USE OF ^{99m}Tc-DTPA FOR MEASURING GASTRIC EMPTYING TIME

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A rapid and easy isotopic method for measuring gastric emptying time (GET) is described. It involves the use of ^{99m}Tc-diethylenetriaminepentaacetic acid (DTPA) and a gamma camera with a computer. Results of animal experiments and 24 studies in 8 normal volunteers are presented. The radiopharmaceutical is neither absorbed from nor adsorbed to the stomach in any significant amount. Our experimental data show less than 1% absorption and less than 1% adsorption of the compound in 30 min. The mean gastric emptying $T_{1/2}$ for a liquid meal in normal subjects was found to be 12 ± 3 min. Since ^{99m}Tc-DTPA fulfills the criteria as an ideal agent for measuring GET and the technique is noninvasive with reproducible results, it may have a potential clinical use.

The saline load test (*1*) has been proposed as a simple and accurate means of identifying the presence of gastric retention. Briefly, this test requires rapid filling of the stomach with a known volume of isotonic saline through a nasogastric tube and after 30 min, aspiration of the gastric contents and measurement of the retained volume. More recently, isotopic methods (*2–5*) used after swallowing a test meal containing one of several poorly absorbed radiopharmaceuticals have been tried as another means for evaluating gastric emptying by measuring radioactivity with an external detector. There are, however, certain disadvantages like false high value due to the use of uncollimated external probe, blind positioning of the probe, high-energy scatter from the adjacent intestinal radioactivity, and unreliable results from counting the dots from a rectilinear scan.

To overcome these difficulties, we have evaluated in the present study the use of ^{99m}Tc-DTPA as a gastric emptying time determining agent in dogs and eight normal healthy human volunteers. A gamma camera coupled to a computer was used for this purpose.

MATERIALS AND METHODS

Radiopharmaceutical. Technetium-99m-labeled diethylenetriaminepentaacetic acid (^{99m}Tc-DTPA) chelate was prepared from the kit (Renotec) supplied by Squibb.

Animal experiments. These were first carried out to study the absorption and adsorption of ^{99m}Tc-DTPA. A group of four dogs was fed ^{99m}Tc-DTPA in 250 ml of normal saline. Serial blood samples up to 60 min were drawn from these dogs and the radioactivity in these blood samples was assayed. At the end of blood sampling, the animals were sacrificed. The radioactivities of the gastrointestinal content, whole stomach without content, thyroid, kidneys, and urine obtained directly from the bladder were determined.

Studies in normal human volunteers. The suitability of ^{99m}Tc-DTPA as an agent for measuring GET was then evaluated in eight normal human volunteers, each having three studies on separate days. None of the subjects were taking anticholinergic drugs or had undergone previous gastrointestinal surgery. Prior approval from the Human Use Subcommittee and the informed consent from the normal volunteers were obtained. The subjects were fasted overnight and smoking was forbidden during this period. After supine positioning under the gamma camera, the subjects consumed 1 mCi ^{99m}Tc-DTPA in 500–700 ml normal saline over a maximum period of 1 min. Dynamic scintiphotos (every 10–20 sec frame) of the abdomen were recorded on a magnetic tape over a period of 20–30 min. At the end

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TABLE 1. TISSUE DISTRIBUTION OF RADIOACTIVITY 30 MIN AFTER ORAL ADMINISTRATION OF ^{99m}Tc-DTPA IN FOUR DOGS

	Percent radioactivity after 30 min			
Dog	Blood & urine	Thyroid & kidneys	GI content	Stomach without content
1	0.59	0.12	94	1.12
2	0.52	0.09	93	1.01
3	0.47	0.08	97	0.86
4	0.39	0.06	101	0.94
Mean	0.49	0.09	96	0.98
± s.d.	±0.08	±0.02	±3.6	±0.11

of the study, a dynamic readout of the computer data (integrated count over the flagged gastric area) was obtained. The gastric activity was plotted against time on a semilog paper. The graph was analyzed and the disappearance half-time of ^{99m}Tc-DTPA from the stomach was determined. The disappearance curves of subjects who had duodenal or jejunal overlap were also analyzed. In two of these subjects, urine and blood samples collected during the study were assayed to detect the concentration of radioactivity.

Effect of geometry on counting rate. Experiments with balloons were carried out to check the effect of geometry on the counting rate. Balloons were filled with 1,000 ml water and 1 mCi ^{99m}Tc-DTPA (uniformly mixed) and counted under a gamma camera. Counting was repeated after withdrawal of 100 ml fluid out of the balloon each time until it was empty.

RESULTS

The results of animal experiments (Table 1) show that only about 0.5% of the ingested radioactivity was recovered from the total blood and urine and less than 0.1% from the thyroid and kidneys. About 96% of the ingested dose was recovered from the gastrointestinal content. The stomach alone (without content) had only about 1% activity indicating insignificant adsorption of ^{99m}Tc-DTPA in the gastric mucosa.

The urine and blood samples in two of these subjects showed insignificant absorption of ^{99m}Tc activity from the gastrointestinal tract. Unfortunately, urine and blood samples were not obtained from the remaining six subjects. At the end of each study, however, a whole-body survey with the gamma camera failed to show detectable cardiac and urinary bladder activity on the photoscope display. Three studies in each subject showed individual variation to be small. The physical data of these subjects are shown in Table 2. The mean age and body weight of these subjects was 26 years and 75 kg, respectively. At least for the first 20 min, the emptying curves were monoexponential. In one subject, followed up to 60 min, the curve showed a biexponential pattern with a delayed second phase.

In the present study, gastric emptying $T_{1/2}$ was expressed as the time necessary for 50% of the initial radioactivity to leave the stomach. The configuration of a typical curve obtained from the computer data is shown in Fig. 1. Abscissa denotes the time in minutes and the ordinate, the relative activity. The $T_{1/2}$ value was found to be 12 min with a standard deviation of 3 min (Table 3). Sequential camera images of the abdomen are shown in Fig. 2 which demonstrates visualization of the entire stomach in early scan and gradual appearance of activity in the intestine. Within 15 min, more than half of the initial activity has left the stomach. Because of the use of a larger volume (700 ml), flagging of the gastric area

TABLE 2. AGE AND WEIGHT DISTRIBUTION OF EIGHT NORMAL VOLUNTEERS

Physical data of eight normal subjects (all male)		
Subject	Age (yr)	Weight (kg)
A	25	70.4
B	24	71.8
C	26	73.2
D	24	82.2
E	25	70.4
F	30	68.6
G	27	72.9
H	27	90.6
Mean	26	75
± s.d.	±2	±7.5

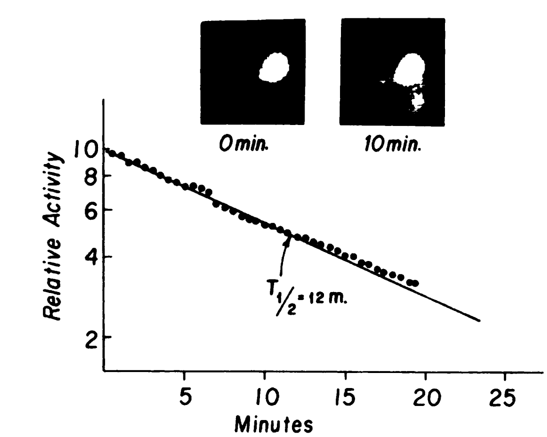

FIG. 1. Typical curve of gastric emptying rate in one subject.

TABLE 3. GASTRIC EMPTYING $T_{1/2}$ IN EIGHT NORMAL VOLUNTEERS

Gastric emptying $T_{1/2}$ determined with ^{99m}Tc-DTPA			
Subject	Study (No)	GET ($T_{1/2}$ in min)	Mean (± s.d.)
A	1	8.0	8.1 ± 2.1
	2	10.2	
	3	6.0	
B	1	16.0	13.5 ± 2.1
	2	12.5	
	3	12.0	
C	1	12.0	12.6 ± 0.9
	2	13.7	
	3	12.0	
D	1	9.0	8.6 ± 1.8
	2	6.6	
	3	10.2	
E	1	12.0	11.3 ± 1.1
	2	10.0	
	3	12.0	
F	1	12.4	13.1 ± 0.9
	2	14.0	
	3	13.0	
G	1	18.0	16.7 ± 1.5
	2	15.0	
	3	17.0	
H	1	10.4	9.8 ± 0.7
	2	9.0	
	3	10.0	

Mean GET ($T_{1/2}$) of all 24 studies 12 ± 3 min.

without intestinal overlapping becomes difficult. The use of an initial volume of 500 ml, however, makes the flagging much easier in terms of including only the gastric area.

Fig. 3 illustrates such a case in which the flagging of the area of interest (i.e., stomach) is shown as an intensified area. In most of the subjects there was no substantial overlap of duodenum or jejunum over the flagged area, particularly when the study was started with 500 ml of test solution. However, with the use of 700 ml of test solution in some individuals there was some degree of duodenal or jejunal superimposition.

The effects of duodenal and intestinal overlap (each on one subject) on gastric emptying $T_{1/2}$ are shown in Figs. 4 and 5, resepectively. There was insignificant variation of $T_{1/2}$ value from these factors. In the case of duodenal overlap, the early part of the curve (Fig. 4) appears horizontal and later the curve started to fall. In case of jejunal overlap, one notices an elevation in the middle of the curve (Fig. 5). In either case, the $T_{1/2}$ is not significantly altered if the proper portion of the curve is selected.

Experiments with balloons showed that there was no significant variation in the count due to changes in the geometry of the balloon. The decrease of radioactivity from the balloon was linearly proportional

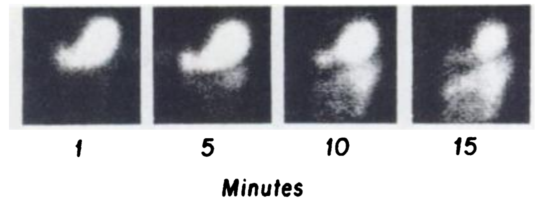

FIG. 2. Gamma camera images of stomach and intestine at different time intervals.

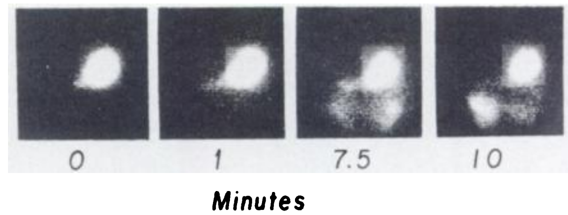

FIG. 3. Sequential gamma camera images of stomach and intestine. Note flagging of stomach with intensified square.

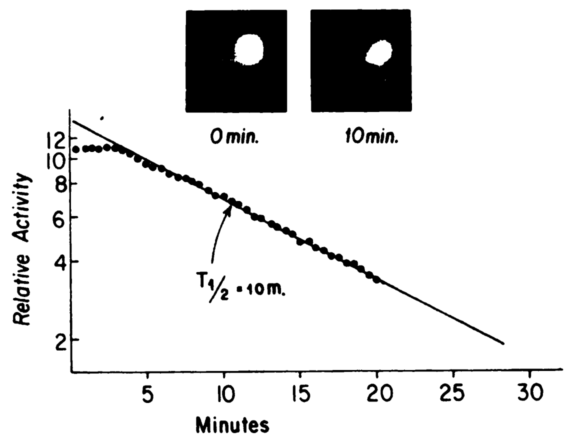

FIG. 4. Appearance of gastric emptying curve in case of duodenal activity overlapping stomach activity. Note initial plateau of curve.

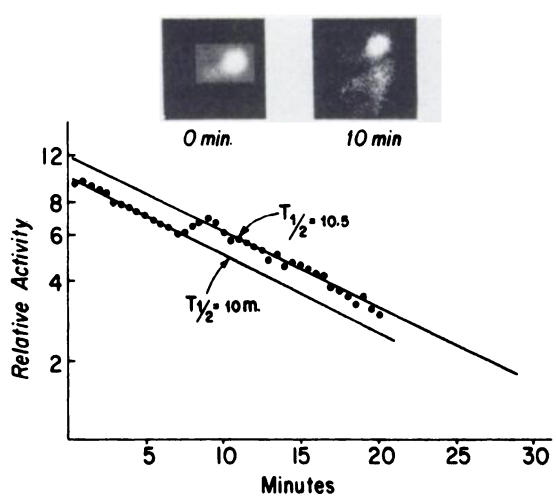

FIG. 5. Linear relationship between counting rate and decrease of volume of stomach phantom.

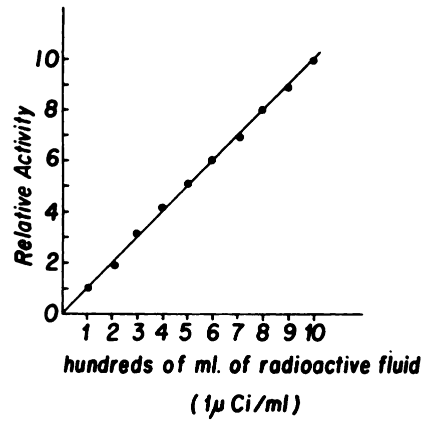

FIG. 6. Typical elevation in middle of curve in case of jejunal overlap.

to the amount of radioactive fluid withdrawn from the balloon (Fig. 6).

DISCUSSION

Abnormalities in the gastric emptying rate have been recognized in certain diseases and postsurgical conditions. Hastened and delayed emptying has been associated with duodenal and gastric ulcers respectively. Delayed gastric emptying is also found in malignant disease of stomach and pyloric stenosis. Symptoms of gastric retention following vagotomy are due to delayed gastric emptying. Thus there exists the need for determining GET following vagotomy and gastrectomy.

The nonisotopic technique of measuring gastric emptying rate is the saline load test (*1*) introduced in 1965. The procedure requires intubation. Moreover, no one can be sure of complete aspiration of the remaining gastric content which is essentially the basis of emptying time determination in such a procedure. X-ray studies using barium state the time when the emptying begins and when it is complete but give no satisfactory idea about the details of emptying rate.

Measurement of GET by isotopic method is a simple means of diagnosing gastric retention. Previously isotopic methods employed the use of ^{51}Cr-chromate (*2*), ^{131}I-IHSA (*3*), ^{113m}In-DTPA (*4*), and ^{129}Cs (*5*). The radioactivity in these techniques was quantitated by fixed external detectors or by sequential rectilinear and camera scanning and counting the dots from the scan. The disadvantage of previous isotopic methods is false high value because of using uncollimated external probe and blind positioning of the probe, thus accounting for radioactivity from the surrounding structures. Disadvantages of scanning technique are that (A) it takes a long time for each scan, thus detailed changes in stomach emptying may be missed; (B) that it cannot measure activity in the whole stomach simultaneously; and (C) physical counting of many dots on scintiscan is a tedious process. Counting dots from the oscilloscope screen of the gamma camera is a crude method also. Disadvantages of ^{51}Cr have been discussed elsewhere (*4*). Moreover, because of their high gamma energies, none of the previously used isotopes are very suitable for gamma camera study.

On the other hand, ^{99m}Tc-DTPA has been previously used for brain scanning, cisternography, and renal function studies. The potential value of this agent for measuring GET has not been reported before. We undertook this study in two phases: to ascertain that it fulfills all the criteria of an ideal agent for measuring GET and to determine the gastric emptying rate of a liquid meal in normal individuals.

Criteria of an ideal agent for measuring GET are (A) it should be nonabsorbable, (B) it should be nonadsorbable, and (C) it should be homogeneously distributed in the meal. Animal experiments showed that ^{99m}Tc-DTPA fulfills these criteria. The nonabsorptive property of ^{99m}Tc-DTPA was also confirmed in two of the subjects by counting blood and urine samples. Virtual absence of radioactivity in the blood and urine also indicates no breakdown of ^{99m}Tc-DTPA to free ^{99m}Tc at lower pH of the stomach.

It is evident from the present study as well as others that GET for a liquid meal (500–750 ml) is a monoexponential function at least for the first 20–30 min. On that basis when one deduces the existing saline load test value (*1*) of GET in terms of $T_{1/2}$, it appears to be faster than our present value. This is probably due to incomplete aspiration of the gastric fluid in saline load test method giving rise to a false faster emptying time.

It has been shown previously that the gastric emptying rate varies significantly with age, position of the patient, the test material, and its volume. In the present study, we have attempted to keep all the factors as constant as possible for each study in every subject. A volume difference of 500 ml and 700 ml did not alter the monoexponential character of the curve at least for the first 20 min.

Although it is difficult to calculate accurately the radiation dose to the stomach, intestine, or other hollow organs in such a procedure, one can make some reasonable estimation from the previously published nuclear data of ^{99m}Tc (*6*) and data for absorbed fraction and organ masses (*7*). Assuming, therefore, 100% retention of the test material in the gut, a maximum possible total-body radiation in a 70-kg man would be 0.012 rads/mCi. Absorbed radiation dose to the small intestine would not be more than 0.029 rads/mCi in such a case.

In conclusion, a rapid and easy isotopic method for measuring GET using ^{99m}Tc-DTPA and a gamma camera is described. It enables observation to be made during and immediately after a test meal. Intubation and suction under fluoroscopic examination are not required. Two important advantages are that counts are recorded automatically and that observations can begin immediately after ingestion of the meal, permitting detailed study of the early phase of gastric emptying. This noninvasive technique appears to be highly satisfactory for the measurement of GET in man.

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