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THE GASTRIC RESPONSE TO PECTIN MEALS OF HIGH OSMOTIC PRESSURE

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Raising the osmotic pressure of a gruel test meal by the addition of glucose, sucrose or sodium chloride will delay gastric emptying and reduce the acidity of the gastric contents. The reduction in the acidity of the gastric contents might be caused by one or more of the following: (1) a reduction in the amount of gastric juice secreted, (2) a reduction in the acidity of the gastric juice secreted, and (3) a reduction in the rate of emptying resulting in a larger volume of the meal remaining in the stomach to dilute the gastric juice secreted. There is experimental evidence that both secretion and emptying are inhibited, but the separate contributions of these two factors cannot be assessed without simultaneous data as to the volume of the meal remaining in the stomach and the quantity and composition of juice secreted from moment to moment. A view commonly held is that of Apperly (1926), who suggested 'that the stomach retains its contents until a suitable osmotic pressure, roughly isotonic with blood, is reached'.

By giving a standard meal containing a dye on successive days, and withdrawing it after progressively longer periods and synthesizing the data so obtained, it has been found possible to measure gastric emptying and secretion (Hunt & Spurrell, 1951; Hunt 1951). This Serial Test-meal makes it possible to follow the progress of gastric emptying and secretion and to determine the effect produced by varying the osmotic pressure of the meals. If, in addition, the osmotic pressure of the gastric contents be followed during the progress of a meal, it is possible to test the Apperly hypothesis in detail. This paper records the results of such an experimental analysis of the 'osmotic effect' of sucrose.

EXPERIMENTAL PROCEDURE

The subjects, medical students or staff, came to the laboratory between 7.30 and 8 a.m. having fasted since the previous evening. After the stomach had been washed out they were given either 750 ml. of a standard pectin meal containing no sugar, or 750 ml. containing 200 g. sucrose/l. The depression of freezing-point of the control meal was 0·05° C., that of the meal containing sugar

1·3° C. The meal without sugar emptied rather quickly, so that withdrawals after 45 min. were not practicable. The meal containing sucrose emptied much more slowly so that the volume of gastric contents was at least 300 ml. after 60 min. However, it appeared pointless to continue after this time since no comparative data about the response to the control meal could be obtained after 45 min. In two of the subjects (J. N. H. and W. R. S.) the original pectin meal with 35 g. sucrose/l. was used as the control and the responses to the meals were followed for 2 hr. In the records the data from these two subjects are marked with an asterisk.

To follow the changes in the osmotic pressure of the gastric contents the depression of the freezing-point was determined in samples from some of these Serial meals and also in samples from a group of fractional gruel meals containing added amounts of sucrose.

RESULTS

The emptying of the meal was slowed by the sucrose but maintained an exponential form: Fig. 1 shows the comparison between the emptying of the

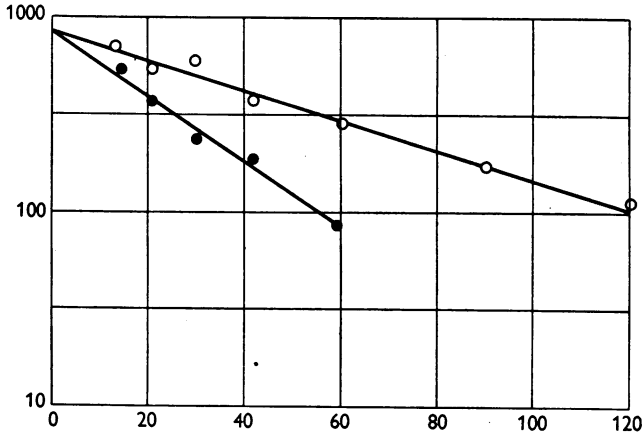

Fig. 1. The influence of sucrose on the emptying of the pectin test meal. Subject J. N. H. Ordinate: volume of meal remaining (ml.) (logarithmic scale). Abscissa: time (min.). ○, 200 g. sucrose/l.; ●, 35 g. sucrose/l.

meals for subject J. N. H. Table 1 gives the number of control and test withdrawals made on each subject and the calculated 'half-lives' for the emptying of the control meals and of those with added sucrose. In all, seventy-six withdrawals were made in ten subjects, every one of whom showed an increase in 'half-life' with the meal containing sugar, the increase varying from twofold to seventeen-fold.

Table 2 shows the calculated 'starting indices' for the two types of meal. It may be seen that with two exceptions the sugar produced a negative deviation of the 'starting index'. Positive 'starting indices' indicate that the rate of emptying is initially less than the ultimate exponential rate; negative 'starting indices' indicate that the initial rate of emptying is greater than the final exponential rate.

TABLE 1. The 'half-lives' of the emptying process of the stomach with meals containing no sucrose and those containing 200 g./l.

Subject	No sucrose: No. of control withdrawals	No sucrose: 'Half-life' (min.)	200 g. sucrose/l.: No. of test withdrawals	200 g. sucrose/l.: 'Half-life' (min.)
A.B.	3	6	4	103
R.W.E.	3	41	3	134
A.J.B.	3	18	3	105
P.R.L.	3	9	3	97
M.W.P.	3	4	3	50
S.M.	4	8	4	105
B.K.O.	4	26	4	69
C.F.A.Y.	3	11	4	68
*J.N.H.	5	18	6	40
*W.R.S.	5	12	6	44
Total	36		40	

* Control meals contained 35 g. sucrose/l.

TABLE 2. 'Starting indices' of the emptying of the stomach with meals containing no sucrose and those containing 200 g./l.

Subject	'Starting indices' (min.): No sucrose *A*	200 g. sucrose/l. *B*	Differences *B–A*
A.B.	+14	−13	−27
R.W.E.	−25	−36	−11
A.J.B.	− 4	−61	−57
P.R.L.	+11	−11	−22
M.W.P.	+17	+ 2	−15
S.M.	+ 3	− 2	− 5
B.K.O.	− 8	+ 6	+14
C.F.A.Y.	+ 7	− 4	−11
*J.N.H.	+ 2	+ 8	+ 6
*W.R.S.	− 3	− 7	− 4

The measurements of secretory activity showed that secretion of the parietal component of gastric juice was reduced when the meal contained sucrose. The rate at which this reduction in secretory activity occurred was not uniform, so it was considered advisable to examine the data in separate periods, 0–15 and 15–30 min. respectively. Table 3 gives for each subject his mean volume of parietal secretion in these two periods; these means were read off individual graphs made from each subject's secretory data. In like fashion the mean amounts of non-parietal component and pepsin secreted are recorded in Tables 4 and 5. Where any doubt could arise as to the statistical significance of the change produced by the sucrose, 'Student's' 't' test (Yule & Kendall, 1947) was applied to the ratio: $\log \frac{\text{test secretion}}{\text{control secretion}}$, a procedure which gives equal weight to halving and doubling a response. The relevant values of 't' and '*P*' are recorded at the foot of the tables.

From Table 3 it may be calculated that the mean volume of parietal component secreted by the group was 25% less for the meal containing sugar than for

TABLE 3. The volume of parietal component formed in response to meals containing no sucrose and those containing 200 g./l.

	0–15 min.			15–30 min.		
Subject	No sucrose *A*	200 g./l. *B*	Log *B*/*A*	No sucrose *C*	200 g./l. *D*	Log *D*/*C*
A.B.	65	52	−0·1	34	13	−0·42
R.W.E.	29	29	0	39	39	0
A.J.B.	32	28	−0·06	46	14	−0·51
P.R.L.	76	70	−0·05	88	28	−0·51
M.W.P.	52	32	−0·21	76	16	−0·68
S.M.	28	18	−0·20	50	12	−0·62
B.K.O.	21	24	+0·06	22	13	−0·23
C.F.A.Y.	13	8	−0·21	5	6	+0·04
*J.N.H.	18	13	−0·14	29	20	−0·16
*W.R.S.	72	25	−0·46	63	22	−0·46

$t=3{\cdot}0$, $P<0{\cdot}02$.

TABLE 4. The volume of non-parietal component formed in response to meals containing no sucrose and those containing 200 g./l.

	0–15 min.			15–30 min.		
Subject	No sucrose *A*	200 g./l. *B*	Log *B*/*A*	No sucrose *C*	200 g./l. *D*	Log *D*/*C*
A.B.	24	18	−0·12	32	5	−0·80
R.W.E.	23	22	−0·01	24	11	−0·34
A.J.B.	28	16	−0·24	12	10	−0·08
P.R.L.	12	13	+0·04	3	8	+0·43
M.W.P.	16	17	+0·04	20	34	+0·23
S.M.	24	20	−0·08	19	10	−0·31
B.K.O.	28	18	−0·20	16	3	−0·70
C.F.A.Y.	28	30	+0·04	23	11	−0·30
*J.N.H.	16	14	−0·06	16	13	−0·10
*W.R.S.	11	6	−0·27	6	2	−0·50

$t=2{\cdot}3$, $P<0{\cdot}05$.

TABLE 5. The pepsin output in response to meals containing no sucrose and those containing 200 g./l.

	0–15 min.			15–30 min.		
Subject	No sucrose *A* (× 1000 units)	200 g./l. *B* (× 1000 units)	Log *B*/*A*	No sucrose *C* (× 1000 units)	200 g./l. *D* (× 1000 units)	Log *D*/*C*
A.B.	12·7	15·0	+0·08	11·6	1·0	−1·05
R.W.E.	6·6	7·0	+0·04	6·9	6·0	−0·06
A.J.B.	5·0	3·2	−0·19	3·9	2·0	−0·29
P.R.L.	9·5	11·0	+0·08	5·5	2·0	−0·44
M.W.P.	7·5	9·5	+0·11	11·5	3·0	−0·58
S.M.	3·0	1·2	−0·40	1·5	1·8	+0·08
B.K.O.	3·5	3·0	−0·07	2·0	1·5	−0·12
C.F.A.Y.	3·0	3·2	−0·03	1·0	1·0	0
*J.N.H.	1·2	0·9	−0·13	1·0	1·0	0
*W.R.S.	8·2	4·6	−0·25	7·3	2·1	−0·53

$t=1{\cdot}1$, $P=0{\cdot}3$.

the control meal in the period 0–15 min. and 65% less during the period 15–30 min. Table 4 shows that the meal containing sugar gave rise to about 16% less non-parietal component than the control meal during the period

0–15 min., and about 37% less non-parietal secretion than the control during the period 15–30 min. The data of Table 4 are the least reliable of all the secretory measurements, since the absolute magnitude of the secretion was often small and a little contamination by swallowed saliva or duodenal regurgitation could result in a relatively large error in the calculated amount of non-parietal secretion. From Table 5 it may be seen that the mean output of pepsin by the group was reduced by only 3% during the period 0–15 min. by the addition of sucrose to the test meal, but during the period 15–30 min. it was reduced by about 60%.

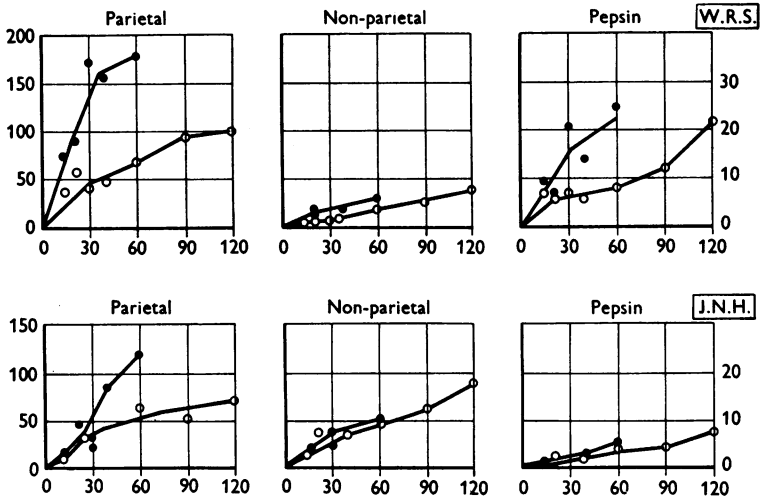

Fig. 2. Cumulative amounts secreted by W. R. S. and J. N. H. Ordinates: volume of parietal and non-parietal components (ml.); amount of pepsin (×1000 units). Abscissa: time (min.). ●, 35 g. sucrose/l.; ○, 200 g. sucrose/l.

Fig. 2 shows the cumulative amounts of each component secreted in response to the test meal containing 35 g. sucrose/l. and 200 g. sucrose/l. by W. R. S. and J. N. H. plotted against time. It may be seen that both subjects showed throughout a reduction in the secretion of parietal component with the meal containing 200 g. sucrose/l. This reduction persisted up to 120 min. and at that time the total parietal secretion was less than 70% of the amount secreted in the 60 min. of the control meal. W. R. S. showed a steady acceleration in the output of pepsin after the initial depression with the meal containing 200g. sucrose/l. J. N. H. showed a similar but unconvincing trend in the same direction. However, the cumulative secretion of pepsin by both subjects at the end of 120 min. with the meal containing 200 g. sucrose/l. was equal to that accumulated at 60 min. with the meal containing 35 g./l. There was a slight initial depression of the secretion of the non-parietal component, but both subjects secreted more non-parietal component in 120 min. with the meal

containing 200 g. sucrose/l. than they did in 60 min. with the meal containing 35 g. sucrose/l.

Fig. 3 shows the respective concentrations of the constituents of gastric secretion in the gastric contents for the two meals, 35 and 200 g. sucrose/l. In subject W. R. S. the concentration of acid at 60 min. was 55 m.equiv./l. in the first meal and 18 m.equiv./l. in the second. The amount of acid secreted was reduced from 175 to 65 ml. and the volume of meal remaining in the stomach to

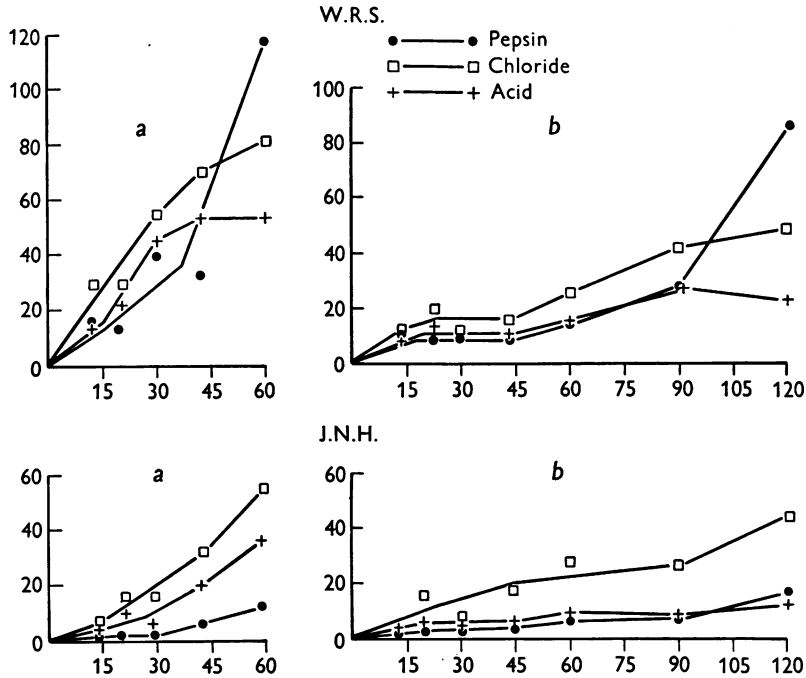

Fig. 3. Concentration of acid, chloride and pepsin in the gastric contents of W. R. S. and J. N. H. Ordinates: concentration of acid and chloride (m.equiv./l.); concentration of pepsin (units/ml.). Abscissa: time (min.). *a*, 35 g. sucrose/l.; *b*, 200 g. sucrose/l.

dilute the retained secretion was increased from 20 to 300 ml. Thus a fifteen-fold increase in the volume of meal remaining in the stomach did not lead to commensurate reduction in the concentration of acid in the gastric contents, thereby indicating that changes in emptying play a small part in altering the acidity of the gastric contents. In subject J. N. H. the reduction in the acidity of the gastric contents at 60 min. was from 38 to 9 m.equiv./l., the secretion of acid was reduced from 115 to 50 ml. and the volume of meal remaining in the stomach to dilute the retained secretion was increased from 80 to 280 ml. These data show the interplay between secretory activity and rate of emptying in deciding the concentration of the constituents of gastric secretion in the gastric contents.

Fig. 4 records the changes in the depression of freezing-point of the gastric contents following a series of fractional gruel test meals containing varying amounts of sucrose. It will be seen that there is a progressive change towards a steady value of the order of $\Delta = 0{\cdot}3°$. With meals of low osmotic pressure there is a rise towards the same value, whereas meals with an initial value of $\Delta = 0{\cdot}3°$ show very little change. With the pectin meal the fall in Δ was from 1·3° to about 0·8° C. in 2 hours.

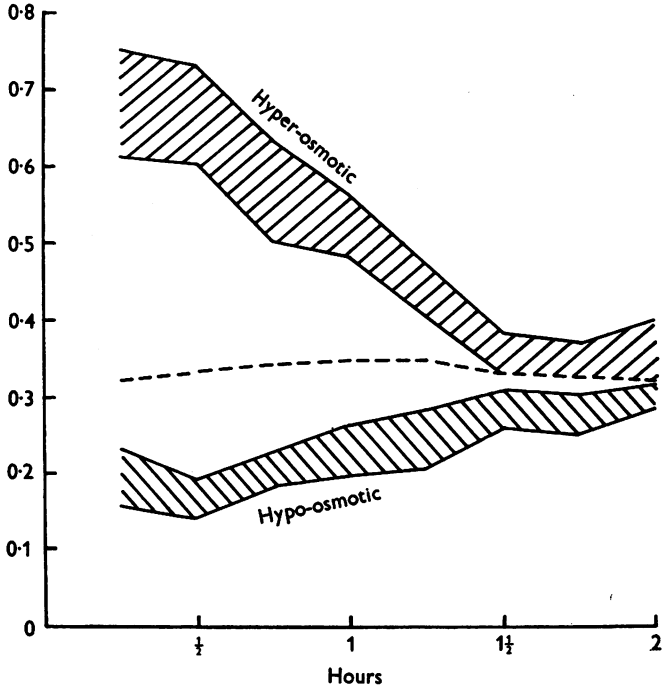

Fig. 4. Changes in the osmotic pressure of the gastric contents with gruel test meals containing sucrose. Ordinate: depression of freezing-point (° C.). Abscissa: time (hr.). Hyperosmotic, $\Delta = 0{\cdot}6$–$0{\cdot}8°$ C.; – – –, $\Delta = 0{\cdot}3°$ C.; Hypo-osmotic, $\Delta < 0{\cdot}2°$ C.

DISCUSSION

The hypothesis enunciated by Apperly (1926), and still exerting an influence on current writing (Wells & Welbourn, 1951; Wollaeger, 1950; Jones, 1951), suggested that a meal of raised osmotic pressure exerted some restraining influence which led to the retention of the gastric contents until by dilution they reached a suitable osmotic pressure, roughly isosmotic with plasma. The experiments described in this paper show that retention is not complete when $\Delta = 1{\cdot}3°$ and that, although there is a progressive reduction of the osmotic pressure of the gastric contents, the achievement of a particular value is not the necessary precursor of gastric emptying, nor is the final value achieved one which is necessarily isosmotic with plasma.

The data obtained by the Serial method show that although emptying is slowed the stomach does not retain a hyperosmotic meal. On the contrary, the rate of flow of the meal into the duodenum is greatest shortly after the meal enters the stomach and becomes progressively less as the volume of the meal in the stomach falls. Thus the osmotic threat to the duodenum, reckoned as rate of entry of sugar, or concentration of sugar entering the duodenum, is maximal at the beginning of the digestive period, i.e. when the emptying process is most vigorous. Thus there is no evidence that the stomach protects the duodenum by first diluting these hyperosmotic pectin meals and then allowing them to flow into the duodenum.

It would still be possible to justify the use of the word 'retain' if it could be shown that the onset of emptying was delayed, but in fact our 'starting index' was given a negative deviation in eight subjects out of ten by the sugar, which is incompatible with significant delay in initiating the emptying of the meal.

Apperly's hypothesis would be justified in part if it could be shown that there was a great outpouring of fluid by the stomach in the initial digestive period. Such an outpouring would lead to an increase in the volume of the gastric contents; this, however, was not found in our experiments. Indeed, to judge from the amounts of acid and chloride secreted, the hyperosmotic meal calls forth less fluid than the control meal. If the stomach were in fact to retain a meal of 750 ml. with a depression of freezing-point of 1·3° C. until this was reduced to 0·6° C. by the addition of normal gastric juice (assumed minimal depression of freezing-point 0·4° C.) the final volume in the stomach would approach 4 l. which would be beyond the tolerance of most persons.

From Fig. 4 it may be seen that the gastric contents do tend to have a constant depression of freezing-point at the end of the digestive period with a value of about 0·3° C. for gruel test meals containing sucrose, which is roughly half the depression of freezing-point of plasma. Whether this particular osmotic pressure is especially suitable for any physiological process is not known but it can be said that the osmotic pressure of a gruel meal having $\Delta = 0{\cdot}3°$ C. suffers minimal alteration in the stomach.

The experiments reported here do not add to what is known of the nature of fundamental mechanism controlling gastric emptying but they do reveal some of the characteristics of the mechanism in operation.

The sequence of events may perhaps be pictured as follows. Following entry of the meal into the stomach, a small amount of material of high osmotic pressure is emptied into the duodenum. Here, acting through some osmo-receptor mechanism, a braking influence is exerted upon the emptying process with the result that in a subsequent equal interval of time a smaller fraction of the gastric contents is ejected—this will be of a slightly lower osmotic pressure owing to gastric dilution and so the osmotic brake will be weaker. Thus in phase with a diminishing osmotic pressure due to dilution of the gastric contents

the duodenal osmotic pressure is gradually reduced, with the result that the emptying pattern retains its exponential form and the osmotic braking is expressed by the increase in 'half-life'. Presumably the 'osmo-receptor' must be a unit possessed of a semi-permeable membrane across which water is drawn by virtue of the high osmotic pressure of the gastric efflux. The unit must be excited by this fluid withdrawal to exert an influence, either humoral or nervous, upon the machinery of gastric emptying. The influence of this 'osmotic brake' can be studied quantitatively by measuring the changes in 'half-life' produced by sucrose.

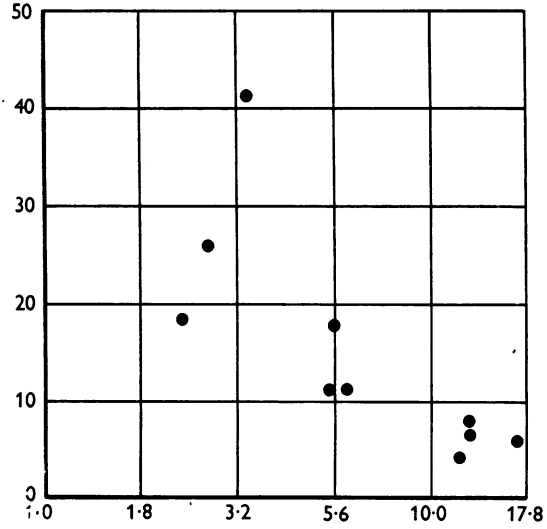

Fig. 5. Control 'half-life' plotted against the change in 'half-life' produced by the addition of 200 g. sucrose/l. of Test meal. Ordinate: control 'half-life' (min.). Abscissa: change in 'half-life' plotted as $\frac{\text{Test 'half-life'}}{\text{Control 'half-life'}}$ on logarithmic scale.

In Fig. 5 the change in 'half-life' produced by adding sucrose, expressed as $\frac{\text{Test 'half-life'}}{\text{Control 'half-life'}}$ on a logarithmic scale has been plotted against control 'half-life'. It may be seen that the shorter the control 'half-life' the greater was the relative slowing of emptying produced by the sugar. Similarly, it was found that the greater the control secretion of parietal component, pepsin and non-parietal component, the greater was the relative reduction in secretion in the period 15–30 min. produced by the standard dose of sucrose. There is thus no question of rapidly emptying or hypersecretory stomachs behaving like runaway horses; they respond perfectly well to a curb in the shape of sucrose, and in fact appear progressively more responsive to that curb as their capacity for running away increases.

Not only is the 'osmotic brake' applied to the machinery of gastric emptying but also to that of gastric secretion, although in the latter the effect of its application lacks the uniformity which is such a striking feature in gastric emptying.

Plotting the change in 'half-life' against the relative reduction in secretion of acid and pepsin in each individual showed that the greater the reduction in secretion the greater was the slowing of emptying. From inspection of Fig. 6 it might be thought that as the increase in 'half-life' reached a certain value before any decrease in secretion of acid was recorded, therefore the threshold for braking was lower for emptying than for secretion. This conclusion, however, is not justifiable for the following reason.

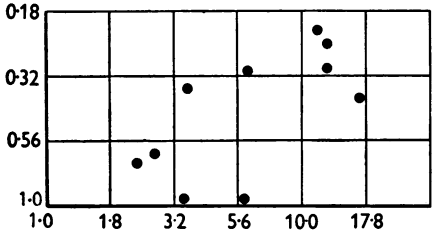

Fig. 6. Inhibition of the secretion of parietal component plotted against change in rate of emptying process produced by adding 200 g. sucrose/l. of Test meal. Ordinate: change in secretion of parietal component plotted as $\frac{\text{Test parietal component (15–30 min.)}}{\text{Control parietal component (15–30 min.)}}$ on logarithmic scale. Abscissa: change in emptying plotted as $\frac{\text{Test 'half-life'}}{\text{Control 'half-life'}}$ on logarithmic scale.

The data on the inhibition of secretion by the sucrose added to the pectin meal is mainly relevant to the first 30 min. of the digestive period, during which time it might be thought that the cephalic phase of secretion would be at its height. However, there are a number of points to suggest that the pectin test meal is not an effective stimulus to the cephalic phase. It was designed to be bland and to excite neither distaste nor appetite: the secretory response was the same when it was given down the tube or swallowed in the ordinary way (Hunt & Macdonald, 1951); and recently Janowitz, Hollander, Orringer, Levy, Winkelstein, Kaufman & Margolin (1950) have shown that gruel test meals excited no cephalic secretion in a subject with a gastric fistula. If the secretion in response to the test meal is not the cephalic phase of secretion it seems probable that distension of the stomach may be an important factor in stimulating the secretion. Thus a meal emptying slowly might be expected to provoke a greater amount of secretion than one of the same initial volume which left rapidly, so that the meal containing 200 g. sucrose/l. may be considerably more effective as a stimulus to secretion than the control meal. It follows, therefore, that it is not possible to make quantitative comparisons of the inhibiting effect of sucrose on gastric secretion by comparing the volume of

secretion in response to the meal containing sucrose with the response to the control meal, because effective distending stimuli are not equal.

It may be noted from Tables 3–5 that the output of pepsin did not apparently come under inhibition as quickly as did the secretion of parietal and non-parietal component. A possible explanation is that the initial part of the output of pepsin was not truly secreted but was merely washed from the tubules and thus not susceptible to inhibition, except in so far as the volume washing out the tubules was reduced.

In the first study from this laboratory with Serial Test meal (Hunt, 1951), it was noted that in five subjects the rate of secretion of pepsin had two peaks, as distinct from the secretion of acid which fell away progressively with time. It is thus interesting to see that whereas in the period 15–30 min. the output of pepsin and secretion of acid in subjects W. R. S. and J. N. H. were both inhibited, later the inhibition of the secretion of parietal component persisted but the rate of secretion of pepsin rose. It does not seem probable that a 'gastrin', acting as we know it in experimental animals, can be the cause of this second peak in the rate of secretion of pepsin, for gastrin typically stimulates the production of a juice poor in pepsin. This observation suggests that there may exist some non-cephalic mechanism other than gastrin to account for the second peak in pepsin secretion and that this second peak is not so susceptible to the 'osmotic brake'.

SUMMARY

1. The 'osmotic effect' of sucrose on gastric secretion and emptying has been studied by means of the Serial Test meal.

2. The emptying of the stomach was slowed by the sucrose but the exponential character of the emptying process was not lost.

3. Evidence was obtained that the achievement of a certain intra-gastric osmotic pressure by dilution was not a necessary precursor of gastric emptying.

4. The secretion of the parietal component, pepsin, and the non-parietal component was reduced by the addition of sucrose, the relative reduction being greater during the period 15–30 min. than during the period 0–15 min.

5. The greater the emptying and secretory activity of the stomach the greater was the relative inhibition produced by the addition of sucrose.

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