An evaluation of ^{113m}In DTPA chelate in the measurement of gastric emptying by scintiscanning

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SUMMARY The sequential scintiscanning technique was used to determine gastric emptying rates in adult human subjects after ingestion of a meal of cornflakes and milk to which a gamma-emitting radioactive isotope had been added.

Comparison of emptying rates using ^{113m}In DTPA chelate and ^{51}Cr sodium chromate showed that significantly slower rates were recorded with chromate, and studies *in vitro* demonstrated adsorption of chromate to the solid component of the meal. The results imply that the liquid phase of the gastric contents after a meal is discharged through the pylorus more rapidly than the solid phase. Scintiscanning with indium chelate provides a measurement of the emptying of the liquid phase of the gastric contents.

Measurement of the rate of gastric emptying after food is now possible by the external detection of radioactive material incorporated into a meal. Fixed detectors (Brömster, Carlberger, and Lundh, 1968), scintiscanning (Griffith, Owen, Kirkman, and Shields, 1966), and a gamma camera (Harvey, Brown, Mackie, Keeling, and Davies, 1970) have been used to locate and quantitate isotope remaining in the stomach at intervals after its ingestion and hence provide a measurement of the rate at which it leaves the stomach. The technique permits the study of gastric emptying after ordinary meals of mixed composition and is thus complementary to methods of serial aspiration (Hunt and Spurrell, 1951) which are limited to liquid meals.

^{51}Cr chromate has been regarded as a suitable isotope to incorporate into a meal because it is not absorbed (Hansky and Connell, 1962) and has a suitable gamma ray emission. However, only 9% of its disintegrations give rise to gamma radiation. In addition, chromate is not suitable for successive tests on the same subject because isotope in the colon would be difficult to distinguish from that in the stomach. The present investigation was undertaken to evaluate the chelate of ^{113m}In indium with diethylene triamine penta acetic acid (DTPA) as an alternative to chromate because of its greater gamma ray emission and short physical half-life of 1.7 hours, which permits study of the same subject on successive days.

Received for publication 11 May 1971.

Methods

ISOTOPES

^{113m}In indium was eluted from a generator and the DTPA chelate prepared by the method of Stern, Goodwin, Scheffel, Wagner, and Kramer (1967). ^{51}Cr sodium chromate was obtained from the Radiochemical Centre, Amersham.

CLINICAL STUDIES

Adult male and female hospital patients were studied. None were taking anticholinergic drugs or had undergone previous upper gastrointestinal surgery. All subjects were given a standard meal of 20 g cornflakes with 15 g sugar to which 150 ml of milk containing 200 microcuries of the appropriate radioactive isotope was added immediately beforehand. The time taken to consume the meal was between four and eight minutes. Each subject was studied on two successive mornings; eight were given the meal with indium chelate on both occasions and 18 subjects were studied using the indium compound on the first day and chromate on the second. A further two subjects were studied first with the indium chelate and then with chromate to which the physically decayed indium compound had been added.

The scanning procedure was similar to that used by Griffith *et al* (1966) except that single detector scanners were used. After ingestion of the meal four scans of the upper abdomen were obtained at ap-

proximately 25-minute intervals with the subject supine. The position of the xiphisternum was marked on each scan as a reference point. During the rest of the time the subjects were free to sit or walk, but smoking was not permitted. The scanner used for most of the studies was basically a Nuclear Chicago type 1700. The detector was fitted with a 3 in. $\times$ 3 in. crystal and a 19-hole focused collimator. The maximum scanning speed of 60 cm/min and a line spacing of 0.8 cm were used. With this instrument each scan took about eight minutes, so that the subject was supine for about a third of the period of observation. Two other scanners were used during the study, a Picker Magnascanner V and a Nuclear Enterprises NE 8271. Each was fitted with a 5 in. $\times$ 2 in. crystal, and medium resolution collimators were used. Higher scanning speeds were available, and a speed of 120 cm/min was employed with a line spacing of 1.0 cm when ^{113m}In had been administered. No subject was examined with more than one scanner.

Absorption of the indium chelate was assessed in four subjects from the isotope content of a four-hour urine collection begun at the time of ingestion of the meal and from a blood sample taken at the end of the four-hour period. Absorbed isotope was assumed to be distributed in the extracellular water volume of the subject.

CALCULATION

The scans from each subject were inspected and an area which included the stomach was marked out on each. The number of dots within this area was counted and correction made for background and for physical decay in the case of ^{113m}In . A plot of logarithm of dot counts against time was then drawn by eye, complete ingestion of the meal being taken as time zero. From this straight line, the half time ($T_{\frac{1}{2}}$) for gastric emptying was measured graphically.

STUDIES *IN VITRO*

The distribution of the isotope within a mixture of

cornflakes, gastric juice, and milk was studied by direct counting of the supernatant fluid after addition of a known quantity of isotope. Similar measurements were made on mixtures of cornflakes with citrate buffers and hydrochloric acid with a pH range of 1 to 6. In all cases the gastric juice had been obtained fresh from patients undergoing penta-gastrin stimulation of gastric secretion as part of their routine clinical investigation. In order to compare directly the distribution of the two isotopes in such mixtures, 1 ml of a solution containing both ^{51}Cr sodium chromate and ^{113m}In indium DTPA chelate was added to a mixture of 2 g cornflakes and 10 ml water and to a mixture of 2 g cornflakes and 10 ml gastric juice. These mixtures were centrifuged, 5 ml of the supernatant was removed and replaced by water, and, after remixing, the whole procedure was repeated until five sequential supernatant samples were obtained. The ratio of ^{51}Cr to ^{113m}In in the samples was then determined, using a Tracerlab Gammaguard fitted with a 3 in. well crystal. The samples were counted in a channel set to include both the 320 keV peak of ^{51}Cr and the 390 keV peak of ^{113m}In . They were then allowed to decay for 24 hours and the ^{51}Cr counted with no interference from the short-lived ^{113m}In . These counts were then subtracted from those obtained the previous day, to give the ^{113m}In activity, standards being used to allow for any change in sensitivity of the apparatus.

Results

GASTRIC EMPTYING RATES

The results obtained from subjects studied with indium chelate on both occasions are shown in Table I. There is good agreement in the two measurements. Absorption of the isotope was less than 2%. Table II shows the comparison of ^{51}Cr chromate with the indium chelate, and demonstrates a significant difference in the results obtained by the two isotopes. There is also considerable variation between subjects in the indium-chromium difference. There was no

Subject	Gastrointestinal Disease	Day 1	Day 2	Percentage Difference ¹ $2 \left(\frac{T_{\frac{1}{2}}(2) - T_{\frac{1}{2}}(1)}{T_{\frac{1}{2}}(1) + T_{\frac{1}{2}}(2)} \right) \times 100$
1	None	27	25	-8
2	Previous duodenal ulcer	26	25	-4
3	Cirrhosis, duodenal ulcer	30	31	+3
4	Prepyloric ulcer	25	23	-8
5	Idiopathic steatorrhoea with subtotal villous atrophy	40	46	+14
6	None	55	49	-12
7	None	25	27	+8
8	None	28	27	-4

Table I Gastric emptying $T_{\frac{1}{2}}$ (minutes) determined with ^{113m}In indium DTPA chelate on two successive days

¹The percentage difference is not significantly different from zero.

Subject	Gastrointestinal Disease	Day 1 (^{113}In DTPA Chelate)	Day 2 (^{51}Cr Chromate)	Percentage Difference ¹ $2 \left(\frac{T_{\frac{1}{2}}(2) - T_{\frac{1}{2}}(1)}{T_{\frac{1}{2}}(1) + T_{\frac{1}{2}}(2)} \right) \times 100$
9	None	38	55	+36
10	Duodenal ulcer and prepyloric ulcer	41	44	+7
11	None	41	65	+45
12	Duodenal ulcer	52	89	+52
13	None	20	32	+46
14	Prepyloric ulcer	20	28	+33
15	None	39	45	+14
16	Alcoholic gastritis	37	62	+50
17	Previous duodenal ulcer	59	26	-77
18	None	26	26	0
19	Previous duodenal ulcer	47	60	+24
20	Gastric ulcer	32	40	+22
21	None	25	41	+48
22	None	35	47	+29
23	Cholelithiasis	39	43	+10
24	Duodenal ulcer	35	43	+21
25	None	35	60	+53
26	None	29	30	+3
27	Duodenal ulcer	20	32	+46
28	None	37	66	+56

Table II Gastric emptying $T_{\frac{1}{2}}$ (minutes) determined with ^{113}m indium DTPA chelate and ^{51}Cr chromate on successive days

¹The percentage difference (subjects 9-26) is significantly greater than zero ($P < 0.01$).

For subjects 27 and 28, physically decayed indium chelate was included with chromate on day 2.

evidence for a pharmacological action on gastric emptying by the indium compound since a difference in the $T_{\frac{1}{2}}$ values was still obtained in two subjects when physically decayed indium chelate was incorporated in the chromate-labelled meal. Subjects included in Tables I and II who did not have any known gastrointestinal disease have a mean indium chelate $T_{\frac{1}{2}}$ value of 33 minutes. No satisfactory

explanation can be offered for the atypical results obtained from subject 17.

Subject 18 gave identical $T_{\frac{1}{2}}$ values with both isotopes and thus provides an opportunity to compare directly data obtained with the two methods. Figure 1 shows the points obtained for the two determinations of $T_{\frac{1}{2}}$ in this subject and illustrates the smaller potential error of the points obtained using indium as a consequence of the greater precision inherent in the greater count rate.

Fig. 1 Counts are indicated $\pm$ their square root.

STUDIES IN VITRO

Chromate was shown to be adsorbed to cornflakes whereas the indium compound was not. Adsorption was particularly marked in a mixture of cornflakes, water, and isotope only and was less when gastric juice, milk, or citrate buffer was incorporated in the mixture. The degree of adsorption was independent of pH.

The differing behaviour of the two isotopes is illustrated by the experiment using an isotope solution containing both ^{51}Cr chromate and ^{113}m indium chelate (Table III). The Cr/In ratio in the first supernatant is clearly lower than that of the isotope

	Cr/In Ratio of Isotope Solution Added	Supernatant Cr/In ratio				
		1	2	3	4	5
Cornflakes and water	0.54	0.32	0.37	0.52	0.80	2.2
Cornflakes and gastric juice	0.54	0.48	0.51	0.62	0.81	1.3

Table III Differing behaviour of two isotopes

solution due to adsorption of the chromate to the cornflakes, but rises in later supernatants as the chromate is eluted back into the aqueous phase.

Discussion

All methods of determining gastric emptying with external counters employ a gamma-emitting radioactive isotope as a marker of the meal. ^{51}Cr chromate has been the most widely used but ^{129}Cs bound to zirconium phosphate has been reported recently and appears to be a satisfactory alternative (Jones, Clark, Kocak, Cox, and Glass, 1970). The use of any non-absorbable tracer has been criticized as giving a falsely high value for $T_{\frac{1}{2}}$ since activity which has passed beyond the pylorus may be included in the field of view. However, in contrast to fixed detectors, scanning methods make it possible to recognize activity in the duodenum or jejunum and thus to minimize this source of error. A technique designed to eliminate this difficulty completely uses ^{131}I human serum albumin but requires gastric intubation in addition to external counting and is a more complicated procedure (Brömster *et al*, 1968).

All external counting methods depend on the assumption that emptying of the isotope from the stomach may be considered to correspond with emptying of the meal. The present work shows that two non-absorbable isotopes may give differing results for the rate of gastric emptying. If the gastric contents, comprising meal, isotope, and secretion, are a completely homogeneous mixture at all times during the period of observation, identical results would be obtained from two non-absorbable radioactive substances, provided that the isotope is not adsorbed to the gastric mucosa and does not affect gastric motility. In the present study the $T_{\frac{1}{2}}$ difference was still found when physically decayed indium chelate was added to the chromate. The higher value given by chromate for $T_{\frac{1}{2}}$, coupled with the demonstration of its adsorption to the solid matter of the meal, implies that the gastric contents do not leave the stomach as a homogeneous mixture but that in most of the subjects the more fluid component empties more rapidly. This is in accord with other observations (Klein, 1926; Thomas, 1957).

The indium isotope has an advantage over chromate in the radiation dosage to the lower alimentary tract, which is considered to be the critical organ for most non-absorbable radioactive materials. However, it is of some importance to examine the relative dosages, particularly as the use of a short-lived nuclide leads to a different critical organ. Absorbed doses were calculated using the ICRP data (1959) for gastrointestinal transit: one hour spent in the stomach, four in the small intestine,

eight in the upper, and 18 in the lower large intestine. The first figure corresponds to an exponential $T_{\frac{1}{2}}$ of 42 minutes, similar to the values we observed in practice. The nuclear data came from Dillman (1969) and the absorbed fractions and organ masses from Snyder, Ford, Warner, and Fisher (1969).

It is difficult to assess the dose to the gastric mucosa from the internal conversion electrons of $^{113\text{m}}\text{In}$ and the 'non-penetrating' radiation from ^{51}Cr , and it was thought best to assume that this was half the dose to the contents of the stomach, assuming the mean volume of the latter to be 150 ml. The results of the dose calculations are shown in Table IV. The figures are critically dependent on the assumptions made concerning the 'non-penetrating' radiation, which will in any case irradiate only a thin layer of the mucosa.

	Dose to Organ (millirads/ μCi)			
	Stomach	Lower Large Intestine	Ovaries	Trunk
$^{113\text{m}}\text{In}$	0.77	0.001	0.001	0.012
^{51}Cr	0.050	1.1	0.027	0.020
Dose ratio In/Cr for equal γ emission	2.1	0.0001	0.05	0.08

Table IV Comparison of doses received by different organs from the two isotopes

The abundance of the $^{113\text{m}}\text{In}$ γ ray is 65% compared with only 9% for ^{51}Cr . For a given initial external count rate it is therefore necessary to administer about seven times as much ^{51}Cr . Table IV therefore includes a comparison of the doses received from the two materials for the same gamma ray emission. Apart from the stomach, other organs receive a higher dose from ^{51}Cr . The dose to the critical organ (stomach for $^{113\text{m}}\text{In}$, lower large intestine for ^{51}Cr) is 10 times as high for ^{51}Cr . However, we have chosen to make use of the advantage of $^{113\text{m}}\text{In}$ to obtain higher counting rates, as the doses from the administration of 200 microcuries of either radionuclide are quite acceptable.

$^{113\text{m}}\text{Indium}$ DTPA chelate thus appears to be a satisfactory material for the measurement of gastric emptying. The results obtained in this study indicate that although gastric emptying appears to fit a single exponential pattern for a given tracer, the gastric contents cannot be regarded as a single homogeneous pool which is discharged through the pylorus and that considerable caution must be exercised in the direct comparison of values obtained with external counting methods which use different isotopes. The indium chelate, being distributed in the water of the gastric contents, reflects the emptying of the liquid phase of the gastric contents.

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