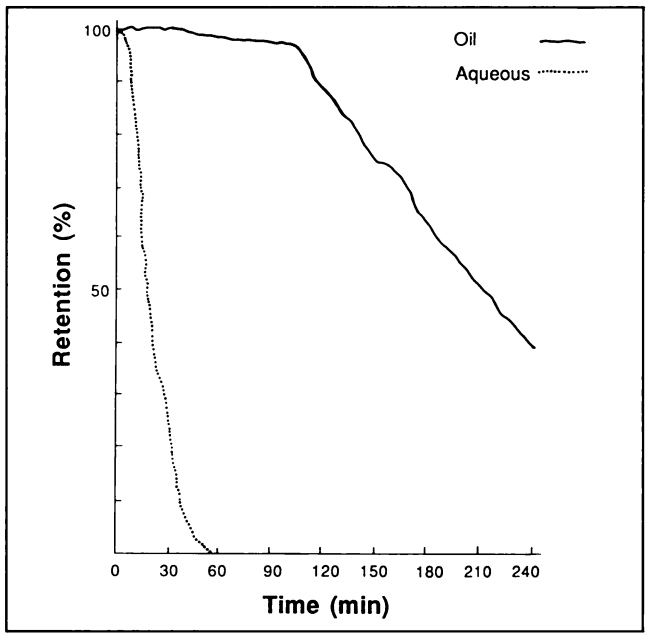

FIGURE 4. Emptying curves for oil and aqueous phases in a volunteer (same as for Fig. 3) who ingested 290 ml of beef consomme soup (labeled with ^{113m}In-DTPA) blended with 60 g of olive oil labeled with ^{99m}Tc(V)thiocyanate.

ble as lipid labels because the pertechnetate formed will rapidly return to the aqueous phase.

Radionuclide methods have confirmed that there are significant differences in the rates at which different food components (digestible solids, nondigestible solids, liquids, and fats) empty from the stomach in humans (*1–7, 12, 16*). Technetium-99m is the preferred radionuclide for imaging purposes because of its low cost, low radiation burden, and favorable gamma ray energy. We believe that ^{99m}Tc(V)thiocyanate is a valuable addition to the range of pharmaceuticals that may be used to study gastric emptying.

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EDITORIAL

Considerations for Accurately Measuring Gastric Emptying

In this issue, Cunningham et al. describe a radiopharmaceutical for measuring the gastric emptying of fat (*1*). The choice of radioactive markers is one of several important considerations in accurately measuring the rate of gastric emptying.

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RADIOPHARMACEUTICAL

First, it is important that food be used as the marker of gastric emptying. Hunt and Stubbs have shown non-nutrient saline meals empty rapidly with exponential (first-order) kinetics, whereas nutrient meals show an initial emptying period that loads the duodenum, followed by a more linear (zero-order) emptying curve (*2*).

Second, solid-phase markers should be used. The mechanism of liquid

emptying is different from solid emptying and liquids may give normal emptying times in the presence of disease (*3*). Liquid emptying is primarily dependent on the effects of gravity and the pressure gradient between the stomach and duodenum.

The control of post-prandial solid emptying is much more complex. Studies in dogs indicate solid food must be reduced to a maximum size of 1 mm before it can enter the duodenum, with the majority of particles passed measuring 0.06 mm or less (*4*). Surprisingly, the fragmentation of food is primarily dependent on the coordinated contraction of the stomach walls. In fact, although enzymatic digestion may contribute to fragmentation, it is not necessary and normal emptying rates can occur in its absence (*6*). This grinding activity is dependent on the antrum rather than the fundus and is controlled by the post-prandial propagation of peristaltic waves (*3*). Solids can also empty the stomach via powerful Phase III interdigestive migrating motor complex (MMC) contractions that occur between meals. These powerful lumen-obliterating contractions are stimulated by motilin. Their purpose is to empty the stomach of indigestible debris and fasting contents. Erythromycin, shown recently to enhance gastric emptying in diabetic gastroparesis, does so by binding to motilin receptors (*7*).

Meal caloric content must also be considered. Using liquid-meal emptying times determined by a tube-indicator recovery technique, Hunt and Stubbs showed gastric emptying was slowed with increasing caloric density (kcal/g) (*8*). Equicaloric concentrations of lipid, carbohydrate, and protein produced equal slowing of gastric emptying rates. This concept is sometimes referred to as the Hunt and Stubbs hypothesis and states that gastric emptying is controlled by the nutrient density (total kcal/total g or ml of food) entering the duodenum (*9*). Studies using radionuclide techniques with solids have been consistent with this hypothesis (*10,11*). A 300-g meal with a total caloric content of 68 kcal emptied with a half-time of 73 min, while a similar-sized meal containing 633 kcal emptied with a half-time of 214 min (*11*).

Studies have indicated that an even more important criterion is meal size or weight (*10,11*). As meal size increases, gastric emptying slows. Meals of 300, 900, and 1692 g caused solid emptying times of 77 min, 146 min, and 277 min, respectively; liquids showed half-emptying times of 40 min, 81 min, and 178 min, respectively (*10*). When caloric content and meal weight are compared, the slowing effect of added calories is not sufficient to overcome the enhancing effect of increasing meal weight. In a study using meals of equicaloric content, a 300% increase in meal weight resulted in a 388% increase in absolute emptying rates, while a 304% increase in total meal calories caused only a 43% reduction in absolute emptying rates (*11*).

Stability of the solid-phase tag is also important. If the tag elutes, it mixes with the liquid phase, giving a partly solid, partly liquid, emptying time. To prevent problems from tag elution, Meyers et al., developed an in vivo technique for labeling chicken liver (*12*). Stability is excellent: 97%–98% of the tag is still associated with the liver after 4 hr of incubation in gastric juice or hydrochloric acid. Unfortunately, the technique is inconvenient, requiring the injection and sacrifice of live chickens. Until recently, alternative techniques have given much higher dissociation percentages (*13,14*).

A simple labeling technique of liver that does not require live chickens has recently been developed (*14*). This technique involves frying liver pate in a mixture of ^{99m}Tc-sulfur colloid. Incubation studies indicate 92%–93% of the tag remains bound at 4 hr. This is more than adequate for gastric emptying studies.

Finally, the radioisotope chosen for marking the food must be considered. Higher-energy isotopes are attenuated less; however, equivalent activities of ^{99m}Tc- and ^{111}In-labeled chicken liver have markedly different dosimetries. Compared to ^{99m}Tc, 500 μCi of ^{111}In-labeled chicken liver results in a stomach dose 4 times higher, a large intestine dose 20 times higher, and a total-body burden 12 times greater (*15*).

TECHNIQUE

Patient positioning must be standardized. A study of the rate of gastric emptying in subjects in four different positions (recumbent, sitting, standing, and alternate sitting-standing) indicated the recumbent position slowed gastric emptying by 102% compared to sitting-standing (*16*). How recumbency slows gastric emptying is unknown, but likely it is related to meal pooling, reduced antral distention, and lack of a gravitational effect. Because exercise, even walking, enhances gastric emptying, it is important that subjects remain quiescent between imaging sessions (*17*).

The interval between imaging can also affect accuracy. Obviously, the fewer the data points, the more likely the true half-emptying time will be missed; the controversy about the presence or absence of an initial solid-phase lag period is partly related to this problem (*18*). Studies with continuous monitoring show a short initial lag phase (8 min), which could be missed easily if sampling is done only at 10–15-min intervals, as is frequently the case. Continuous monitoring has another advantage: it prevents the patient from falsely enhancing gastric emptying by walking between imaging sets.

Patient motion during acquisition or inaccurate repositioning will cause errors, usually falsely shortened emptying times (*19*). This is because stomach activity will move outside the outline of the stomach region of interest, falsely lowering the counts measured.

Repositioning is frequently done by marking the stomach region with a wax pencil on the persistence scope. The patient is positioned with the stomach activity within this area at the beginning of each imaging session. A better method is to tape a small

point-source marker of ^{57}Co or ^{99m}Tc on the patient's skin (*3*). The location of the marker is drawn on the persistence scope at the first imaging session. Then the patient is positioned with the marker in the drawn region each time. If both anterior and posterior imaging are performed, a second marker should be placed on the patient's back. Not only do the markers permit accurate vertical and horizontal repositioning, they allow any patient motion during image acquisition to be discovered. Motion artifacts can be corrected by drawing a new region of interest for each image set.

Depending on the radionuclides used, decay correction may be necessary. Isotopes with short half-lives, such as ^{99m}Tc or ^{113m}In, must be decay-corrected or the emptying time will be underestimated (*20*). This is especially important for patients with significantly delayed emptying. Indium-111, on the other hand, with its 2.7-day half-life, does not require correction.

In simultaneous solid-liquid phase studies using ^{99m}Tc and ^{111}In as the markers, a correction for crosstalk must also be made (*20*). Using more activity of the lower energy isotope than the higher-energy radionuclide helps minimize the effects of down-scatter. In addition, estimates can be made of the amount of down-scatter into the lower energy window; these counts can then be subtracted from the measured counts in the lower-energy window. Since correction factors depend on the relative amounts of activity used for each radionuclide, the window width, and the recorded percentage of scatter into the lower window, it is best to experimentally determine the degree of crosstalk from phantom or patient studies and use this number for correction.

Gastric emptying studies are a dynamic process in which the radiolabeled food progresses from an initial posterior position in the fundus to the more anteriorly-located antrum. If imaging is performed from the anterior position only, an artifactitious increase in counts occurs as the radionuclide's depth within the body decreases and attenuation plus scatter are reduced (*3,20*).

How important are these effects? Studies indicate gastric emptying rates are underestimated (half-times overestimated) by an average of 38% using a standard 300-g meal (*21*). Errors as large as 87%, however, are seen in individual patients. The effect varies with meal size (*20,21*).

There are several approaches for correcting for depth and attenuation. We use opposed detectors and geometric mean correction. At each imaging session, anterior and posterior counts in the stomach are recorded. The geometric mean is calculated by: (anterior counts × posterior counts)1/2. Phantom studies indicate the calculated geometric mean gives count rates that vary less than 2% for depths of 2.5–20 cm (*21*).

An alternative approach for correction of depth and scatter (as well as septal penetration) is to use the peak-to-scatter (P/S) ratio (*20,22,23*). Studies of ^{113m}In with its 392-keV photon, indicate attenuation is less important than scatter and septal penetration, when compared to ^{99m}Tc. Errors of 30%–40% have been found with ^{113m}In. Studies indicate a correction factor generated from the P/S ratio may give equivalent results to geometric mean correction (*22,23*). Investigations into the use of the P/S ratio in linear profile scanning, however, indicate the P/S ratio method may be more sensitive than the geometric mean technique to variations in source volume and other distribution effects (*24*). In particular, the P/S ratio can be changed by scatter from sources completely outside the field-of view of the camera. Therefore, it is not clear that the P/S ratio method offers any advantage compared to the simpler geometric mean correction technique.

PHYSIOLOGIC VARIABLES

In establishing and applying normal emptying values, several points must be considered. First is the time of day of the study. Circadian rhythm affects gastric emptying as it does other physiologic processes (*25*). In a study of healthy subjects who underwent identical gastric emptying studies at 8 a.m. and at 8 p.m., evening emptying rates were significantly slower than morning rates. Therefore, it is important that gastric emptying studies always be scheduled at the same time each day to ensure that established normal values apply.

Even more important is to establish different normal values for males and pre-menopausal females. In the past, it was assumed men and women had identical rates of gastric emptying. Normal values were usually established in male volunteers and then applied to both sexes; however, studies of normal pre-menopausal women have shown they have significantly slower gastric emptying than men. Since post-menopausal women have much more rapid emptying, equal to that of men, female sex hormones appear to inhibit gastrointestinal motility (*27*).

Estradiol and progesterone may slow gastric emptying by two mechanisms. Estradiol receptors have been identified in gastrointestinal tissues and progesterone receptors are likely present as well (*26*). Female sex hormones may, therefore, directly affect motility. Second, motilin, a gastrointestinal hormone with smooth muscle-stimulating effect is decreased in pregnancy. Progesterone may act indirectly in slowing gastric emptying by decreasing plasma levels of motilin (*26*).

Finally, subjects need to be at ease during the gastric emptying exam. Physical stress slows gastric emptying, and mental stress may do the same (*28*).

Gastric emptying studies are a useful tool for investigating normal physiology and detecting gastrointestinal disease. Strict attention to detail when carrying out the studies is necessary, however, to ensure accurate results.

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