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THE GASTRIC EMPTYING OF SMALL VOLUMES GIVEN IN QUICK SUCCESSION

BY LESLEY ERSKINE AND J. N. HUNT*
From the Department of Physiology, Guy's Hospital Medical School, London

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SUMMARY

1. Ten subjects were given solutions of 33 mM-trisodium citrate or 505 mM-glucose, by tube into the stomach; either 25, 50, 100 or 200 ml. were instilled. The gastric contents were recovered, after 3 min with the trisodium citrate solution and after 10 min with the solution of glucose, then the stomach was washed out with 250 ml. water. Each volume was instilled six times in quick succession on one day with the trisodium citrate solution, and four times on another day with the solution of glucose. The recovered volume of the original meal, which contained Phenol Red, was assessed from the amount of dye in the combined recovery and wash. Each day's procedure was replicated on three days.

2. About half of the trisodium citrate solution was recovered after 3 min and about half the solution of glucose after 10 min, independent of the volume instilled.

3. Glucose slowed gastric emptying. The effect was seen when amounts as low as 1·5 g passed into the duodenum in 10 min.

4. Within-subject, the volumes of trisodium citrate (a distending gastric stimulus) recovered at 3 min allowed predictions of the volumes of glucose solution (a gastric distending and a duodenal osmotic stimulus) recovered at 10 min.

5. The volumes recovered on one day fell progressively with successive instillations of 25, 50 and 100 ml.

6. The results showed that the control system governing gastric emptying responded to volume and osmotic stimuli even when the intragastric volumes were as small as those in the stomach during the interdigestive periods.

INTRODUCTION

The rate of gastric emptying of test meals from the stomach is regulated by duodenal receptors which are stimulated by the composition of the gastric contents which pass through the pylorus. Receptor systems that respond to lipids, to acids and to the osmotic properties of the luminal contents are postulated (Hunt & Knox, 1968). However, the experimental studies of the actions of these receptors were made with test meals of large volume, usually 750 ml. Because gastric emptying was initially rapid under these conditions (Hunt & Macdonald, 1954), a relatively large stimulus was delivered to the duodenal receptors. It was therefore possible that the

* Present address: Department of Physiology, Baylor College of Medicine, Houston, Texas 77030, U.S.A.

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control system discovered with large meals did not operate with small meals. The present experiments were designed to study the control of the rate of gastric emptying of volumes of 25–200 ml. The mean volume of gastric contents during fasting is 22 ml. (Williams & Hunt, 1973).

METHODS

Two types of meal were used:

(1) 33 mM-trisodium citrate pH *ca.* 7. This solution was emptied rapidly from the stomach because it was close to a minimal stimulus to the duodenal receptors whose activation slowed gastric emptying (Hunt, 1956; Hunt & Pathak, 1960). Buffering by citrate ion minimized the effect of acid on gastric emptying (Hunt & Knox, 1962). The rate of emptying of trisodium citrate solution was used as an index of the emptying of the uninhibited stomach.

(2) 100 g glucose monohydrate/l. (505 mM) pH *ca.* 7. This solution was a potent stimulus to duodenal osmoreceptors (Meeroff, Go & Phillips, 1975; Barker, Cochrane, Corbett, Dufton, Hunt & Roberts, 1978). Duodenal stimulation slowed gastric emptying by increasing duodenal resistance to filling and by reducing antral propulsive activity (Weisbrodt, Wiley, Overholt & Bass, 1969).

Phenol Red, *ca.* 60 mg/l., was added to each meal as a marker to allow the volume of the given meal recovered from the stomach to be measured (Hunt & Knox, 1962; Ivey & Schedl, 1970).

The subjects, who were medical students, a nurse and the authors, came fasting to the laboratory early in the morning. The stomach was washed out with 250 ml. distilled water and an instillation of solutions of trisodium citrate or of glucose, at 37 °C, was given by tube into the stomach from a funnel 30 cm over the subject's head. Recovery of the gastric contents was started 3 min after the beginning of instillation of the rapidly emptying trisodium citrate meals, and 10 min after the beginning of instillation of the slowly emptying glucose meals. The stomach was then washed out with 250 ml. water to ensure maximal recovery. As soon as recovery of the wash-out was complete, the next meal of the same volume was given. This cycle of instillation, recovery and wash-out was repeated four times in succession for glucose meals and six times for trisodium citrate meals, the volume given remaining constant. Four volumes, 25, 50, 100 and 200 ml., on different days were given in random order. The recovered gastric content and its wash-out were pooled to obtain the total amount of Phenol Red recovered, determined as a product of the concentration of Phenol Red in the pooled material and its volume. This amount was divided by the concentration of Phenol Red in the original solution to give the volume of original instillation recovered.

About half of the trisodium citrate solution left the stomach in 3 min and about half of the glucose solution left in 10 min, so that comparisons of their action could be made when equal volumes had passed into the duodenum. The composition of the solutions, the initial wash-out which preceded each instillation, and the short time intervals minimized any effects which gastric secretion might have on the recoveries. Glucose 100 g/l. was an inhibitor of gastric secretion (Shay, Gershon-Cohen, Fels & Siplet, 1942): 200 ml. was one quarter of the maximal volume stimulus to secretion (Hunt & Macdonald, 1952). With test solutions free of protein, pepsin is not known to have any effect on gastric emptying. These experiments were approved by the local Ethical Committee.

Expression of results

The term 'meal number' will be used to refer to the first, second, third, etc. instillation on a given day. Each volume of original test solution recovered was expressed as a percentage of the mean of the six or four volumes recovered on that day from the subject. The mean of the percentages of meal recovered on the three days, for each meal number, was calculated for the four volumes of the two test meals used, 25, 50, 100 and 200 ml. The means for ten subjects were pooled and plotted against meal number (Fig. 1). The aim was to minimize the effects of between-day and between-subject variance.

RESULTS

The effect of volume given on volume recovered

With volumes given betwen 25 and 200 ml. about half of the trisodium citrate solution was recovered after 3 min and about half of the glucose solution was

TABLE 1. Volumes of test instillations recovered. Coefficient of variation = standard deviation × 100/mean. S.E. values in parentheses are hypothetical standard errors had there been 180 observations with glucose as there were with trisodium citrate. Coefficients of variation allow the relative magnitudes of the contributions of between-subject differences, day-to-day differences and the method (including the effect of meal number, under 'other') to be appreciated. The over-all coefficient of variation is less for instillations of 200 ml. of glucose solution than for instillations of 200 ml. of trisodium citrate solution ($P < 0{\cdot}01$). For smaller volumes, neither composition nor volume had a significant effect on coefficients of variation

	Trisodium citrate (33 mM) (3 min)					Glucose (505 mM) (10 min)				
Volume instilled (ml.)	n	Mean recovery (ml.)	S.E. of mean	Source of variance	Coefficient of variation	n	Mean recovery (ml.)	S.E. of mean	Source of variance	Coefficient of variation
200	180	99	±3·0	Subjects	14·5	120	121	±2·7	Subjects	12·1
				Days	23·2			(2·2)	Days	11·7
				Other	29·8				Other	18·1
100	180	43·4	±1·8	Subjects	36·2	120	44·4	±2·1	Subjects	21·6
				Days	30·4			(1·7)	Days	37·8
				Other	31·6				Other	28·8
050	180	25·3	±0·99	Subjects	30·0	120	22·4	±1·21	Subjects	30·4
				Days	24·9			(0·98)	Days	40·2
				Other	26·9				Other	31·3
25	180	12·4	±0·54	Subjects	33·1	120	10·3	±0·64	Subjects	42·7
				Days	30·6			(0·52)	Days	33·0
				Other	37·1				Other	41·7

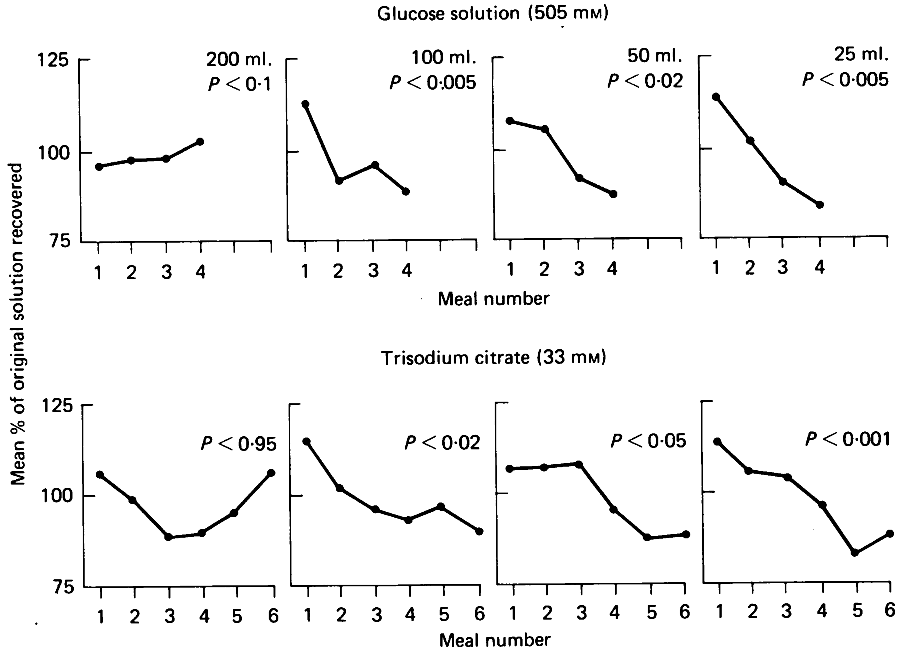

Fig. 1. The effect of mean number and volume of instillation on the volume of original solution recovered after 3 min for trisodium citrate (33 mM), and after 10 min for glucose solution (505 mM). Ordinate: mean percentages of original solution recovered. The results for each day were expressed as percent of mean for that day within-subject. These percentages were averaged over three days to give the value on the ordinate ($n = 30$). Abscissa: number of instillations in series of four for glucose or of six for trisodium citrate solution. Volumes over each frame are those of the meal given at time zero. P values relate to the significance of the progressive fall in volume recovered with increase in meal number.

recovered after 10 min. The mean volumes recovered are shown in Table 1, columns 3 and 8.

The effect of meal number on volume recovered

For 25, 50 and 100 ml. the recovery of meal as percentage of mean for the day fell with each successive meal on that day, from about 115 % of the mean with the first to about 85 % with the last (Fig. 1). The relative magnitude of this change in volume recovered with meal number was not dependent upon the original volume nor upon the composition of the meal over the range 25–100 ml.

For meals of 200 ml. of trisodium citrate solution, there was a fall in percentage recovered with the first three successive meals ($P < 0·02$), then the volume recovered increased progressively with meal number. For the 200 ml. meals of glucose, there was no effect of meal number (Fig. 1).

In plots of percentage of mean volume recovered on one day against meal number, before they were pooled in Fig. 1, there were 154 subject days with progressive falls and eighty-six subject days with progressive increases in volume recovered without distinction between glucose solutions and trisodium citrate solutions.

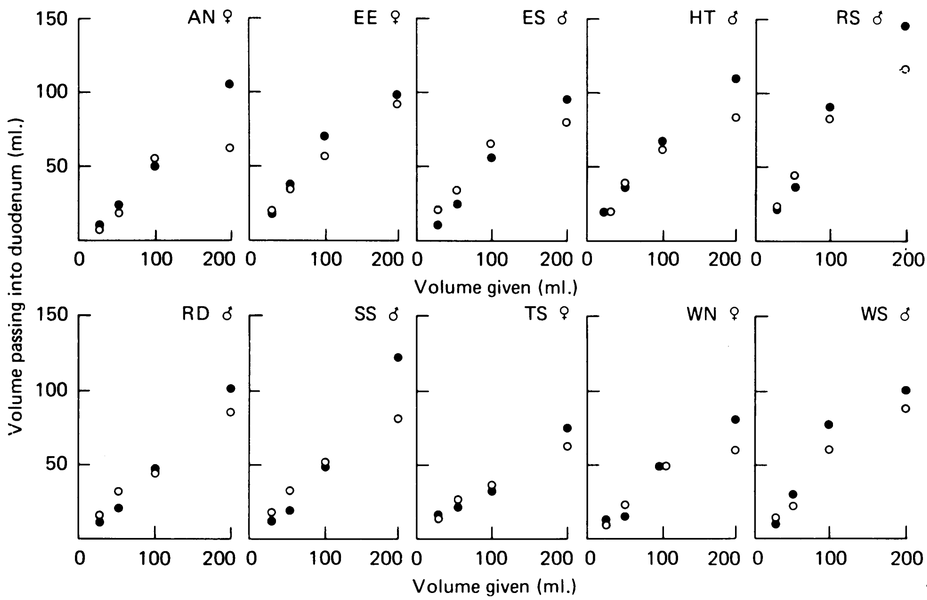

Fig. 2. Comparison of mean volumes of original solutions passing into duodenum in 3 min for trisodium citrate (six tests; 33 mM; filled circles) and 10 min for glucose solution (four tests; 505 mM; open circles). Ordinate: volume entering duodenum (ml.). Abscissa: volume instilled (ml.).

The effect of composition of meals on volume recovered

In Fig. 2, the effect of meal number is disregarded. It can be seen that the mean volume of trisodium citrate solution passing into the duodenum in 3 min was about half that given, which was about the same as the mean volume of glucose solution passing in 10 min, with 25, 50 and 100 ml. Other experiments with recoveries at 5, 10, 15 and 20 min showed that gastric emptying of these small volumes was indistinguishable from rectilinear with time. Thus the rate of gastric emptying was three times slower with the solution of glucose (505 mM) than with the solution of trisodium citrate (33 mM), with volumes of 25, 50 and 100 ml.

With 200 ml. the mean volume of glucose solution emptying in 10 min was less than the corresponding value for solutions of trisodium citrate. This slow emptying of the glucose solution with 200 ml., relative to that with 25, 50 and 100 ml., was significant ($P < 0{\cdot}02$) even when the analysis was confined to first recoveries of the three experimental days.

DISCUSSION

The effect of composition of the test solutions

In the present experiments, about 15 % per min of the instilled volumes of the trisodium citrate solution and about 5 % per min of the instilled volumes of the glucose solution emptied into the duodenum. In principle this was similar to the initial emptying with large volumes (Hunt & Macdonald, 1954; Bell & Watson, 1976). The slower emptying of the solution of glucose was presumably the result of the stimulation of duodenal osmoreceptors (Meeroff *et al.* 1975; Bell & Mostaghni, 1975; Barker *et al.* 1978). The threshold for these receptors was surprisingly low, since 1·5 g glucose passing into the duodenum in 10 min decisively slowed the gastric emptying of the 25 ml.

The trisodium citrate solution was predominantly a distending stimulus to gastric receptors and smooth muscle. Yet it may be seen from Fig. 2 that within-subject, the rate of emptying of the trisodium citrate solution allowed precise predictions of the rate of emptying of the solution of glucose which was also a potent stimulus to duodenal receptors. The implication appeared to be that gastric factors determined the between-subject differences ($P < 0·01$) in the initial rates of gastric emptying of both solutions. The similarity of the coefficients of variation (Table 1) for recovered volumes of trisodium citrate solution and of glucose solution was consistent with the gastric response being the main source of variation between subjects, with little contribution from duodenal receptors.

In spite of washing out the stomach with a constant 250 ml. between each volume instilled, the rate of emptying was a constant fraction of the instilled volumes. It appeared therefore that the control system responded to the intragastric volume with a short latency and a short after discharge. The strong effect of intragastric volume on the *initial* rate of gastric emptying was in contrast to the rate of gastric emptying measured over 30 min or more, which was largely determined by the stimulation of duodenal receptors by the chyme leaving the stomach (Hunt & Stubbs, 1975).

The effect of meal number on gastric emptying

The progressive decrease in volume recovered with meal number could not have been caused by loss of reactivity of duodenal osmoreceptors, since it was seen with the trisodium citrate solution, which had little effect on them. It has been seen before with pairs of large meals in succession (Hunt & Macdonald, 1954). Cannon (1911) described a somewhat similar phenomenon in the stomach *in vitro*, that is, without any input from the extrinsic vagus nerves.

Conclusions

The initial phase of gastric emptying is largely dominated by the intragastric volume over the range 25–1250 ml. Gastric emptying can be slowed by 1·5 g glucose passing from the stomach to the duodenum in 10 min.

By comparing the gastric emptying of two test meals of different composition in each subject, it was possible to reach the following tentative conclusions:

(1) the progressively more rapid emptying with meal number was a property of the stomach and was not caused by a decreasing response of duodenal receptors;

(2) the constant fractional emptying with increase in volume of test solution was a property of the stomach;

(3) the main between-subject differences in rates of gastric emptying could be attributed to gastric properties and were not a function of variations in response of duodenal receptors.

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