

J. Physiol. (1954) 126, 459-474

THE INFLUENCE OF VOLUME ON GASTRIC EMPTYING

BY J. N. HUNT AND I. MACDONALD

Department of Physiology, Guy's Hospital, London, S.E. 1

(Received 27 May 1954)

The emptying of the stomach must depend upon the pressure gradient between the stomach and the duodenum, the dimensions of the pyloric canal and the physical properties of the gastric contents. The pressure gradient will be influenced by any factors that affect the expulsive effort of the stomach and/or the resistance of the intestine to filling.

The expulsive effort of the stomach is basically related to the volume of the gastric contents, but many factors may change this effort-volume relationship. Any such factor will clearly have a dual effect upon the stomach: first, by changing the reactivity of that organ to any particular volume; and secondly, by altering from moment to moment the volume to which the stomach has to react as a result of the changed rate of emptying.

The state of affairs in the duodenum and upper intestine operates to regulate gastric emptying in two ways: first, a combination of the volume within the intestine and the pressure therein, that is, the 'receptive capacity' of the intestine, directly decides the resistance to outflow from the stomach; secondly, changes within the intestine for example, of pressure, pH, concentration of solutes or of fat are known to exert an indirect influence upon gastric activity. In addition, Gregory (1950) has shown that intra-gastric stimuli such as distension indirectly affect the 'receptive capacity' of the intestine. Thus the emptying of the stomach must be influenced by the interplay between: (1) the intra-gastric volume affecting the stomach and the intestine; and (2) the intra-intestinal situation influencing the intestine and the stomach.

From this summary of the mutual relationship between the stomach and the intestine it may be seen that the interpretation of any studies of gastric emptying demands a knowledge of the relationship between the behaviour of the gastro-intestinal unit and the intra-luminal volumes. The experiments reported in this paper were made to explore this relationship by studying the gastric emptying patterns in response to different volumes of test-meals.

While it is inherently impossible to separate completely the gastric and intestinal aspects of this process of emptying, one or other may be emphasized experimentally. An account is given of some experiments, placing emphasis on the intestinal contribution by studying the reaction to a second meal given at a short interval after the intestine has received a known amount of a previous meal.

METHODS

The test-meal used in the greater part of this work was a 2% solution of pectin, 3.5% sucrose, with phenol red added as a marker. The reasoning behind this composition and the method of preparation and analysis of the meal have been set out elsewhere (Hunt & Spurrell, 1951). This pectin meal appears to stimulate mainly by distension (Macdonald & Spurrell, 1953). A recent study shows that the pectin, which was originally added to give viscosity to the meal, exerts no detectable influence on emptying or secretion (Hunt, 1954). Information concerning the influence of the volume of the test-meal ingested on the gastric secretory response has already been published (Hunt & Macdonald, 1952).

Procedure

The subjects were volunteer medical students without history of peptic ulceration. They came to the laboratory in the morning, having fasted since the previous evening and, when the stomach had been washed out with 250 ml. of tap water, they drank the chosen test-meal. After a measured interval during which salivary aspiration was maintained the gastric contents were withdrawn. From a knowledge of the amount of phenol red contained in the original meal and the amount of phenol red in the recovered gastric contents, the volume of the original meal in the gastric contents at the time of recovery was calculated. The procedure was repeated on subsequent days but the intervals between swallowing the meal and its recovery were varied. The data so obtained were synthesized into a serial record for each individual of the volume of meal remaining in his stomach during the digestive period.

RESULTS

Five studies were made, the relevant experimental details of which are summarized in Table 1. In order to describe gastric emptying numerically the volume of the original test-meal remaining in the stomach has been plotted on a logarithmic scale against time on a linear scale. The points fall closely about

TABLE 1. Data on the test-meals used in the experiments

Series	A	B	C	D	E
No. of subjects	3	7	8	9	1
No. of withdrawals	53	65	42	58	14
Temperature of meal (° C)	37	20	20	20	37
Concentration of sucrose in meal (g/l.)	35	35	0	0	35, 100
Volume of meals (ml.)	330, 750, 1250	330, 750	750, 1250	750, 750	1250

a straight line indicating exponential emptying so that the rate of emptying of the meal is a constant proportion of the volume of the meal within the stomach. The straight lines were fitted by the method of least squares and the slopes of the lines were described in terms of the time required for the volume of the meal remaining in the stomach to fall by half, that is the 'half-life'. By

extrapolating the fitted straight line it is possible to calculate the value on the time axis corresponding to the original volume of meal ingested, which time value we call the 'starting index'.

Series A, B, C and E

Figs. 1-3 show the results for three subjects each given test-meals of 330, 750 and 1250 ml. containing 3.5% sucrose. It may be seen that as the volume of the meal was increased so the proportion of the meal emptying per minute, represented by the slope of the line, decreased. It may also be seen that the emptying of the final portion of the 1250 ml. meal was more rapid than was demanded by the extension of the exponential pattern. Fig. 4 which sets out data of series E obtained for the emptying of serial meals of 1250 ml. of water without pectin, and with two different concentrations of sucrose, confirms that with this large volume the proportion of the meal leaving the stomach per minute increases towards the end of the digestive period, and suggests that this feature is unaffected by the increase in sugar content of these meals or by the omission of pectin. With 750 ml. meals this final departure from an exponential pattern was not usually seen until less than about 20 ml. of the original meal remained in the stomach.

The numerical data obtained by the 160 experiments of series A-C in seventeen subjects are set out in Tables 2-4. In general the experiments of series B and C confirm in the larger groups of subjects what has been said about the findings in the three subjects of series A.

Series D

Eight medical students and J.N.H. were given pairs of successive meals of 750 ml. The sugar was omitted from these meals to simplify the interpretations of the results since it was thought that 40-50 g of sucrose passing into the intestine might produce hyperglycaemia or reactionary hypoglycaemia. The first of each pair of successive meals served as the 750 ml. controls of series C. As a result of omitting the sucrose the 750 ml. meals left the stomach rather more quickly than the usual 750 ml. meals with 35 g sucrose/l. This rapid emptying was an advantage in that the stimulus to the intestine was large, but a disadvantage in that the time available for comparison between the first and second meal was limited to a digestive period of about 45 min. In addition, reproducible results are less easily obtained when the emptying is very rapid, presumably because small differences in swallowing, initiation of emptying, or recovering the meal are proportionately more significant in determining the volume of the gastric contents.

In synthesizing the data for each subject all the first meals of each pair of successive meals are comparable. The data obtained by the second withdrawal of each day are not strictly comparable with each other because the second

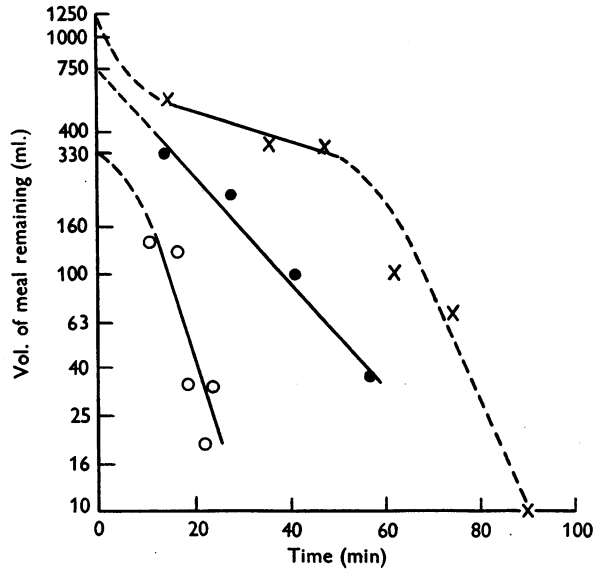


Fig. 1. The gastric emptying patterns for pectin meals of 1250, 750 and 330 ml. Subject M.B.R.M. Ordinate: volume of meal remaining in the stomach (ml.), log scale. Abscissa: time, min.

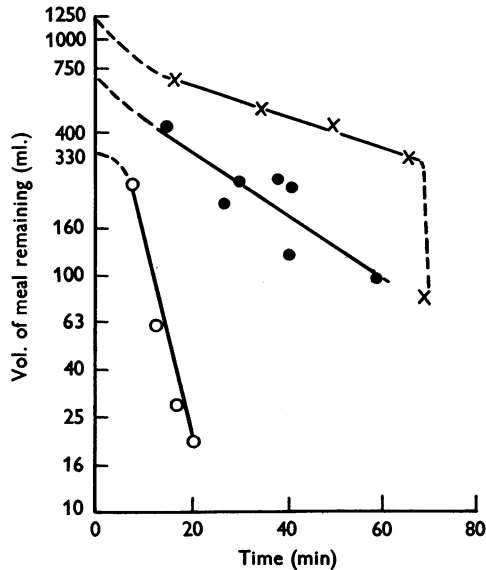


Fig. 2. The gastric emptying patterns for pectin meals of 1250, 750 and 330 ml. Subject R.E.O. Ordinate: volume of meal remaining in the stomach (ml.), log scale. Abscissa: time, min.

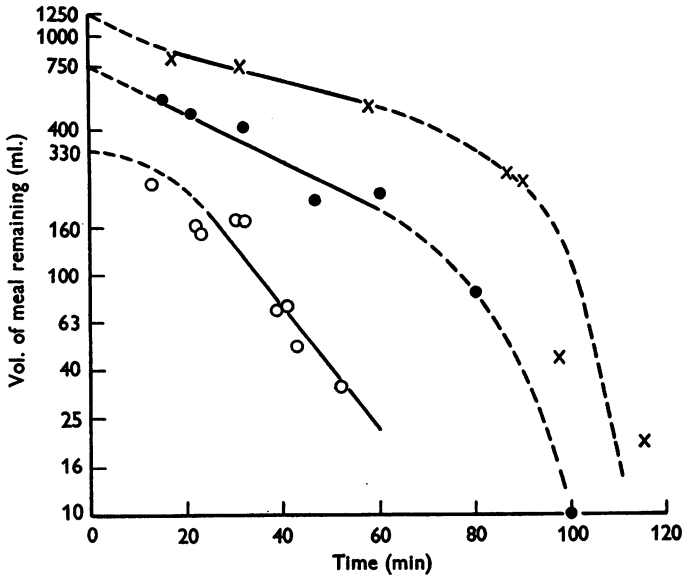


Fig. 3. The gastric emptying patterns for pectin meals of 1250, 750 and 330 ml. Subject J.M. Ordinate: volume of meal remaining in the stomach (ml.), log scale. Abscissa: time, min.

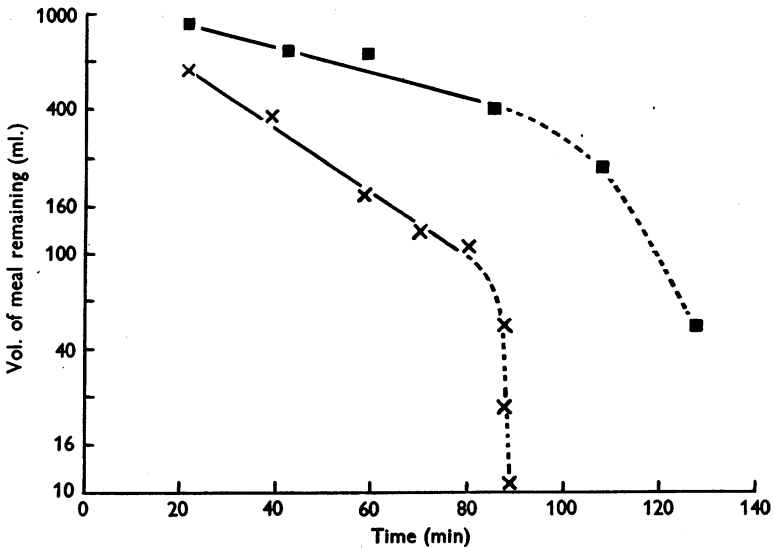


Fig. 4. The gastric emptying patterns for water meals of 1250 ml. containing 35 g and 100 g sucrose/l. Subject J.N.H. Ordinate: volume of meal remaining in the stomach (ml.), log scale. Abscissa: time, min. ■, 100 g sucrose/l.; ×, 35 g sucrose/l.

TABLE 2. Series A. Data on the emptying of pectin meals of 330, 750 and 1250 ml.

Subject	Age (years)	Wt. (lb.)	Ht.	Volume of meal (ml.)			Volume of meal (ml.)			Volume of meal (ml.)		
				330	750	1250	330	750	1250	330	750	1250
				'Half-life' (min)			'Starting index' (min)			Volume of meal leaving the stomach in period 0-15 min (ml.)		
M.B.R.M. (M.)	25	196	6' 0"	4.7	13.3	49.0	+6.1	+0.4	-45.0	240	425	700
R.E.O. (M.)	22	154	5' 8"	3.3	22.4	47.0	+5.8	-6.5	-25.0	183	365	555
J.M. (M.)	22	174	6' 2"	12.4	30.2	56.5	+12.6	0	-14.8	40	217	383

TABLE 3. Series B. Data on the emptying of pectin meals of 330 and 750 ml.

Subject	Age (years)	Wt. (lb.)	Ht.	Volume of meal (ml.)		Volume of meal (ml.)		Volume of meal (ml.)	
				330	750	330	750	330	750
				'Half-life' (min)		'Starting index' (min)		Volume of meal leaving the stomach in period 0-15 min (ml.)	
S.F.E. (F.)	20	126	5' 4"	7	68	+12	-49	79	366
H.C.C. (F.)	21	110	5' 3"	10	17	+6	+6	154	225
B.A.M.A. (F.)	21	129	5' 2"	6	34	+11	-17	121	352
A.P.O.S. (M.)	26	150	5' 10"	9	23	-4	-30	247	560
R.H.F. (M.)	29	140	5' 8"	9	9	-2	+3	239	573
I.C.F. (M.)	28	143	6' 0"	9	17	+6	+3	172	282
J.N.H. (M.)	34	145	5' 9"	14	22	-4	-7	202	378

Table 4. Series C. Data on the emptying of pectin meals of 750 and 1250 ml.

Subject	Age (years)	Wt. (lb.)	Ht.	Volume of meal (ml.)		Volume of meal (ml.)		Volume of meal (ml.)	
				750	1250	750	1250	750	1250
				'Half-life' (min)		'Starting index' (min)		Volume of meal leaving the stomach in period 0-15 min (ml.)	
A.B. (M.)	39	172	5' 10"	6	20	+14	+5	75	490
R.W.E. (M.)	19	130	5' 10"	41	75	-25	-43	370	490
A.J.B. (F.)	28	119	5' 3"	18	17	-4	-4	378	675
P.R.L. (M.)	22	144	5' 9"	9	15	+11	+3	213	558
S.M. (F.)	29	133	5' 6"	8	34	+3	-20	482	626
B.K.O. (F.)	25	144	5' 8"	26	96	-8	-75	338	612
C.F.Y. (M.)	24	143	5' 7"	11	16	+7	+6	293	580
J.N.H. (M.)	34	145	5' 9"	12	26	+3	-9	375	590

recovery on one day might be preceded by a first meal of 15 min duration whilst the second recovery on another day might be preceded by a first meal of 30 min or 45 min duration. However, the data on the amount of meal remaining in the stomach plotted against time fit equally well to an exponential pattern for both the first and the second recoveries. A probable implication of this finding is that the varying duration of the first digestive period does not, in this context, disturb the exponential emptying of the second meal sufficiently for us to detect it. Alternatively, though the points for the second meal may lie on an exponential curve, there is nothing in the

TABLE 5. Series D. The influence of two successive meals on gastric emptying

Subject	Age (years)	Wt. (lb.)	Ht.	No. of pairs of withdrawals	'Half-life' (min)		Student's 't' of difference between half-lives	'Starting index' (min)		Data on the emptying of the gastric contents during the initial part of the digestive period			
					1st meal	2nd meal		1st meal	2nd meal	1st meal		2nd meal	
										Time (min), T_1	Volume of gastric contents at T_1 (ml.)	Time (min), T_2	Volume of gastric contents at T_2 (ml.)
A.B. (M.)	39	172	5' 10"	3	6	8	0.6	+14	+8	17	650	18	490
R.W.E. (M.)	19	130	5' 10"	3	41	10	4.3	-25	+5	15	371	15	378
A.J.B. (F.)	28	119	5' 3"	3	18	7	4.3	-4	+7	15	435	18	375
P.R.L. (M.)	22	144	5' 9"	3	9	3	15.0	+11	+15	16	575	17	570
M.W.P. (M.)	22	164	6' 0"	3	4	6	5.1	+17	+10	19	560	14	580
S.M. (F.)	29	133	5' 6"	4	8	8	0.1	+3	+6	15	330	16	395
B.K.O. (F.)	25	144	5' 8"	4	26	7	3.0	-8	+12	20	505	18	445
C.F.Y. (M.)	24	143	5' 7"	3	11	5	1.6	+7	+11	17	500	17	420
J.N.H. (M.)	34	145	5' 9"	3	12	7	2.0	+3	+6	15	455	15	455

data to make it certain that the intra-gastric conditions at 30 min for the second meal were reached by passing through conditions which had been found to exist at 15 min for the second meal on an earlier day. Nevertheless, records of the emptying for the second meal have been synthesized from these data. It had been expected that the emptying of the second meal would be retarded by the presence of the first meal in the intestine. However, in Table 5, columns 7 and 8 show that the second meal had a shorter 'half-life' than the first meal in six subjects out of nine. The exceptional subjects already had short 'half-lives' for the first meal so that there was little opportunity to show an increase in the rate of emptying of the second.

DISCUSSION

The importance of obtaining reproducible results from day to day

Under the conditions of the experiments described in this paper the emptying pattern of the stomach in response to a standard test-meal is usually stable from day to day. When the volume of the test-meal taken is changed the main pattern of emptying remains exponential, but as the volume ingested becomes larger the percentage of the gastric contents leaving the stomach per minute becomes smaller. The important result of this study is to show that the gastrointestinal unit is not as capricious in its motor behaviour as it has sometimes appeared to be. Once this point has been established it is possible to synthesize data obtained on successive days to build up a general account of gastric emptying. Further, it will be seen below that differences between subjects are quantitative but not qualitative so that an intensive study of a few subjects may provide the basis for generalization.

The emptying pattern of the stomach

The stomach has a basic pattern of emptying during which a constant fraction of the volume of the test-meal remaining in the stomach empties in each minute. This basic pattern does not usually begin as soon as the test-meal is ingested so that there is also an initial phase of emptying to consider. Nor does the exponential phase of emptying continue to the end of the digestive period. Thus it is convenient to describe the gastric emptying of the test-meal in three phases.

Three phases of gastric emptying

(1) There is an initial phase of emptying which may be either faster or slower than would be expected by an extrapolation towards zero time of the basic exponential pattern which follows the initial phase. From the mean of the results for all our subjects taking a meal of pectin solution containing 35 g sucrose/l. it may be said that when the original volume of pectin meal taken is more than 750 ml. the initial rate of emptying is greater than would be expected from extrapolating the basic exponential pattern. When the volume of meal taken is less than 750 ml. the stomach takes a few minutes to reach the rate of emptying required by the basic exponential pattern.

(2) Then follows the basic pattern. During this phase a constant fraction of the meal in the stomach empties per minute. Assuming that the secretion in the stomach is intimately mixed with the meal, the same fraction of the secretion in the stomach empties per minute. Thus the fraction of the test-meal emptying per minute is also the fraction of the gastric contents emptying per minute. The value of this fraction diminishes as the volume of meal ingested is made larger. This basic pattern of emptying may apparently begin almost immediately on taking the meal when 750 ml. of standard pectin meal is given.

(3) There is a final phase of emptying during which the efflux is greater than would be expected from an extrapolation of the preceding basic pattern. In four subjects when the original volume of meal was 1250 ml. this final phase appeared to begin when the volume of meal remaining in the stomach was between about 300 and 100 ml. When the original volume of meal was 750 ml. the final phase was not usually observed until the volume of meal remaining in the stomach had fallen to less than 20 ml. With the 330 ml. meal the final phase was not detected.

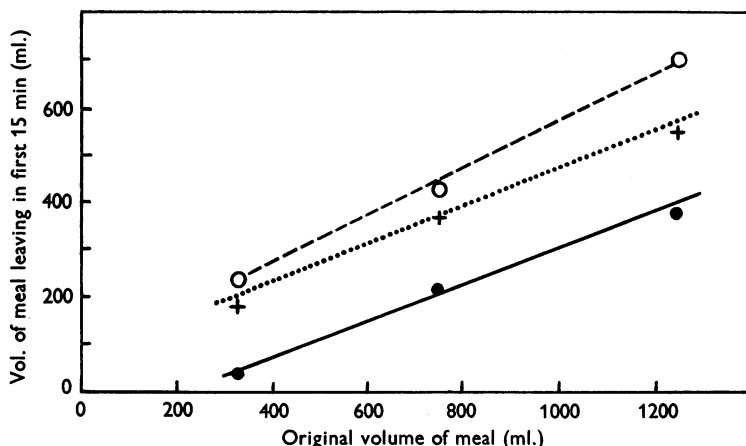


Fig. 5. The volume of meal leaving the stomach during the first 15 min of the digestive period plotted against the original volume of the meal. Ordinate: volume of meal leaving the stomach during the first 15 min of the digestive period, ml. Abscissa: original volume of test-meal, ml. ○, M.B.R.M.; +, R.E.O.; ●, J.M.

Emptying during the early part of the digestive period

Fig. 5 shows the volume of meal which left the stomach during the first 15 min plotted against the original volume ingested for the three subjects of Table 2. It may be seen that the volume which left during the period 0–15 min is related linearly to the volume ingested. This type of relationship is compatible with the idea that the mechanism of emptying during the initial period may be similar throughout the whole range of original volume from 330 to 1250 ml., that is, it is just as orderly for the large as for the small meal. This early emptying is possibly more under the influence of gastric factors than is the subsequent emptying when the volume in the stomach is smaller and that in the intestine larger. Thus the differences between the lines of Fig. 5 may be very tentatively attributed to gastric factors.

The relation between the initial phase of emptying and the basic pattern

The relation of the initial phase of emptying to the basic exponential pattern is described by the 'starting index'. A negative index is found when the

initial rate of emptying is greater than would be expected by an extrapolation towards zero time of the basic emptying pattern. A positive index occurs when the initial emptying is slower than would be expected by such an extrapolation. The 'starting index' therefore depends partly, but only partly, on the slope of the regression line relating log volume of meal and time, i.e. on the 'half-life' of the basic emptying pattern. Apart from this dependence there is a relationship between the 'starting index' and the 'half-life' for the gastric response to any pectin meal, which is shown in Fig. 6 for the three subjects of Table 2.

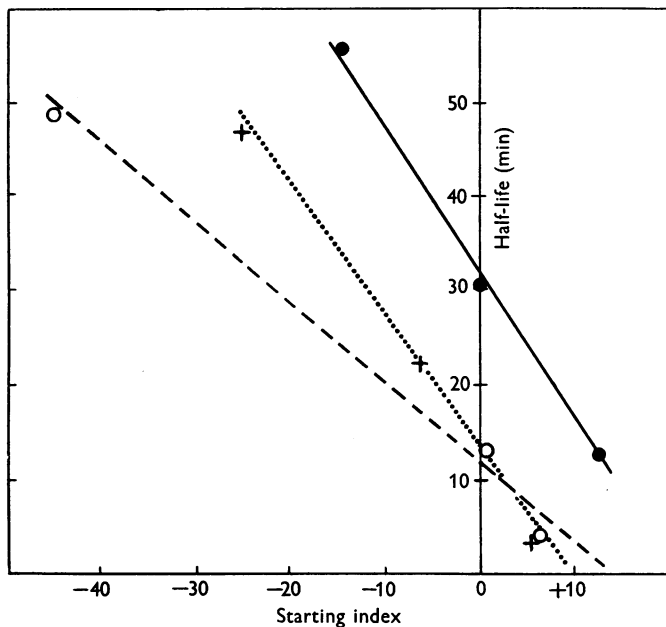


Fig. 6. 'Half-life' plotted against 'starting index' for pectin meals of original volumes of 1250 ml., 750 ml. and 330 ml. Ordinate: 'half-life', min. Abscissa: 'starting index', min. ●, J.M.; +, R.E.O.; ○, M.B.R.M.

As the 'half-life' becomes longer the 'starting index' moves from positive to negative. In physiological terms, as the fraction of the meal in the stomach which empties per minute during the basic emptying pattern becomes smaller, so the initial rate of emptying becomes relatively greater. Broadly speaking, one might suggest that the larger the volume that is taken into the stomach the more does it seem that the gastric propulsive force initially dominates the intestinal retarding influence.

A linear relationship between 'half-life' and 'starting index' occurs in all our data. This may be seen for the main body of data in Fig. 7 based on sixty-two serial meals made up from 391 withdrawals of which 226 have previously been reported (Hunt & Spurrell, 1951; Hunt, Macdonald & Spurrell, 1951).

When $x = \text{'starting index'} + 75 \text{ min}$ (to eliminate negative values of x) and $y = \text{'half-life' (min)}$ it was found that $y = 86.4 - 0.910x$. The standard error of the first constant was ± 1.0 , and that of the second constant ± 0.056 . From this equation it may be calculated that when the 'starting index' is zero the 'half-life' will be 18.2 min. When the concentration of sucrose is raised to 200 g/l. the relationship between 'half-life' and 'starting index' is altered quantitatively as may be seen from the points in the upper part of Fig. 7 (data from Hunt *et al.* 1951). Amongst all the variables such as alteration of

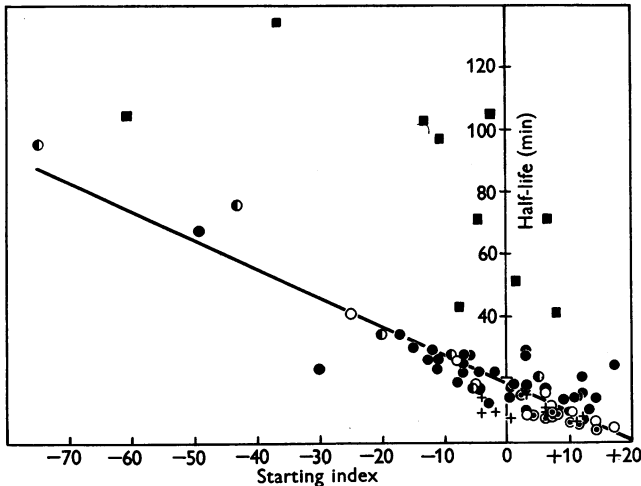


Fig. 7. 'Half-life' plotted against 'starting index' for a variety of test-meals. Ordinate: 'half-life', min. Abscissa: 'starting index', min. ●, 750 ml., 35 g sucrose/l.; +, 330 ml., 35 g sucrose/l.; ⊙, 1250 ml., no sucrose; ○, 750 ml., no sucrose; ■, 750 ml., 200 g sucrose/l.; ⊙, 750 ml., no sucrose, 2nd of two successive meals.

the volume of meal, routine of administration, etc., which are incorporated in the data of Fig. 7 only high concentrations of sucrose alter the relationship between 'half-life' and 'starting index'. But as far as is known the receptors responding to sucrose are sited distal to the pylorus (Quigley & Phelps, 1934). Accepting this view it would appear that the position of the line which could be fitted to the points for meals containing high concentrations of sucrose in Fig. 7 is evidence of the vigour of the intestinal inhibition of gastric emptying.

The emptying of the gastric contents

If one could obtain sufficient data on gastric emptying it would be possible to set up and test hypotheses concerning the influence of the distending volumes in the stomach and in the intestine on the rate of emptying of the gastric contents. Data on the emptying of the meal do not by themselves appear at first sight to be of much value in this context since the distending agent is gastric *contents*, that is meal plus secretion.

It has been indicated that when the volume of the meal in the stomach is plotted on a logarithmic scale against time on a linear scale a straight line is obtained over a considerable part of the digestive period. This finding provides a convenient method of estimating the average volume of meal leaving the stomach during any minute of the exponential period of emptying. This, together with the average simultaneous concentration of phenol red in the gastric contents, obtained graphically, allows the volume of the gastric contents leaving during any minute of the period of exponential emptying to be calculated.

TABLE 6. Data on the emptying of the gastric contents (M.B.R.M.)

Line	Meal	Volume (ml.)		Time (min) <i>T</i>	Rate of efflux (ml./min) at <i>T</i>
		Gastric contents	Gastric effluent		
1	750	150	720	40	7.5
2	330	150	230	13	22.0
3	1250	450	904	40	6.3
4	750	450	355	12	24.0
5	750	425	390	13	22.0
6	330	150	230	13	22.0

Table 6 sets out data for M.B.R.M. on the emptying of the gastric contents, based on the values of Table 2, in such a way as to draw attention to some of the factors influencing gastric emptying. Comparison of lines 1 and 2, and 3 and 4 shows that for a given volume of gastric contents the rate of efflux is slower in those instances where the intestine has received the larger volume of gastric effluent. This may be taken as evidence of the action of the entero-gastric reflex of Thomas, Crider & Mogan (1934). But this is not the only distinction between lines 1 and 2, and between lines 3 and 4, since the duration of the digestive periods differ. A comparison of lines 1 and 3 eliminates this variable. In line 3 a gastric content of 450 ml. empties slightly more slowly into a gut which has received 900 ml. than a gastric content of 150 ml. into an intestine which has received 720 ml. Thus when the initial volume is 1250 ml. the transfer of gastric contents is actually slower at 40 min than when the initial volume of meal is 750 ml. Whether this difference is the result of the greater initial distension of the stomach by the 1250 ml. meal, or whether it is the result of the difference of 180 ml. between the respective volumes of gastric effluent is an open question. In lines 5 and 6 the data have been chosen to give equal rates of efflux and equal digestive periods which are short relative to those of lines 1 and 3. Even under these conditions the rate of efflux does not appear to be simply related to the ratio of the volume of the gastric contents to the gastric effluent.

The data of Table 6 are qualitatively interesting since they allow certain simple hypotheses to be tested but they are not ideal for setting up quantitative relationships. The data on the volume of the gastric contents are useful

and reliable but the data on the volume of the gastric effluent are of limited use. First, they are not a direct measurement since they are calculated from the volume of the gastric contents and the initial volume of the meal. Secondly, they are not the true distending volume within the intestine since they are augmented by intestinal secretion and diminished by absorption. Finally, it seems possible that the receptors which influence the gastric propulsive effort in response to intestinal distension are confined to the upper part of the small intestine (Marbaix, 1898) so that to assess the stimulus to these receptors knowledge of the distribution of the gastric effluent in the small intestine is a prerequisite.

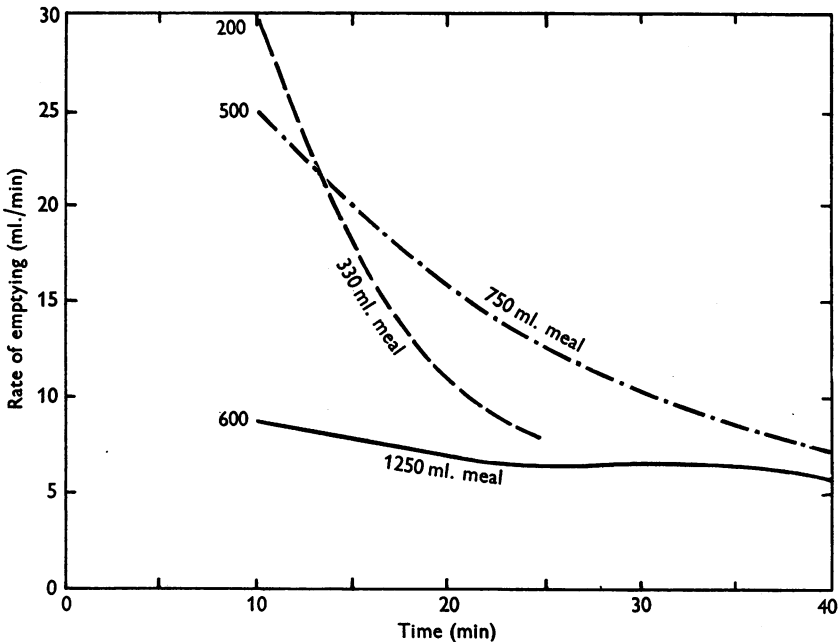


Fig. 8. The emptying patterns of the gastric contents after meals of original volume 330, 750 and 1250 ml. Ordinate: rate of emptying, ml./min. Abscissa: time after ingestion of meal, min. The figures at the start of each curve is the volume in ml. of the gastric contents at 10 min.

The patterns of gastric efflux

The pattern of the changing rates of efflux of the gastric contents with varying initial volumes of meal for subject M.B.R.M. is set out in Fig. 8. It appears that meals of large volume in this subject ran very rapidly into the intestine during the initial phase of the digestive period which was accompanied by a rise of 20 mm Hg in his diastolic blood pressure and profuse sweating. The subject remarked that he normally sweated after meals. It may be noted that with the 1250 ml. meal, after this initial phase of emptying the rate of

emptying of the gastric contents falls only slowly from about 9 ml./min to 6 ml./min. These rates of emptying are probably less than the maximum rate of water absorption in the intestine so that it is not justifiable to regard the change in the rate of emptying as resulting from a stomach containing a slowly declining volume emptying into an intestine containing a constant effective distending volume.

It is worth noting that Salamanca (1949) found that in dogs a 250 ml. test-meal of tea and bread flowed out very rapidly during the first minute or two after ingestion. Such a meal in his dogs would correspond in relative volume to our 1250 ml. meals in man.

The results of giving two meals in succession

It has been shown by Thomas *et al.* (1934) that in conscious dogs the contractions of the pyloric antrum are augmented by allowing the gastric effluent to escape from a duodenal fistula instead of passing into the intestine. An extension of this finding would suggest that duodenal distension inhibits gastric emptying. This has in fact been demonstrated in cats (Spurrell, 1935). Some of the data in Table 6 can be used to support the same hypothesis. It was therefore surprising to find that the 'half-life' of the emptying process of the second of two meals in succession was apparently *shorter* than that for the preceding meal, a finding which confirms the results of Marbaix (1898). We had expected the remnants of the gastric effluent of the first meal in the gut to hamper the emptying of the second meal. There is no consistent evidence of this in the measurements of 'half-life' shown in Table 5 which are in general shorter for the second meal than the first. It is true that the 'starting index' is in general more positive for the second of the two meals but this is to be expected from the relationship between 'starting index' and 'half-life' shown in Fig. 7.

It might be possible to explain the results obtained with two successive meals by saying that the remnants of the first meal in the intestine were responsible for the slowness of establishing emptying of the second meal at the full exponential rate, shown as a more positive 'starting index', and that the shortening of the 'half-life' for the second meal was comparable to the increased vigour of a stretch reflex after inhibition, a type of 'rebound phenomenon'. Inspection of the last four columns of Table 5 which show the volumes of meal emptied at the beginning of the digestive period for the first and second meals does not suggest that there was any marked retention of the gastric contents in those subjects whose 'half-life' for the second meal was markedly shorter for the second meal than it was for the first meal, e.g. R.W.E. and B.K.O. It seems more likely that the retarding influence of the intestine upon gastric emptying is reduced after a large volume has entered the intestine. This would make the rapid emptying of the second meal comparable to the third phase of emptying seen in Figs. 1-4 with meals of 1250 ml.

The control of gastric emptying

The regulation of gastric emptying is very largely under the control of factors which operate through the intestine. Distension of the intestine, or the presence of fat, sugars or hyper-osmotic salt solutions within the intestine reduces the co-ordinated propulsive activity of the gastric antrum and duodenum. The resistance to filling of the intestine is increased by sham feeding, gastric distension or the presence of hyper- and hypo-osmotic solutions within the intestine (Gregory, 1950). Thus the intestine plays a dual role, as the site of receptors regulating gastric activity and as a variable resistance to the gastric effluent. Moreover, the threshold of these regulating mechanisms is low; 35 g sucrose/l., which gives an osmotic pressure one-third that of plasma, gives an appreciable slowing of gastric emptying when compared with distilled water during the first 15 min of the digestive period (Hunt, unpublished). Taking all these points together it would seem reasonable at the moment to regard the stomach and the small intestine as a single functional unit.

The sensitivity of the gastro-intestinal unit to intra-luminal stimuli makes the exponential emptying pattern of the stomach for test-meals a very remarkable performance, since during this phase of emptying the composition of the gastric effluent often changes considerably. This consideration should invite a note of caution in the assessment of the significance of the exponential pattern. It is possible to set up a hypothesis in which the fundamental pattern of gastric emptying is exponential with the actual percentage of the gastric contents emptying per minute being determined by a variety of intra- and extra-gastric factors. Alternatively, it is possible to suppose that the fundamental pattern of the emptying of the stomach in isolation is other than exponential and that the pattern discovered by experiments is dictated by the continuous interplay of intra- and extra-gastric factors giving a pattern which is, under our conditions, indistinguishable from exponential.

Conclusions

The rate of gastric emptying of a standard test-meal is reproducible and is influenced by the interplay between: (1) the volume of the meal taken; (2) the ratio of the volume in the stomach to the volume that has flowed into the intestine; (3) the distension of the stomach and/or intestine which preceded the ingestion of the meal.

SUMMARY

1. Reproducible gastric emptying patterns in response to test-meals of 330, 750 and 1250 ml. were established.
2. The larger the original volume of the meal, the greater was the initial rate of emptying.

3. During the period of exponential emptying the larger the original volume of the meal the smaller was the proportion of the meal which emptied per minute.

4. When two 750 ml. test-meals were given in succession, in the majority of subjects the second meal emptied more rapidly than the first meal.

5. The relevance of these findings to the regulation of the rate of emptying of the stomach is considered.

We are indebted to our students who acted as subjects for their unfailing co-operation. We wish to thank Prof. W. R. Spurrell for his continuous encouragement and for much improvement of the manuscript.

Part of the expenses of this work was defrayed under the terms of the Gillson Scholarship awarded by the Worshipful Society of Apothecaries of London to J. N. Hunt.

REFERENCES

- GREGORY, R. A. (1950). Some factors influencing the passage of fluid through intestinal loops in dogs. *J. Physiol.* **111**, 119-137.
- HUNT, J. N. (1954). The viscosity of a test-meal, its influence on gastric secretion and emptying. *Lancet*, **266**, 17.
- HUNT, J. N. & MACDONALD, I. (1952). The relation between the volume of a test-meal and the gastric secretory response. *J. Physiol.* **117**, 289-300.
- HUNT, J. N., MACDONALD, I. & SPURRELL, W. R. (1951). The gastric response to pectin meals of high osmotic pressure. *J. Physiol.* **115**, 185-195.
- HUNT, J. N. & SPURRELL, W. R. (1951). The pattern of emptying of the human stomach. *J. Physiol.* **113**, 157-168.
- MACDONALD, I. & SPURRELL, W. R. (1953). 'Sham feeding' with the pectin meal. *J. Physiol.* **119**, 259-265.
- MARBAIX, O. (1898). Le passage pylorique. *Cellule*, **14**, 249-330.
- QUIGLEY, J. P. & PHELPS, K. R. (1934). The mechanism of gastric motor inhibition from ingested carbohydrates. *Amer. J. Physiol.* **109**, 133-138.
- SALAMANCA, F. E. DE, jun. (1949). Estudio de fisiología gástrica en el perro. *Arch. Méd. exp.* **12**, fasc. 3, pp. 17-68.
- SPURRELL, W. R. (1935). Duodenal reflexes. *J. Physiol.* **84**, 4-5P.
- THOMAS, J. E., CRIDER, J. O. & MOGAN, C. J. (1934). A study of reflexes involving the pyloric sphincter and antrum and their rôle in gastric evacuation. *Amer. J. Physiol.* **108**, 683-700.