Enterogastric Reflux and Gastric Clearance of Refluxate in Normal Subjects and in Patients with and without Bile Vomiting Following Peptic Ulcer Surgery

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A noninvasive scintigraphic technique was used to estimate enterogastric reflux and subsequent gastric evacuation of refluxate in 35 normal, healthy subjects and 55 patients previously treated by vagotomy or partial gastrectomy. Reflux was provoked by a milk drink and quantitated by counting 99mTc-EHIDA activity within the gastric area during gamma camera imaging. Seven normal subjects (20%) showed reflux of 5–18% of initial activity (mean: 10%), with peak values occurring at 5–30 minutes (mean: 14 minutes) following the milk. Gastric evacuation of activity in these subjects was monoexponential (τ = 0.993, T½ = 24.1 minutes). Reflux occurred more frequently than normal in patients with truncal vagotomy and drainage (22/28 patients) and partial gastrectomy (28/21 patients). All of 16 patients with Billroth II anastomoses exhibited reflux, which was excessive compared with refluxing normal subjects (mean: 25%; p < 0.01) and occurred later into the study (mean: 34 minutes; p < 0.01). Ten of 11 asymptomatic patients showed reflux of similar amounts of activity (mean: 21%) compared with 16 patients who complained of bile vomiting (mean: 22%). However, asymptomatic patients exhibited gastric evacuation of refluxate at a rate similar to that of refluxing normal subjects, while bile vomitters showed significant gastric retention of refluxate at 25–30 minutes following peak gastric activity (p < 0.05). This result confirms that postoperative bile vomiting is essentially a problem of gastric emptying.

BILE VOMITING following upper gastrointestinal tract surgery necessarily involves the occurrence of enterogastric reflux. The syndrome is common, reported to occur in 9–14% of all patients undergoing all types of operation for peptic ulcer disease.1 Vomiting may occur at any time but most typically occurs shortly after starting a meal. It has been suggested that, in patients susceptible to bile vomiting, accumulation of bile within the stomach or gastric remnant interferes with gastric emptying.2 It is not clear whether such patients differ from asymptomatic patients with respect to the amount of intragastric bile accumulation or only with respect to impaired gastric evacuation of refluxate.

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Differing opinions have been expressed about the pathogenetic significance of enterogastric reflux following peptic ulcer surgery.3,4 It is not at all clear whether reflux alone may cause symptoms of whether reflux is a cofactor or merely an effect of an underlying cause of symptoms. Enterogastric reflux may be observed in normal, healthy subjects. It occurs most consistently shortly after the administration of a test meal.5 “Normal” reflux may differ from “abnormal” reflux in frequency, amounts, and duration.

In the present study, enterogastric reflux and subsequent gastric evacuation of refluxate have been assessed in normal subjects and in patients with and without symptoms following peptic ulcer surgery, using a noninvasive scintigraphic technique.6

Subjects and Methods

Normal Subjects

Forty-five control studies were carried out on 35 normal, healthy volunteers. These were 16 men (mean age: 38 years, range: 23–66 years) and 19 women (mean age: 42 years, range: 21–74 years). Ten subjects were studied twice. No control subject gave a present or recent past history of gastrointestinal symptoms, and all enjoyed good health. None had a history of abdominal surgery. None was on any drug treatment. Informed consent was obtained from all control subjects and patients, and the study was approved by the Regional Hospitals Ethical Committee and the Department of Health and Social Security.

Patients

Studies were carried out on 55 patients who had previously undergone peptic ulcer surgery. Operations were
truncal vagotomy with pyloroplasty (TV + P), partial gastrectomy with Billroth I gastroduodenostomy (BI-PG), truncal vagotomy with gastroenterostomy (TV + GE), partial gastrectomy with Billroth II gastrojejunostomy (BII-PG), proximal gastric vagotomy (PGV), and truncal vagotomy without drainage (TV). There were 40 men (mean age: 51 years, range: 19-75 years) and 15 women (mean age: 52 years, range: 25-70 years). Eleven patients were free of symptoms at the time of study, which was at least 2 months after operation. The remaining 44 patients had a variety of postvagotomy/postgastrectomy symptoms, which were fully appraised by conventional investigations, including barium radiology and endoscopy as well as more specific investigations such as acid output studies and dumping provocation tests, when appropriate. Clinical details are summarized in Table 1.

Methods

All subjects fasted and refrained from smoking for 4 hours prior to receiving the test injection. The radiopharmaceutical agent $^{99m}$Tc = EHIDA (Radiochemical Centre, Amersham, United Kingdom) was given as a single intravenous injection of 2 millicuries (74 MBq). Subjects then waited for 30 minutes to allow hepatic uptake and secretion and gallbladder accumulation of the agent to develop. Imaging was carried out using an IGE 535 Gamma Camera (International General Electric Company) fitted with a standard low energy collimator. This was linked to a Nodcrest Nuclear Medicine Data Acquisition and Analysis System.

Thirty minutes after the injection, subjects were positioned standing, facing the gamma camera, and a control view of the abdominal field was obtained over 1 minute. Subjects then drank 300 ml fresh milk at room temperature, taking 2-4 minutes to finish the drink. At 5 minutes following the start of the control view, the abdominal field was again imaged for 1 minute. Thereafter, serial 1-minute views were obtained at 5-minute intervals until 1 hour after the initial control view. Subjects sat in a chair between views.

Analysis

During the course of the study, a cumulative display of abdominal field activity was observed. In studies during which anatomically well-defined gastric activity developed, the area of gastric activity was mapped at the time of its clearest definition. The complete series of 1-minute images was then reviewed, and activity within the superimposed gastric map was counted for each viewing. Gastric area activity, expressed as a percentage of the total abdominal field activity counted during the initial control view, was plotted to give a time-versus-activity curve characterizing the rate, pattern, and magnitude of reflux and subsequent clearance of refluxed activity from the stomach. Corrections were applied for isotope decay.

For each study, the presence or absence of identifiable reflux was noted. The proportions of refluxers noted among clinical groups were compared using Fisher's exact test (two tailed). Among refluxing subjects, the percentage peak of refluxed activity and the time elapsed from ingestion of the milk to peak activity were recorded. Groups of these values were compared using Wilcoxon's two sample rank test (two tailed). Gastric evacuation of refluxed activity was examined by normalizing postpeak values of gastric activity to peak values, taking peak activity as 100% at time zero. Semilog plots of values were derived and between group points of difference tested using Wilcoxon's two sample rank test to individual normalized values.

Results

Normal Subjects

Reflux of activity into the stomach was identified in studies on seven of the 35 normal subjects (20%: 5 men, 2 women). Five refluxers and five nonrefluxers were re-
studied. Two of the five refluxers and none of the non-refluxers showed reflux on retesting. Figure 1 shows mean gastric activity (± 2 SEM) plotted against time for the nine positive studies.

The mean of individual peak values for gastric activity was 9.2% (range: 4–18%), occurring at a mean time of 15 minutes (range: 5–30 minutes) following the milk drink. The amount and pattern of gastric activity in studies judged to be positive was quite distinct from the small amount of background activity counted in a comparable left upper quadrant area of the abdominal field in negative studies.

For the nine positive studies on normal subjects, the rate and pattern of gastric evacuation of refluxed activity are shown in Figure 2. Linear regression analysis computing the natural logarithms of normalized values, confirmed that the clearance curve was well described by a single exponential (r = 0.993) having a T½ value of 24.1 minutes.

Patients

The results of studies on patients are shown in Figure 3 and Table 2.

Patients with BI-PG exhibited reflux significantly more frequently than did normal subjects (p = 0.03), but patients with TV + P did not. Neither group differed significantly from refluxing normal subjects in terms of the amount of refluxed activity observed or the time to peak gastric activity among refluxers. However, the numbers of patients in these two groups were small.

When considered as two separate groups, patients with TV + GE and those with BII-PG exhibited reflux significantly more frequently than did normal subjects (Table 2). Indeed, all patients with BII-PG exhibited reflux. Values for peak gastric activity in these groups were higher than those for refluxing normal subjects, significantly so for patients with BII–PG (p < 0.01) or when considered together (p < 0.05). The time elapsed to peak gastric activity was significantly prolonged (p < 0.01) for patients

![Figure 1](image1.png)

**Fig. 1.** Refluxing normal subjects (9 studies): intragastric activity expressed as per cent of initial total field activity (mean ± 2 SEM) plotted against time.

![Figure 2](image2.png)

**Fig. 2.** Refluxing normal subjects (9 studies): gastric clearance of refluxed activity. Intragastric activity normalized to peak values and plotted on a logarithmic scale (mean values ± 95% confidence limits) against time following peak gastric activity. Linear regression analysis computing natural logarithms of normalized values: r = 0.993, T½ = 24.1 minutes.

![Figure 3](image3.png)

**Fig. 3.** Presence and amount of reflux among patients studied. Open circles denote asymptomatic patients. TV + P = truncal vagotomy with pyloroplasty; BI–PG = partial gastrectomy with Billroth I gastroduodenostomy; TV + GE = truncal vagotomy with gastroenterostomy; BII–PG = partial gastrectomy with Billroth II gastrojejunostomy; PGV = proximal gastric vagotomy; TV = truncal vagotomy without drainage. *Reflux not quantified for two refluxing patients.
with BII-PG irrespective of the presence (mean time elapsed: 34 minutes) or absence (mean time elapsed: 33 minutes) of symptoms. Symptomatic patients with TV

+ GE showed a similar tendency, but the difference was not statistically significant.

Differences were sought between patients with symptoms and those without symptoms and also between those patients complaining of bile vomiting and patients with other or no symptoms. All patients with bile vomiting showed reflux, while 10/26 patients with other symptoms did not (p = 0.007). However, only one of 11 asymptomatic patients failed to show reflux. There were no significant differences between these groups in terms of the amount of refluxed activity (Fig. 4) or the time elapsed to peak gastric activity. Indeed, asymptomatic patients with TV + GE or BII–PG exhibited somewhat higher peak gastric activity (mean value: 29%) than those with symptoms (mean value: 20%). Among patients complaining of bile vomiting, however, there was a tendency toward failure of gastric evacuation of refluxed activity during the second half of the study hour. In this respect, patients with TV + GE or BII–PG who were complaining of bile vomiting differed significantly from those who were symptom-free, the latter group exhibiting gastric evacuation of refluxed activity at a rate similar to that observed in refluxing normal subjects (Fig. 5). Refluxing patients with symptoms other than bile-vomiting showed variable gastric evacuation of refluxate with mean values intermediate between and not significantly different from those for bile vomitors and those for asymptomatic patients.

Discussion

The test we have used to assess enterogastric reflux has been described in detail elsewhere. Compared with alternative techniques, the test is simple and carries a high degree of patient acceptability. The identification of enterogastric reflux of \(^{99}\)Tc \(^{m}\)-EHIDA activity is based on visual recognition of its occurrence from scintigraphic
images. We have not judged studies to be positive when there was doubt and believe that any false-negative results are unlikely to have been associated with more than a minor degree of reflux. We attribute the clear definition of reflux in positive studies to the proximal migration of refluxate within the stomach, which tends to occur when patients are sitting or standing. The test examines the response to a milk drink in the upright subject, and we have not, of course, addressed the possibility of pathophysiological significant reflux occurring under different conditions.

The quantitation of reflux using biliary excretion scintigraphy is subject to errors from various sources. However, the potential magnitude of these errors seems hardly sufficient to cast doubt on the findings from these studies. We have based our expression of reflux on the hepatobiliary sequestration of activity at a fixed time following injection. We believe this to be a valid index of the agent’s activity as a biliary marker, each patient thus providing his own reference value. This method is simpler than others described. The percentage values for reflux obtained by different methods are not strictly comparable, although in practice the differences are unlikely to be great.

Our studies on normal subjects showed that 20% of individuals exhibited reflux. Repeat studies suggested that reflux occurred in reflux-prone individuals, but the numbers involved were too small to draw a firm conclusion. The amount of reflux and time to peak intragastric activity for refluxing normal subjects were very similar to those reported by Tolin and colleagues. Our studies on refluxing normal subjects have shown that, after peak intragastric activity has been achieved, refluxed activity is emptied from the stomach in an orderly manner. The rate of gastric emptying of refluxate in these studies is similar to the normal gastric emptying rate of milk reported by McArthur et al.

The results of our studies on patients confirm that enterogastric reflux occurs more commonly than normal following operations that disrupt or bypass the normal gastric outlet, although this finding just failed to reach statistical significance for patients with TV + P.

The results obtained from the small group of patients studied following PGV are in keeping with the suggestion that this procedure is not associated with any increase in the frequency or amount of reflux. However, reflux was seen in both of the asymptomatic patients with truncal vagotomy alone. Although no statistical significance can be attached to this observation, it may indicate that absence or limitation of reflux depends, at least in part, on normal antral motility.

The amount of refluxed activity seen in patients with TV + P or BI-PG was similar to that observed in refluxing normal subjects. Values for peak gastric activity were higher in patients with TV + GE and highest in those with BI-GE. These results are broadly in agreement with previous reports. For patients with BI-GE, the time elapsed to peak gastric activity was significantly longer than that for refluxing normal subjects. This is a very similar finding to that reported by Tolin and colleagues, who noted the same pattern in symptomatic and asymptomatic patients, a finding confirmed by the present studies. In disagreement with these and other workers, however, we found that the amount of reflux observed was related only to the type of previous operation, being independent of the presence, nature, and severity of postoperative symptoms.

Most interestingly, however, we have noted that patients complaining of biliary vomiting showed impaired gastric evacuation of refluxed activity, compared with asymptomatic patients with comparable previous surgery and a similar or greater amount of reflux. This finding gives support to the hypothesis that postoperative bile vomiting is essentially a problem of gastric emptying but at the
same time indicates that this is not simply an effect of intragastric accumulation of bile.

References