Changes in gastric emptying rates with age

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Summary
1. A dual isotope technique which measures simultaneously the emptying of solids and liquids by the stomach was used to study gastric emptying in 35 subjects in the age range 21–84 years, who were all fit, mobile volunteers and were not taking any drugs.

2. Solid and liquid emptying were significantly slower in older subjects, but this finding is unlikely to be of clinical significance because the changes were small and emptying rates were usually within the normal range for younger subjects.

Key words: age, gastric emptying, stomach.

Abbreviation: DTPA, diethylenetriamine penta-acetic acid.

Introduction
Gastric emptying of solids and liquids is dependent on motor functions of different portions of the stomach. Emptying of solid food is preceded by antral propulsive and retropulsive mincing [1], and the main factor controlling the emptying of liquids is the pressure gradient across the gastroduodenal junction, which is largely dependent on the tone of the fundus [2]. Gastric emptying tests which utilize a double isotope technique permit the simultaneous measurement of solid and liquid meal components and are capable of detecting clinically significant abnormalities of gastric emptying [3–5]. It has been demonstrated that rates of solid and liquid emptying in patients with symptomatic gastric emptying disorders are usually outside the range of values found in normal volunteers [6].

There is conflicting information both on the effects of age on gastric emptying and the clinical implications of any change. Reviews of pharmacokinetics in the elderly have suggested that there is a significant delay in gastric emptying with increasing age [7–10], mainly as a conclusion from the results of indirect studies reporting a delay in the rate of absorption of drugs in aged subjects [11]. However, the validity of these studies has been questioned [12–14]. Some investigators who have directly measured the influence of age on gastric motility have found no change, either in laboratory animals [15] or humans [16, 17], whereas others [18] have reported a marked delay in the emptying of liquids. These studies have either used subjects who were in hospital [17] or taking drugs [18], or have employed relatively inaccurate methods to measure gastric emptying [16, 17]. We have therefore studied the effect of age on gastric emptying using an accurate technique and appropriate subjects, in an attempt to clarify the discrepancy in these findings.

Methods
Preparation of solid marker and liquid marker
Twenty-seven millicuries of $^{99m}$Tc-sulphur colloid were injected into a wing vein of a live chicken, as described by Meyer et al. [1]. After 20 min the chicken was killed and the liver removed. The amount of liver containing 1–1.5 mCi of $^{99m}$Tc-sulphur colloid was mixed into 100 g of ground beef and the resulting 'hamburger'
cooked on a griller. The total energy content of the solid meal (25 g of protein, 21 g of fat) was approximately 1130 kJ (270 kcal). The liquid marker was 0.5–0.75 mCi of $^{113m}$In-labelled diethylenetriamine penta-acetic acid (DTPA) mixed in 150 ml of 10% D-glucose solution. The whole body radiation dose was calculated to be approximately 40 mrad for each study.

Subjects

All subjects were non-smokers, not receiving medication, and had no evidence of gastrointestinal or significant medical disease. There was no evidence of neurological disease or history of diabetes mellitus and in all subjects the morning fasting plasma glucose level was less than 6.5 mmol/l. Subjects older than 65 years of age were volunteers from an Elderly Citizen's Club. Informed consent was obtained in all cases and the study was approved by the Research Review Committee of the Royal Adelaide Hospital. The 35 subjects (20 male, 15 female), mean age 50 years (range 21–84), who participated in the study were divided into two groups. Twenty-two ‘control’ subjects (14 male, 8 female), mean age 34 years (range 21–62) and mean body weight $66 \pm 3$ kg, and 13 ‘elderly’ subjects (six male, seven female), mean age 77 years (range 70–84) and body weight.

Performance of test

The gastric emptying test was performed at either 10.00 hours (after the subject had fasted from 24.00 hours the previous day) or 12.30 hours (after the subject had eaten a light, standard breakfast at 07.30 hours). The study was performed in the sitting position with the detector behind the patient [4, 5]. The subject ate the solid meal, which was easily masticated, over a 5 min period and then drank 150 ml of 10% D-glucose solution containing $^{113m}$In-DTPA. Data collection commenced at the beginning of food ingestion. At 30 min intervals, data acquisition was interrupted for 5 min to allow the subject to stand or sit away from the camera. Each study was continued for at least 2 h.

Data acquisition and analysis

A scintillation camera interfaced to a computer was used for data collection. The energy window alternated regularly between that of $^{113m}$In (393 keV) and $^{99m}$Tc (140 keV) by using an automatic switching device. During the first postcibal 10 min, the energy window alternated every 5 s. Subsequently, this interval was increased to 50 s. At the end of data acquisition, 100 mCi of $^{99m}$Tc-DTPA in 150 ml of water was given orally and a 1 min left lateral image of the upper abdomen was taken to allow for attenuation correction [5].

The computer data comprised list mode files which were reformatted to produce separate dynamic studies for the solid and liquid components. Corrections were made for $^{113m}$In-Compton scatter, attenuation, patient movement and radionuclide decay [5].

By using the computer display, a region-of-interest was drawn to include the whole stomach but excluding the small intestine. For each frame of the study the total counts in the region-of-interest were determined. Histograms for the solid and liquid components of the meal (expressed as a percentage of the total meal remaining within the stomach vs time) were subsequently printed. The value for 100% retention of the meal was derived from the maximum count rate achieved in the first 20 min of the study. Several parameters were derived from these histograms. For the solid component these parameters were: the lag period before onset of emptying, the time for 50% emptying ($T_{50}$), and the percentage retention of food at 100 min after meal completion. For the liquid component, the $T_{50}$ and the amount of tracer remaining at 10 and 20 min after ingestion were obtained.

Statistical methods

Data were analysed by using Student’s $t$-test and linear regression analysis.

Results

Solid emptying

In all subjects solid emptying was slower than liquid and was characterized by a lag period followed by linear emptying (Fig. 1a). There was a significant delay of solid food emptying in the elderly subjects with prolongation of the solid $T_{50}$ ($P < 0.0025$), and increased retention of solid at 100 min ($P < 0.0025$) (Table 1, Fig. 1a).

Liquid emptying

The emptying of liquid was non-linear with a slope that decreased with time and usually followed a mono-exponential pattern (Fig. 1b). Liquid emptying was delayed in the elderly subjects with prolongation of the solid $T_{50}$ ($P < 0.0025$), and increased retention of liquid at 100 min ($P < 0.0025$) (Table 1, Fig. 1b). The falls in percentage retention of liquid between 10 and 20
Age and gastric emptying

FIG. 1. Gastric emptying curves for solid and liquid in control (—, age range 21–62 years) and elderly (……, age range 70–84 years) subjects. Results are mean values ± SEM.

TABLE 1. Solid and liquid emptying in control (age range 21–62 years) and elderly (age range 70–84 years) subjects

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Elderly</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>22</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Solid lag period (min)</td>
<td>35 ±3</td>
<td>32 ±5</td>
<td>N.S.</td>
</tr>
<tr>
<td>Solid T50 (min)</td>
<td>78 ±4</td>
<td>103 ±8</td>
<td>&lt;0.0025</td>
</tr>
<tr>
<td>Solid retention at 100 min (%)</td>
<td>33 ±3</td>
<td>50 ±4</td>
<td>&lt;0.0025</td>
</tr>
<tr>
<td>Liquid T50 (min)</td>
<td>19 ±1</td>
<td>25 ±3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Liquid retention after 10 min (%)</td>
<td>68 ±2</td>
<td>80 ±4</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Liquid retention after 20 min (%)</td>
<td>47 ±2</td>
<td>56 ±4</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

min and 10 and 100 min were not significantly different between the two groups.

Relationship between age and solid and liquid emptying

Analysis of the gastric emptying curves of all 35 subjects revealed a positive correlation between age and solid (T50; \( r = 0.42, P < 0.01 \)) and liquid emptying (percentage remaining at 10 min; \( r = 0.36, P < 0.05 \)). The regression line indicated that the solid T50 was approximately 32% greater at age 70 than at age 20 years (Fig. 2).

A positive correlation existed between solid and liquid emptying rates in both elderly and control subjects (T50; \( P < 0.01 \)). There was no difference in emptying rates between men and women and there was no correlation between subject body weight or surface area and solid or liquid gastric emptying rates in either the elderly or control subjects.

Discussion

Simple observation tells us that many physiological functions are retarded with age, and direct measurements of function from the immune system [19] to the musculoskeletal system [20] confirm this. There is a paucity of information on the effect of ageing on the gastrointestinal system. A reduction in oesophageal peristalsis in patients over 70 years of age has been documented [21]. The absorption of nutrients such as 3-methyl-glucose, galactose, calcium and iron [7, 8] is reduced with increasing age, suggesting that some small intestinal transport processes may be less functional in the elderly [22]. Most of the available data concerning age-related changes in
the structure and function of the stomach pertain to the gastric mucosa. Atrophic changes in the gastric mucosa are more common with increasing age [23], and both basal and maximal (histamine stimulated) acid secretion are reduced [24].

We have demonstrated that increasing age is associated with a reduction in gastric emptying of both solid and liquid meal components. The delay in liquid emptying was in the early phase of gastric emptying. These findings did not relate to differences between the two groups in subject sex or body weight.

The emptying of solids and liquids is dependent on different portions of the stomach. A major factor controlling the emptying of liquids is the pressure gradient across the gastroduodenal junction, which is dependent on the tone of the proximal stomach [2]. In contrast, digestible solids may be emptied by a dual process: a grinding and mixing function of the antrum which reduces solid food to small particles and an emptying process by which the small particles are emptied with the liquid [1]. The emptying process for solids may be dependent on propulsive forces mainly dependent on fundal tone. The delay of solid emptying in elderly subjects may therefore reflect either a reduction in mixing function of the antrum and/or a reduction in proximal stomach tone. Our findings suggest that changes in function of the proximal stomach and possibly the antropyloric musculature accompany the ageing process.

A deficiency of all radionuclide methods is that gastric emptying of the solid and liquid marker is measured and the effects of dilution by gastric secretion cannot be quantified. This limitation applies particularly to water soluble radiolabelled markers and it is thought that gastric emptying of solids is more reliably evaluated and largely independent of the volume of intragastric liquid [1]. Therefore differences in gastric secretion rates could theoretically have influenced the results. However, the delay in liquid emptying observed in the elderly subjects was apparent soon after meal consumption when the effects of gastric secretion would be minimal.

Some previous investigators [16, 17] found no change in gastric emptying with increasing age. Van Liere & Northup [17] used fluoroscopy to measure gastric emptying of a high carbohydrate meal into which barium sulphate had been incorporated. It is not surprising that these authors found no correlation between gastric emptying and age, as contrast studies using barium have limited usefulness in determining even major alterations in gastric emptying because of the inability to quantify emptying accurately. Halvorsen et al. [16] studied gastric emptying of water using an intubation technique in 19 subjects (age range 22–63 years). The small changes in liquid emptying we have observed may not have been apparent [16] both because of the non-physiological nature and inherent inaccuracies of the technique used and the smaller age range of the subjects studied. More recent studies have used radioisotopes to measure gastric emptying. Wright et al. [25] found no correlation between solid or liquid gastric emptying rates and age in 31 control subjects, but the maximum age was 62 years. Evans et al. [18] found that gastric emptying of a liquid meal was considerably delayed in elderly patients, but these findings must be viewed with uncertainty as all of their elderly patients had multiple pathological conditions (six out of 11 had Parkinson’s disease) and the patients’ physical illness and the medications they were taking may have affected gastric emptying. For this reason, we selected a patient group which had no significant medical illness and was not taking any medication. Moore et al. [26] recently reported a delay in liquid emptying in fit male
elderly subjects. These authors used a radioisotope method similar to our own but studied a smaller group of subjects and perhaps because of this did not observe any change in solid food emptying.

Our results indicate that the effect of ageing should be taken into account when defining normal ranges or in selecting control subjects for gastric emptying studies.

The rate of gastric emptying can be an important determinant of oral drug absorption in humans [11]. Divoll et al. [12] noted that elderly subjects (mean age 71 years) have a slight but significant reduction in oral paracetamol absorption. This observation is consistent with the delay in liquid emptying we have demonstrated, as paracetamol absorption correlates with the rate of gastric emptying [27]. However, there appears to be no significant alteration in the absorption kinetics of oral oxazepam, lorazepam [13], diazepam [14], tetracycline [28], or L-dopa [29] in elderly subjects and apart from paracetamol it seems likely that the slight delay in gastric emptying does not significantly affect drug absorption.

It must therefore be emphasized that the changes in gastric emptying we have demonstrated are small and unlikely to be of clinical significance. In fit, elderly subjects, gastric emptying rates for solids and liquids are usually within the 'normal' range found in younger control subjects, and the previously reported major delay in gastric emptying in elderly patients [18] was likely to be due to associated disease and/or drugs rather than ageing itself.

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References


