Gastric Emptying in Children

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This article reviews the evaluation of gastric emptying in children with emphasis on scintigraphic techniques. The mechanism of emptying as well as how quantitation may vary with patient positioning, the composition of the standard meal and possibly the size of the meal are discussed. Preliminary data suggest that for children under the age of 2 yr, meal size is less critical. Although normal ranges need to be determined by individual laboratories, values reported in the literature may be used as a guide. Quantitation is useful for the follow-up of patients on therapy.

Key Words: gastric emptying; scintigraphy; children

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When a meal enters the stomach, the fundic smooth muscle relaxes. There is thus only a small rise in pressure as the volume increases. Gastric receptive relaxation has been shown to be absent in the newborn and this may explain, in part, why gastroesophageal reflux is more frequent in newborns than in older infants (*1*). An increase of tonic intraluminal pressure in the fundus is necessary for the emptying of liquids, whereas antral peristalsis is necessary for the emptying of solids. Antral contractions, initiated by solids, may also, however, play a role in liquid emptying (*2*). There are no peristaltic contractions in the stomach in the first 2–4 days of life (*3*). Gastric peristalsis in the distal half of the stomach, in coordination with the pylorus, is important for both propagation and mixing. The antropyloric region restricts the emptying of particles larger than 1 mm in diameter. Larger particles are triturated and then emptied with the liquid phase. The trituration process, during which time solid emptying does not occur, gives rise to the lag phase. There is usually no lag phase as milk empties, and it would seem that functions of the fundus are important. However, solids are formed in the stomach during digestion, which may explain, in part, the varying rates of emptying with different types of milk feedings.

It is clear that motor functions of the proximal stomach, antrum, pylorus and duodenum are closely integrated and not independent (*4*). The gastric motor response is mediated largely through the vagus. Several gastrointestinal hormones such as gastrin, secretin, cholecystokinin and gastric inhibitory peptide, delay gastric emptying (*5*). Although liquids empty more rapidly than digestible or indigestible solids, other factors relating to the meal are important. Emptying is prolonged with larger meals, although it is the caloric content that is important rather than the weight (*6,7*). Increasing osmolality delays emptying in adults (*8–10*) but within limits does not affect premature infants and normal newborns (*11,12*). Cow's milk empties at a slower rate than human milk, even though they are isocaloric (*13*). Emptying is more rapid with whey-based than with casein-based formulas, even with similar osmolality, caloric or fat content (*14*). An exception is acidified milk, which also has been found to empty rapidly (*15*). Gastric emptying also is delayed with fatty acids having specific carbon chain lengths (*16*), with physiological concentrations of L-tryptophan (*17*) and with increasing concentrations of acid solutions (*18*). It is clear that for the quantitation of gastric emptying, the size and composition of the meal should be standardized. However, as discussed later, when studying sick infants and children, this is not always possible.

ASSESSMENT OF GASTRIC MOTOR FUNCTION

The earliest methods to study gastric emptying and gastric secretion required the aspiration of gastric contents. Marker dilution tests have been widely used in infants and children (*19*). Other techniques for assessing gastric function have been reviewed briefly (*20*). Sonography is noninvasive and provides a detailed but short-term evaluation of antropyloric function (*21*). Motor abnormalities have been evaluated in children with dyspeptic symptoms (*22*).

Widespread application is limited because it is operator-dependent, and the observation time is short. The role of MRI has not yet been determined, although it has been used to measure gastric emptying and the intragastric distribution of the meal (*23*). Electrical impedance methods can measure gastric emptying (*24*), and although a good correlation with scintigraphic methods has been used, both liquid and solid emptying are subject to considerable noise (*25*). More recently, electrogastrography has been used clinically. Gastric electrical activity now can be reliably recorded from surface electrodes, and there have been several reports in children of abnormal rhythms associated with delayed emptying and various symptom patterns (*26,27*). The dominant frequency of about 3 cpm is observed in children and adults, but in newborn infants there is a developmental pattern, with the percentage of 2–4 cpm increasing with age, that could be attributed to the normalization of tachygastria (*28*). Digital antral scintigraphy recently has been described in adults. Processing the data using a refined Fourier transform allows the visualization of antral contractions. In healthy individuals, antral frequency and amplitude correlated inversely with the lag phase, emptying rate and total gastric emptying course. Potentially, this technique allows the characterization of gastric motility and the evaluation of pathophysiological mechanisms of gastric disorders (*29*). Whether this technique will have an application in pediatric nuclear medicine remains to be seen. Scintigraphic techniques with radiolabeling of the liquid, solid or both components of the meal have become the mainstay of the evaluation of gastric function in clinical practice. They have been adapted for use in infants as well as older children.

SCINTIGRAPHIC EVALUATION OF GASTRIC EMPTYING

Delayed gastric emptying may be suspected in infants presenting with vomiting, abdominal discomfort, early satiety with long intervals between meals and chronic constipation. Abnormally rapid emptying may be seen infrequently, associated with "dumping" and diarrhea.

In infants, the usual milk or formula feeding is suitable as the test meal. When ^{99m}Tc-sulfur colloid is added, the mixture

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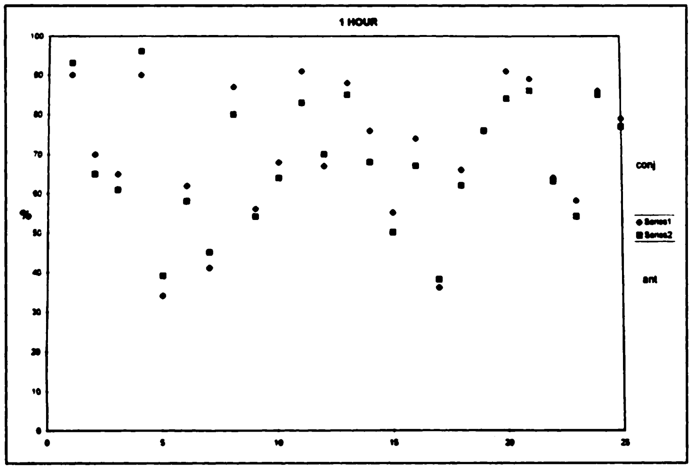

FIGURE 1. Scatterplot showing the percentage of gastric residual at 1 hr, comparing anterior counting with the conjugate mean in 25 infants. The differences are small and anterior counting alone is satisfactory.

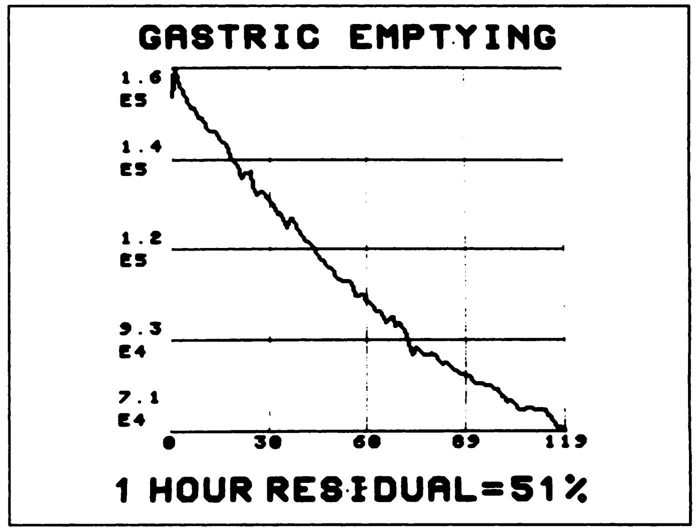

FIGURE 2. Normal gastric emptying.

remains stable in an acid medium. Because the evaluation of gastric emptying is usually performed in conjunction with that for gastroesophageal reflux, the dose may vary from 7.4 MBq (200 μCi) to 37.0 MBq (1.0 mCi). Smaller doses can be used when gastric emptying alone is of interest (3.7–7.4 MBq). Ideally, the volume administered should be standardized according to the patient's age or size. In practice, many patients are on modified diets, and the test meal is adjusted accordingly. The tracer is placed in the usual food and is preferably given orally, or if necessary by tube feeding. Some prefer to give one-half the unlabeled feeding followed by the radioactive dose in a small volume and then the remaining food. This avoids inadequate total activity of the tracer should the total feeding volume not be consumed (*30*). Patients usually are positioned supine, although it has been shown that right lateral and upright imaging significantly increases the rate of emptying, and it has been suggested that the study be complemented with further imaging in these projections (*31*). Even with supine imaging, the rate of emptying may increase in the second hour, so that if emptying is delayed at 1 hr it should be extended until the end of the second hour (*32,33*). A normal gastric residual at 2 hr should be indicative of normal gastric emptying, provided that the time-activity curve does not have an abnormal configuration. The camera may be positioned anteriorly or posteriorly. Conjugate counting does not significantly change the result when compared with anterior imaging alone (*34*), so obtaining both anterior and posterior images is not necessary (Fig. 1). Computer acquisition of the data is continuous in infants and small children, at a framing rate of 30–60 sec in 128- or 64-word mode matrix.

When analyzing the study, a region of interest is placed around the stomach, as seen in the immediate postfeeding image. A time-activity curve, corrected for decay, is generated from this region. If there has been significant patient movement or if the region overlaps small-bowel activity in later frames, it is necessary to generate separate regions at approximately 15-min intervals. The decay-corrected data then are plotted on semilog paper for analysis. As mentioned earlier, it may be necessary to include data up to 2 hr. Gastric emptying has been expressed as the half emptying time ($T_{1/2}$), the percentage of the initial activity remaining at specific time points (R%) or the activity emptied by the stomach at these times (100 − R%). Because milk usually empties in an exponential or biexponential manner, $T_{1/2}$ measurements may be meaningful. Some individuals, however, display different emptying patterns, so that abnormal individuals are not always separated from normal individuals with this parameter. It is usual to express gastric emptying as either R% or (100 − R%) over 60–120 min. A graphical representation of the process will reveal any abnormal pattern of emptying (*35*).

Normal gastric emptying rates in infants and children have been difficult to establish because of the unavailability of normal control subjects. For ethical reasons, normal individuals cannot be studied. It also is not possible to directly compare interinstitutional results because of a lack of standardization of the technique with regard to patient positioning and the test meal. It is important for individual laboratories to determine an acceptable normal range. There are reports in the literature that may act as a guide. In one study, normal infants were fed 50 ml milk labeled with ^{113m}In-micro colloid, and gastric emptying was found to be exponential 10–100 min after feeding, with a $T_{1/2}$ of 87 ± 29 min. A diphasic pattern was found in a small number of infants, which was attributed to swallowed air (*36*). Extrapolation of these data indicate a gastric residual of between 48% and 70% at the end of 1 hr. My own data support this range in infants. In another study, using a ^{99m}Tc-sulfur colloid tag and milk feeding volumes according to age, patients who were evaluated retrospectively were thought to have normal emptying. At 1 hr, the gastric residual was between 36% and 68%. In a small number of older children, the range was between 42% and 56% (*35*). Dextrose labeled with ^{99m}Tc-sulfur colloid was found to empty with a residual of 27%–81% at 1 hr in children under 2 yr of age. In children older than 2 yr, the range was between 11% and 47%, suggesting that the normal rate of emptying is age related (*37*). This age-related dependence also has been reported by others (*38*). Thus, when deciding on the normal rate of gastric emptying in infants and children, both the composition and volume of the test meal as well as the age range should be considered.

Not only is the gastric residual at a given time point important in determining whether emptying is normal but so is the shape of the gastric time-activity curve. Emptying may be intermittent, and a delayed plateau emptying pattern has been described with gastric outlet obstruction as with the antral membrane (*35*). Time-activity curves, corrected for decay, may show the emptying to be normal, delayed at 1 and 2 hr, delayed at 1 hr but normal at 2 hr, or there may be a plateau pattern as described with intermittent gastric obstruction (Figs. 2–5).

In older children, the emptying of a solid, or a combined solid and liquid meal, can be measured. For solids, it is important that

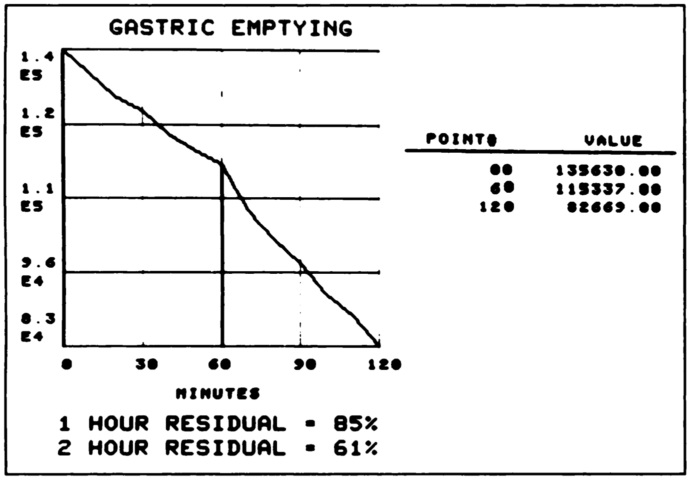

FIGURE 3. Gastric emptying is delayed, with increased gastric residuals at 1 and 2 hr.

the radiolabel remain firmly associated with the solid phase. For clinical studies, the labeling of eggs, either the whole egg or the egg white, with ^{99m}Tc-sulfur colloid has been satisfactory for quantitation (*39*), although not as firm as labeled chicken liver. Other possibilities are in vitro-labeled chicken liver (*40*), an iodinated fiber (*41*) or ^{99m}Tc-labeled bran (*42*) or pudding (*38*). When combined solid and liquid emptying is evaluated, the solid phase is usually labeled with ^{99m}Tc-sulfur colloid and the liquid (water) with ^{111}In-DTPA. The ^{99m}Tc-to-^{111}In activity ratio should be at least 6:1 to minimize the downscatter from the ^{111}In into the ^{99m}Tc window. Suitable doses in children are 11.1 MBq (300 μCi) of ^{99m}Tc-sulfur colloid and 1.85 MBq (50 μCi) ^{111}In-DTPA. Because there is some variation between emptying in the upright and supine positions, standardization of the imaging geometry also is important, as is the meal composition and size (*43,44*). Because liquids generally empty more readily than solids, solid emptying alone should probably be quantitated in children to reduce the radiation burden. However, liquids do influence the rate of gastric emptying, so the standard meal should include unlabeled liquid. A suggested meal is based on two whole eggs as a sandwich and 300 ml water per 1.73 m^2, scaled according to the patient's size. Imaging is begun immediately the meal is consumed. Thirty-second images are obtained with the patient supine and is repeated every 10 min for 2 hr. Between images, patients are upright. Gastric emptying is determined from the decay-corrected counts in each frame.

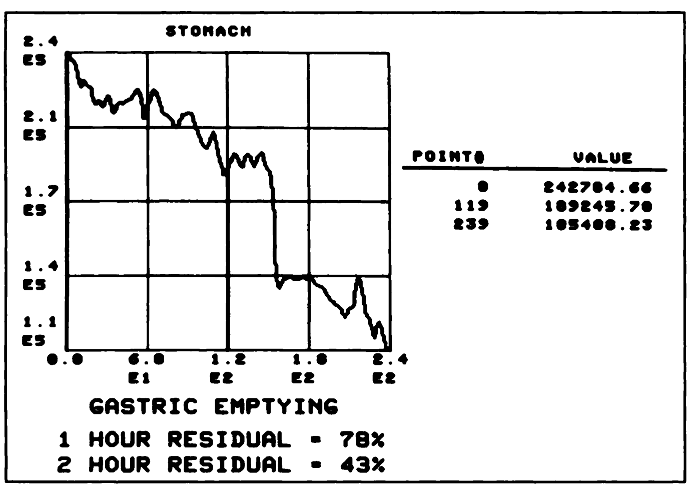

FIGURE 4. Gastric emptying is somewhat delayed at 1 hr, with a residuial of 78%. There is more rapid emptying in the second hour, with a residual of 43%. In this case, gastric emptying is considered normal.

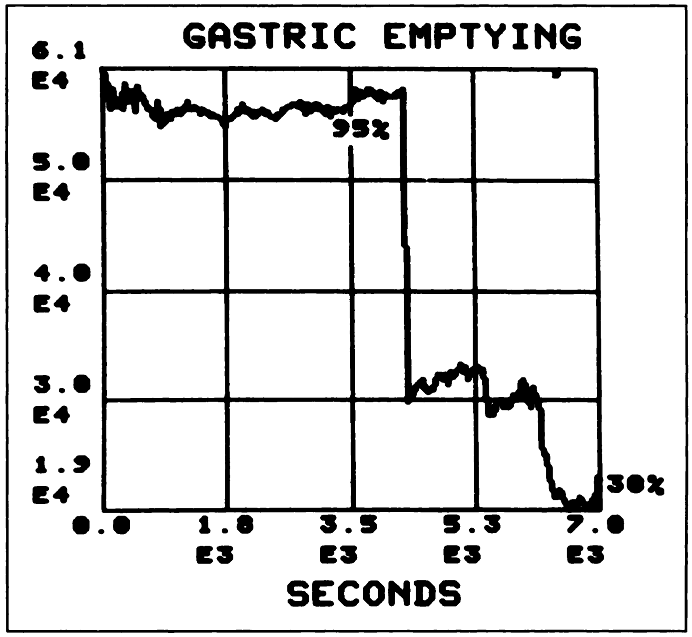

FIGURE 5. Example of intermittent gastric emptying, or a plateau pattern. It has been described with intermittent outlet obstruction, such as an antral web.

Using a reregistration program, the study can be displayed in cine mode and a time-activity curve can be constructed. As in the case of infants, normal children have not been studied, so that the physiological range of solid emptying has not been reported. As a guide, one may use the control values in normal young adult volunteers using the anterior projection (*39*). These values for both liquids and solids, expressed as the percentage residual gastric activity over time, are depicted in Figure 6. In adults, it has been shown that correction for attenuation is necessary as food moves from the relatively posterior fundus to the more anterior gastric antrum. Corrective techniques described include geometric mean counts (*45*), peak-to-scatter ratios (*46*), lateral (*47*) and left anterior oblique views of the stomach (*48*). I have studied several children and believe that in younger patients, anterior imaging alone is satisfactory (Fig. 7). A correction is probably important with large meals, obesity and older patients.

Sources of error using the radionuclide technique include

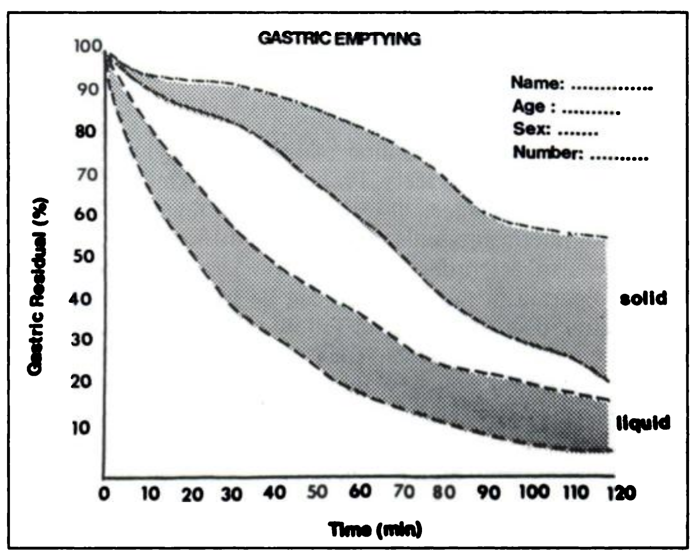

FIGURE 6. Normal gastric emptying of solids and liquids in young volunteers, expressed as percentage gastric residual with time (adapted from Ref. 39).

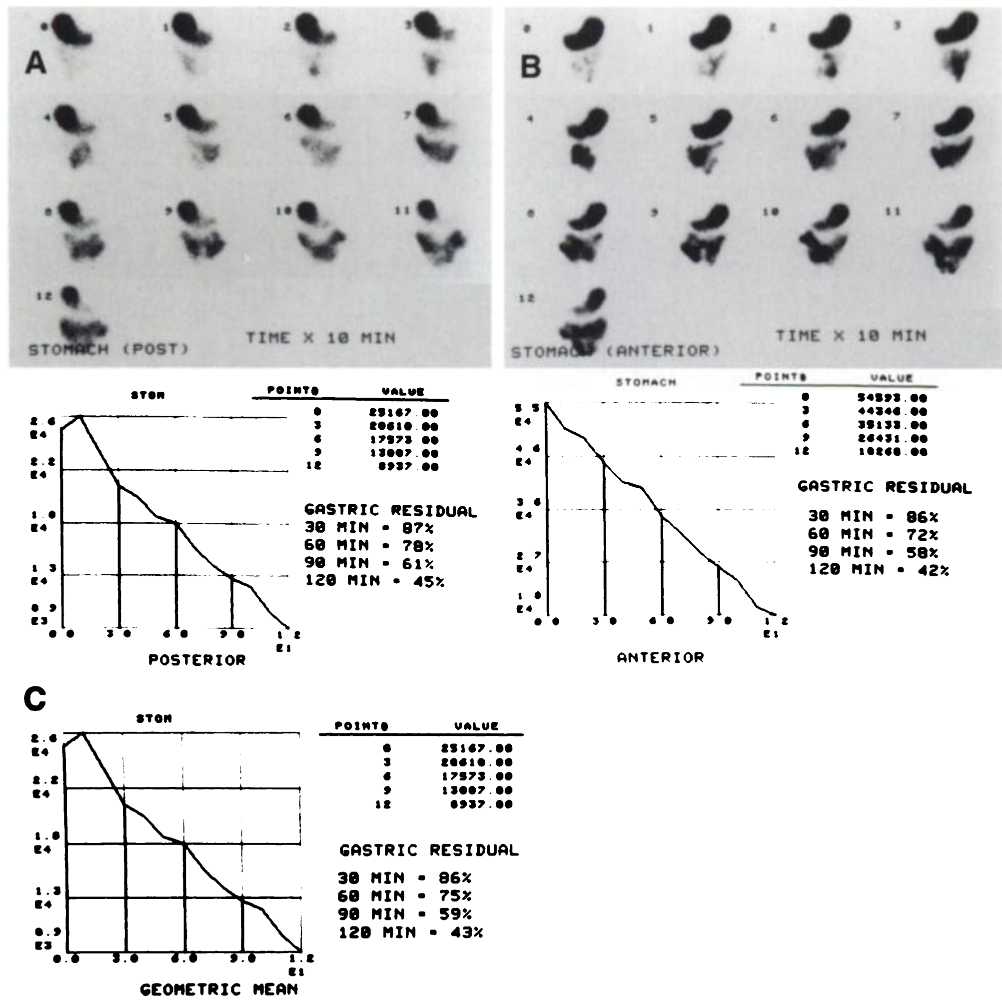

FIGURE 7. The curves show the gastric emptying of a solid meal in a 1-yr-old boy, as determined from: anterior, posterior and geometric mean counts. Anterior imaging alone is usually satisfactory for determining the emptying of solids in young children.

overlap of gastric and duodenal activity, scatter from adjacent bowel activity into the stomach, scatter when two radionuclides are used, and postero-anterior movement within the stomach. Errors from scatter of gut activity are small (*49*). With blurring of the gastric border, it may be useful to extend the acquisition somewhat to allow clearance from the duodenum. With dual isotopes, scatter correction factors must be determined with phantom studies with the specific collimator and gamma camera to be used. These corrections must be subtracted before decay corrections are performed (*39*). Decay correction is essential for the shorter lived isotope.

CONCLUSION

The scintigraphic evaluation of gastric emptying in infants and children is used widely. Problems with standardization of the food and differences in technique, with regard to positioning, make interinstitutional comparisons difficult. Each laboratory needs to determine its own normal range, although the values reported in the literature can be used as a guide. The quantitative data are useful in follow-up studies to assess the effect of prokinetic agents, such as cisapride or metoclopramide. Recent data suggest that there may be an association between tachygastria and gastric motor quiescence (*50*). It remains to be seen whether more detailed scintigraphic analysis, such as antral contractility, is possible in children and whether this will lead to more targeted therapy.

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Erratum

The p value in the 4 hr column of the Lung row in Table 1A in the article, "Early Detection of Bleomycin-Induced Lung Injury in Rat Using Indium-111-Labeled Antibody Directed Against Intercellular Adhesion Molecule-1," by Weiner et al. (*JNM* 1998;39:723–728) was printed incorrectly. The correct p value is < 0.001.