

## THE VOLUME AND ENERGY CONTENT OF MEALS AS DETERMINANTS OF GASTRIC EMPTYING

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### SUMMARY

1. Results were collected from thirty-three published and unpublished studies of gastric emptying. The volumes of the meals ranged from 50 to 1250 ml., and composition varied from pure carbohydrates to ordinary food.

2. From the published composition of the meals, their nutritive density, as kcal/ml. (4.18 KJ/ml.) was computed: it ranged from zero to 2.3 kcal/ml.

3. The volume of each meal, or test meal, delivered to the duodenum in 30 min was determined, assuming that gastric emptying was exponential.

4. The greater the nutritive density of a meal, the less was the volume transferred to the duodenum in 30 min. The original volume of meal given was not a determinant of the rate of emptying (ml./min).

5. The slowing of gastric emptying with a meal of high nutritive density was not sufficient to prevent an increased rate of delivery of energy to the duodenum (nutritive density  $\times$  volume delivered in unit time) with a meal of high nutritive density.

6. Assuming an appropriate relationship for the interaction of a stimulus (kcal/ml.) and duodenal receptors, it was possible to predict a rate of gastric emptying for each meal, given its nutritive density. Knowing the initial volume of the meal, it was possible to predict the mean half time for its emptying.

7. There were eight sets of anomalous results: in four the volumes of meal given were less than 200 ml.; explanations of the anomalies in the other four results could not be provided.

8. The results are consistent with equal slowing of gastric emptying by the duodenal action of the products of digestion of isocaloric amounts of fat, protein and carbohydrate, for example, 4 g fat or 9 g carbohydrate, both 36 kcal, taking carbohydrate and protein as 4 kcal/g and fat as 9 kcal/g.

## INTRODUCTION

Dietary carbohydrates and triglycerides added to test meals slow gastric emptying: the higher the concentration of carbohydrate or of triglyceride, the slower is the emptying. This regulation of emptying depends upon the intraduodenal concentrations of the digestion products, either monosaccharides acting through their osmotic pressure (Carnot & Chassevant, 1905; Elias, Gibson, Greenwood, Hunt & Tripp, 1968; Barker, Cockrane, Corbett, Hunt & Roberts, 1974), or salts of fatty acids (Quigley & Meschan, 1941), acting on duodenal receptors (Hunt & Knox, 1968). Excitation of these duodenal receptors partially inhibits the pumping action of the gastric antrum and considerably augments the motor activity of the proximal part of the duodenum, so increasing the resistance to the transfer of the gastric contents to the duodenum (Weisbrodt, Wiley, Overholt & Bass, 1969).

The above account of the regulation of the gastric emptying of food raises several quantitative questions.

(a) What concentrations of fat and of carbohydrate will produce equal slowing of gastric emptying?

(b) Will the slowing of gastric emptying, produced by raising the concentration of fat or of carbohydrate in the gastric contents, offset the consequences of increased concentrations of these ingredients? For example, will doubling the concentration of fat halve the volume delivered to the duodenum in unit time, thus maintaining constant the rate of transfer of energy?

(c) Does the amount of fat or of carbohydrate delivered to the duodenum in unit time depend upon the initial volume in which the material is given?

It is concluded below that isocaloric (isojoulic) concentrations of carbohydrate and of triglyceride produce equal slowing of gastric emptying. For example, 9 g carbohydrate/100 ml. slows gastric emptying to the same extent as 4 g triglyceride/100 ml., both equivalent to 36 kcal/100 ml. For a given nutritive density (kcal/ml.) the rate of emptying (ml./min) is independent of the initial volume.

## METHODS

*The pattern of gastric emptying*

For our purpose it was necessary to make a decision about the pattern of gastric emptying. There is a considerable body of data consistent with an exponential pattern (Marbaix, 1898; Salamanca, 1943; Hunt & Spurrell, 1951; George, 1968; Griffith, Owen, Campbell & Shields, 1968; Brömster, 1969; Harvey, Mackie, Brown, Keeling & Davies, 1970; Tinker, Kocak, Jones, Glass & Cox, 1970; Van Dam, 1972, for man; Weisbrodt *et al.* 1969, for dog). However, it is possible to arrange conditions so that the phase of exponential emptying is preceded by a phase more rapid than is required

by extrapolation of the exponential pattern to zero time. This is seen, for example, with meals of 1250 ml. of water (Hunt & Macdonald, 1954), with meals containing boiled starch rapidly introduced into the stomach (Hunt, 1960), or with a variety of small meals taken rapidly (Moberg & Carlberger, 1974). The pattern described by Hopkins (1966), in which the value of the square root of the intragastric volume of meal falls linearly with time, depends on including the results where the recoveries of meal are 20 ml. or less.

This paper is intended to be relevant to the gastric emptying of food during the first 60 min of the emptying process. For this purpose the assumption of an exponential pattern seems appropriate, especially if food is eaten, and not instilled. There is at least one dissenting group to set against the ten cited above (Moberg & Carlberger, 1974). The implications of alternative patterns of emptying are examined in Appendix I.

#### *Calculating the rate of gastric emptying from the half-time of the meal in the stomach*

It has become customary in some laboratories to describe the emptying of meals in terms of the time required for the initial volume of meal in the stomach to fall to half. The volume of meal leaving the stomach in 30 min may be computed from a plot of log volume of meal remaining in the stomach against time. Two points on this straight line are log of initial volume at zero time, and log ( $\frac{1}{2}$  initial volume) at the half time. By interpolation or extrapolation, the log volume remaining at 30 min may be found. The antilog gives the volume remaining, and subtraction from initial volume, the volume of meal emptied into the duodenum in the period 0–30 min.

It is usually not possible to deal with the variations in the initial emptying, as values for 'starting index' (Hunt & Spurrell, 1951) are rarely published. It seems likely that the moment of 'gastric filling' is so indefinite with a meal of food as to make the 'starting index' unmeasurable.

#### *Calculation of the nutritive density of meals*

Table 1 is a summary of thirty-three results taken from the literature and from unpublished studies in this laboratory. The calculation of the nutritive densities (kcal/ml.) of meal from published details is based essentially on 4 kcal/g protein and of carbohydrate, and 9 kcal/g fat (Medical Research Council, 1945). A mole of xylose, mol.wt. 150, has been considered equivalent to a mole of glucose, on the grounds that they both probably produce equal slowing of gastric emptying by their action on duodenal osmoreceptors (Barker *et al.* 1974). Since glucose is commonly used as its monohydrate, mol.wt. 198, all concentrations given in g/l. have been multiplied by 180/198 before attributing 4 kcal/g to glucose, mol.wt. 180. The macrogol stearate in the meals of Moberg & Carlberger (1974) has been ignored, although it probably slows gastric emptying like a salt of a fatty acid (Hunt & Knox, 1968).

#### *The data*

The first nineteen results in Table 1 are for meals with nutritive density 2.3–0.14 kcal/ml., volumes 300–750 ml., and the results include three sets for ordinary food. Emptying of food was studied by external scanning of an isotope in the meal, which is the least invasive method currently available. The remaining fourteen results in Table 1 refer to meals of water, meals with volumes less than 330 ml., or meals whose emptying rates are not adequately described by our hypothesis, for reasons that are not apparent to us. An example is given in line 33 of Table 1 (Davies, Kirkpatrick, Owen & Shields, 1971). Results in an earlier paper by the same authors (Griffith *et al.* 1968) (line 5) using 550 ml. instead of 300 ml. meals, fit the present scheme.

## DISCUSSION AND RESULTS

The discussion which follows is intended to justify progressively more comprehensive quantitative relations between the nutritive density of meals and several ways of specifying the emptying behaviour of the stomach. The relations considered first are included because they allow easier appreciation of some metabolic consequences of this description of the regulation of gastric emptying.

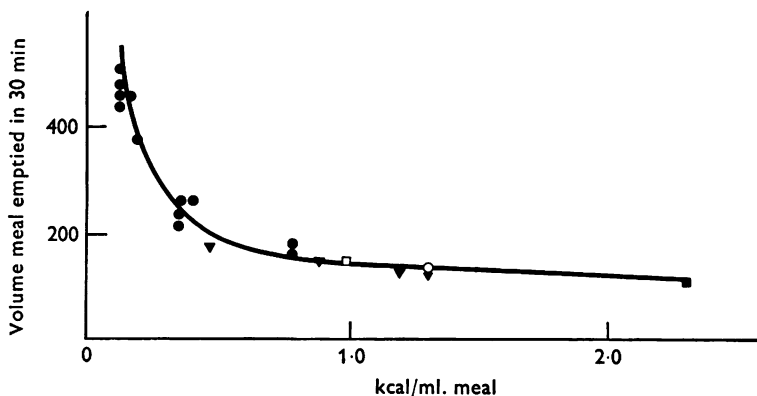


Fig. 1. Relation between volume of meal entering the duodenum in 30 min and the nutritive density of the meal. Ordinate, volume entering duodenum in 30 min (ml.) ( $V_{E30}$ ). Abscissa, kcal/ml. meal ( $K$ ).  $V_0$  ● 750 ml., □ 550 ml., ○ 500 ml., ■ 350 ml., ▼ 300 ml.

*A relation between nutritive densities of meals and the volumes emptied in 30 min*

Fig. 1 shows that the volume of original test meal emptied in 30 min was less with meals of high nutritive density than with meals of low nutritive density over the range 0.14–2.3 kcal/ml. of meal (Table 1, lines 1–19). Specification of the meal in terms of kcal/ml. gives a smooth curve for meals of pure carbohydrate and for ordinary food with as much as 60% of the energy as triglyceride (Table 1, line 1). Fig. 1 seems to provide justification of the notion that the volume emptied into the duodenum per unit time is independent of the ratio of fat to carbohydrate in the original meal, provided the nutritive density is fixed. The various symbols distributed along the curve of Fig. 1 indicate the different volumes of original meal. Their fit to the line is not disturbed by variation in the volumes of the original meals over the range 300–750 ml. In these data nutritive density alone determines volume of meal emptied in 30 min, independent of the initial volume of meal.

*Amounts of energy transferred to the duodenum in periods up to 45 min*

When the nutritive densities of meals are multiplied by the volumes emptied in, say 15 or 45 min, the numbers of calories transferred to the duodenum in these periods are obtained. Such results are given in Fig. 2 (Table 1, lines 1–19). More energy was transferred to the duodenum in 15 or 45 min with meals of high nutritive density than with meals of low density. Thus the reduction in the volume delivered per unit time (Fig. 1) was not sufficient to offset completely the raised nutritive density. Fig. 2 allows

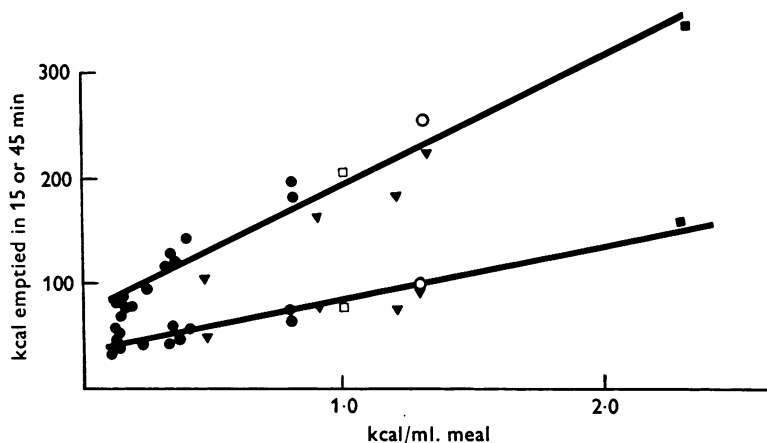


Fig. 2. Relation between amounts of energy (kcal) entering the duodenum in 15 and 45 min and the nutritive density of the meal. Ordinate, amounts of energy (kcal). Abscissa, kcal/ml. meal.  $KV_{E15} = 32.44 + 49.05 K$  (s.e. slope  $\pm 2.03$ ).  $KV_{E45} = 71.56 + 121.63 K$  (s.e. slope  $\pm 6.88$ ).  $V_0$  ● 750 ml., □ 550 ml., ○ 500 ml., ■ 350 ml., ▼ 300 ml.

the rate of delivery of energy to the duodenum to be appreciated, but each line is dependent upon specifying a time, for example, 45 min. This treatment was inappropriate for meals of less than 300 ml., since the stomach was virtually empty before the 45 min period was complete. What was needed was an index of the rate of gastric emptying applicable to all volumes of meal, and not limited to a specific period or to a specific pattern of emptying (Appendix I). Such an index has been used to construct Fig. 3.

*A form of logistic relation between the nutritive density of food and initial gastric efflux (volume of original meal/time to half empty) ( $V_0/t_{0.5}$ )*

An acceptable theoretical basis for the empirical relation between nutritive density and rate of gastric emptying can be derived as follows.

The imposition of a rectilinear relationship between the logarithm of the magnitudes of a stimulus and the relevant responses is often appropriate.

TABLE 1. Summary of results on gastric emptying, taken from the literature

Composition	kcal/ml.	Initial volume ( $V_0$ ) ml.	Half-time min ( $t_{0.5}$ )	s.e. $\pm$	Number of subjects	Authors	Notes
1. Egg breakfast	2.30	350	56	—	5	Harvey <i>et al.</i> (1970)	—
2. Egg breakfast	1.30	500	65	—	5	Tinker <i>et al.</i> (1970)	—
3. Glucose and milk	1.30	300	36	—	37	Brömster (1969)	—
4. Soy bean oil, etc.	1.20	300	43	—	7	Moberg & Carlberger (1974)	Computed on the basis of 19 g xylose, 24 g glucose, macrogol stearate zero
5. Egg breakfast	1.00	550	66	2.4	19	Griffith <i>et al.</i> (1968)	—
6. Soy bean oil	0.90	300	34	—	6	Moberg & Carlberger (1974)	See above
7. Sucrose	0.80	750	82	10	10	Hunt, Macdonald & Spurrell (1951)	—
8. Glucose	0.80	750	80	10	4	Barker <i>et al.</i> (1974)	—
9. Xylose	0.47	300	23	—	8	Moberg & Carlberger (1974)	Osmotic action 1 mole xylose (150 g) equivalent to 1 mole glucose (180 g)
10. Glucose	0.40	750	49	10	4	Barker <i>et al.</i> (1974)	—
11. Glucose	0.36	750	54	5	14	Berger (1969)	—
12. Glucose	0.36	750	48	3	27	Hunt (1957)	—
13. Glucose	0.36	750	55	—	8	Hunt, Knox & Oginski (1965)	—
14. Glucose	0.20	750	29	5	4	Barker <i>et al.</i> (1974)	—

TABLE 1 (continued)

							Reference
15. Glucose	0.14	750	23	3	5		Hunt (1960)
16. Starch	0.14	750	20	4	5		Hunt (1960)
17. Sucrose	0.14	750	22	2	9		Hunt (1956)
18. Sucrose	0.14	750	22	1.3	21		Hunt & Spurrell (1951)
19. Sucrose	0.14	750	18	2	7		Hunt & Macdonald (1954)
20. Sucrose	0.14	300	9	—	7		Moberg & Carlberger (1974)
21. Glucose	0.36	200	13	2	8		L. J. Erskine & J. N. Hunt (unpublished)
22. Triolein	0.22	750	26	4	6		J. N. Hunt & M. T. Knox (unpublished)
23. Glucose	0.18	750	22	2	11		Ramsbottom & Hunt (1970, 1974)
24. Water	0.00	750	11	2	20		George (1968)
25. Water	0.00	750	15	2	8		Hunt & Macdonald (1954)
26. Water	0.00	750	12	5	5		Hunt (1960)
27. Water	0.00	1250	23	3	8		Hunt & Macdonald (1954)
28. Sucrose	0.14	330	17	4	7		Hunt & Macdonald (1954)
29. Glucose	0.40	100	12	2	9		L. J. Erskine & J. N. Hunt (unpublished)
30. Glucose	0.40	50	9	2	9		L. J. Erskine & J. N. Hunt (unpublished)
31. Water	0.00	200	7.5	—	6		L. J. Erskine & J. N. Hunt (unpublished)
32. Water	0.00	150	6.0	—	6		L. J. Erskine & J. N. Hunt (unpublished)
33. Egg breakfast	1.00	300	46	5	11		Davies <i>et al.</i> (1971). Note these are the same authors as Griffith <i>et al.</i> (1968) (no. 5)

As pointed out by Bayliss (1960), this logarithmic relationship can be considered as the central part of a more general relationship, known as logistic, which gives a sigmoid relation between the magnitudes of a stimulus and the relevant responses.

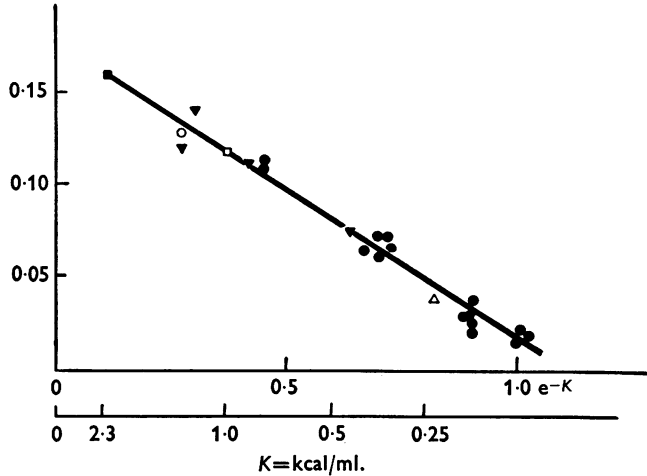


Fig. 3. Relation between ratio time to half empty/volume of original meal and  $e^{-K}$ , where  $K = \text{kcal/ml. meal}$ . Ordinate,  $t_{0.5} (\text{min})/V_0 (\text{ml.})$ . Abscissa,  $e^{-K}$  or  $K (\text{kcal/ml. meal})$ .  $t_{0.5}/V_0 = 0.1797 - 0.1670e^{-K}$  (s.e.  $\pm 0.0050$ ).  $V_0$  ● 750 ml., □ 550 ml., ○ 500 ml., ■ 350 ml., ▼ 300 ml., △ 200 ml.

In the present context the stimulus can be regarded as a function of nutritive density,  $K$ , but contrary to the more common situation, increase in  $K$  causes a reduced rate of gastric emptying, using  $V_0/t_{0.5}$  as the index of initial efflux from the stomach. Hence the logistic relation between nutritive density and rate of gastric emptying is conveniently given by (see Appendix II)

$$\frac{V_0}{t_{0.5}} = \frac{c_1}{1 - c_6 e^{-c_5 K}}, \quad (1)$$

where  $V_0 = \text{initial volume of meal (ml.)}$ ,  $t_{0.5} = \text{time to half empty (min)}$ ,  $K = \text{nutritive density of meal (kcal/ml.)}$ ,  $c_1$ ,  $c_5$  and  $c_6$  are constants.

It is shown in Appendix II, how  $c_5$  was determined to be 1.00.

Relation (1) is curvilinear, but it can be made rectilinear by plotting  $t_{0.5}/V_0$  against  $e^{-K}$  which gives:

$$t_{0.5} = V_0(0.1797 - 0.1670e^{-K}), \text{ s.e. of slope } \pm 0.0050 \quad (2)$$

for the twenty-five points of Fig. 3 (Table 1, 1-21, 24-27) including results for meals of water with initial volumes 750 and 1250 ml. The mathematical implications of eqn. (2) are explored in Appendix II.



*A test of prediction of times to half empty*

The predicted half-times for the twenty-five meals of Fig. 3 were obtained by putting the appropriate values for  $V_0$ , initial volume and  $K$  nutritive density, into eqn. (2). The mean difference between observed and predicted half-times was 0.3 min (s.d.  $\pm$  3 min). There was no systematic deviation of the predicted from the observed half-times, whose mean was 36, range 11–82 min.

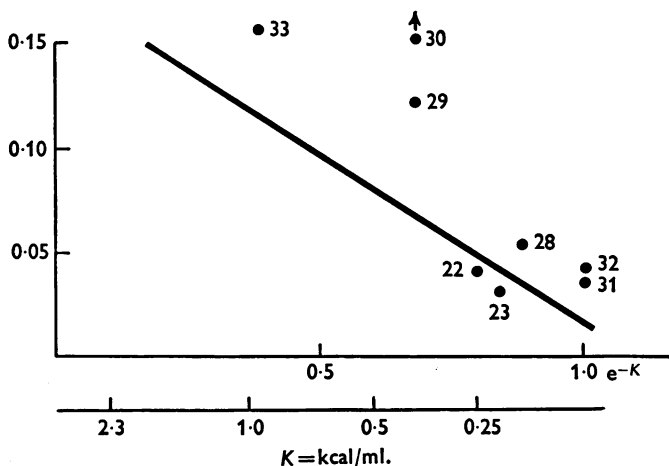


Fig. 4. Relation between ratio time to half empty/volume of original meal and  $e^{-K}$ , where  $K$  = kcal/ml. meal, for anomalous results. The regression line is that fitted to the results of Fig. 4. Numbers on the Figure indicate the lines of Table 1.

*Anomalous results*

Fig. 4 is a repetition of Fig. 3, the regression line being identical, but the points are the anomalous ones from Table 1. Lines 29 and 30 (Table 1) are for meals of 100 ml. and 50 ml. with 0.4 kcal/ml., so that the relationship of Fig. 3 is valid at volumes of 200 but not at volumes of 100 ml. or less. The numbers of Fig. 4 refer to the lines of Table 1.

*Possible spurious correlation*

It is apparent that initial volume,  $V_0$ , appears as the denominator on the ordinate and as part of an exponent  $e^{-K}$  on the abscissa of Fig. 3:  $K$  is total kcal in meal/initial volume ( $V_0$ ). The effect of having  $V_0$  common to ordinate and abscissa has been examined by plotting  $t_{0.5}$  against  $C$ , total energy content of meals, for seventeen meals with volumes of 750 ml. (Table 1). This gave:

$$t_{0.5} = 10.93 + 0.122C \quad \text{s.e. slope } \pm 0.0071.$$

This relation is very highly statistically significant in spite of  $V_0$  having been eliminated. A similar regression for five meals of 300 ml., Table 1, gave a regression equation:

$$t_{0.5} = 4.95 + 0.095C \quad \text{s.e. slope} \pm 0.025,$$

$P < 0.025$  one tailed.

By analysis of variance the populations of the two regressions were found to differ at the 1% level of significance. Thus volume is an independent variable in computing  $t_{0.5}$ . It seems reasonable to conclude that the good fit of the points on to the line of Fig. 3 owes little or nothing to spurious correlation.

*An interaction between receptors responding to the digestion products of carbohydrates and of fats in the diet*

This examination of the results in the literature has shown that, given the nutritive density (kcal/ml.) of a meal, its rate of gastric emptying can be predicted in terms of ml./30 min as in Fig. 1, or in terms of kcal/15 or 45 min as in Fig. 2. This dependence of gastric emptying on nutritive density (kcal/ml.) presumably results from the interaction of two systems of duodenal receptors, one responding to the osmotic pressure of the mono-saccharide products of the digestion of dietary carbohydrates (Mallinson, 1968), and the other responding to the fatty acid anions formed during the digestion of fat (Hunt & Knox, 1968; Knox & Mallinson, 1971). But these systems will respond to energetically inert material: the osmoreceptor responds to potassium chloride as though it were glucose (Barker *et al.* 1974): the fatty acid receptor responds to detergents such as dioctyl sulphosuccinate (J. N. Hunt, unpublished). Under normal conditions the receptors are responding to properties usually, but not always, associated with the energy of food.

Consistent with the results shown in Figs. 1 and 2 is the notion that isocaloric concentrations of fat and carbohydrate give equal slowing of gastric emptying, for example 4 g fat/100 ml. meal must give slowing equal to that caused by 9 g carbohydrate/100 ml., both equivalent to 36 kcal/100 ml. If this is so, it follows that any isocaloric mixtures, no matter what the ratios of fat to carbohydrate, will give the same slowing of gastric emptying.

*Is there a response to dietary protein?*

In computing the nutritive densities for Table 1, each g protein was counted as 4 kcal in the orthodox manner, although at that time slowing of gastric emptying by protein had not been demonstrated. However, M. I. Grossman (personal communication) observed that bovine serum

albumen slowed gastric emptying in the cat. Recently M. A. Fisher & J. N. Hunt (unpublished) have found that in a man casein is equivalent gram for gram to glucose in slowing gastric emptying.

*The effect of the volume of the original meal on gastric emptying*

With the values from Table 1, it is possible to draw a family of straight lines describing the relation between nutritive density of meals and the amount of energy (kcal) delivered to the duodenum in 10, 15, 20 min, etc. Inspection of the 15 min line in Fig. 2 for the two meals, 300 ml. and 500 ml., with nutritive density 1.3 kcal/ml., shows the two points overlapping. The conclusion to be drawn is that gastric emptying is giving a constant transfer of volume to the duodenum in 15 min, in spite of the two initial volumes of the meals being 300 and 500 ml. And presumably equality of volume emptied would be found with other intervals of time. However, consideration has shown that with different initial volumes there is only one emptying pattern which can give, for one nutritive density, equal volumes emptied over a range of time intervals. The required emptying pattern is one in which the volume emptied per min is constant throughout the period of emptying, no matter what the initial volume,  $V_0$ .

TABLE 2. Some numerical implications of the change of half-time with initial volume for meals of 300 and 500 ml. with nutritive density 1.3 kcal/ml.

	<i>A</i>	<i>B</i>
Half-time (min)	36	65
Initial volume ( $V_0$ )	300	500
Volume emptied (ml.) in period		
0-5 min	28	26
0-10 min	53	51
0-15 min	75	74
0-20 min	96	96
0-30 min	132	137
0-60 min	205	236

Volumes emptied are computed on the assumption of exponential emptying.

The results shown in Table 2 allow this point to be studied further. Table 2 is based on the assumption that the emptying patterns are exponential, and it refers to 300 ml. and 500 ml. meals with 1.3 kcal/ml. The half-times for columns *A* and *B* were taken from Table 1. It may be seen that the volumes emptied for the two meals are similar, but not identical, up to 30 min, but by 60 min the 500 ml. meal has emptied 31 ml. more than the 300 ml. meal. From study of Table 2 it may be concluded that the results of Fig. 2 do not diverge from the values required for exponential emptying, provided it is realized that the points for meals of different volumes necessarily diverge from the rectilinear relationship.

Turning again to Fig. 2, it may be seen that the two points for the meals with 1.3 kcal/ml., which are virtually identical at 15 min, have diverged by 45 min, the larger meal having the more rapid emptying.

The relationships of Figs. 1 and 2 are consistent with exponential emptying pattern, allowing that the two linear relations, and any others in the family, are only approximate. Table 2 allows an assessment of the approximation at various times after the meal is given.

*The relation between the time to half empty ( $t_{0.5}$ ) and the initial volume of meal*

The relation  $t_{0.5} = (0.1797 - 0.1670e^{-K}) V_0$  (2) gives a satisfactory prediction of the measured time to half empty for twenty-five of the results from Table 1. But it seems unlikely that the organism computes the time to half empty a meal through an analogous process.

It seems probable that Fig. 1 throws more light on the physiological basis of the regulation of the transfer of energy from the stomach to the duodenum. Fig. 1 shows that the volume received by the duodenum is determined by the nutritive density of the meal, but is independent of the initial volume of the meal. Given that the pattern of gastric emptying is close to exponential, and that the actual rate of emptying is independent of initial volume, it appears that the half-time of the emptying process is being regulated in such a way as to offset changes in initial volume. However, it is easier to visualize that the volume received by the duodenum is held constant for any nutritive density. This view of events fits with that of Weisbrodt *et al.* (1969) who reported a fifteenfold increase in duodenal contractions with a slowly emptying meal containing sodium oleate, as compared to contractions with one containing sodium citrate. The notion that contractions can retard transport is documented for both the small (Gregory, 1950) and for the large bowel (Connell, 1962).

The work of Weisbrodt *et al.* (1969) also supports the idea that the pattern of emptying of the stomach is intrinsically exponential. They reported that antral contractions became progressively less with time as a rapidly emptying meal of sodium citrate solution left the stomach. The gastric emptying of a sodium citrate meal (33 mm) can be regarded as the best approximation to the emptying of a stomach disconnected from the duodenum, because the sodium citrate offers a minimal stimulus to the duodenal osmoreceptors (Hunt & Knox, 1968).

*The anomalous results*

The present results fit together so well that it is necessary to exclude the method of analysis as a cause. However, in Fig. 3 the three variables, volume of original meal, nutritive density and time to half empty appear to be independent, although the calculation of time to half empty does

require knowledge of initial volume. It is therefore reassuring that the results of line 33, by the same authors as the results of line 5 (Table 1) do not fit well on to the regression line of Fig. 3, as shown in Fig. 4. It makes it less likely that some artificial correlation has been created by the method of analysis. The low variances of the measured half-times can be appreciated from Table 1.

*Consequences of the regulation of gastric emptying*

X. Johansson & Y. Lagerlof (personal communication), from measurements of the absorbing capacity of the first 70 cm of duodenum and small intestine, have concluded that the rate of absorption of energy can be limited by the rate of gastric emptying.

APPENDIX I

The rate of emptying of the stomach is a function of the volume within the stomach and the composition of the meal.

We may tentatively write

$$\frac{dV}{dt} = -cV^n, \quad (1.1)$$

where  $t$  is time,  $V$  is volume in the stomach,  $c$  is a constant which is a function of the composition of the meal and  $n$  is an unknown but constant exponent.

If we ignore secretions we may integrate (1.1) and insert the following substitutions:

$$\begin{aligned} V &= V_0 \quad \text{at} \quad t = 0, \\ V &= V_t \quad \text{at} \quad t = t, \\ V_t &= 0.5 V_0 \quad \text{at} \quad t = t_{0.5}. \end{aligned}$$

Thus (for  $n \neq 1$ ):

$$V_t^{1-n} = V_0^{1-n} \left( 1 - (1 - 0.5^{1-n}) \frac{t}{t_{0.5}} \right). \quad (1.2)$$

If we differentiate eqn. (1.2) we obtain:

$$\frac{dV}{dt} = \frac{V_0}{t_{0.5}} \frac{1 - 0.5^{1-n}}{1-n} \left[ 1 - \frac{(1 - 0.5^{1-n})t}{t_{0.5}} \right]^{n/(1-n)}, \quad (1.2)$$

i.e. in the first instant ( $t = 0$ ) the emptying rate,  $\dot{V}_0$ , is given by:

$$\dot{V}_0 = \frac{V_0}{t_{0.5}} \left( \frac{1 - 0.5^{1-n}}{1-n} \right). \quad (1.3)$$

For  $n = 1$ ,  $\dot{V}_0 = \log_e 2 \cdot V_0/t_{0.5}$ . The constant by which  $V_0/t_{0.5}$  is multiplied,  $m$ , is in the range 0.5–1.0 for  $n = 0.0$ –2.0. Evidence cited in the text suggests  $n = 0.5$ –1.0, i.e.  $m = 0.5857 - \log_e 2$ .

Now the volume emptied by time  $t$ ,  $V_{E(t)}$ , is given by

$$V_{E(t)} = V_0 - V_t. \quad (1.4)$$

We may further re-write (1.2) as:

$$V_t = V_0 \left( 1 - \frac{1-n}{V_0} \dot{V}_0 \cdot t \right)^{1/(1-n)}. \quad (1.5)$$

If we expand (1.5) to the first term and insert in (1.4) we obtain:

$$V_{E(t)} = \dot{V}_0 \cdot t. \quad (1.6)$$

That is, for small values of  $t$ ,  $V_{E(t)}$  is the product of time and the initial emptying rate and is independent of the particular model of gastric emptying which is chosen, and independent of the initial volume of the meal. It is shown in the text that  $\dot{V}_0$ , initial gastric efflux, is a function of the nutritive density of the meal alone. Hence  $V_{E(t)}$  is specified by time and the nutritive density of the meal alone (if  $t$  is small).

#### APPENDIX II

Using kinetic theory of receptors, the relationship between a stimulus, of magnitude  $S$ , and a physiological response, magnitude  $R$ , may be given by the following equation (Riggs, 1963):

$$R = \frac{a_1 S}{a_2 + S} + a_3, \quad (2.1)$$

where  $a_1$ ,  $a_2$  and  $a_3$  are constants. Examples are the Michaelis Menten enzyme kinetic equation, the Longmuir gas absorption equation or the  $O_2$  dissociation curve of myoglobin. However, eqn. (2.1) is inconvenient to test statistically since  $a_2$  must be determined iteratively and the higher values of  $S$  cluster together on the regression line and are underweighted in the calculations. We may expand and differentiate (2.1):

$$dR/dS = b_1 S + b_2 S^2 + b_3 S^3. \quad (2.2)$$

Two roots,  $R$  minimum and  $R$  maximum, satisfy (2.2). We take the simplest case of this condition.

$$dR/dS = b_1 S + b_2 S^2, \quad (2.3)$$

eqn. (2.3) solves as:

$$R = \frac{c_1}{1 + c_2 e^{-c_3 S}}. \quad (2.4)$$

Eqn. (2.4) is the logistic equation which has been used, for instance, by Leibovic (1972) in relating input to output across a synapse. The simplest case (first degree) of eqn. (2.2) gives:

$$R = d_1 + d_2 \log S. \quad (2.5)$$

Eqn. (2.5) is used in the Weber–Fechner Law of Psychophysics or the log-dose response of bio-assay methods. However, eqn. (2.5) provides a non-sensical prediction for  $S = 0$  or  $S = \infty$  as Bayliss (Bayliss, 1960) points out. Finney (1971) remarks that equations of the form (2.1, 2.4 and 2.5) are indistinguishable over the middle ranges of  $S$ , so that our selection of eqn. (2.4) was determined by its behaviour at extreme values of  $S$  and its convenience of fitting.

Using (2.4) we chose as  $R$ , the gastric emptying rate in the first instant,  $V_0/t_{0.5}$  (see Appendix I). We put  $c_3S = c_4 + c_5K$ , where  $K$  is the calorie density of a meal. Hence (2.4) is re-written as

$$\frac{V_0}{t_{0.5}} = \frac{c_1}{1 + c_6 e^{-c_5 K}}, \quad (2.6)$$

where  $c_6 = c_2 \cdot e^{-c_4}$ .

If the data are plotted in an equation of type (2.6) it is found that  $c_1$  remains almost independent of changes in  $c_5$ . Hence if  $c_1$  is known  $c_5$  can be obtained by a regression analysis of the equation:

$$K = \frac{1}{c_5} \log c_6 - \frac{1}{c_5} \log \left( \frac{c_1 t_{0.5}}{V_0} - 1 \right). \quad (2.7)$$

Using our data we obtained  $c_1 = 5.5648$ ,  $c_5 = 1.00$  and  $c_6 = -0.9293$ . Hence

$$\frac{V_0}{t_{0.5}} = \frac{5.5648}{1 - 0.9293 e^{-K}}, \quad (2.8)$$

which is easily transformed into relation (2) in the text.

The observed average values for  $K = 0$  fit well within the standard error of the predicted value. The maximal practical value of  $K$  (i.e. 9.6 kcal/ml. in a pure triglyceride) gives  $V_0/t_{0.5}$  less than 0.1 % different from the value predicted for  $K = \infty$ .

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