Gastric emptying: a clinical perspective

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Introduction
A patient with upper gastrointestinal symptoms for which no cause can be found is at risk of having his complaints labelled 'functional'. This is a term with imprecise and variable meanings but in this context it is usually intended to imply that the physician accepts that the symptoms seem gastrointestinal in origin but that no specific disorder of structure or function has been found to account for them. In addition, the term is sometimes intended to convey that, having failed to make a diagnosis, the physician’s interest in the case has effectively come to an end. Such patients are common problems, and it therefore seems remarkable that an assessment of motor function of the upper gastrointestinal tract is so seldom included in their investigation. There is general acceptance of the possibility that motility disorders may be responsible for symptoms, and oesophageal motility studies have earned a place in clinical investigation, but why is it that the complex motor activity of the stomach is still such a 'no go' area for clinical gastroenterology? There are several reasons but the two dominant ones must be the absence of simple procedures by which gastric motor function may be assessed and, perhaps more important, great uncertainty about which aspects of motor function are likely to have clinical relevance. Thus, for many years, the motor functions of the stomach have been largely ignored and, inevitably, there has been relatively little progress in our understanding of the nature, clinical significance or treatment of abnormalities. In marked contrast, the last decade has seen considerable progress in our understanding of the physiology of gastric motility and gastric emptying and it is therefore timely to consider the possible clinical relevance of current knowledge.

Normal gastric emptying
When food is ingested, it is accommodated in the normal stomach by relaxation of the fundus and upper body. This relaxation, triggered in part by the act of swallowing and in part by proximal gastric distension [1] is effected principally by inhibitory motor neurons of the vagus nerve, which act especially on the oblique muscle layer of the proximal stomach [2]. These nerves are neither cholinergic nor adrenergic and the neurotransmitter is presently unknown. Although relaxation occurs proximally, cholinergic vagal neurons innervating the more distal part of the stomach promote the occurrence of peristaltic contractions [3]. Both relaxation in the proximal stomach and the peristaltic activity more distally can be modulated by various gastrointestinal hormones, although at present the contribution made by the hormones released in response to meal ingestion has not been established.

Ordinary meals comprise a mixture of liquid and solid components and it has become clear that somewhat different mechanisms are involved in emptying liquids and solids from the stomach. Moreover, there may be differences in the behaviour of different solid components of the same meal, and this complexity has caused problems in the interpretation of published investigations. For example, studies of gastric emptying based on test meals of mashed potato, chunks of meat or relatively inert dietary constituents such as cellulose or bran are all likely to be said to reflect the emptying of 'solids', but in fact the physical nature of the solid food (i.e. particle size, shape, consistency etc.) appears to be of major importance in determining its rate of emptying from the stomach.

The tonic intragastric pressure, determined mainly by the degree of relaxation of the proximal stomach, appears to be a major influence on emptying of the liquid component of the gastric contents [4]. It is especially important in the first few minutes after meal ingestion, a period sometimes termed the early or initial phase of gastric emptying, and may also contribute to the emptying of liquids thereafter. During the early
phase of emptying, small solid particles empty in parallel with liquids whereas larger particles are retained within the stomach, possibly as a result of simple mechanical filtration by the relatively narrow distal antrum and pylorus. After the initial phase of emptying, which probably lasts no more than 10 min, peristaltic contractions of the distal stomach are thought to contribute to the emptying of liquids [5] and to determine the fate of ingested solids [4, 6–8]. Small solid particles are expelled through the pylorus (though they are emptied more slowly than liquids [9]) and larger particles are wholly retained within the stomach. This relative retention of all solids in comparison with liquids appears to be a property of normal peristaltic activity. However, solids are subjected to the grinding action of the distal antral contractions, which serve to break up susceptible solid foods to fine particulate material which then becomes suspended in the liquid phase of the gastric contents. Thus the physical form of food such as meat will change progressively with time, whereas foods relatively resistant to the grinding action of the antrum, such as fibrous vegetable matter, will show much less change.

The efficiency of the gastric antrum in “liquefying” food such as liver has been well demonstrated both in the dog and in man, where ingested liver is reduced to particles less than 2 mm in size before being emptied through the pylorus [7, 10]. However, such complete liquefaction is not a prerequisite of the emptying of solids, since inert particles 3 mm or so in size are emptied from the stomach at rates comparable with those for ingested liver [11, 12]. Larger solid particles resistant to grinding may well be retained within the stomach until all other gastric contents have been emptied, when they are forced through the pylorus by the powerful contractions of the interdigestive motor complex [13].

A further complication is apparent from recent studies of gastric emptying of lipids [14, 15]. Much dietary fat is liquefied at body temperature, yet the lipid phase of gastric contents is emptied from the stomach more slowly than the aqueous phase. It is not yet clear whether this is wholly explained by the tendency of fats to float to the top of the aqueous phase, but the observations serve to re-emphasize the heterogeneity of normal gastric contents as well as indicating that neither solids nor aqueous liquids reflect the behaviour of fats.

**Measurement of gastric emptying**

The heterogeneous nature of the gastric contents after ordinary food presents an obvious problem when the measurement of gastric emptying is considered. Given the differing behaviour of liquids and solids, it would seem that an adequate assessment of gastric emptying must at least consider these two elements separately. Yet the more comprehensive the measurement, the more complicated (and perhaps impractical) it is likely to be.

Gross abnormality of gastric emptying is readily recognized in the course of routine radiological examination with barium suspension, but, in less extreme situations, useful measurement of emptying is difficult. In any case, the relevance of the measurement to the behaviour of more physiological meals is questionable. The use of food barium mixtures [16] or small radio-opaque particles mixed with food [11, 17] may provide a better indication of the emptying of ordinary meals, but neither approach has gained much popularity. The simplest methods of formal measurement are based on aspiration of gastric contents through a nasogastric tube at a fixed time after ingestion or installation of a known volume of test solution [18]. In a research context, this approach has provided useful information about the physiology of gastric emptying, but it has not earned a lasting place in clinical practice. Developments of the basic technique such as the double sampling method [19, 20] are far from easy to undertake and, of course, are limited to the study of liquid test meals. Another method, employing simultaneous gastric and duodenal intubation [21], can be used for mixed solid–liquid meals but is again far too complicated for routine use.

The best prospect for clinical application would appear to be the radioisotopic methods of gastric emptying measurement, which use a gamma camera to detect and measure isotope remaining in the stomach at intervals after its ingestion. Many studies using these scintigraphic methods have been published in recent years, so that there is now a reasonable awareness of the advantages and limitations of the technique. Quite obviously it is emptying of the isotope that is measured and the assumption is made that this provides a proper representation of emptying of the test meal or some component of it. However, many water soluble isotopes used to represent the aqueous phase of the gastric contents become partially and reversibly adsorbed to solid foods within the stomach, so that measured emptying rates reflect in part emptying of the aqueous phase and in part emptying of the solid. Sodium chromate and technetium diethylene triamine penta-acetic acid (DTPA) are typical examples. Even indium DTPA, now widely used as an aqueous phase marker, is not entirely free of this problem, being
partially adsorbed to some solid foods, notably bread [22]. In addition, it is important to recognize that gastric emptying measurements made with indium DTPA and similar markers record emptying of the aqueous phase of the test meal, not of the whole gastric contents. No account is taken of the volume of gastric secretion which is continuously added to the meal within the stomach, a volume which may vary very considerably from one individual to the next. Thus the rate of emptying of the aqueous component of the meal bears an uncertain relationship to the rate at which fluid is discharged through the pylorus.

Firm radioisotope labelling of solid foods such as chicken liver [23] or egg white [24] permits the gamma camera method to be used to measure the emptying of solid food. As discussed above, such foods are normally liquefied within the stomach and some authors have argued that it would therefore be better to use dietary constituents resistant to intragastric grinding (such as cellulose fibre or bran) to study the gastric emptying of solids. However, in the context of detecting abnormalities of emptying, it remains to be shown that the one type of solid has any advantage over the other.

The measurement of radioactivity within the stomach by external detection does present some technical problems, which may introduce inaccuracy to the measurements. When unilateral detection is used, as with a gamma camera placed anterior to the subject, movement of radioactivity within the stomach as emptying proceeds may be associated with a changing attenuation of the gamma emissions. This usually results in the measurement being an underestimate of the true emptying rate, though the magnitude of the error depends on the conditions of the study and on the isotope being used [25-27]. The problem can be overcome if bilateral detection is used, i.e. using the gamma camera to count from both the anterior and posterior aspects of the subject, but of course this further complicates the method.

Although recognition of the limitations and imprecisions of gamma camera gastric emptying measurements is clearly important, the two outstanding advantages of the technique are its non-invasive nature, which renders it readily acceptable to patients, and that, once the method is set up, it is relatively simple to perform. Thus gamma camera methods do have the potential for practical application.

Abnormal gastric emptying
The abnormalities of gastric emptying which occur after gastric surgery are predictable from a knowledge of the physiology of gastric emptying. Thus, after vagotomy, emptying of the gastric contents during the early phase of emptying is accelerated because the normal relaxation of the proximal stomach in response to meal ingestion has been compromised. The early emptying abnormality is enhanced when gastric 'drainage' is facilitated by pyloroplasty or gastroenteroscopy. After the early phase, emptying of both liquids and solids tends to be slower than normal in patients who have undergone truncal vagotomy, because the vagal activity which normally promotes antral contraction is lost, whereas no such abnormality is seen after highly selective vagotomy, in which antral innervation is preserved. Thus gastric emptying is much less deranged after the highly selective operation and the relative normality of emptying is presumed to be responsible for the much lower incidence of post-operative dumping and diarrhoea. An association has been established between the magnitude of gastric emptying during the early phase and the occurrence of dumping and diarrhoea after vagotomy and pyloroplasty [28-30], and although the relationship is not clear cut [31] it seems reasonable to accept that rapid emptying makes a contribution to the genesis of such symptoms. However, there has been remarkably little investigation of the clinical value of gastric emptying measurements in the assessment of patients with troublesome post-operative problems.

In most patients who have undergone vagotomy and pyloroplasty, the differentiation between solid and liquid emptying is preserved [32], indicating that this aspect of antral function persists despite vagal denervation. However, discrimination is reduced or lost in individuals who have undergone antrectomy. My colleagues and I have also observed reduced solid-liquid discrimination in some diabetic patients [33], in some patients with post-vagotomy problems [32] and an intriguing total loss of discrimination in one patient with recurrent bezoar formation for which no explanation was apparent. The implication that this individual had an isolated but unexplained impairment of antral contractile function is obvious.

Gross gastric stasis is usually due to mechanical obstruction and may be apparent clinically or radiologically without recourse to formal gastric emptying measurements, but, in the absence of mechanical obstruction, delayed gastric emptying may be demonstrable by scintigraphic methods when routine barium studies appear normal [33]. Chronic gastroparesis may occur in association with various neurological,
metabolic and muscular disorders and its discovery in such patients may come as no surprise. However, the recent recognition of idiopathic gastroparesis in patients with unexplained upper gastrointestinal symptoms who are otherwise well [16, 34–36] indicates that the problem is of more general importance. In some cases the onset of symptoms appeared to follow a viral illness; in others an abnormal antral pacemaker was apparently responsible for generating an antral tachyarrhythmia. In many cases the abnormality was unexplained. It is just this type of patient, with persistent or recurrent nausea, and complaints of epigastric fullness, bloating or vomiting, that will be considered ‘functional’ if traditional investigations fail to identify an abnormality.

Most investigators using modern methods of measurement are acutely conscious of the fact that transfer of the gastric contents to the duodenum is the outcome of a highly complex inter-relationship of influences on gastric and duodenal muscle and that abnormalities of emptying, particularly stasis, may more often reflect a disorder outside the alimentary tract than one within it. The problems posed by the undoubted relationships between the psyche and upper gastrointestinal motor function are particularly daunting. For example, what should we make of the anxious patient who complains of nausea, anorexia and bloating and has delayed gastric emptying? Does he require treatment for his anxiety, the gastric motor abnormality or both? Does delayed gastric emptying in anorexia nervosa reinforce the patient’s disinclination to eat to such an extent that attempts to normalize the gastric emptying with drugs such as metoclopramide or bethanecol are desirable? These and many similar questions present formidable challenges to the collaborative efforts of gastroenterologists and psychiatrists.

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A poor understanding of the nature and clinical significance of gastric emptying abnormalities is inevitably accompanied by considerable uncertainty about the actions and practical value of the drugs usually employed in treatment. Metoclopramide is an obvious example. Although this drug is widely held to accelerate gastric emptying, and pharmacological studies have clearly shown that it promotes gastric contractions [37], its effects in the circumstances in which it is commonly prescribed are largely unknown. In patients with delayed gastric emptying, metoclopramide is of real symptomatic benefit [16] but in a recent study of our own, symptomatic improvement produced by metoclopramide in patients with diabetic gastroparesis bore no apparent relationship to changes in gastric emptying. The place of other drugs with cholinergic activity (such as bethanecol) in the treatment of gastric emptying abnormalities is even more uncertain and, similarly, the value of dopamine antagonists such as domperidone, which may affect antro-duodenal co-ordination [38], has yet to be established. The widespread clinical use of various anticholinergic and other drugs as gastrointestinal ‘anti-spasmodics’ to treat ‘functional’ symptoms is convincing evidence that most current therapy is empirical.

Our understanding of the clinical implications of abnormal gastric emptying and disturbed gastric motility is presently very limited and it would be wrong to pretend otherwise. However, the measurement of gastric emptying is now feasible with gamma camera methods and in several major centres this is complemented by manometric and electrical recording methods which can help to characterize abnormalities. Thus the possibility of making progress now exists. We could perhaps begin by reaffirming that to describe persistent upper gastrointestinal symptoms as ‘functional’ without demonstrating any abnormality of function is intellectually inadequate for the physician and all too often of meagre benefit to the patient. If we are to do better, measurements of gastric motor function will be required.

References

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