Research articles

Novel approach to quantify duodenogastric reflux in healthy volunteers and in patients with type I gastric ulcer

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SUMMARY A new method is described which allows simultaneous measurement of gastric emptying and duodenogastric reflux and avoids transpyloric intubation. After intragastric instillation of a liquid lipid meal in six healthy volunteers the fractional gastric emptying rate was 2.9 ± 0.3 in the upright and $2.5 \pm 0.6 \text{ SEM} \times 10^{-2}/\text{min}$ in the supine position, respectively ($p > 0.5$). The duodenogastric reflux rate (expressed as fraction of the intraduodenal amount of duodenal marker) was 0.30 (range 0.03–0.81) and 0.22 (0.01–0.55) $\times 10^{-2}/\text{min}$, respectively ($p > 0.2$). Atropine (40 $\mu\text{g}/\text{kg}$) decreased the supine gastric emptying rate to 1.1 ± 0.2 ($p < 0.05$) and increased the supine duodenogastric reflux rate to 2.74 (0.04–9.80) $\times 10^{-2}/\text{min}$ ($p < 0.05$). Fasting duodenogastric reflux rate was similar in the supine and upright position, 0.49 (0.04–0.89) and 0.42 (0.06–0.97) $\times 10^{-2}/\text{min}$, respectively ($p > 0.5$). Fractional gastric emptying rate was similar in 10 volunteers and 17 patients with type I gastric ulcer (2.1 ± 0.4 vs $1.7 \pm 0.2 \text{ SEM} \times 10^{-2}/\text{min}$, $p > 0.2$). Their duodenogastric reflux rates were also similar, 0.65 (0.01–5.24) vs 1.10 (0.01–10.83) $\times 10^{-2}/\text{min}$ ($p > 0.5$). We conclude therefore that (1) gastric emptying and both fasting and postprandial duodenogastric reflux are independent of the posture; (2) fasting and postprandial reflux are of similar magnitude; (3) atropine shows gastric emptying and increases duodenogastric reflux; and (4) patients with type I gastric ulcer have neither slowed gastric emptying nor increased duodenogastric reflux.

Duodenogastric reflux has been claimed to play a major role in the pathogenesis of gastric ulcer¹⁻³ but exact measurement of reflux is still a problem. Methods used in previous studies were either qualitative,⁴ or invasive,⁵ or did not measure reflux but concentrations of bile in gastric juice,³ or had technical problems.⁶ In the present paper a method is described which allows quantitative measurement of duodenogastric reflux during emptying of a liquid test meal or in the fasting state and does not interfere with the gastroduodenal junction. This method was standardised in healthy volunteers. Duodenogastric reflux was measured both in the fasting and in the fed state, in dependence of the

posture and during infusion of atropine. Duodenogastric reflux in healthy volunteers was then compared with reflux in patients with type I gastric ulcer.

Methods

GASTRIC INTUBATION

The experiments lasted for 120 minutes. They were started at 8.30 am after an overnight fast. In postprandial experiments a single lumen oesophago-gastric tube was used and in fasting experiments a double lumen tube was used. The tube was positioned with its tip in the lowest part of the stomach. Its position was checked by fluoroscopy. The fasting gastric contents were removed by intermittent suction for 15 minutes using an Egnell pump model EMP 171 687.

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Received for publication 9 August 1982

GASTRIC MARKER

Experiments in fasting subjects The instillation port of the gastric tube was near the cardia and the aspiration port was near the pylorus. The perfusion consisted of 50 μCi $^{51}\text{CrCl}_2$ in 200 ml saline. It was given at a rate of 1.5 ml/min. The gastric aspirates were pooled in 10 minute fractions.

Experiments in postprandial subjects At time zero, a 400 ml test meal was instilled into the stomach. It consisted of 200 ml Intralipid® 20% (Hausmann) and 200 ml tap water and was labelled with 10 μCi $^{51}\text{CrCl}_2$. Intralipid® 20% is an aqueous emulsion of soy-bean oil (200 g/l), egg lecithin (12 g/l), and glycerol (25 g/l). It has 2000 kcal/l and an osmolality of 280 mosm/l. The intragastric volume was determined at 10 minute intervals using a marker dilution technique modified from George.⁷ A 400 ml stock solution of 5% Intralipid® was labelled with 90 μCi $^{51}\text{CrCl}_2$. After withdrawal of a sample of the gastric contents, a bolus of the labelled solution was instilled. For two minutes, six to eight cycles of aspiration and reinjection were performed by quickly filling and emptying a 50 ml syringe. Then another sample was withdrawn. In the first to the fourth mixing manoeuvre the aspiration and instillation volumes were 10 ml and 20 ml, respectively. In the fifth to the eighth mixing manoeuvre the volumes were 15 and 30 ml, and in the ninth to twelfth manoeuvre 20 and 40 ml, respectively.

DUODENAL MARKER

HIDA ($^{99\text{m}}\text{Tc}$ -Sn-2,6-diethylacetanilidoiminodiacetate, from Solco Nuclear, Switzerland) was used as duodenal marker. When infused intravenously it is cleared by the liver and enters the duodenum *via* the bile.

For the intravenous infusion, HIDA was dissolved in 500 ml saline. The activity was 1 mCi in postprandial and 0.5 mCi in fasting studies. Total radioactivity of the solution was measured with a gamma camera equipped with a diverging low energy collimator (Searle) behind a water layer of 10 cm (depth of the duodenum, see below). The infusion was started 30 minutes before the beginning of the experiment at a rate of 200 ml/h. During the experiment abdominal radioactivity was scanned with the gamma camera at five minute intervals for one minute (at minute three, eight, 13, 18, . . . , 113, 118). The data were stored on disc by a computer (gamma 11, Digital Equipment Co, Maynard, Mass.). In addition, the radioactivity was continuously monitored on a screen. Two tablets containing 3 μCi of ^{57}Co were glued to the right and left side of the abdomen, respectively. The activity spots of these tablets were marked on the screen

with a pencil. Thus, the position of the subject could easily be reproduced for each gamma camera recording.

POSTURE

In supine studies the subjects remained in the supine position throughout the experiment. In upright studies the subjects sat on a chair. They stood up one minute before the gamma camera recording and were positioned identically for each recording by means of the ^{57}Co activity spots as described above. Two minutes later, after the end of the gamma camera recording, they sat down again.

SUBJECTS STUDIED**A HEALTHY VOLUNTEERS**

Fasting Six healthy volunteers (aged 22–42 years) were studied in the fasting state both in the upright and supine position in randomised order.

Postprandial Ten healthy volunteers (aged 25–39 years) were studied in the supine position. Six of these subjects were also examined in the upright position. The two studies were performed in randomised order. In the latter six subjects the supine studies were repeated during infusion of atropine. For this purpose 40 $\mu\text{g/kg}$ atropine sulphate were added to the infusion.

B PATIENTS

After obtaining informed consent 17 patients with type I gastric ulcer⁸ were studied in the postprandial state in the supine position. Each ulcer was proved by endoscopy. Biopsies were taken from the ulcer itself (centre and wall) and from the surrounding macroscopically intact mucosa. Biopsies were read 'blindly' by a pathologist. In none of the cases was malignancy suspected on the basis of the macroscopical or microscopical aspect. No patients had experienced previous abdominal surgery or had gastric outlet obstruction. Details of the patients are given in the Table.

The time between two studies in the same subject was at least one week. The study protocol was approved by the local ethical committee.

EVALUATION*Gastric and duodenal marker*

After completion of the study $^{99\text{m}}\text{Tc}$ radioactivity was counted over the descending part of the duodenum by computer analysis of the stored data. The region of interest consisted of 150 cells on the screen. Triple samples of 1 ml of all solutions (marker solutions, tests meals, gastric aspirates) were counted in a gamma scintillation spectrometer (model 5375, Packard) for one minute. The counts of ^{51}Cr were corrected for background and

Table Characteristics and mean duodenogastric reflux rates of the patients studied

Patient sex, age (yr)	Concomitant diseases	NOSAC*	Reflux rate ($\times 10^{-2}/\text{min}$)
1 PV M 57	Hypertension	No	10.83
2 MM F 79	Coronary heart disease	No	4.05
3 EH M 63	—	No	1.57
4 EH F 75	Coronary heart disease	No	0.55
	Oesophagitis		
5 ED M 57	—	No	0.43
6 CA F 49	Schizophrenia	No	0.32
7 BH F 69	Diabetes	No	0.27
8 KS M 67	Arthrosis	Yes	0.21
9 WW M 70	Arthrosis	Yes	0.12
10 JM M 62	Arthrosis	Yes	0.06
11 PS F 57	Oesophagitis	No	0.05
12 WZ M 77	—	No	0.05
13 HF M 51	Arthrosis Obesity	Yes	0.03
14 GH M 54	—	No	0.02
15 LB F 71	Cerebral atherosclerosis	No	0.02
16 EM M 73	—	No	0.01
17 BT F 21	—	No	0.01

* NOSAC = treatment with non-steroidal anti-inflammatory compounds. Patients no. 3 and 7 are husband and wife. The husband (no. 3) developed symptoms two weeks after his wife.

irradiation of ^{99m}Tc and *vice versa*. The counts of ^{99m}Tc as measured both by the gamma camera and by the scintillation spectrometer were corrected for the decay of the nucleotide.

ACID

Acidity was determined by titrating 1 ml samples of gastric aspirates with 0.01 molar NaOH to pH 7.0 using an automatic burette (Instrumenten-Gesellschaft, Zürich).

MATHEMATICS

Fasting experiments The recovery rate is $w = V_a[^{51}\text{Cr}]_a / V_i[^{51}\text{Cr}]_i$, where V_a is the volume aspirated from the stomach, V_i is the volume instilled into the stomach, $[^{51}\text{Cr}]_a$ is the concentration of ^{51}Cr in the gastric aspirate, and $[^{51}\text{Cr}]_i$ is the concentration of ^{51}Cr in the gastric perfusion fluid. The amount of ^{99m}Tc refluxed into the stomach per minute is $^{99m}\text{Tc}_G = [^{99m}\text{Tc}]_a V_a / w$, where $[^{99m}\text{Tc}]_a$ is the concentration of ^{99m}Tc in the gastric aspirate. The duodenogastric reflux rate expressed as fraction of intraduodenal ^{99m}Tc is $r = ^{99m}\text{Tc}_G / ^{99m}\text{Tc}_D$ (min^{-1}), where $^{99m}\text{Tc}_D$ is the amount of ^{99m}Tc in the duodenum. The gastric volume secretion rate is $s = V_a / w - V_i$ (ml/min). The acid secretion rate is $h = A V_a / w$ (mmol/min, where A is the acidity of the gastric aspirate).

Postprandial experiments The total intragastric volume, V is calculated from the gastric marker concentration before and after mixing, and from the volume and marker content of the mixing fluid as described by George.⁷ The intragastric amount of gastric marker G_G is (1) $G_G = V[^{51}\text{Cr}]_a$, where $[^{51}\text{Cr}]_a$ is the concentration of ^{51}Cr in the gastric aspirate. The intragastric amount of duodenal marker (D_G), expressed as fraction of the intraduodenal amount of duodenal marker (D_D), is (2) $D_G = V[^{99m}\text{Tc}]_a / D_D$, where $[^{99m}\text{Tc}]_a$ is the concentration of ^{99m}Tc in the gastric aspirate. Two assumptions were made: (a) gastric emptying rate, duodenogastric reflux rate, and gastric secretion rate remain constant during the relatively short time interval of 10 minutes (otherwise they represent average values for this period); (b) gastric emptying is proportional to the actual intragastric volume. Thus, the change in the intragastric amount of gastric marker is described by (3) $dG_G/dt = gG_G$, where g is the fractional gastric emptying rate (min^{-1}) and hence (4) $G_2 = G_1 e^{-gt}$, where the indices 1 and 2 refer to the beginning and the end of the time interval t , respectively. As the aqueous and the lipid phase of the gastric contents empty together¹⁰ a common emptying rate for both phases was calculated. The test meal empties from the stomach like the gastric marker. Thus, its amount M remaining in the stomach is (5) $M_2 = M_1 e^{-gt}$. The difference $V - M$ is the volume of gastric secretion fluid plus the small amount of refluxed duodenal juice. All other volume and marker changes are described by the equation (6) $dA_i/dt = -gA_i + a_i$, where i represents either duodenal marker (expressed as fraction of its intraduodenal amount), or acid, or secretion volume, A_i is the intragastric amount of i , and a_i is the rate by which i is delivered to the stomach. Equation (6) is solved as follows: (7) $a_i = ((A_{i2} - A_{i1} e^{-gt})/g)/(1 - e^{-gt})$. The volume secretion rate includes fluid secreted by the stomach and refluxed duodenal juice.

The equations were applied to the data using a SESAM computer (Hannes Keller AG, Switzerland).

VALIDATION STUDIES

GASTRIC MIXING

Different volumes of the test meal were instilled into the stomach. The marker dilution technique was performed as outlined above. Then the stomach was emptied by manual aspiration. The calculated volume was compared with the measured volume.

BINDING OF HIDA AND ^{51}CR TO THE GASTRIC MUCOSA

In four experiments saline containing 2% poly-

ethylene glycol 4000 (PEG), a currently used non-absorbable marker,¹¹ was labelled with HIDA and $^{51}\text{CrCl}_2$. A volume of 200 ml of this solution was instilled into the stomach. Samples of 10 ml were withdrawn at five minute intervals until the stomach was empty and analysed for PEG,¹² $^{99\text{m}}\text{Tc}$, and ^{51}Cr , respectively.

SECRETION OF $^{99\text{m}}\text{Tc}$ BY GASTRIC MUCOSA

In six Heidenhain pouch dogs, 1 mCi of HIDA dissolved in 15 ml normal saline was infused intravenously at a rate of 6 ml/h over 2½ hours. Gastric juice was collected from the pouch for two hours beginning 30 minutes after the start of HIDA infusion. It was pooled in 10 minute fractions. From the 30th to the 60th minute of collection, 20 µg/kg/h, and from the 60th to the 120th minute, 80 µg/kg/h of 4-methyl-histamine dihydrochloride were infused intravenously. In the samples, acidity and concentration of $^{99\text{m}}\text{Tc}$ were determined and the outputs of acid and HIDA were calculated. For each 10 minute period, $^{99\text{m}}\text{Tc}$ recovered from the pouch was expressed as fraction of $^{99\text{m}}\text{Tc}$ infused so far and compared with the acid secreted by the pouch by linear regression analysis. The same calculations were performed for the studies in fasting human volunteers.

DISTANCE BETWEEN SKIN AND DUODENUM

The distance between skin and duodenum was determined by abdominal computed tomography in 50 subjects. Tomograms with abnormal abdominal findings were excluded from this series. Before tomography the subjects ingested a barium suspension which allowed identification of the descending duodenum. The distance between the skin and the anterior and posterior duodenal wall was measured.

CALCULATION OF THE REFLUX RATE

In three postprandial studies (one patient, and two volunteers treated with atropine) duodenogastric reflux was high and the stomach did not overlap the ascending duodenum. In another patient in which the stomach did not overlap the ascending duodenum 5 mCi of HIDA instead of 1 mCi were infused. Thus, in these four studies the intragastric $^{99\text{m}}\text{Tc}$ could be scanned. The change in the counts over the stomach were compared with the calculated duodenogastric reflux rate.

STATISTICS

In the validation studies linear regression analysis was used. Duodenogastric reflux rates, intragastrically accumulated duodenal marker, and intragastric concentration of $^{99\text{m}}\text{Tc}$ were compared by

using the Wilcoxon's rank sum test. The other data were normally distributed and were thus compared by Student's *t* test. Paired tests were used when appropriate. Values are given as means $\pm$ SEM and as means (range), respectively.

Results

VALIDATION STUDIES

The validation of gastric mixing is given in Fig. 1. HIDA and ^{51}Cr do not bind to the gastric mucosa as shown in Fig. 2. Figure 3 shows that $^{99\text{m}}\text{Tc}$ appearing in the Heidenhain pouch is closely related to acid secretion, suggesting secretion of HIDA and/or free pertechnetate by the gastric mucosa. In man gastric recovery of $^{99\text{m}}\text{Tc}$ was much higher than in dogs and not related to the acid secretory rate. Thus, nearly all gastric $^{99\text{m}}\text{Tc}$ in man is refluxed from the duodenum and not secreted by the gastric mucosa.

The distance between skin and anterior duodenal wall was 10.3 ± 0.3 cm and the diameter of the duodenum was 1.75 ± 0.07 cm. The data were normally distributed. The validation of the calculated duodenogastric reflux rate is shown in Fig. 4. It should be noted that the measured values but not the calculated values depend on the gastric emptying rate.

FASTING EXPERIMENTS

The recovery rate of the perfused marker was 0.88 ± 0.03 . The posture did not affect the duodenogastric reflux rate. The rate amounted to 0.49

Fig. 1 Validation of gastric mixing. Measured volume expressed as (volume instilled before mixing + volume aspirated after mixing)/2 is compared with the volume calculated from the marker dilution.

Fig. 2 Validation of the gastric and duodenal marker. A linear regression analysis between the concentrations of PEG and ^{51}Cr , respectively, is shown. ^{51}Cr values are expressed as per cent of ^{51}Cr concentration within saline test meal. Similar correlation exists between the concentrations of PEG and ^{99m}Tc .

Fig. 3 Gastric secretion of acid and ^{99m}Tc . Close correlation is found in Heidenhain pouch dogs ($\bullet$, $y = 1.1 \times 10^{-5} + 1.3 \times 10^{-5} \times x$, $r = 0.62$, $p < 0.01$, t value of the slope $= 5.81$, $p < 0.001$). Gastric recovery of ^{99m}Tc in man ($\circ$) is much higher than in dogs and not related to acid secretion.

($0.04\text{--}0.89$) in the supine position and to 0.42 ($0.06\text{--}0.97$) $\times 10^{-2}/\text{min}$ in the upright position ($p > 0.5$).

POSTPRANDIAL EXPERIMENTS

Posture The gastric emptying rates are shown in Fig. 5a. The mean rates did not significantly differ between upright and supine studies (2.9 ± 0.3 vs $2.5 \pm 0.6 \times 10^{-2}/\text{min}$, $p > 0.5$). The volume emptied (7.0 ± 0.6 vs 5.8 ± 0.9 ml/min, $p > 0.3$) and the duodenogastric reflux rates, 0.30 ($0.03\text{--}0.81$) vs 0.22 ($0.01\text{--}0.55$) $\times 10^{-2}/\text{min}$ ($p > 0.2$, Fig. 5b) were also similar. Thus, postprandial and fasting reflux were similar.

Atropine Atropine decreased fractional gastric emptying rate from 2.5 ± 0.6 to $1.1 \pm 0.2 \times 10^{-2}/\text{min}$ ($p < 0.05$, Fig. 5a). The volume emptied was decreased from 5.8 ± 0.9 to 3.1 ± 0.3 ml/min ($p < 0.05$). Atropine increased duodenogastric reflux rate from 0.22 ($0.01\text{--}0.55$) to 2.74 ($0.04\text{--}9.80$) $\times 10^{-2}/\text{min}$ ($p < 0.05$, Fig. 5b). The volume secretion rate during infusion of atropine was 1.9 ± 0.1 ml/min. In the control studies, it was 3.9 ± 0.9 ($p < 0.05$). The acid secretion rate was reduced by atropine from 0.62 ± 0.25 to 0.27 ± 0.15 mmol $\text{H}^+ / 10$ min ($p < 0.05$).

The time courses of the intragastric volumes and the intragastrically accumulated amount of the duodenal marker of the supine studies without and with atropine, respectively, are shown in Fig. 6.

Gastric ulcer The mean gastric emptying rates and duodenogastric reflux rates of the 10 volunteers and the patients with gastric ulcers are shown in Fig. 7. In addition, the reflux rates of the patients are given in the Table. Statistically, they do not differ significantly. The mean emptying rates were 2.1 ± 0.4 and $1.7 \pm 0.2 \times 10^{-2}/\text{min}$ ($p > 0.2$) and the mean reflux rates were 0.65 ($0.01\text{--}5.24$) and 1.10 ($0.01\text{--}10.38$) $\times 10^{-2}/\text{min}$ ($p > 0.5$), respectively. Gastric volume and acid secretion tended to be lower in the patients but the difference was not statistically significant. The intragastric concentration of the duodenal marker was 180 ($8\text{--}1144$) nCi/ml in controls and 460 ($4\text{--}2730$) in patients ($p > 0.4$). Duodenogastric reflux rates and gastric emptying rates did not significantly differ between patients treated or not treated with non-steroidal anti-inflammatory compounds.

Discussion

Of the many methods proposed to measure duodenogastric reflux, only those of Löhlein *et al.*,¹³ Muhammed *et al.*,¹⁴ and Tolin *et al.*⁶ lend themselves to measure reflux rates in the absence of a transpyloric tube. They have the following disadvantages, however: (1) Gastric emptying and volume secretion cannot be measured because the concen-

Fig. 4 Validation of calculation of duodenogastric reflux rate in four subjects where gastric scanning was feasible. Reflux rate (■) is compared with the change in intragastric ^{99m}Tc radioactivity as measured by scanning (●); (a) is from a patient with high duodenogastric reflux rate (no. 1), (b) is from an elderly patient with low reflux in whom 5 mCi of HIDA had been infused (no. 8), (c) and (d) are from two atropine studies in volunteers.

Fig. 5 Fractional gastric emptying rates (a) and postprandial duodenogastric reflux rates (b) in volunteers studied in upright and supine position and in supine position during infusion of atropine. Each point represents mean of a 120 minute experiment. Values of same subject are connected with solid lines. ns = statistically not significant.

tration of the gastric marker is unknown. (2) The method of Tolin *et al*⁶ fails – at least in our hands – in more than half of the cases because there is a superposition between antrum and ascending part of the duodenum or between fundus and liver. (3) With low reflux rates the fraction and thus the amount of the duodenal marker inside the stomach is very small. Thus, accurate measurements require a high amount of duodenal marker. This poses ethical problems in young healthy volunteers.

The method described in the present paper avoids transpyloric intubation and has additional advantages: small intragastric amounts of the duodenal marker can be measured; furthermore, the determination of the concentration of the gastric marker allows the distinct calculation of gastric emptying and volume secretion.

A series of validation experiments was performed. ^{51}Cr and ^{99m}Tc which were used as gastric and duodenal markers did not bind to the gastric mucosa (Fig. 2). The syringe induced mixing of the gastric marker within the gastric contents was complete and reliable (Fig. 1). The duodenal

Fig. 6 Time course of intragastric volume (a), amount of original test meal remaining in stomach (b), and intragastrically accumulated duodenal marker (c) expressed as fraction of intraduodenal amount of duodenal marker in studies without (○—○) and with atropine (●—●), respectively. Means $\pm$ SEM, * $p < 0.05$.

marker is secreted by the gastric mucosa to a negligible extent (Fig. 3). Gastric ^{99m}Tc , therefore, can be assumed to originate quantitatively from the duodenum. When the calculated duodenogastric reflux rates were compared with the change in the intragastric amount of duodenal marker a close correlation was found (Fig. 4). The use of the calculated reflux rate instead of the measured value has three distinct advantages: the calculated but not the measured value is corrected for gastric emptying; small rates can be measured; and super-

positions between stomach and small intestine do not affect the results.

Our method has, on the other hand, the following limitations: the reflux rate cannot be calculated in ml/min because the duodenal concentration of the duodenal marker is unknown. The marker reflux as calculated is proportional to the volume reflux provided that the distance between skin and duodenum and the diameter of the duodenum show little interindividual variation. It could be shown that this is in fact the case. An improvement of our method would consist of measuring the duodenal radioactivity simultaneously from the abdomen and from the back, but such an apparatus was not available.

Duodenogastric reflux was found in all volunteers both in the fasting and the postprandial state. Interindividual variations were large (Figs 5b, 7b) while intraindividual variations were relatively small (Fig. 5b). They are, at least in part, because of the fact that duodenogastric reflux is discontinuous (Fig. 4). Other authors reported increased duodenogastric reflux in the upright position.^{15,16} We were unable to confirm these findings. Furthermore, in contrast with the dog,^{17,18} reflux was of similar magnitude in the fasting state and after a meal. Thus, reflux is neither affected by posture nor by the emptying of a liquid meal.

Gastric emptying was also independent of posture (Fig. 5a). Other authors did observe an acceleration in the upright position.^{19,20} A possible explanation of this apparent difference may be related to the composition of the meal. A lipid meal may by activation of duodenal osmoreceptors slow gastric emptying and thus override the effect of posture.¹⁹

Atropine markedly increased the duodenogastric reflux rate (Fig. 5b). In addition, it decreased the

Fig. 7 Gastric emptying rates (a) and duodenogastric reflux rates (b) in control subjects and gastric ulcer patients. Each point represents mean of 120 minute experiment. ○ = treatment with non-steroidal anti-inflammatory compounds.

gastric emptying rate (Fig. 5a) and the gastric secretion rate. Consequently, the total intragastric volume was higher during atropine administration than in control experiments (Fig. 6a). More of the original meal remained in the stomach (Fig. 6b) and, most importantly, the amount of the duodenal marker appearing in the stomach was much higher than in control experiments (Fig. 6c). During the second hour of the experiment more than a third of the duodenal marker was present in the stomach. We have previously reported similar findings on the effect of atropine on duodenogastric reflux, gastric emptying and gastric secretion in the dog.²¹ Atropine probably exerts its effect by inhibiting smooth muscle contractile activity.²²⁻²³ Interestingly, atropine has very little to no effect on the pyloric muscle.²² This, together with our failure to observe an increased duodenogastric reflux during emptying of a fatty meal casts some doubt on a major role of the pylorus in preventing duodenogastric reflux in man.

Patients with gastric ulcer had similar gastric emptying rates when compared with healthy controls (Fig. 7a). This is in agreement with previous reports where no delay in the emptying of liquid test meals was found in type I gastric ulcer.²⁴⁻²⁶ Delayed emptying of solids has been reported in this type of ulceration²⁶⁻²⁸ but this was not studied in the present paper.

Gastric ulcer patients did not differ from controls in their duodenogastric reflux rates (Fig. 7b). Some patients had very high reflux rates but this was also observed in the control group. The same holds true for the intragastric concentration of the duodenal marker. Most authors claim duodenogastric reflux to be increased in gastric ulcer patients.^{1-4 5 16 26 29} They have, however, either used the Capper test^{4 15 16} which allows no quantitative assessment of reflux or they measured intragastric bile acids.^{1-3 26 29} Bile staining of gastric juice is not an accurate measurement of duodenogastric reflux.¹⁷ When reanalysing the data of Black *et al*^{1 3 29} we found that the data are not normally distributed. Thus, only some patients had high 'reflux', a finding quite similar to our results. Also, Duane³⁰ showed that even in patients with Billroth II resection – and thus high duodenogastric reflux – the intragastric concentration of bile acids and lysolecithin rarely reaches values necessary to produce mucosal damage. Thus, there is no evidence that gastric ulceration in general is because of increased duodenogastric reflux. Other factors such as non-steroidal anti-inflammatory compounds³¹ and infectious agents^{32 33} may be equally or even more important. This is consistent with the view that 'gastric ulcer are many different diseases'.³⁴

In conclusion, duodenogastric reflux is a physiological event in healthy man. Gastric emptying and duodenogastric reflux are not affected by gastric emptying of a liquid meal and by the posture. In contrast, they can profoundly be changed by atropine. Gastric ulcer patients have on the average neither slowed gastric emptying nor increased duodenogastric reflux. In some patients, though, duodenogastric reflux might play a pathogenetic role.

This study was supported by Swiss National Foundation, grants no. 3.158/077 and 3.940/080, and by Deutsche Forschungsgemeinschaft grant no. Mu 629/1-1. We are indebted to Mrs M Lukachich for her excellent technical assistance.

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