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THE COMPOSITION OF GASTRIC JUICE

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It has recently proved possible to estimate the composition of the two hypothetical components of human gastric juice which according to Hollander's (1938) concept could account for the main variations in the concentrations of the inorganic ions (Fisher & Hunt, 1950). These calculations were based on the values for the concentrations of acid and chloride in gastric juice secreted in 1 hr. (Ihre, 1938). Now Dr Ihre has kindly made available the results for the individual samples of gastric juice making up his hourly totals and this has allowed a more searching examination of the data since the statistical calculations may be made for each individual instead of for groups of subjects. It seemed possible that the more detailed examination might disclose individuals diverging largely from the mean of their group or differences between groups which were not shown by the original examination. It is of practical importance to make this effort since the values originally calculated are employed in the analysis of the results of the Serial Test meal (Hunt, 1951). Since the Serial Meal method is to be applied to patients with peptic ulcers it was especially necessary to decide whether the inorganic components of gastric juice in such patients differed from those in normal subjects.

STATISTICAL METHODS

Hollander's (1938) hypothesis was based on the finding that when he plotted the concentration of acid in samples of juice against the concentration of chloride ions in electrical equilibrium with metallic cations, i.e. so-called 'neutral chloride', the points fell on a straight line. Fisher & Hunt (1950) have described the assumptions necessary for the calculation of the composition of the components of the gastric juice from the regression equation describing such a line. When it is required to compare the compositions of the two components which can be calculated from such regression lines, it is possible to compare the lines without actually computing the composition of the components. The regression lines drawn to pass through a plot of concentration of 'neutral chloride' against concentration of acid have been specified by giving the calculated intercepts of the lines with the two axes. In making this calculation the regression equation was chosen to make the appropriate intercept the dependent variable. The intercepts cannot be interpreted as indicating directly the composition of either of the two components.

THE DATA

Three stimulated gastric secretion first with histamine and then with insulin in successive hours in 24 normal subjects, 20 patients with gastric ulcers, and 20 with duodenal ulcers. Some subjects had more than 1 pair of tests. It is difficult to be sure that a specimen of gastric juice obtained from man is not contaminated by duodenal contents and saliva. Three reduced the significance of this contamination by aspirating the stomach for 20 min. or more before beginning collection, and by continuous suction from the duodenum and the mouth. Nevertheless there were a number of samples that he noted to be contaminated, or in which it may be inferred that there was contamination, because the concentration of chloride was less than 100 m.equiv./l. Some subjects produced only three samples, of which it was necessary to reject one because of contamination. In such a case it was not worth while to calculate the regression line since it was not possible to estimate its reliability. A preliminary selection based on the above considerations left 210 samples of juice from normal subjects, 111 samples from patients with gastric ulcers, and 170 samples from patients with duodenal ulcers.

Since it was conceivable that different stimulants might alter the composition of the two components it was necessary to see whether there was any significant difference between the regression line for 'histamine juice' and that for 'insulin juice' within individual subjects. Separate regression lines were calculated for histamine and insulin juice for each of 24 normal subjects. There was no systematic difference between the intercepts for the histamine and insulin stimulated juices. This result suggested that nothing would be lost by pooling data derived from the juice secreted under the influence of histamine and insulin.

A regression line was fitted to the pooled histamine and insulin data for each subject. The means of the intercepts of the regression lines on the neutral chloride axis and the acid axis calculated separately for the normal subjects, the patients with duodenal ulcers, and those with gastric ulcers are shown in Table 1 with their standard errors.

TABLE 1. Pooled histamine and insulin data. Mean intercepts (m.equiv./l.)

	No. of records	Mean neutral chloride intercept	Mean acid intercept
Normal subjects	26	121 (± 3)	171 (± 2)
Patients with gastric ulcers	15	124 (± 4)	154 (± 5)
Patients with duodenal ulcers	15	124 (± 4)	162 (± 9)

The mean intercept on the acid axis for the gastric ulcers is significantly different from that for the normal subjects. The total volume of secretion in patients with gastric ulcers is less than in the normal group, with less acid component and more alkaline component. A possible explanation of the

difference shown in Table 1 between the mean acid intercepts for normal subjects and patients with gastric ulcers might be that the extra-gastric contamination was relatively more important in patients with gastric ulcers since their total volume of juice is relatively small.

One effect of extra-gastric contamination is to upset the linear relationship between the concentrations of neutral chloride and acid. Thus, selecting subjects from each group with high correlation coefficients might be expected to produce groups in which the difference between the acid intercept for the patients with gastric ulcers and the normal subjects is smaller if the difference were due to contamination. Since the main effect of contamination is to lower the neutral chloride intercept, such a selection would also be expected to raise the mean neutral chloride intercept for all three groups above the values observed without selection. Both these expectations are fulfilled as may be seen from the results shown in Table 2.

TABLE 2. Pooled insulin and histamine data mean intercepts for subjects with a correlation coefficient greater than 0.97 (m.equiv./l.)

	No. of records	Mean neutral chloride intercepts	Mean acid intercepts
Normal subjects	12	127	170
Patients with gastric ulcers	4	133	161
Patients with duodenal ulcers	5	132	166

Since low correlation coefficients increase the variance of the intercept it seemed reasonable to calculate weighted means of the intercepts, the weight being inversely proportional to the variance of each intercept comprising the mean, in an attempt to equalize the significance of contamination in each of the groups.

TABLE 3. Weighted mean intercepts for pooled histamine and insulin data (m.equiv./l.)

	Mean neutral chloride intercept	Mean acid intercept
Normal subjects	124 ± 2	168 ± 2
Patients with gastric ulcers	132 ± 3	163 ± 4
Patients with duodenal ulcers	128 ± 4	168 ± 4

As may be seen from Table 3, the three groups apparently are similar when treated in this way except that the neutral chloride intercept for normal subjects is lower than might be expected. This could be explained as follows. Normal subjects usually produce highly acid juice with low concentrations of 'neutral chloride'. When these points are plotted they fall as shown by the circles in Fig. 1. However, many subjects produce a sample of juice which contains a low concentration of acid at low rates of secretion, especially at the beginning of the experiment. Such a sample is thus peculiarly affected by contamination with saliva and duodenal contents, both of which would lower

the concentration of acid and chloride. Such a specimen would be plotted as shown by the cross in Fig. 1. It can readily be appreciated that such a point would have little influence on the correlation coefficient but would lower the neutral chloride intercept considerably, at the same time raising the acid intercept. Thus a negative correlation between the neutral chloride intercept and the acid intercept might be expected. This does exist, as can be seen from Table 4, and is highest for the normal subjects as might be anticipated.

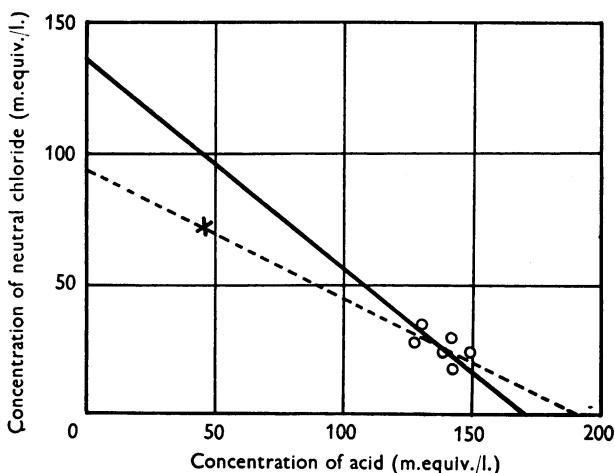


Fig. 1. The effect of one contaminated sample of gastric juice on the intercepts of a regression line. \circ uncontaminated samples; \times contaminated sample.

The results so far considered suggest that contamination might account for differences between the mean intercepts for the regression lines for the different groups. This would presumably have less effect at high rates of secretion if the

TABLE 4. Correlation coefficients for acid intercepts plotted against neutral chloride intercepts

	No. of records	Correlation coefficient
Normal subjects	43*	-0.6
Patients with gastric ulcers	15	-0.5
Patients with duodenal ulcers	20*	-0.4

* Includes lines plotted with insulin data separated from histamine data.

volume of contamination were roughly constant. To test this hypothesis, samples of juice from normal subjects stimulated with insulin and histamine were grouped according to their rates of secretion and the regression lines were calculated for all samples with rates of secretion greater than 50 ml./20 min., etc. The results are shown in Table 5. It may be seen that the greater the rate of secretion the higher the values for the mean intercepts and the less the standard error, which would be expected if the significance of contamination was reduced at high rates of secretion.

The secretion of saliva during the period of insulin stimulation was measured and found to be less than during the histamine stimulation. In addition the insulin-stimulated secretion was collected after the stomach had been thoroughly washed out by histamine juice. Thus, to make a comparison between the groups in which contamination had a minimal effect, samples of insulin-stimulated juice with rates of secretion greater than 40 ml./20 min. were selected and regression lines fitted.

TABLE 5. Intercepts calculated from samples selected according to rates of secretion (normal subjects, histamine and insulin data) (m.equiv./l.)

Rate of secretion	No. of samples	Neutral chloride intercept	Acid intercept
Greater than 50 ml./20 min.	48	136 ± 5	170 ± 2
30-40 ml./20 min.	43	124 ± 9	165 ± 3
Less than 20 ml./20 min.	57	105 ± 19	158 ± 7

TABLE 6. Insulin data, rates of secretion greater than 40 ml./20 min. (m.equiv./l.)

	No. of samples	Neutral chloride intercept	Acid intercept
Normal subjects	54	135 ± 6	167 ± 2
Patients with gastric ulcers	31	127 ± 5	163 ± 5
Patients with duodenal ulcers	53	131 ± 4	161 ± 3

TABLE 7. Intercepts calculated for samples of 'insulin juice' divided according to concentration of pepsin (m.equiv./l.)

	Normal subjects	Patients with gastric ulcers	Patients with duodenal ulcers
	Neutral chloride intercepts		
High pepsin	131 ± 8	109 ± 13	134 ± 3
Low pepsin	134 ± 10	122 ± 5	107 ± 10
	Acid intercepts		
High pepsin	171 ± 4	170 ± 11	162 ± 3
Low pepsin	165 ± 3	161 ± 4	169 ± 7

It may be seen from Table 6 that when every effort is made to eliminate the effects of contamination the three groups do not differ significantly.

There is a further possibility which deserves consideration. Patients with duodenal ulcers secrete much more pepsin than the other groups. Since the pepsin is presumably secreted in solution, some fluid must be secreted with the pepsin and it is conceivable that in patients with duodenal ulcers this volume might be significant. Accordingly the samples of insulin juice with a rate of secretion greater than 40 ml./20 min. were divided into those with concentrations of pepsin less than 50 units/ml. and those with more than 50 units/ml., and regression lines were fitted.

It may be seen from Table 7 that there is only one significant difference between the pairs of intercepts, that for the neutral chloride intercept of patients with duodenal ulcer. Since low concentrations of pepsin are surprisingly associated with high concentrations of acid in samples of juice obtained from

these subjects the situation is comparable to that discussed in relation to Table 3, so that the difference is probably not significant in this context. It thus appears probable that the pepsin is secreted in a relatively negligible volume of fluid, which is in accord with the findings of Linde (1950) in cats.

DISCUSSION

Nothing has come to light in this examination to suggest that composition of the two components calculated for normal subjects differs from that calculated for patients with peptic ulcers. It is clear that even with Ihre's painstaking technique the contamination of gastric juice which occurs has very important effects on the results of the calculation of the composition of the two components using these methods. In the paper by Fisher & Hunt (1950) it was concluded that the composition of the non-parietal component secreted after histamine was probably different from that secreted after insulin. It seems possible from the present analysis that the difference found was the result of the higher incidence of salivary contamination on the samples obtained after histamine because they preceded the insulin stimulated samples. The important effects of contamination have prevented any useful estimate of the variation in the components of the gastric juice.

SUMMARY

1. The figures obtained by Ihre (1938) for the composition of gastric juice in normal subjects, patients with gastric ulcers and patients with duodenal ulcers have been analysed in detail.
2. A study of the effects of contamination of gastric juice by saliva and duodenal contents upon the method of arriving at the composition of the two hypothetical components has been made.
3. There is no evidence that there is any difference between these three groups of subjects in the composition of the two hypothetical components of the gastric juice.

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