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METHODS FOR STUDYING GASTRO-INTESTINAL MOTILITY: STOMACH

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INTRODUCTION

Standardized methods for measurement of gastric motor functions are required for correct diagnosis of disordered gastric emptying, as the diagnostic value of subjective abdominal and epigastric symptoms and physical findings is poor.

The methods that are used clinically can be separated into three categories:

- Measurement of gastric emptying
- Measurement of antroduodenal luminal pressures
- Measurement of gastric electric activity

Scintigraphic measurement of gastric emptying is presently the only of these methods that has proven clinical value. Other methods of luminal pressure measurements and electric activity mainly have a research potential but may add to the diagnostic value of radionuclide measurements of emptying.

MEASUREMENT OF GASTRIC EMPTYING

Scintigraphic technique

Scintigraphic measurement of gastric emptying is a convenient non-invasive method for evaluation of gastric emptying. The method permits concomitant measurements of solid as well as liquid meals. However, the diagnostic value seems greater for the emptying of solid gastric contents than for liquids (*Horowitz* et al., 1985). The radionuclide mostly used as marker is ^{99m}Tc because of its low cost, easy accessibility and convenient physical half-life. ^{99m}Tc labelled macroaggregated albumin is easily incorporated into liquid or solid meals, preferably containing egg albumin to which the marker substance can bind. We have used an egg omelette with added flavour to achieve a truly solid meal of 250 g corresponding to 310 kcal, to which 10-12 MBq of ^{99m}Tc is added. The omelette is cooked in a microwave oven and is tolerated by most patients. Alternatively, pancakes can be used, which is preferred by children, but may not be used in studies of diabetic patients, and require extra-ordinary utensils for the radioactive cooking.

The test meal is eaten within 10 min together with 150 ml of liquid and thereafter registration is started using anterior-posterior and posterior-anterior projections for 1-min periods at intervals of 5 min until the lag phase is passed, followed by projections at 10-min intervals until 120 min.

The gamma camera is linked to a computer system which enables registration of abdominal radioactivity. The stomach is recognized by its characteristic shape and the region of interest is outlined (Figure 1). The counts within this region reflect the amount of food

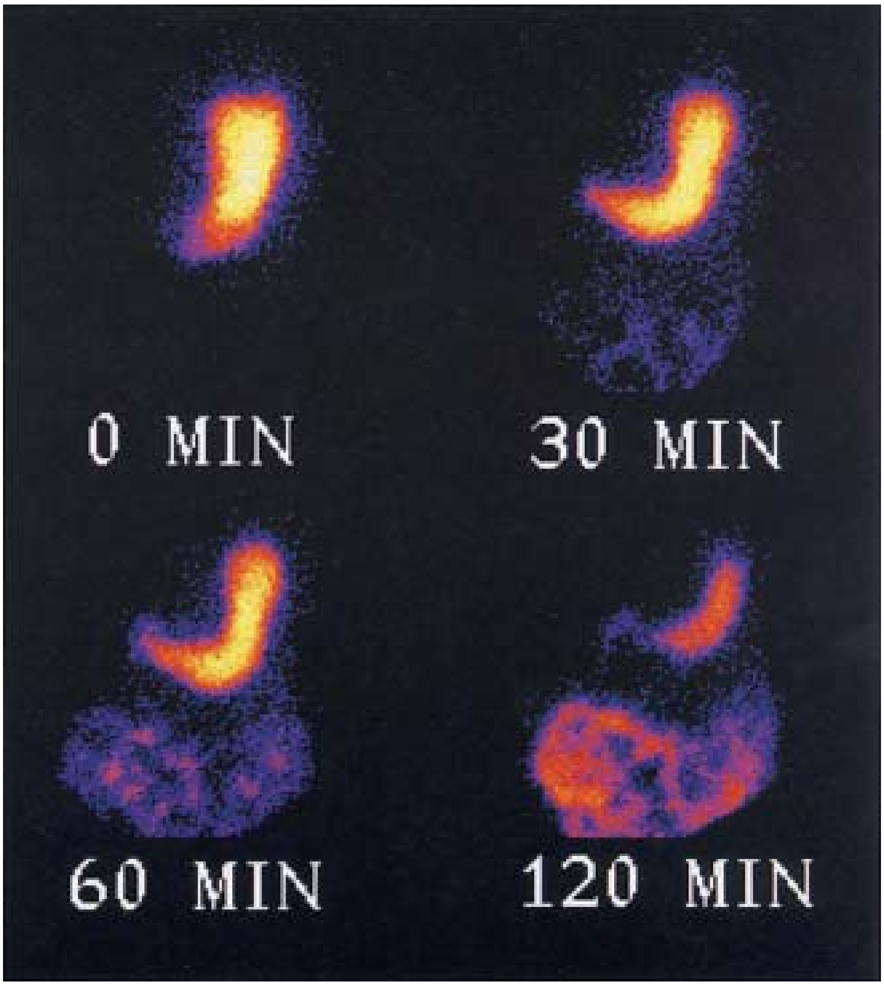


Figure 1: Scintigraphic registration of gastric emptying using a 12 MBq ^{99m}Tc-labelled omelette. Scintiscans taken at 0, 30, 60 and 120 min after food intake.

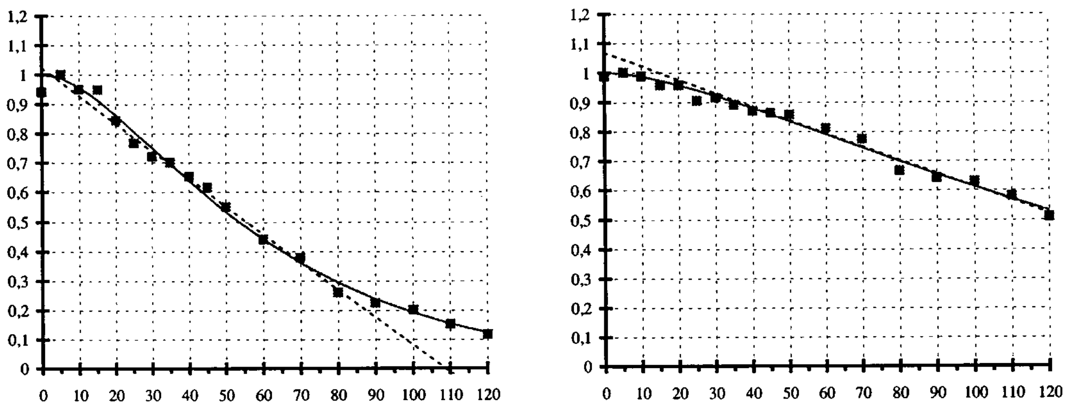
retained in the stomach. The gastric radioactivity registered by anterior and posterior projections, are multiplied and the square root of the value is taken to achieve the geometric centre of the region-of-interest. The computed values are plotted against time to determine the rate of gastric emptying (*Collins* et al., 1983).

Gastric emptying of liquid contents may be measured simultaneously with the emptying of solids, because liquids are already taken with the test meal. In such cases, ^{111}In-DTPA is added to the liquid marker. The gamma camera system separately detects the two nuclides of different energies (*Horowitz* et al., 1985).

The use of large field-of-view gamma cameras minimizes technical errors and may permit simultaneous measurements of small intestinal transit (*Read*, 1989).

Measurement of solid meals are more

A B



Lag phase: 13.0 min
Emptying rate: 27.3%/h
T50: 55.5 min

Lag phase: 36.8 min
Emptying rate: 56.4%/h
T50: 124.8 min

Figure 2: Illustrations showing the gastric emptying process in a healthy male (A) and female (B). Indices for the gastric emptying is given below the graphs.

sensitive than measurements of liquids in the detection of abnormal gastric emptying. Therefore, if a single tracer should be employed a solid marker is preferred (*Malmud* and *Fisher*, 1981).

Measurements of gastric emptying of solids usually demonstrate a characteristic appearance with a lag phase followed by a linear emptying phase. The mathematic evaluation of gastric emptying includes the lag phase period which we defined until 90% retention (min), as well as the post-lag linear rate of gastric emptying (%/min), the half-emptying time (T50; min) and the gastric retention at 120 min (%). The gastric emptying rate during the linear emptying phase has been estimated to be about 1-2 kcal/min. Figure 2 shows the typical appearance of two gastric emptying curves in a male (A) and female (B).

On a research basis, in order to further evaluate the association between motor function of the stomach and gastric emptying, scintigraphy has been combined with manometric techniques (*Houghton* et al., 1988).

The common problems inherent with scintigraphy is that the method is expensive and time-consuming, and occupies detection equipment that has a limited availability. Also, studies with administration of radionuclides cannot be carried out during pregnancy.

The methodological problems that limit the sensitivity and specificity of isotope gastric emptying tests include in particular the movement of the radionuclide marker within the stomach, which leads to variations in the counts detected because of the different thickness of tissue between the stomach and the gamma camera for which corrections must be made (*Collins* et al., 1983). Another drawback with the method is that external scintigraphy cannot measure the volume of gastric secretion within or emptied from the stomach. This gastric secretion progressively dilutes the gastric markers and may affect the outcome of the emptying characteristics.

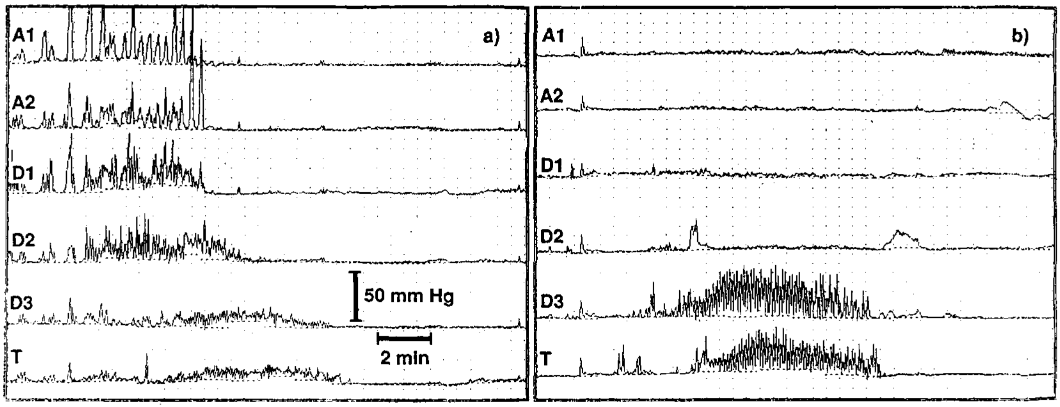


Figure 3: Recordings of antroduodenal motility in a healthy subject (a) and a patient with diabetic gastroparesis (b). Registration sites in the proximal (A1) and distal (A2) antrum, proximal (D1), middle (D2) and distal (D3) duodenum, and at the angle of Treitz (T).

Absorption kinetics of orally administered drugs

In humans there is limited absorption of drugs administered orally. The rate of appearance of the drug in plasma therefore serves as an indicator to measure the rate of gastric emptying (*Nimmo*, 1976). Paracetamol is most commonly used for detection of the gastric emptying rate because the drug can usually be analysed on a routine basis at clinical laboratories. A limitation of the method is that it only permits measurements of the liquid phase of emptying. An advantage with the method is that it can be performed in most clinical settings with availability of limited analytical equipment.

Determination of the rate of gastric emptying by measurement of plasma concentrations of intestinally absorbed paracetamol has been considered fairly inaccurate and unsatisfactory for appropriate measurements of gastric emptying. However, with the use of a suitable nutrient-liquid test meal and carefully calibrated standard curves for plasma concentrations of paracetamol, the method can be optimized. We have used paracetamol 24 mg/kg body weight, i.e. about 1.5 g, given perorally with Borgström's test meal containing 400 kcal of liquid nutrients. The absorption kinetics of paracetamol are usually evaluated as T_{max} (min), C_{max} (mmol/l) and area under curve (AUC; mmol/l.min), but may be further optimized by swapping the cumulated absorption curve for the drug which then reflects the gastric emptying rate. This mathematical operation also permits calculation of the half-emptying rate (T50; min) for the drug.

Another way of optimising the measurement of gastric emptying with this technique is to carefully coordinate the emptying process to the respective phase of the migrating motor complex (MMC) during which the drug is given. However, this may only be done on a research basis because recordings of the MMC require gastro-intestinal intubation for luminal pressure recordings of the antroduodenal region (*Medhus* et al., 1995).

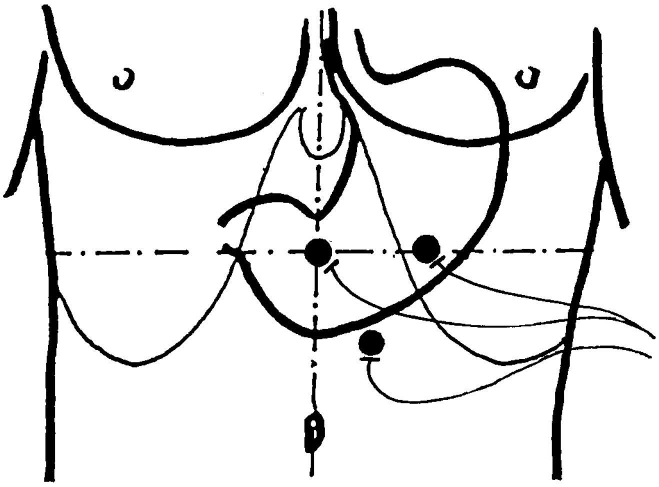


Figure 4: Placement of surface electrodes for recording of electrogastrogram.

MEASUREMENT OF ANTRODUODENAL LUMINAL PRESSURE

The technique of recording antroduodenal pressure changes aims at selectively identifying different motor activities responsible for the process of gastric emptying. Hence, motor activity of the antrum churns ingested foodstuffs and is thereby of importance for the duration of the lag phase. Thus, manometry is valuable for the detection of basic mechanisms underlying abnormal gastric emptying (*Hellström*, 1991).

Manometry is usually carried out with external pressure transducers linked to a multiple lumen manometric catheter or by miniature solid-state transducers. Manometry of the antroduodenal region can be carried out during fasting as well as after food intake. Contractions in other parts of the stomach do not evoke any pressure changes and are not possible to detect employing this method (*Fone* et al., 1990). The purpose of fasting motility studies is to evaluate the existence of MMC, and the involvement of the antral region in this migrating complex (Figure 3). Normally about 60% of MMCs start in the antrum, while 100% occur at the angle of Treitz (*Kellow* et al., 1986). Because the MMC cycle length in man varies greatly with mean values ranging from 80-120 min, prolonged studies have to be carried out to permit accurate measurements of the MMC cycle length and the characteristics of phase 3 activity (*Hellström* et al., 1991). Antroduodenal motility studies can also be carried out after food intake. This is mainly done in order to investigate the initiation of fed motility in the antrum and duodenum in response to food intake, and evaluated as an increase of motility index. The lack of an appropriate motility response after food intake is generally considered as a neurogenic disturbance of gastric motor activity, that should be associated with prolonged gastric emptying.

The problem inherent with the manometric technique is the positioning of the sensors in the antroduodenal region, since it is impossible to maintain a stable position with one pressure recording point in such mobile anatomical structures as the antrum and duodenum. Due to this fact multiple pressure sensors

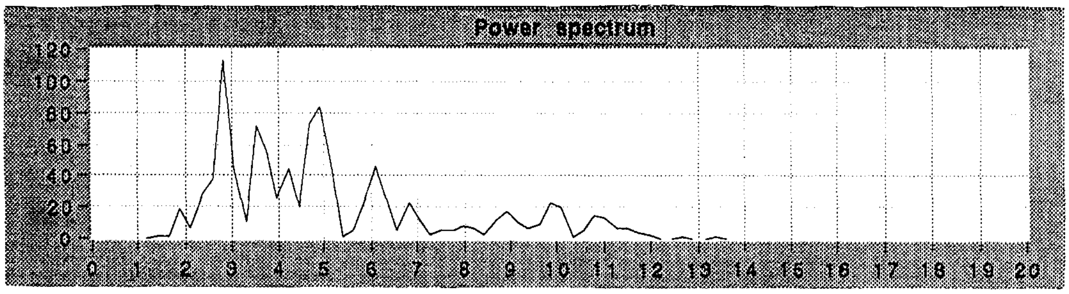


Figure 5: Distribution of electric frequencies in antral smooth muscle as registered by electrogastrography. Note the dominating frequency of 3 cycles per min.

are positioned in the stomach and duodenum. Because normal motility will push the manometric tube aborally, its position in the gastro-intestinal tract has to be continuously monitored and corrected. The position of the manometric tube can be easily determined by the characteristics of the pressure waves during phase 3 of MMC: high amplitudes at a 3 per minute-rhythm in the antrum, and low amplitudes at a 12 per minute-rhythm in the duodenum.

With the manometric tube in correct position, patients with diabetic gastroparesis have been considered to lack the antral component of the MMC and exhibit postprandial antral hypomotility (*Camilleri* and *Malagelada*, 1984). Other forms of slow gastric emptying as seen in idiopathic gastroparesis, different types of myopaties, and in anorexia nervosa may also show antral hypomotility.

Antroduodenal manometry is a clinical procedure that directly evaluates the motor components, as antral hypomotility or pylorospasm, underlying disordered gastric emptying. The main drawback for its clinical use is that the method is invasive.

MEASUREMENT OF GASTRIC ELECTRIC ACTIVITY

Electrogastrography (EGG) is made via surface electrodes attached to the skin at the positions shown in Figure 4. The obtained signal is filtered in an analogue system and thereafter converted to a digital signal that is analysed using computer software that permits overlapping of the signal and presentation of the signal as a fast Fourier analysis in a running spectrum (Figure 5). The result gives an indication of the function of the gastric pacemaker, which determines the basal electric rhythm that governs gastric contractions (*Smout* et al., 1980).

The gastric pacemaker located on the proximal part of the greater curvature generates a basal electric rhythm (slow waves) at a pace approximately 3 cycles per min. This electric rhythm governs the frequency of contractions in antral smooth muscle. It is generally considered that this pacemaker activity is not a property of the smooth muscle cells *per se*, but a function of specialized pacemaker cells, the so-called interstitial cells of Cajal. The basal electric rhythm does not produce contractions, but rather paces rapid depolarisations, i.e. spikes, which correspond to contractions of smooth muscle cells. Spiking occurs at the peak of the basal electric rhythm, and thus the normal frequency registered by EGG is 3 cycles per min.

EGG registered with a sampling frequency of 1 Hz is only capable to record the basal electric rhythm and cannot be used to detect the occurrence of contractions in the stomach. Pathologic electrical rhythms, such as bradygastria, or tachygastria, can be detected by EGG and may be of importance for the emptying process of the stomach.

EGG has been considered mainly a research tool, but with its non-invasive technique and common handiness, it may be used also clinically to detect disordered electrical rhythms of the stomach.

ACKNOWLEDGEMENTS

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