythromycin.<sup>25–27</sup> The present study suggests that monitoring the postprandial rise in EGG amplitude could be helpful in finding the minimal dose of such a drug not only subjectively but also objectively.

Whether delayed gastric emptying in patients is caused by a diminished postprandial increase in GEA, as assessed by EGG, or if both alterations are only

different manifestations of an underlying motility disorder, can only be speculated. The hampered gastric emptying may not be understood as the sole cause of complaints in this subgroup of patients with FGID, as in diabetic gastroparesis, often serving as a model for FD-associated gastroparesis, only a part of the patients develop dyspeptic complaints.<sup>2,5,28,29</sup>

Functional dyspepsia and IBS are often treated as different entities. Many studies focus only on one of these two disease entities defined by prevailing symptoms. In the present study the symptom scores clearly differentiated between patients and the control group. However, patients with FD also reported IBS symptoms in the questionnaire and vice versa. Several patients even fulfilled the diagnostic criteria of FD and IBS. Some authors indicated a high degree of coincidence of IBS and FD, as assessed by symptoms.<sup>11,30</sup> In the present study the lack of a postprandial rise in GEA, as determined by EGG, which is highly correlated with delayed gastric emptying, was observed not only in patients with FD or symptoms of FD and IBS, but also in IBS patients. These results are in good accordance with the hypothesis that at least subgroups of FD and IBS have a common pathological basis, besides visceral sensory dysfunction.<sup>1,2</sup>

In summary, the present data suggest that the lack of a postprandial increase in the EGG amplitude could be useful in identifying a disturbed gastric emptying in patients presenting with symptoms of FD or IBS.

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## REFERENCES

- 1 Azpiroz F. Role of visceral sensory dysfunction in functional dyspepsia and irritable bowel syndrome. In: Goebell H, Holtmann G, Talley N, eds. *Functional Dyspepsia and Irritable Bowel Syndrome. Concepts and Controversies*. Dordrecht: Kluwer Academic Publishers, 1998: 87–92.
- 2 Camilleri M, Neri M. Motility disorders and stress. *Dig Dis Sci* 1989; **34**: 1777–86.
- 3 Coffin B, Azpiroz F, Guamer F, Malagelada JR. Selective gastric hypersensitivity and reflex hyporeactivity in functional dyspepsia. *Gastroenterology* 1994; **107**: 1345–51.
- 4 Holtmann G, Talley JN, Goebell H. Association between *H. pylori*, duodenal mechanosensory thresholds and small intestinal motility in chronic unexplained dyspepsia. *Dig Dis Sci* 1996; **41**: 1285–91.

- 5 Klatt S, Pieramico O, Guethner C, Glasbrenner B, Beck K, Adler G. Gastric hypersensitivity in nonulcer dyspepsia. An inconsistent finding. *Dig Dis Sci* 1998; **42**: 720–3.
- 6 Pieramico O, Ditschuneit H, Malfertheiner P. Gastrointestinal motility in patients with non-ulcer dyspepsia: a role for *Helicobacter pylori* infection? *Am J Gastroenterol* 1993; **88**: 364–8.
- 7 Leahy A, Besherdas K, Clayman C, Mason I, Epstein O. Abnormalities of the electrogastrogram in functional gastrointestinal disorders. *Am J Gastroenterol* 1999; **94**: 1023–8.
- 8 Lin X, Levanon D, Chen JD. Impaired postprandial gastric slow waves in patients with functional dyspepsia. *Dig Dis Sci* 1998; **43**: 778–84.
- 9 Heymann-Mönnikes I, Arnold R, Florin I, Herda C, Melfsen S, Mönnikes H. The combination of medical treatment plus multicomponent behavioral therapy is superior to medical treatment alone in the therapy of irritable bowel syndrome. *Am J Gastroenterol* 2000; **95**: 981–94.
- 10 Kruis W, Thieme C, Weinzierl M, Schussler P, Holl J, Paulus W. A diagnostic score for the irritable bowel syndrome. Its value in the exclusion of organic disease. *Gastroenterology* 1984; **87**: 1–7.
- 11 Geldof H, van der Schee EJ, van Blankenstein M, Grashuis JL. Electrogastrographic study of myoelectrical activity in patients with unexplained nausea and vomiting. *Gut* 1986; **27**: 799–808.
- 12 Smout AJ, Jebbink HJ, Samson M. Acquisition and analysis of electrogastrographic data: the Dutch experience In: Chen JD, McCallum RW, eds. *Electrogastrography, Principles and Applications*, 1st edn. New York: Raven Press, 1994: 3–30.
- 13 Feldman M, Smith HJ, Simon TR. Gastric emptying of solid radiopaque markers: studies in healthy subjects and diabetic patients. *Gastroenterology* 1984; **87**: 895–902.
- 14 Smith HJ, Feldman M. Influence of food and marker length on gastric emptying of indigestible radiopaque markers in healthy humans. *Gastroenterology* 1986; **91**: 1452–5.
- 15 Annese V, Janssens J, Vantrappen G *et al.* Erythromycin accelerates gastric emptying by inducing antral contractions and improved gastroduodenal coordination. *Gastroenterology* 1992; **102**: 823–8.
- 16 Tack J, Janssens J, Vantrappen G *et al.* Effect of erythromycin in controls and in diabetic gastroparesis. *Gastroenterology* 1992; **103**: 72–9.
- 17 Chen JD, McCallum RW. Clinical applications of electrogastrography. *Am J Gastroenterol* 1993; **88**: 1324–36.
- 18 Mintchev MP, Kingma YJ, Bowes KL. Accuracy of cutaneous recordings of gastric electrical activity. *Gastroenterology* 1993; **104**: 1273–80.
- 19 Jebbink HJ, Bruijs PP, Bravenboer B, Akkermans LM, vanBerge-Henegouwen GP, Smout AJ. Gastric myoelectrical activity in patients with type I diabetes mellitus and autonomic neuropathy. *Dig Dis Sci* 1994; **39**: 2376–83.
- 20 Chen J, McCallum RW. Gastric slow wave abnormalities in patients with gastroparesis. *Am J Gastroenterol* 1992; **87**: 477–82.
- 21 Abell TL, Malagelada JR. Electrogastrography. Current assessment and future perspectives. *Dig Dis Sci* 1988; **33**: 982–92.
- 22 Pfaffenbach B, Wedmann B, Adamek RJ, Wegener M. The significance of electrogastrographically determined amplitudes – is there a correlation to sonographically measured antral mechanical contractions? *Z Gastroenterol* 1995; **33**: 103–7.
- 23 Chen J, McCallum RW. Response of the electric activity in the human stomach to water and a solid meal. *Med Biol Eng Comput* 1991; **29**: 351–7.
- 24 Lin X, Chen JZ. Abnormal gastric slow waves in patients with functional dyspepsia assessed by multichannel electrogastrography. *Am J Physiol Gastrointest Liver Physiol* 2001; **280**: G1370–5.
- 25 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.
- 26 Rothstein RD, Alavi A, Reynolds JC. Electrogastrography in patients with gastroparesis and effect of long-term cisapride. *Dig Dis Sci* 1993; **38**: 1518–24.
- 27 Richards RD, Davenport K, McCallum RW. The treatment of idiopathic and diabetic gastroparesis with acute intravenous and chronic oral erythromycin. *Am J Gastroenterol* 1993; **88**: 203–7.
- 28 Fox S, Behar J. Pathogenesis of diabetic gastroparesis: a pharmacologic study. *Gastroenterology* 1980; **78**: 757–63.
- 29 Werth B, Meyer-Wyss B, Spinass GA, Drewe J, Beglinger C. Non-invasive assessment of gastrointestinal motility disorders in diabetic patients with and without cardiovascular signs of autonomic neuropathy. *Gut* 1992; **33**: 1199–203.
- 30 Talley NJ, Phillips SF. Non-ulcer dyspepsia: potential causes and pathophysiology. *Ann Intern Med* 1988; **108**: 865–79.