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THE SECRETORY PATTERN OF THE STOMACH OF MAN*

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The secretory work of the stomach is the attainment of concentrations of acid and pepsin in the gastric contents sufficient to reduce an ingested meal to chyme within the time available. The concentrations achieved in the gastric contents depend not only on the amounts secreted but also upon the volume of the meal ingested and the rate at which it and admixed secretions leave the stomach. By means of the gruel fractional test meal the resultant of these contributions to the concentrations of acid, pepsin and chloride in the gastric contents may be assessed but it is quite impossible by the fractional method to measure separately the contributions either of the secretory or of evacuatory functions.

In the data hitherto available there are two deficiencies which prevent the measurement of the amounts secreted in response to a meal. First, the volume of the gastric contents is not measured when the concentrations of the constituents of the gastric secretions in the gastric contents are measured by the fractional method. Thus the amount of any constituent in the stomach cannot be calculated. Second, an unknown amount of secretion passes out of the stomach through the pylorus with the gastric contents. By means of the Serial Test meal described in this paper these two deficiencies have been remedied.

The principle of the Serial Test meal. A standard test meal is given at a fixed time to the same subject on successive days, the time of complete withdrawal of the meal being progressively later on each day. By incorporating a dye in the meal the amounts of chloride and acid contained in the volume of the gastric contents leaving the stomach during any interval between withdrawals may be calculated. Then by synthesizing the data obtained from each withdrawal on the same subject into one record a complete picture of his gastric activity may be formed.

Although from the results of Serial Test meals the amounts of acid, chloride and pepsin secreted by the stomach may be calculated, it is usual to measure

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secretions in terms of the *volume* formed and it has proved possible to calculate the volume of gastric juice from the amounts of chloride and acid secreted. This volume has been further divided into two hypothetical components, an acid component and an alkaline component, and the secretory response of the stomach has been expressed in terms of the volumes of these two components formed, and of the proteolytic activity of the enzymes produced.

The results of a study of gastric emptying by Serial Test meals in 21 healthy subjects have already been described (Hunt & Spurrell, 1951). This present paper describes the extension of the technique to secretory studies and sets out the results obtained in 190 withdrawals from 21 healthy subjects. The observations were made simultaneously with those for the study of gastric emptying.

METHODS

Experimental methods. The experimental procedure and the method of making the test meal have already been described (Hunt & Spurrell, 1951). The concentrations of acid and chloride in the gastric contents were measured by electrometric titration (Hunt, 1949) and the concentration of phenol red by a method already described (Hunt, 1947).

The proteolytic activity of the gastric contents was estimated by a modification of the Anson & Mirsky (1932) method using a substrate of plasma proteins. As the proteins proved to be uniform, whether prepared in England or the U.S.A., the method allowed the proteolytic activity of the gastric contents to be expressed in terms of reproducible arbitrary standard units (Hunt, 1948*a*). It was found that comparisons of the proteolytic activity of gastric juices could not be made with commercial pepsin as a standard owing to the presence of a peptic synergist in human gastric juice (Hunt, 1948*b*).

The proteolytic activity of the gastric contents is the resultant of the amount of enzymes and their inhibitors present. In this work the term 'pepsin' refers to values calculated from the actual proteolytic activity of the gastric contents. All estimations of proteolytic activity were made in duplicate. At 4° C. the proteolytic activity has been found to be stable for periods up to 14 days.

Arithmetical methods. The method of calculating the volume of the gastric contents leaving the stomach during an interval of time has already been described (Hunt & Spurrell, 1951).

The amount of chloride secreted by an individual during any one interval, i.e. between t_1 and t_2, was calculated in the following way:

Amount of Cl^- secreted between t_1 and t_2
= Amount in stomach at t_2 + Amount passing the pylorus between t_1 and t_2
− Amount in stomach at t_1

Amount in stomach at t_2
= Vol. of gastric contents at t_2 × Concentration of Cl^- in the gastric contents at t_2

The amount in the stomach at t_1 was calculated similarly.

$$\text{Amount of } Cl^- \text{ passing pylorus between } t_1 \text{ and } t_2 = \text{Vol. passing pylorus} \times \frac{\text{Conc. of } Cl^- \text{ at } t_1 + \text{Conc. of } Cl^- \text{ at } t_2}{2}$$

This same method was applied to the calculation of the amounts of acid and pepsin secreted by each subject. It assumes that all of these substances had their origin in the stomach, an assumption which will be discussed later.

The emptying behaviour of the stomach was almost always reproducible from day to day. This was usually found to be true of the secretory activity of the stomach but occasionally there was some variation. In such cases it was necessary to apply certain restrictions of selection when

calculating. The rules of selection were based upon consideration of the following situations which would provide reasons for the rejection of the immediately antecedent meal as a basis for the arithmetical analysis.

1. Higher concentrations in the gastric contents at 15 min. than at 30 min. of
   (*a*) Cl^-
   (*b*) proteolytic activity,

or (*c*) acid. (This has been applied only to the first 45 min.)

2. Lower concentrations of phenol red at 15 min. than at 30 min.
3. Smaller amounts of phenol red in the stomach at 15 min. than at 30 min.
4. Rise in concentration of acid in the gastric contents out of proportion to the rise in the concentration of Cl^- on the basis of the assumption that the parietal secretion contains 170 m.equiv./l. Cl^- and 160 m.equiv./l. H^+ (Fisher & Hunt, 1950).
5. A fall in the concentration of Cl^- in the gastric contents when it is below 125 m.equiv./l. Since the minimum concentration of chloride in the gastric juice is 125 m.equiv./l. any fall below this level must be due to dilution with saliva or duodenal juice.
6. A fall in the concentration of phenol red without a comparable rise in the concentration of Cl^-. It is impossible for the concentration of phenol red to fall between one sample and the next without any concomitant rise in the concentration of Cl^- unless the initial concentration is more than 125 m.equiv./l.
7. Time intervals of less than 10 min. between withdrawals.

For the sake of clarity only the results of two recoveries at 15 and 30 min. have been used as an example.

Since acid may be neutralized and proteolytic enzymes may probably be inactivated, it is possible for apparently negative amounts of these constituents to be secreted. Measurements concordant with this were noted occasionally in the later samples. Hence 1 (*b*) and 1 (*c*) were not applied throughout the meal.

These rules were applied with discretion where the differences in concentrations in the gastric contents were small. In a few cases the amount of proteolytic enzymes secreted was calculated with a starting-point different from that for other constituents since the secretion of these enzymes appeared to have varied independently of the other constituents.

Having calculated the amounts of these three constituents secreted by the subjects it was necessary to estimate the volume of gastric secretion in which these amounts were contained. It has been suggested (Fisher & Hunt, 1950) that the gastric juice may be considered as a mixture of two components, parietal and non-parietal, in so far as the main inorganic constituents are concerned. The volumes of these two hypothetical components can be calculated if the amounts of chloride and acid are known, using the following equations

$$\text{Volume of parietal component} = 4{\cdot}521\ \text{H} + 1{\cdot}628\ \text{Cl},$$
$$\text{Volume of non-parietal component} = 5{\cdot}778\ \text{Cl} - 6{\cdot}147\ \text{H},$$

when Cl and H are the number of m.equiv. of chloride and acid secreted. Using these equations and the amounts of chloride and acid secreted by the subjects, the volumes of parietal and non-parietal secretion have been calculated and the values so obtained, and the values for pepsin secreted, plotted cumulatively against time. From these plots mean cumulative graphs were calculated for each individual for the components of secretion. Fig. 1 (*a–d*) gives examples of such individual records. In order to assess the variability about the cumulative means for each subject, the deviation of each experimentally determined point from the mean was found and expressed as a percentage of the mean at the relevant point in time. Sums of the squares of these percentages were computed and divided by the total number of points plotted. The value obtained for each subject was called the 'consistency index'.

RESULTS

In Table 1 the total volumes of parietal component, non-parietal component and the amounts of pepsin secreted by each subject are shown together with

the 'consistency indices'; the mean 'consistency indices' are greatest for pepsin and least for parietal component. The mean total volume of parietal component secreted was 135 ml. (S.D. ± 77), the mean total volume of non-parietal component was 103 ml. (S.D. ± 41) and the mean total amount of pepsin 24,000 units (S.D. ± 16,800).

TABLE 1. Total volumes of parietal component, non-parietal component and amounts of pepsin secreted in response to the pectin test meal

Subject	No. of meals	Volume of parietal component (ml.)	'Consistency index'	Volume of non-parietal component (ml.)	'Consistency index'	Amounts of pepsin (units)	'Consistency index'
J.G.L.	6	290	856	116	440	30,000	8
E.C.	5	250	308	140	455	81,000	544
B.L.M.	6	250	258	88	1,034	40,500	24
F.D.B (*a*)	4	234	0	46	0	50,600	0
P.H.	8	210	72	140	3,558	43,500	987
P.S.E. (*a*)	5	196	81	38	1,696	29,000	993
R.C.S.	7	190	422	64	1,007	14,000	5,106
K.J.	8	188	179	180	477	34,000	158
E.R.H. (*a*)	6	166	71	104	0	26,500	45
W.R.S.	12	148	67	50	1,202	32,000	279
J.E.S.	8	140	129	120	2,005	22,000	69
F.L.D.S.	13	132	1,882	122	1,938	22,000	955
M.J.P.	7	110	510	50	1,376	16,000	1,455
E.C.S.	7	106	1,027	104	1,460	23,000	971
E.M.	8	96	3,594	210	658	16,000	5,260
H.S.R.	9	93	305	100	192	15,000	181
R.W.B.	8	88	1,263	104	6,299	26,000	2,465
G.B.S.	6	76	120	62	141	9,500	208
C.H.O.	9	68	4,569	108	226	6,000	4,257
F.J.A.B.	5	65	491	130	49	12,800	1,534
J.N.H.	25	55	190	70	106	2,200	1,696
F.D.B. (*b*)	4	42	6	112	91	12,300	60
P.S.E. (*b*)	6	36	48	104	93	10,500	2,551
E.R.H. (*b*)	8	20	2,038	104	672	2,000	14,749*
Mean	—	135	770	103	1,048	24,000	1,241
Standard deviation as % of mean	—	±57	—	±40	—	±70	—

* Omitted from mean.

TABLE 2. Mean amounts of parietal and non-parietal component and pepsin secreted by 21 subjects plotted cumulatively against time

Time (min.) ...	15	30	45	60	75	90
Parietal component (ml.)	37	69	92	111	129	149
Standard deviation as % of mean	±53	±49	±51	±54	±48	±41
Non-parietal component (ml.)	20	36	50	63	79	105
Standard deviation as % of mean	±32	±28	±30	±34	±34	±35
Pepsin (units)	5,790	11,090	16,530	19,740	20,060	—
Standard deviation as % of mean	±68	±60	±63	±65	±64	—

From the individual curves for cumulative secretion, the means for the group can be calculated for any intervals of time. In Table 2 these means have

been set out for each secretory component for intervals of 15 min. up to 75 min. The standard deviations expressed as a percentage of the mean are roughly constant for each component; the biggest variation between individuals being in the secretion of pepsin, the least in the secretion of parietal component.

The data derived graphically for individuals were studied to establish the times of the maximum rates of secretion for the three components. For the parietal component 13 records showed maximal rates of secretion in the first 15 min. period, 7 in the 2nd period, 1 in the 3rd period and 3 in the 4th and 5th periods. There was no remarkable difference between the mean maximal rates of secretion of these groups but the total volume of parietal secretion formed by the 4 subjects (F.D.B. (*a*), B.L.M., J.G.L. and H.S.R.) having maximal rates of secretion in the 3rd, 4th and 5th periods was 217 ml. (S.E. of mean ± 43), compared with a mean of 107 ml. (S.E. of mean ± 16·5) for those secreting maximally in the 1st period. Ten subjects had maximum rates of secretion of parietal component greater than 3 ml./min., the highest rate being 5·4 ml./min., the lowest peak being about 1 ml./min. The rates of secretion of acid had only one peak during the meal. Considering the group as a whole, three-quarters of the total volume of parietal fluid was secreted in the first third of the 'emptying time'.

When considering the data on the rates of secretion of non-parietal component, which were extracted from the records for individuals it must be pointed out that the stomach was washed out with saline (125 m.equiv.NaCl/l.) at the beginning of the meal in about the first 50 of the experiments. The volume of non-parietal secretion shown to be secreted during the first 15 min. was particularly influenced by this factor and in some subjects may well have been recorded as 10–20 ml. higher than it was. Eight records showed their maximal rates of secretion of non-parietal component during the first 15 min.; of these three showed a second lower peak during the 60–75 min. period. The remaining records showed maximal rates of secretion in the periods between 30 and 120 min., twelve records having their peaks after 60 min. The maximum observed rates of secretion for non-parietal component lay between 1 and 2 ml./min. The general conclusion to be drawn is that the rate of secretion of the non-parietal fluid tended to increase towards the end of the meal but some subjects nevertheless may have had relatively high rates of secretion in the first 15 min.

When the rates of secretion of pepsin were examined it was found that 7 subjects had maximum rates of secretion during the first 15 min., 8 during the 2nd period, 4 in the 3rd, 2 in the 3rd and 4th periods, and 2 subjects in the 5th period. The maximum rates of secretion lay between 1000 and 50 units/min. It was also found that 5 subjects had two peaks in their rate of secretion of pepsin.

This consideration of the peaks in the rates of secretion in individual subjects should serve to emphasize that smooth curves are typical of very few persons.

All the subjects of this research were normal in that they had no symptoms of illness, so that each of the individual records is a record of normality. It is possible to some extent to divide the cumulative graphical records for individuals into groups having certain features in common. Using the particular scales chosen (Fig. 1*a–d*), for the most part the line denoting the parietal component is the highest, followed by that for pepsin, the line representing non-parietal component being the lowest of the three, which rise more or less together. There are 15 such records, of which a typical example is given in

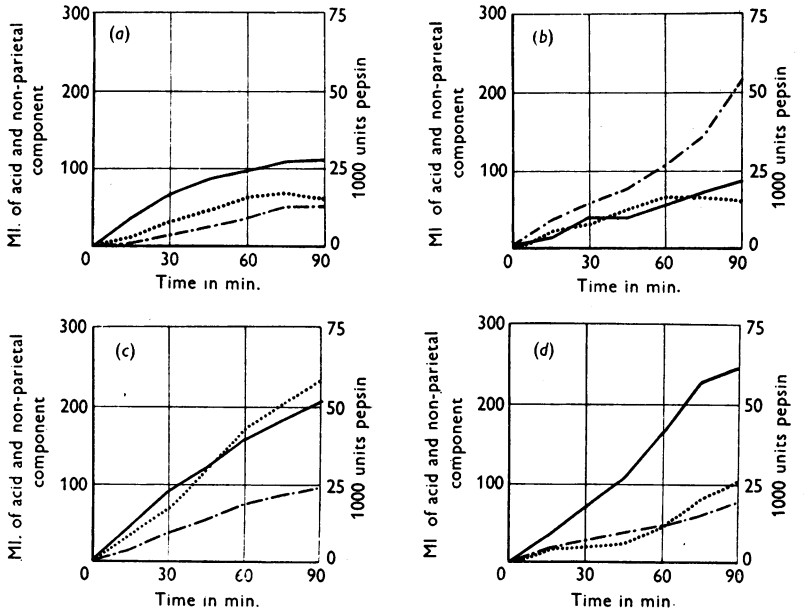

Fig. 1. Cumulative curves of secretion of parietal and non-parietal components, and of pepsin, in four subjects. (*a*) M.J.P.; (*b*) E.M.; (*c*) E.C.; (*d*) J.G.L. ——, parietal; - - - -, non-parietal; ....., pepsin.

Fig. 1*a*. In the 9 other records the secretion of acid and pepsin is more or less depressed relative to the secretion of the non-parietal component (Fig. 1*b*). There are three subjects, F.D.B. (*a*), R.W.B. and E.C. in whom the secretion of pepsin is high relative to the secretion of acid (Fig. 1*c*) and 2 subjects, J.G.L. and R.C.S., in whom the secretion of acid is high relative to the secretion of pepsin (Fig. 1*d*).

The results described so far have involved some selection in the analysis which has its advantage in that it allows the 'consistency indices' for each component to be calculated for each subject and enables the variations between individuals to be appreciated. The selections, however, are open to criticism and therefore a more secure analysis of the mean results for the whole group of 21 subjects was made.

Means of the experimental observations made on the gastric contents were calculated and were so combined as to try to give equal weight to each subject in spite of the different number of meals given to each. However, after the 60–75 min. period the subjects who empty the more slowly have a disproportionate influence on the mean since the subjects emptying quickly no longer contribute. The results are shown in Table 3.

TABLE 3. Mean results of Serial Test meals on 21 subjects

Time of withdrawal (min.) ...	15	30	45	60	75	90
Volume recovered (ml.)	539	385	291	196	147	121
Concentration of Cl^- (m.equiv./l.)	14·5	29·9	43·3	59·1	62·0	72·9
Acid (m.equiv./l.)	7·6	18·4	25·8	34·1	33·6	25·5
Pepsin (units/ml.)	9·7	18·7	28·1	40·8	46·9	62·8
Phenol red as percentage of conc. ingested	88·5	76·5	67·0	61·1	56·9	47·9
Rate of emptying of gastric contents (ml./min.)	19·3	14·7	9·3	7·9	4·0	3·3
Volume of parietal secretion (ml./15 min.)	39	40	26	20	6	3
Volume of non-parietal secretion (ml./15 min.)	26	14	15	13	5	19
Total volume of secretion (ml./15 min.)	65	54	41	33	11	22
Rate of secretion of pepsin (units/min.)	443	316	283	256	105	69

It may be seen that the rate of secretion of parietal component fell after 30 min. The total volume secreted up to 90 min. was 134 ml., which agrees well with Table 1.

The fall in the rate of secretion of non-parietal fluid was proportionately less and there was an increase in the calculated rate of secretion during the 75–90 min. period. The total volume of non-parietal secretion formed was 92 ml. as compared with 103 ml. in Table 1. The discrepancy is the result of the analysis of the mean results in Table 3 not being carried past 90 min., after which time a number of subjects still secreted considerable volumes. The selective incidence of this error on the non-parietal component and not on the parietal component is to be expected since the majority of the parietal component was secreted at the beginning of the meal.

The rate of secretion of pepsin fell with time but not to the same extent as did rate of secretion of the parietal component. The mean amount of pepsin secreted, calculated from Table 3, was 22,000 units, as compared with the mean value of 24,000 units from Table 1. This difference has the same cause as was described for the non-parietal component.

The interrelations of the components of the gastric juice. Up to this point the experimental data have been analysed in terms of two hypothetical components of the gastric juice, and pepsin. Nothing has been said of the composition of the total secretions entering the stomach. Such questions as 'What was the

total volume of gastric juice secreted by individual subjects?' and 'What was the concentration of acid and pepsin in the juice?' remain to be considered.

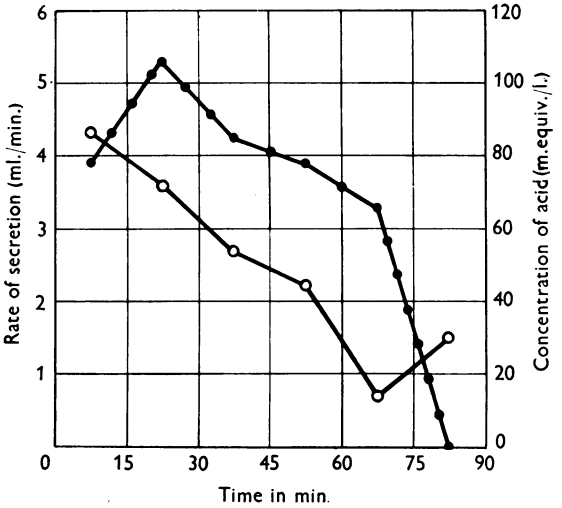

Fig. 2. Rate of secretion of gastric juice and concentration of acid in gastric juice, with the pectin test meal. Means for 21 subjects. o——o, rate of secretion; •——•, concentration of acid.

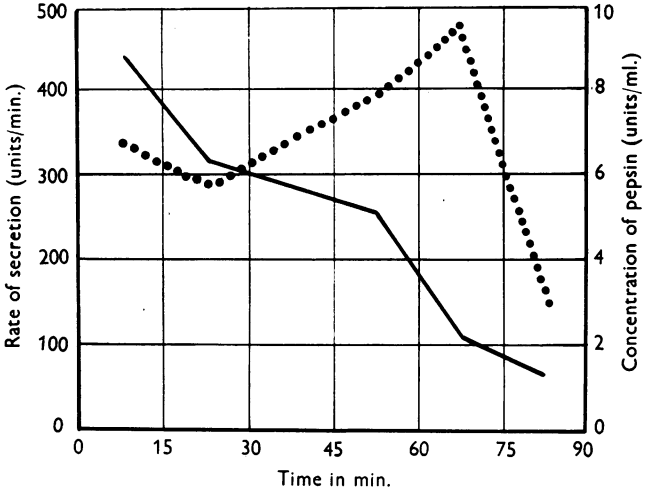

Fig. 3. Rate of secretion of pepsin and concentration of pepsin in gastric secretion in response to pectin test meals. Means for 21 subjects. ••••, concentration of pepsin; ——, rate of secretion.

In Fig. 2 the changes in the rate of secretion of the gastric juice and its concentration of acid calculated from the results of Table 3 are shown. It may be seen that the rate of secretion and the acidity of the gastric juice fell considerably towards the end of the meal. In order to bring out quite clearly that

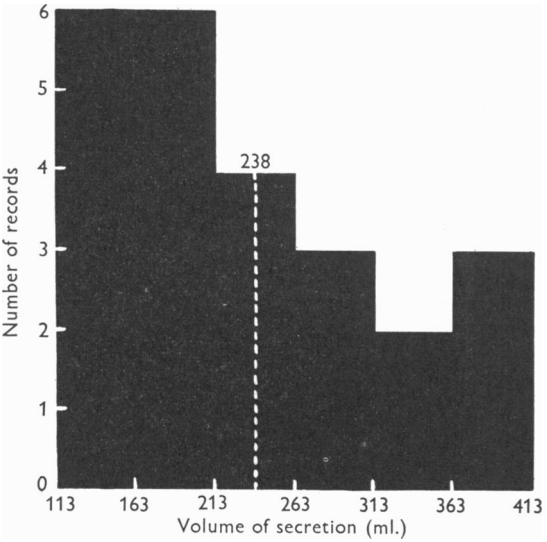

Fig. 4. Frequency distribution of volumes of gastric secretion in response to the pectin meal (21 subjects). Mean 238 ml. Standard deviation ±86 ml.

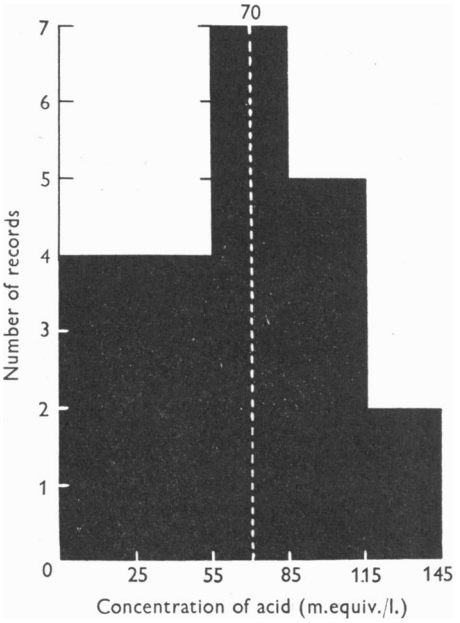

Fig. 5. The mean concentration of acid in the gastric juice of 21 subjects taking the pectin test meal. Mean, 70 m.equiv./l. Standard deviation ±36 m.equiv./l.

the rates of secretion cannot be directly appreciated from the concentrations of the acid and chloride in the gastric contents, Fig. 2 should be compared with Fig. 7. It may be seen that the rise in the concentration of chloride and acid in the gastric contents was almost linear in the first 60 min. although the rate of secretion was falling. This was the result of the diminishing volume of the test meal remaining to dilute the entering secretion and to the diminishing concentration of acid and chloride in the gastric secretion.

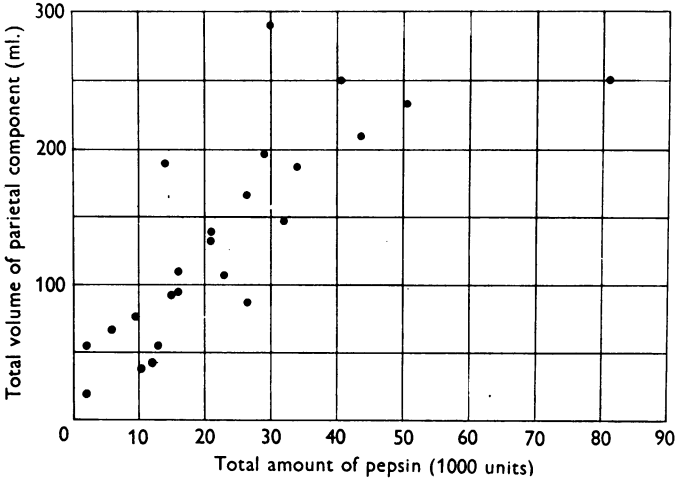

Fig. 6. Secretory response to the pectin test meal. Total volume of parietal component plotted against total amount of pepsin.

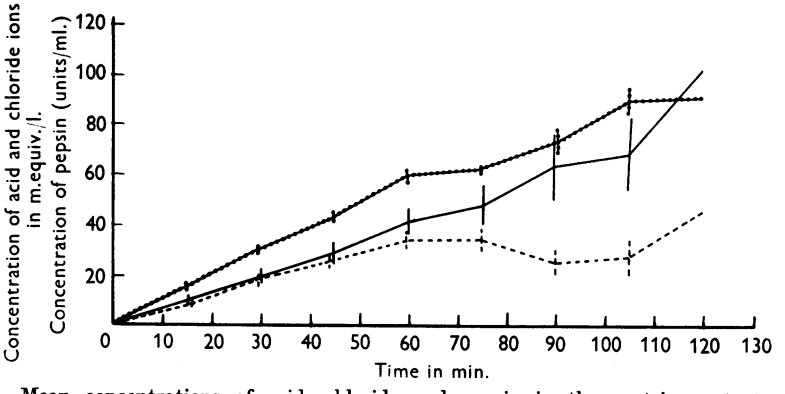

Fig. 7. Mean concentrations of acid, chloride and pepsin in the gastric contents of 21 subjects plotted against time. ——, pepsin (units/ml.); •–•–•–•, chloride (m.equiv./l.); – – – – –, acid (m.equiv./l.). Vertical lines represent standard errors of the means.

In Fig. 3 the rate of secretion of pepsin and the concentration of pepsin in the gastric juice have been plotted against time. It may be seen that the rate of secretion of pepsin fell with time but the concentration of the pepsin in the gastric juice reached a peak after 60 min.

Fig. 4 gives the frequency distribution of the total volumes of the gastric juice secreted by individual subjects using the data of Table 1. It may be seen that the mean total volume of secretion formed in response to 750 ml. of bland pectin test meal was 238 ml. whilst one subject secreted over 400 ml. In Fig. 5 the frequency distribution of the concentrations of acid in the gastric juice of individual subjects is shown. The mean concentration of acid over the whole digestive period was 70 m.equiv./l. It was calculated that a mean of over 17 m.equiv. of acid was secreted by this group of subjects in response to the meal. When the data of Figs. 4 and 5 were examined together, it was found that in general the larger the volume of gastric juice secreted, the higher was its acidity. In Fig. 6 the total volume of parietal component secreted has been plotted against the total amount of pepsin secreted in response to the meal for each subject. With the exception of three points out of a total of 24 the relationship is linear. The mean concentrations of acid, chloride and pepsin in the gastric contents of each subject at 15, 30, 45 min., etc., were derived graphically. The mean concentrations for the whole group of subjects at 15, 30, 45 min., etc., were then calculated. The results are shown in Fig. 7 with the standard errors of the means.

DISCUSSION OF THE METHOD

Arithmetical assumptions

The Serial Test meal has made it possible to estimate the secretory activity of the stomach in terms of the amounts secreted. However, the results are separated from the observations by much tedious arithmetic based on a number of assumptions, some of which have already been considered (Hunt & Spurrell, 1951). The remainder will now be briefly examined.

It is assumed that the amount of chloride, for example, leaving the stomach through the pylorus may be calculated from the product of the mean concentration and the volume passing the pylorus. It may be objected that the secretory response must have a latent period, so that the first flush of gastric contents past the pylorus must contain very little chloride, with the result that the amount of chloride calculated to leave the stomach is in excess of the actual amount leaving. To some extent this may be true but there are two counts on which this objection may be answered. First, emptying itself probably does not begin immediately, and second, the latent period of the secretory response is probably shortened by the previous wash-out.

It is assumed that the gastric contents are a homogeneous mixture. This is not always the case but such error as there is in this assumption of complete mixing is relatively ineffective in disturbing the results of the calculation of the amounts secreted. To take the most extreme case possible, complete absence of mixing during the first 15 min. of the emptying of the meal, assuming a rate of emptying of 26 ml./min., would lead to an error of 28 % in calculating the amount

of a constituent secreted. Since such extremely unfavourable conditions are almost impossible the error is usually much less.

Physiological assumptions

The origin of the chloride in the gastric contents. In the calculation of the volume of gastric juice secreted during the Serial Test meal it is assumed that the chloride recovered with the gastric contents has its origin within the stomach. This assumption deserves careful examination.

It may frequently be seen from the results of gruel fractional test meals that the acidity of the gastric contents falls towards the end of the meal whilst the concentration of chloride may continue to rise up to 100 m.equiv./l. or more. The fall in the concentration of acid is the result of neutralization, dilution or both. The rise observed in the concentration of chloride is the result of the addition of a solution of chloride containing more than 100 m.equiv. Cl^-/l. Since fluids containing 100 m.equiv./l. of chloride and unspecified concentrations of bicarbonate have been recovered from the duodenum of man (Lagerlof, 1942), the stomach of dogs (Hollander, Lauber & Stein, 1948) and the stomach of man (Ihre, 1938), it is not possible to decide upon the origin of the neutralizing fluid without considering further experimental evidence.

The work of Baird, Campbell & Hearn (1924), Shay, Katz & Schloss (1932), and MacLagan (1934) indicates that in man the bulk of the neutralizing fluid is of intragastric origin.

It is assumed that no hydrogen ions are absorbed in the stomach. Professor Teorell informed me that according to his diffusion theory the probable magnitude of error in this assumption was 0·57 m.equiv. of H^+/hr. which seems of little consequence in this context.

Advantages of the method

It is possible to calculate the volume of secretion by using data for the dye in the stomach directly.

Volume secreted between time t_0 and t_1
= Volume of gastric contents at t_1 + volume passing pylorus between t_0 and t_1 − volume ingested at t_0.

Using this method, the calculated volume of secretion has been found to be systematically higher than that calculated from amounts of Cl^- and H^+ secreted. Using the data of Table 3 the discrepancy in the first 15 min. is 13 ml., i.e. 20% of the volume of secretion but only 2% of the volume of the gastric contents. The direct dye method is most unsatisfactory since any small absolute error in the estimation of the three terms of large magnitude on the right of the equation remains absolutely the same but becomes a very large percentage of the volume calculated to have been secreted (see Hollander & Glickstein, 1940). This difficulty is avoided in the Serial Test meal by calculating the volume of secretion from the amounts of chloride and acid secreted.

Apart from the results which it makes available for the first time, the Serial method has advantages over the fractional method. It is virtually a tubeless test-meal since the tube is not present in the stomach during the digestive phase. Secondly, the peptic activity of the gastric contents is measured in units which may be reproduced with precision in other laboratories, whilst the meal itself can be similarly standardized.

DISCUSSION OF THE RESULTS

The Serial Test meal has been found to provide a workable method of obtaining simultaneous quantitative data on gastric secretion and emptying in man. This has not previously been possible even in experimental animals. From the data obtained with the Serial Meal it is apparent that the main secretion of acid and pepsin occurs at the beginning of the digestive period and the rates of secretion fall off as the meal progresses. This is quite different from the impression gained from a study of curves of gastric acidity obtained by the usual fractional methods.

The use of the Serial Test meal depends upon the constancy of the gastric response and in general this has been found to be steady. In two subjects (W.R.S. and J.N.H.) it is known to have been almost unchanged for 3 years. On the other hand in 3 subjects alteration in the stress of life has been associated with a change from one consistent level of activity to a much lower consistent level. Two of these (E.R.H. and P.S.E.) have already been considered (Hunt & Spurrell, 1951) and the third, F.D.B., age 38, suffered from a severe attack of mumps between records *a* and *b*. In the case of F.D.B. it is reasonable to assume that the results obtained before his attack of mumps represented his normal activity but it is impossible to choose between the two patterns of activity of E.R.H. and P.S.E. As the latter were foreign born it does not seem possible to compare the results of their personality tests with those made on the remainder of the group who were born in this country. There is also some evidence that subject B.L.M. had a much reduced secretory response shortly after these tests were completed and coincident with his marriage. In one subject the anticipation of a routine psychometric test reduced the secretion of acid and pepsin to about 10% of the expected response on that day. Such variations in the response of the stomach are well recognized but it was a surprise to find that they were so frequent in such a small group of subjects. When alterations in secretion were observed the acid and pepsin were involved to the same extent, a point which may have some significance in the analysis of the controlling mechanisms.

When considering data on acid and pepsin it is essential to have in mind one important distinction between them. So far as is known there is no storage of acid in the gastric mucosa so that an increase in the amount of acid in the stomach is good evidence of secretion by the parietal cells. On the other hand

pepsin can exist preformed in the tubules of the gastric glands and is washed out by the first flush of acid, as occurs for example after the injection of histamine. Thus an increase in the amount of pepsin in the stomach does not necessarily signify that secretory impulses are affecting the pepsin-producing cells. The pepsin produced in response to the meal is probably partly flushed out and partly the result of true secretion. In those 5 subjects who had two peaks to their rates of secretion of pepsin following the meal the second peak was almost certainly a true secretory response whilst in the other subjects, if such a response occurred, it presumably fused with the pepsin initially washed out.

There is much evidence to suggest that the secretion of acid and pepsin depend upon separate controlling mechanisms, a view which is in accord with the finding that in response to the pectin meal the peaks for the rates of secretion of the acid and pepsin in individual subjects were not closely related in time. Hard up against this concept must be brought the conclusion to be drawn from Fig. 6. The relationship between the total amount of acid and pepsin secreted in response to the meal is relatively fixed for 21 out of 24 records. It therefore seems likely that there is some influence which co-ordinates the response of the two separate mechanisms controlling the secretion of acid and pepsin; for example, levels of vascularity of the mucosa might be responsible for the relationship between the two secretions. Such a mechanism, if it operated by altering the reactivity of the secreting cells, would give rise to a constant relationship between the amount of acid and pepsin secreted in response to a stimulus acting on the gastric mucosa directly, e.g. histamine. In fact such a relationship has been found to exist (Hunt, 1950*b*). The hypothetical influence must therefore be able to intercede between the parietal cell and histamine.

Since temporary changes in the response of the stomach to the test meal show this relationship between the secretion of acid and pepsin, a purely anatomical explanation, that mucosae having large numbers of pepsin-producing cells have corresponding numbers of parietal cells, is not the complete explanation of the observations.

There is little evidence to show how the pectin meal stimulates the secretion of gastric juice. The main property of the meal is its physical bulk. This might be expected to operate by giving rise to the anticipation of a large meal, by setting up an afferent discharge during swallowing, and by distending the stomach. The afferent stimuli set up during swallowing are not apparently of any significance in this context, since giving the meal down the tube does not alter the gastric response (Hunt & Macdonald, 1951).

It is perhaps relevant to ask whether the secretory pattern disclosed by these experiments is well adapted to the digestion of a meal. The high rate of secretion of acid and pepsin at the beginning of the digestive period increases the proteolytic activity within the stomach quickly when the volume of meal in the

stomach is large, a process which is normally aided by the presence of the resting juice. With ordinary meals the gastric juice does not immediately mix uniformly with the meal so that the actual acidity and proteolytic activity around the food mass must be higher than is suggested by the results of fluid test meals. The second peak in the rate of secretion of pepsin, when it occurs, would serve to increase the rate of proteolysis when it was tending to fall as a result of the increasing concentration of the end products of digestion.

The small absolute increase in the rate of secretion of the alkaline component towards the end of the digestive period is effective in neutralizing the gastric contents because it occurs at a time when the volume of the gastric contents is small.

The pectin meal is, by design, a very poor substitute for food. The author finds that even when 1200 ml. of the meal passes into his duodenum, it leaves him ravenously hungry for a real breakfast. However, the traditional gruel meal is no better in this respect, and the results with the pectin meal in terms of the concentrations of acid and chloride in the gastric contents and emptying time are remarkably similar to those obtained with the gruel meal by Baird *et al.* (1924). The main virtue of the pectin meal is that it offers the possibility of adding fat, carbohydrate, etc., to a stimulus which at the moment is almost pure bulk.

The description of the secretory response in terms of Hollander's two-component hypothesis has the advantage that it draws attention to the fact that the amount of acid which can be recovered from the stomach is not the amount secreted, since it may be partly neutralized by the alkaline component. This alkaline fraction of the gastric juice may have some clinical importance since it has been found in a recent study that it is present in nearly double the normal proportion in the histamine- and insulin-stimulated juice of patients with peptic ulcers (Hunt, 1950*a*). The main value of the Serial Test meal is that it has provided the basic pattern of gastric activity in man in terms of the amounts secreted and emptied from moment to moment. This is the first time that it has been possible to give quantitative expression to these two phases of gastric activity. It now becomes possible to appreciate how the composition of the gastric contents, which is the resultant of these two activities, is achieved. This provides a basis upon which to superimpose variables such as the composition, or method of administration, of the test meal.

SUMMARY

1. A method of estimating the gastric secretory response to a test meal, in terms of amounts of acid, chloride and pepsin secreted as the meal progresses, is described.

2. The volume of the gastric secretion can be calculated from the amounts of acid and chloride secreted.

3. The volume of secretion can be subdivided into two components, the acid parietal component and the alkaline non-parietal component.

4. The results of the application of the method to a group of 21 normal subjects are given.

5. The method and the significance of the results is discussed.

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