Relationship between gastric emptying of solids and gall bladder emptying in normal subjects

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SUMMARY Very little is known about the normal temporal and quantitative relationships between gastric emptying and gall bladder emptying. Using a non-invasive double isotope technique these relationships were investigated in 22 normal healthy adults. $^{99}Tc^m$ EHIDA was used as the biliary tracer and $^{113}In^m$ labelled bran as the gastric content tracer. Gastric emptying was monoexponential with a $t\frac{1}{2}$ of 45±3 minutes (mean±SEM). In 15 subjects the gall bladder emptied in relation to eating according to a double exponential function. In these subjects 15·0±1·6% of gall bladder contents emptied before gastric emptying began. They could be further divided into two clear cut types (p<0·001), according to the ejection fraction at 10 minutes and the $t\frac{1}{2}$ of the first exponential. Emptying of the gall bladder was faster and more of its contents were ejected in subjects with a type I response (n=9) than in subjects with a type II response (n=6). In the remaining seven subjects the gall bladder began to empty spontaneously, unrelated to eating. These observations suggest that gall bladder emptying: (a) may have a cephalic phase, (b) can be expressed as a double exponential function, (c) may occur unrelated to eating, (d) which occurs only in relation to eating would appear to be either fast (type I) or slow (type II).

It has always been assumed that the emptying of gastric contents into the duodenum triggers several physiological events including contraction of the gall bladder, which allows bile to be mixed with duodenal contents. The temporal and quantitative relationships between gall bladder emptying and gastric emptying, however, have not been clearly established in man. The normal relationships may be disturbed in disease and may be responsible for some of the undesirable side effects after gastric surgery – for example, bilious vomiting or malabsorption of fat.[1-3]

Before results of studies in such patients can be understood, it is necessary to investigate normal healthy subjects. The purposes of this study were: (a) to measure gastric emptying and gall bladder emptying in normal subjects after a physiological solid meal using a double isotope non-invasive technique with $^{99}Tc^m$ EHIDA (2,6-diethylphenyl-carbamoylmethyliminodiacetic acid) as the biliary

tracer and $^{113}In^m$ labelled bran as the gastric content tracer, and (b) to relate the emptying pattern of the stomach to that of the gall bladder.

Methods

PHANTOM STUDIES
It was first necessary to determine the quantity of the two isotopes to be used and the optimal settings of the gamma camera. A stomach sized phantom, fashioned from Perspex and filled with varying quantities of either $^{99}Tc^m$ or $^{113}In^m$ or both, was placed at several depths in a water bath and a series of gamma camera images obtained. These tests gave information about: (a) the required window settings for the gamma camera, (b) the amount of downscatter to be expected from the $^{113}In^m$, and (c) the amount of septal penetration to be expected from the $^{113}In^m$ high energy gamma rays to determine a possible correction factor.

From these initial studies it was decided to use 74 MBq (2 mCi) of $^{99}Tc^m$ with a window width of 10% and 9·2 MBq (250 μCi) of $^{113}In^m$ with a window width of 20%.

SUBJECTS

Twenty eight healthy adults (21 men and seven women) of mean age 26 ± 1 years ($\pm$SEM) volunteered to take part. The Royal Liverpool Hospital Ethical Committee gave approval for the study (January 1982) and informed consent was obtained from each subject.

Twenty two subjects were studied in the following manner. Each subject fasted overnight for at least 12 hours. The study began at 0900 hours and lasted 120 minutes. The subject lay semirecumbent beneath a large field of view gamma camera (Searle LFOV, GD Searle, Unithoorn, Holland) fitted with a medium energy parallel hole collimator. The gamma camera was linked to a computer system (Digital PDP 11/34, Maynard, Massachusetts). Each subject received an intravenous injection of 74 MBq (2 mCi) of ^{99}Tc EHIDA (prepared from a commercially available kit supplied by Amersham, UK).

Filling of the gall bladder was determined by observing the accumulation of counts in a region of interest drawn around the gall bladder image displayed on a video screen. When the counts in the gall bladder region of interest reached and were maintained at a relatively constant value (count accumulation less than 1% per minute) which occurred at 52 ± 1 minutes, each subject was given a solid test meal (Table 1) consisting of porridge (Readybrek) mixed with bran labelled with 9·2 MBq (250 μCi) of ^{113}In^{m} (see below), two cheese sandwiches and a cup of tea (the tea was consumed over the last two minutes of eating). Data were then acquired simultaneously from the ^{113}In^{m} gastric content tracer and the ^{99}Tc^{m} bile tracer at the rate of one frame per minute on a 64×64 data matrix. All data were stored on a hard magnetic disk for later analysis.

In a further six subjects ^{99}Tc^{m} EHIDA was given without any subsequent meal.

^{113}In^{m} LABELLED BRAN

The technique for labelling the bran was identical to that previously described for ^{99m}-Technetium,[4] except that ^{113}In^{m} was used. In brief, 5 grams of bran were mixed with 37 to 55 MBq of ^{113}In^{m}. To this mixture were added 2 ml acetate buffer. The

mixture was then mechanically shaken for five minutes, centrifuged and the supernatant discarded. Several washes were carried out to remove any free ^{113}In^{m} not bound to the bran. Washing was repeated until the specific radioactivity of the bran was constant to within 5%. The resultant labelled bran was mixed with the porridge.

To determine the stability of the binding of ^{113}In^{m} to the bran, the following experiments were performed: (a) incubation of the ^{113}In^{m} bran with varying concentrations of hydrochloric acid at 37°C, and (b) incubation of the ^{113}In^{m} bran with gastric juice at 37°C.

After 60 minutes incubation in hydrochloric acid between pH 3·3 and 5·0. no more than 7% of the label was detached. In gastric juice at pH 2·01, only 5·6% of the label was removed after 30 minutes incubation.

REGIONS OF INTEREST (Fig. 1)

Using an electronic selection device the following regions of interest were drawn; gall bladder (A), liver adjacent to gall bladder for overlap subtraction (B), stomach (C), liver/stomach overlap (D), composite liver and gall bladder (E+D+A+B), small intestine (F), and background (G). From time-activity curves constructed by the computer, gall bladder filling and emptying curves were derived. Duodenogastric reflux was
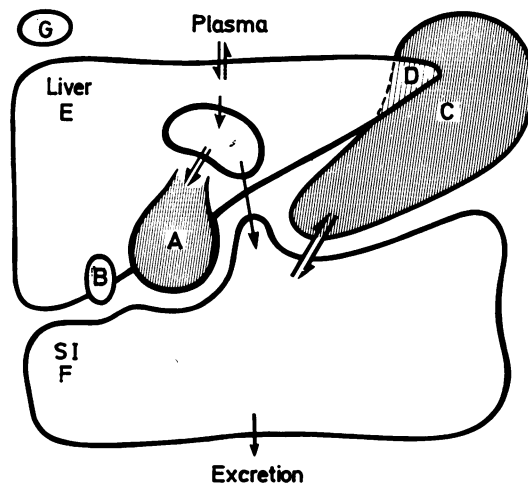

Fig. 1 *Regions of interest (ROI) selected to generate raw data curves. Using an electronic selection device the following ROIs were selected; A, gall bladder; B, liver/gall bladder overlap; C, stomach; D, liver/stomach overlap; E+D+A+B, composite liver and gall bladder; F, small intestine; G, background.*

Table 1 *Characteristics of test meal*

Protein	30·0 g
Fat	40·5 g
Carbohydrate	76·4 g
Energy content	2·8 MJ
Volume	550·0 ml

measured by dividing the $^{99}Tc^m$ counts in the gastric regions of interest by the maximum count in the composite liver and gall bladder regions of interest (expressed as a percentage).

CURVE ANALYSIS

Gastric emptying could be expressed as a monoexponential function (computer least squares fit program [r=0·98]); therefore gastric emptying was described by a half-emptying time. Gall bladder emptying followed a double exponential function (computer program using Prony's method[5]); therefore gall bladder emptying was described as two half-emptying times. The rate of gall bladder filling was calculated from the percentage change in counts over the gall bladder regions of interest from the onset of gall bladder filling until maximum counts were obtained. Gall bladder partitioning (the fraction of the total amount of tracer taken up by the liver that enters the gall bladder) was determined by dividing the maximum gall bladder count by the maximum count obtained in the composite liver and gall bladder regions of interest (expressed as a percentage). Gall bladder ejection fraction (GBEF) was derived from the equation,

$$GBEF\ (\%) = \frac{C(t_i) - C(t_f)}{C(t_i)} \times 100$$

$C(t_i)$ = counts at time i
$C(t_f)$ = counts at time f where i>f.

All isotope count curves were corrected for decay. The times from the start of the meal until gastric and gall bladder emptying commenced were recorded.

REPRODUCIBILITY

Reproducibility studies were undertaken in seven subjects. The mean interval between the first and second study was 21 (range 14–28) days. Intraobserver error in selecting the regions of interest was determined by calculating the coefficient of variation of five different estimations of a value determined from five attempts at drawing the same region of interest. Interobserver error was also calculated in the same manner from the attempts of five experienced observers at drawing the same region of interest.

STATISTICS

Results are expressed as mean±SEM, unless otherwise stated. A non-parametric Mann-Whitney U-test was used to test for significance.

DOSIMETRY

Dosimetry calculations using Medical Internal

Radiation Dose Committee tables[6] resulted in the following doses of radiation: target organ, 2·2 rads; whole body dose, <0·05 rads.

Results

GASTRIC EMPTYING

The mean time taken to eat the meal was 7·5±0·3 minutes. Gastric emptying began 8·3±0·3 minutes after the start of the meal. The t½ of gastric emptying was 45±3 minutes (Fig. 2).

GALL BLADDER EMPTYING

It was evident from the outset that the subjects could be divided into two distinct groups with respect to the onset of gall bladder emptying. In one group (group A, n=15) the gall bladder began to empty only when a meal was presented. In the other group (group B, n=7) the gall bladder emptied spontaneously before the counts reached a relatively constant value in the gall bladder region of interest. In this group the onset of gall bladder emptying was in advance of, and therefore unrelated to, the meal.

In group A subjects the gall bladder began to empty 1·4±0·8 minutes after the start of the meal. Indeed, 15·0±1·6% of gall bladder contents had left the gall bladder before the stomach began to empty. In these subjects the gall bladder emptying pattern could be expressed as a double exponential function and there were two definite subgroups, of
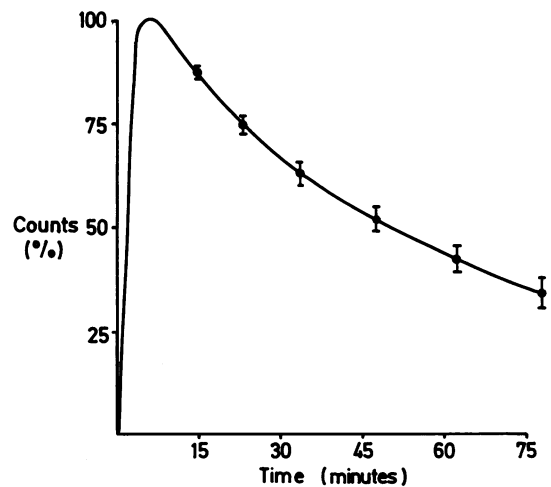

Fig. 2 *Mean curve of gastric emptying in the 22 normal subjects. All raw data curves were normalised to 100% (peak counts = 100%). Results shown are the mean±SEM (emptying part of curve only).*

which one subgroup emptied their gall bladder faster and more completely than the other. These subgroups were characterised by calculating two parameters: (a) half-emptying time of the first exponential, and (b) ejection fraction over the first 10 minutes of gall bladder emptying (Table 2, Figs. 3 and 4).

In the first subgroup (type I [n=9]), the $t\frac{1}{2}$ of the first exponential was 5·5±0·7 minutes and the 10 minute ejection fraction was 40·7±4·5%. In the second subgroup (type II [n=6]), the $t\frac{1}{2}$ of the first exponential was 14·0±1·0 minutes and the 10 minute ejection fraction was 11·7±1·6%. There was no overlap in these values between the two groups and the parameters were significantly different (p<0·001). The half-emptying times of the second exponentials were also significantly different between the two subgroups (p<0·02).

In group B subjects gall bladder emptying started spontaneously 33·5±3·7 minutes after the injection of $^{99}Tc^m$ EHIDA. In three subjects, after 19·3±4·3% of contents had left the gall bladder, the counts remained constant in the gall bladder regions of interest; in three other subjects, the gall bladder had started refilling with $^{99}Tc^m$ EHIDA; and in one subject emptying continued; when eating began. The subsequent gall bladder emptying curve in all cases followed a variable monoexponential function.

QUANTITATIVE RELATIONSHIP BETWEEN GASTRIC AND GALL BLADDER EMPTYING

In those subjects in whom only presentation of the meal appeared to stimulate gall bladder emptying (group A), the gastric emptying and gall bladder emptying curves were superimposed thus allowing the quantitative and temporal relationship between the two emptying processes to be defined (Fig. 5). The curve of gall bladder emptying was divided into three phases relative to the gastric emptying curve: phase 1, the time during which gall bladder emptying occurs before gastric emptying begins; phase 2, the emptying of the gall bladder during the first 15 minutes of gastric emptying (when most
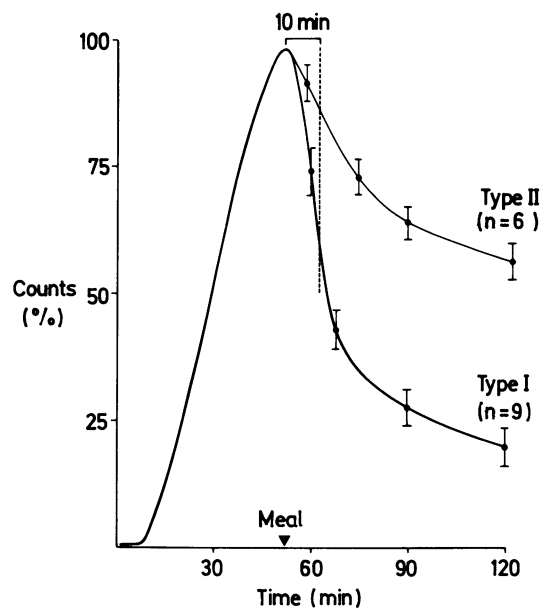

Fig. 3 *Gall bladder emptying patterns in 15 subjects who emptied in relation to eating (group A). All subjects emptied their gall bladders according to a double exponential function. Division into types I and II was on the basis of two parameters; (a) t½ of the first exponential and (b) ejection fraction over the first 10 minutes of emptying (vertical dotted line). Results shown are the mean±SEM (emptying part of curves only).*

of the rapid emptying of the first exponential of gall bladder emptying had taken place); phase 3, remaining gall bladder emptying until the end of the study (Fig. 5).

The mean duration of phase 1 for both subgroups (types I and II) was 6·5±0·7 minutes, during which 15·0±1·6% of gall bladder bile was emptied. During phase 1 – that is, gall bladder emptying before the onset of gastric emptying – subjects with a type I response emptied 18·6±1·6% of gall bladder contents while subjects with a type II response emptied only 9·6±1·2% of gall bladder contents (p<0·002) (Fig. 6). During phase 2 – that is, first 15 minutes of gastric emptying – subjects with a type II response emptied from their gall bladder and stomach a similar percentage of gall bladder and gastric contents, whereas in the subjects with a type I response the gall bladder was emptying more rapidly, with the result that more bile left the gall bladder during this time interval than in subjects with a type II response (p<0·001) (Fig. 6).

Gastric emptying was not significantly different

Table 2 *Group A gall bladder emptying patterns*

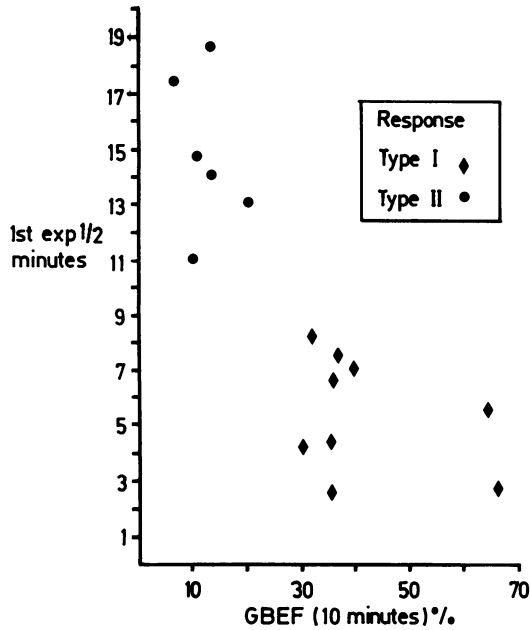|	1st exp t½ (min)	GBEF (10 min)* (%)	2nd exp t½ (min)
Type I (n=9)	5·5±0·7	40·7±4·5	118±22
Type II (n=6)	14·0±1·0	11·7±1·6	243±38
Mann-Whitney U-test	p<0·001	p<0·001	p<0·02

* Gall bladder ejection fraction at 10 minutes.

Fig. 4 *First exponential t½ and gall bladder ejection fraction at 10 minutes in the 15 group A subjects (see Table 2). Division into types I and II was on the basis of these two parameters. GBEF (10 minutes) = gall bladder ejection fraction at 10 minutes.*

between subjects with a type I or type II response. During phase 2, there was no significant correlation between the emptying rates of the gall bladder and stomach (type I, r=−0·31; type II, r=0·33).

GALL BLADDER FILLING
In those subjects in whom gall bladder emptying occurred in relation to eating (Group A), the mean time for gall bladder activity to reach a plateau was 51·9±1·2 minutes. In nine of these subjects the gall bladder filled at a uniformly constant rate (2·5±0·1%/min). In the remaining six subjects the filling of the gall bladder took place in a stepwise manner (Fig. 7). The 'steps' in the filling curve corresponded to the appearance of the bile tracer in the small intestine. The bile tracer appeared in the small bowel during the gall bladder filling phase only in those subjects with stepwise filling. Moreover, it always corresponded with the 'steps' in the filling curve during which no gall bladder filling or emptying was occurring. In the nine subjects in whom the gall bladder filled smoothly and uniformly it was observed, first that no $^{99}Tc^m$ EHIDA was detected in the duodenum until gall bladder emptying had started after the meal, and secondly, more $^{99}Tc^m$ EHIDA entered the gall bladder (71·0±2·7%) than in the group who had
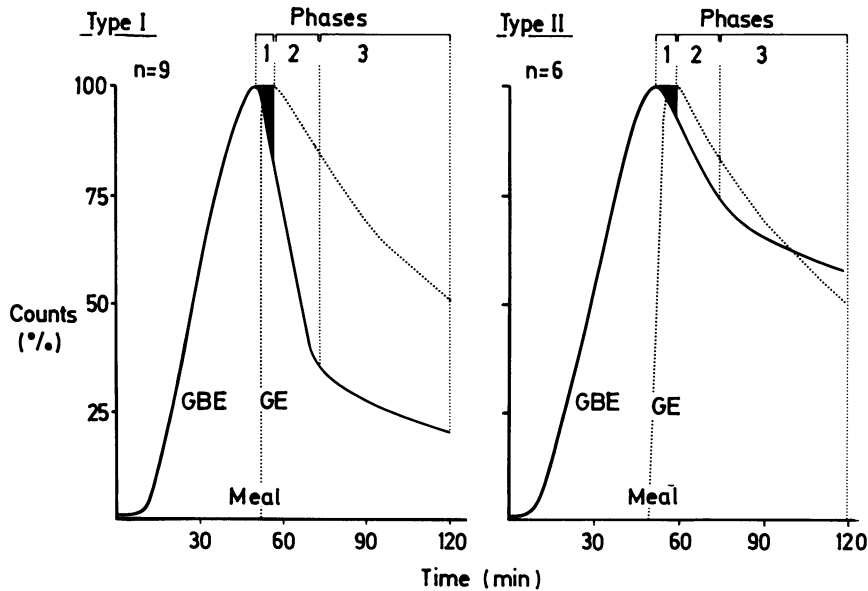

Fig. 5 *Superimposition of gall bladder emptying (solid line) and gastric emptying (dotted line) curves (group A subjects). Phase 1 (emphasised in black) represents gall bladder emptying before gastric emptying. Phase 2 includes gall bladder emptying from the onset of gastric emptying until 15 minutes have elapsed. Phase 3 is the remaining gall bladder emptying until the end of the study.*

Fig. 6 *Fraction of contents of stomach and gall bladder emptied during the three phases described in Fig. 5. During phase 1 there was by definition no gastric emptying, but type I subjects emptied a greater quantity of gall bladder bile than type II subjects (p<0·002). During phase 2, type I subjects emptied a greater quantity of bile from the gall bladder than type II subjects (p<0·001).*
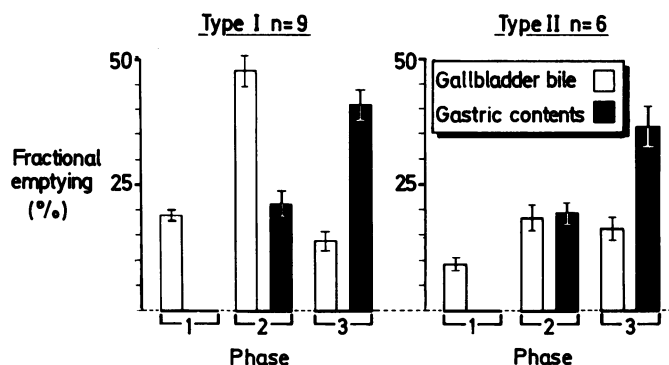
stepwise filling (58·3±4·2%) (p<0·05). There was a similar distribution of both uniform and stepwise filling patterns in subjects with type I and type II emptying patterns.

In the group B subjects, filling was uniform until premature gall bladder emptying occurred.

$^{99}Tc^m$ EHIDA WITHOUT TEST MEAL

In the six subjects who received $^{99}Tc^m$ EHIDA without a meal, the gall bladder did not begin to empty after the plateau had been reached in four of the subjects. In the remaining two subjects, the gall bladder emptied approximately 50 minutes

Fig. 7 *Patterns of gall bladder filling in group A subjects. The solid line represents filling at a constant rate and was not associated with gall bladder bypass (hepatic bile directly entering the duodenum without being stored in the gall bladder). The dotted line represents stepwise filling and was associated with gall bladder bypass.*

after the start of the test, one with 30% ejection and the other with 80% ejection (measured from onset of gall bladder emptying until end of study).

DUODENOGASTRIC REFLUX

No duodenogastric reflux of $^{99}Tc^m$ EHIDA was detected before eating in either group A or group B subjects.

REPRODUCIBILITY (Table 3)

Reproducibility studies were carried out in five subjects from group A and two subjects from group B. All subjects in group A reproduced a group A pattern (gall bladder emptying only related to eating and after a double exponential function). One subject in group B reproduced the same pattern on the second occasion but the other subject changed to a group A pattern. Intraobserver and interobserver error were 1% for both gastric emptying and gall bladder emptying.

Discussion

This study has shown that a non-invasive dual-isotope technique, using $^{99}Tc^m$ EHIDA and $^{113}In^m$ labelled bran, is a reproducible method for the simultaneous study of gastric and gall bladder emptying. Formerly gall bladder emptying has been difficult to measure because of the lack of an accurate and valid technique. Since the introduction of iminodiacetic acid (HIDA) labelled with $^{99}Tc^m$,[7] quantitative analysis of gall bladder emptying has been reported by many investigators,[8-10] who have, however, used exogenous cholecystokinin (CCK) rather than a meal as the stimulus for gall bladder contraction. By using a labelled solid test meal to stimulate gall bladder emptying, it is possible to examine the relationship between gastric emptying and gall bladder emptying under physiological conditions.
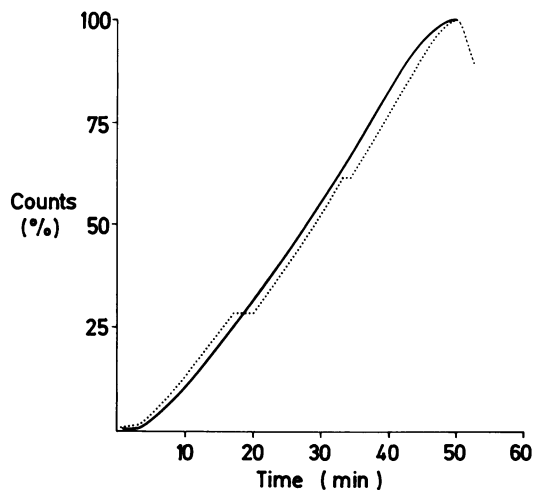
Table 3 *Reproducibility studies (group A subjects)*

Subjects	Gastric emptying (t½ min)		Gall bladder emptying					
			1st exp (t½ min)		GBEF (10 min) (%)*		2nd exp (t½ min)	
	I†	R‡	I	R	I	R	I	R
1 Type II	33	38	14·4	12·2	13	11	234	212
2 Type I	27	21	6·9	7·6	33	39	115	173
3 Type II	50	50	13·0	14·6	10	11	125	112
4 Type I	27	24	5·3	7·6	30	39	173	183
5 Type I	36	39	4·3	5·0	35	30	53	69
Student's paired *t* test	NS		NS		NS		NS	
Error§	6%		9%		8%		9%	

* Ejection fraction at 10 minutes. † = First study. ‡ = Second study.
§ Error calculated as half of the difference between the two values, expressed as a percentage of the mean value.

The subjects in this study could be divided into two groups according to whether the gall bladder emptied only in relation to eating (group A) or spontaneously before presentation of the meal (group B).

In the group A subjects during the interdigestive period, the gall bladder filled in one of two ways: (a) uniform or (b) stepwise. In the nine subjects who filled uniformly, the gall bladder partitioning (fraction of the total amount tracer taken up by the liver that enters the gall bladder) and filling rates were similar to those reported by Shaffer.[8] In these subjects it would appear that all the hepatic bile entered the gall bladder. In the six subjects who experienced stepwise filling, gall bladder partitioning was reduced because of hepatic bile bypassing the gall bladder. As counts over the gall bladder region of interest did not decrease during the 'steps' of stepwise filling, the tracer which appeared in the duodenum during this period must have been hepatic bile that had not entered the gall bladder. The most important factor controlling gall bladder filling may be the tonic state of the sphincter of Oddi as it is the only valve in the biliary compartment determining the flow of bile. The results suggest that in the six subjects in whom the gall bladder filled in a stepwise manner, the sphincter of Oddi occasionally relaxed allowing the release into the duodenum of hepatic bile that had not been previously stored in the gall bladder.

It is therefore suggested that in the interdigestive period bile may be excreted into the duodenum, either by cyclical relaxation of the sphincter of Oddi without concomitant gall bladder emptying or by gall bladder emptying.

In those subjects in whom the gall bladder emptied in relation to eating (group A), the pattern of gall bladder emptying was consistently double exponential. In this group there appeared to be two subgroups of emptying patterns – that is,

rapid, large-volume ejection (type I) and slow, small-volume ejection (type II). The subjects in both subgroups were well matched for sex, age, height, and weight. Gall bladder filling rates and distribution of uniform and stepwise filling patterns were similar in both subgroups. Reproducibility studies indicated that these patterns were consistent. A prospective study is necessary to prove that there are indeed two subgroups of gall bladder emptying patterns.

Double exponential gall bladder emptying has recently also been observed in 22 women by Everson and his colleagues using an ultrasound technique.[11] These investigators, however, did not observe a dichotomous distribution of the double exponential gall bladder emptying patterns. The reason for this discrepancy is not entirely clear.

It should be emphasised that there is no readily apparent physiological reason for gall bladder emptying to fit a double exponential function. The biphasic gall bladder emptying pattern could be also described as an initial rapid emptying phase (first exponential) and a slower second emptying phase (second exponential). Because all the isotope has not been excreted by the liver when gall bladder emptying begins, there is the possibility that the gall bladder may refill. This is unlikely during the rapid emptying, first exponential phase. Close inspection of the slower, second exponential phase often reveals some small phasic variation suggesting that some refill does occur, although overall there is net emptying as described by the emptying curve.

As gastric emptying was the same in both subgroups of subjects, in subjects with a type I response there was a greater amount of gall bladder bile emptied into the duodenum, to mix with gastric contents, than in subjects with a type II response.

A consistent finding in those subjects in whom

the onset of gall bladder emptying was related only to eating (group A) was that gall bladder emptying occurred before gastric emptying began. The early onset of gall bladder emptying may imply that a cephalic neural reflex initiates gall bladder emptying. The only previous reports of a cephalic phase to gall bladder emptying are those of McMaster and Elman in 1926[12] and Puestow in 1931.[13] These workers observed that, in dogs, bile would gush from the sphincter of Oddi on the sight, smell, or after only a few mouthfuls of food. It is unlikely that a known gastrointestinal hormone, especially CCK, would be secreted in sufficient amount rapidly enough to stimulate the early phase of gall bladder emptying. The only report in the literature relating the onset of gall bladder contraction to plasma CCK concentrations is that of Weiner and his colleagues.[14] Using ultrasound to monitor gall bladder emptying and a liquid test meal of triglyceride (Lipomul), they found that gall bladder emptying was well advanced before any significant rise in plasma CCK was detected. The evidence that one of the main hormonal actions of CCK is to cause gall bladder emptying, still awaits conclusive proof.[15]

The role of the autonomic nervous system in controlling gall bladder emptying is uncertain. Neural control of gall bladder emptying is considered to be of minor importance.[16] This study suggests, however, that neural mechanisms may be more important than previously recognised. In sham feeding experiments we have found that gall bladder emptying occurs without swallowing food (unpublished data). Further investigation is needed to determine the exact nature of neural mechanisms in gall bladder emptying and also any other 'preduodenal' mechanisms.

The emptying of gall bladder bile into the duodenum in advance of gastric emptying, may represent an important physiological mechanism for mobilising the bile salt pool and returning some of the bile salts quickly into the enterohepatic circulation for continuing secretion by the liver to cope with the remaining bulk of gastric emptying.

A direct quantitative relationship between exogenous CCK and gall bladder emptying – that is, dose-response relationship – has been previously shown in man.[17] It may have been expected in this study that there would be a quantitative relationship between gastric emptying and gall bladder emptying, that is, the more rapid gastric emptying (to produce a large volume of duodenal chyme), the greater would be the release of the hormones responsible for gall bladder emptying. In our studies where the stimulus to gall bladder emptying was a meal, no such relationship

was seen. During phase 2, no correlation was found between the amounts of material entering the duodenum from the stomach or from the gall bladder.

The emptying of the gall bladder prematurely before the meal was presented (group B subjects, and in some of the subjects who received ^{99}Tc^m EHIDA without a meal), is not unexpected. Other investigators have observed that bile is discharged into the duodenum during the interdigestive period in relation to the interdigestive migrating motor complex (IMMC) both in the dog[18] and in man.[19 20]

Interestingly our reproducibility studies in group B subjects revealed that it is possible to change to a group A pattern. This suggests that a group A pattern (onset of gall bladder emptying only in relation to eating, double exponential emptying pattern) is probably the usual response to eating a meal; however, if an IMMC occurs immediately before eating, a group B pattern (premature gall bladder emptying then variable monoexponential gall bladder emptying pattern in relation to eating a meal) will be seen.

Griffith and coworkers in 1966[21] first described the use of isotopes to measure gastric emptying, and in 1970 the gamma camera, introduced by Harvey[22] added further precision to these studies. In this study a recently validated technique for using isotope labelled bran was used[4] to provide a solid meal of physiological size and content. Although many workers report that gastric emptying of solids can be expressed as a linear function,[23–26] Weiner and his colleagues have shown that solids composed of small particles empty in a monoexponential manner.[27] This is in accord with our results for bran which has a small particle size. It is unlikely that there is any significant error in the gastric emptying curve because of elution of the label and subsequent emptying in a liquid phase.

There are several potential technical errors in measuring gastric emptying: (a) inaccuracies in quantifying the emptying pattern may result from using only an anterior detector[28 29] because of changing attenuation of the gamma rays as the gastric contents move anteriorly. In the present study, a high energy isotope ^{113}In^m, was used so that errors associated with anterior movement of food in the stomach were reduced.[30] (b) An underestimate of the amount of tracer in the gastric region of interest can arise from septal penetration when a high energy isotope is used to monitor and quantify gastric emptying.[28] This problem was investigated using phantoms and a derived correction factor was applied to the gastric emptying curves. As there was only a marginal

difference between septal penetration corrected and raw count curves, a septal penetration correction factor is not considered necessary. (c) When two isotopes of different energies are used simultaneously a certain fraction of the high energy gamma rays will have their energy degraded such that they will be detected in the low energy window and counted as low energy gamma rays (down-scatter). From phantom studies, the down-scatter fraction (in the same region of interest) from the $^{113}In^m$ into the $^{99}Tc^m$ window was calculated at 15%. From relative counting statistics, the down-scatter from the $^{113}In^m$ into the gall bladder regions of interest $^{99}Tc^m$ window was negligible.

In conclusion, we have shown that the initial onset of gall bladder emptying may occur either in relation to eating or spontaneously. When the onset of gall bladder emptying occurs only in relation to eating, the gall bladder starts emptying well before gastric emptying begins and there appear to be two types of emptying patterns; one in which the gall bladder empties faster and ejects more contents than the other. There also appears to be no correlation between gastric emptying and gall bladder emptying rates in these subjects. During the interdigestive period, filling of the gall bladder may be uniform or stepwise depending on whether all hepatic bile enters the gall bladder or not.

This reproducible, non-invasive method for measuring simultaneously gastric emptying and gall bladder emptying may therefore prove useful for studying the relationship between gastric and gall bladder emptying. Concurrent measurement of hormone levels may help to elucidate basic physiological mechanisms. This technique should also be useful for investigating whether gastric operations alter gastric emptying/gall bladder emptying relationships and may be of value in increasing the understanding of the pathophysiology of the symptoms which some patients unfortunately experience after such surgery.

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