THE ELECTROLYTES OF ALKALINE HUMAN GASTRIC JUICE

J. R. C. GARDHAM AND M. HOBSLEY

Department of Surgical Studies, The Middlesex Hospital, London

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SUMMARY

1. The electrolytes were measured in alkaline gastric juice from eleven subjects with various gastric disorders; seven of these subjects had histamine-fast anacidity. The aim was to investigate the relation between alkaline gastric aspirates and the alkaline component predicted by the two-component hypothesis of gastric secretion.

2. The electrolyte concentrations differed from one subject to another: decreasing concentrations of sodium, chloride and alkali were correlated with increasing potassium concentrations.

3. The observed variations were completely explicable in terms of dilution of gastric juice by saliva. It is therefore concluded that the uncontaminated gastric juice was similar in all subjects.

4. The purest specimens of alkaline gastric juice closely resembled the alkaline component predicted by the two-component hypothesis. It is unlikely that diffusion in exchange for primary acid secretion could have produced the same results.

Two main alternatives have been advanced to explain the electrolyte composition of human gastric juice. The two-component hypothesis (Hollander, 1932) proposed that gastric juice consists of separate acid and alkaline components. A quantitative statement of this hypothesis (Makhlouf, McManus & Card, 1966) defined the two components, and the validity of this approach in a number of different human subjects has since been confirmed (Hobsley & Silen, 1970). By contrast, it has been claimed that a primary acid secretion is altered by back-diffusion of hydrogen ions in exchange for sodium ions (Teorell, 1947), and it has been demonstrated that this process can occur under experimental conditions, (Davenport, Warner & Code, 1964; Chapman, Werther & Janowitz, 1968).

The majority of previous work has been concerned with the electrolytes in acid gastric juice. By contrast there is very little information about the electrolytes in alkaline human gastric juice. Alkaline juice can always be aspirated from patients with pernicious anaemia (Callender,

Correspondence: Dr J. R. C. Gardham, Department of Surgical Studies, The Middlesex Hospital, London, W.1.
Retief & Witts, 1960), and can occasionally be aspirated, under resting circumstances, from many other subjects.

It seemed that a study of the electrolytes in alkaline juice might provide new and direct evidence of the existence and composition of the alkaline component. This paper reports data from a small series of subjects who secreted alkaline gastric juice, and demonstrates that the variations in electrolyte concentrations followed a distinct pattern. The interpretation is discussed, and it is shown that such a pattern would be produced by a mixture of variable proportions of saliva with an alkaline component of constant composition.

**MATERIALS AND METHODS**

The results of tests on eleven subjects are reported. The clinical diagnoses are indicated in Table 1. Seven of the subjects had total anacidity throughout the tests: the remaining four had basal anacidity, but did secrete acid in response to stimulation. The results reported in this paper are only those from alkaline specimens (pH > 7.0).

After overnight fasting, a nasogastric tube was passed into the stomach and the position checked radiologically. With the subject in a semi-recumbent position, the stomach was emptied and the initial aspirate discarded. Thereafter, aspiration was by continuous mechanical suction, aided by frequent air insufflation to clear the tube. Samples were collected at 15-min intervals. Each test included a minimum of three consecutive alkaline samples without visible bile staining. In eight tests intravenous histamine diphosphate (0.04 mg h\(^{-1}\) kg\(^{-1}\)) was given by a slow injection pump (C. H. Palmer Ltd.) into the tubing of a continuous infusion of 5% Dextrose. In one test ametazole hydrochloride ('Histalog') 50 mg was given subcutaneously. In the remaining two tests no gastric stimulant was given as the subjects were already known to have histamine-fast anacidity, and gave their permission for the test to be conducted for research purposes.

In all tests phenol red 0.15% w/v solution was instilled into the upper part of the stomach at a rate of 4.8 ml/h by a Palmer pump via a fine vinyl tube, and the measurements of dye in the samples were used to estimate the completeness of aspiration (Hobsley & Silen, 1966, 1969).

Four subjects were asked during the test to expectorate small samples of saliva for analysis, but in no test was any attempt made to prevent swallowing of saliva. The reasons for this decision are set out in the discussion section. In the interpretation of the results, the presence of saliva has been taken into account.

Analyses were performed as follows: pH on a direct reading pH meter (Electronic Instruments Ltd., Model 27A, fitted with a Jena dual micro-electrode) and titratable alkalinity with 0.01M-HCl to pH 7.0, or to the end point of phenol red. Sodium and potassium were measured on a flame photometer (Evans Electroselenium Ltd., Mark II) and chloride on a potentiometer (Evans Electroselenium Ltd., chloride meter). Phenol red concentration was measured on a spectrophotometer (Unicam Instruments Ltd., Model S.P. 600), with readings at wavelengths of 550 and 410 m\(\mu\) incorporating a correction for extinction by blood in the samples (Crawford & Hobsley, 1968).

**Calculation of results**

The concentration of sodium, potassium, chloride, and titratable alkali in a sample was multiplied by the volume to give the quantity of each in mEq, in each single sample. The sum of
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the quantities in successive samples was then divided by the total volume, and the result expressed as the mean concentration in mEq/l for the test. The phenol red marker dye contributed small amounts to the volume, sodium and alkali in the aspirated fluid, and therefore, after estimating the volume of phenol red in each sample, appropriate subtractions were made before the final calculation of mean concentration. In addition to the measured volumes of aspirate, volumes corrected for incomplete aspiration by the observed recovery rate of phenol red are also given. The validity of this correction is discussed below.

RESULTS

The results are summarized in Table 1.

Electrolyte concentrations

The subjects have been arranged for convenience by the mean sodium concentration of the gastric juice, which ranged from 146-48 mEq/l. The ranges of mean concentrations for the other electrolytes were: potassium 26-7-11-1 mEq/l, chloride 147-56 mEq/l, and titratable alkali 18-3-3-3 mEq/l. In individual subjects, successive specimens closely resembled one another, and the use of mean concentrations does not conceal any appreciable variations.

Examination of correlations between any pair of the four electrolyte concentrations resulted in six regression equations. Five of these six pairs had correlation coefficients which were statistically significant: the regression equations for these pairs of electrolytes are given in Figs. 1-5, and the regression lines are drawn as solid lines.

\[
\begin{align*}
\text{[Na}^+\text{] vs. [Cl}^-\text{]} & : r = +0.970 : P<0.001 \quad \text{(Fig. 1)} \\
\text{[Alkali] vs. [Cl}^-\text{]} & : r = +0.677 : P<0.05 \quad \text{(Fig. 2)} \\
\text{[Alkali] vs. [Na}^+\text{]} & : r = +0.610 : P<0.05 \quad \text{(Fig. 3)} \\
\text{[K}^+\text{] vs. [Cl}^-\text{]} & : r = -0.759 : P<0.01 \quad \text{(Fig. 4)} \\
\text{[Na}^+\text{] vs. [K}^+\text{]} & : r = -0.706 : P<0.05 \quad \text{(Fig. 5)}
\end{align*}
\]

The one remaining correlation was not statistically significant at conventional levels.

\[
\text{[Alkali] vs. [K}^+\text{]} : r = -0.557 : 0.05<P<0.1
\]

The three correlations in which potassium was included were negative, the remainder were positive.

Volume

The aspirated volumes varied from 0.5 to 15.8 ml/15 min, and the corrected volumes from 3.4 to 21.0 ml/15 min. The volumes did not correlate significantly with the electrolyte concentrations.

Response to histamine or ‘Histalog’

Nine subjects received histamine or ‘Histalog’ during these tests, and in five of these there was no consequent change in the volume, pH, or electrolyte concentrations of the alkaline juice. The remaining four subjects, who had alkaline basal juice, later produced acid in response to histamine. This paper reports only the results from the alkaline samples.
TABLE 1. Composition of alkaline gastric juice in eleven patients

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Acid secretion after histamine (mEq/h)</th>
<th>Number of alkaline samples</th>
<th>Aspirated volume (ml/15 min)</th>
<th>Corrected volume (ml/15 min)</th>
<th>Maximum pH</th>
<th>Mean concentrations</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td>Na (mEq/l)</td>
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<tr>
<td>1</td>
<td>73</td>
<td>M</td>
<td>Pernicious anaemia</td>
<td>0</td>
<td>8</td>
<td>6.4</td>
<td>6.8</td>
<td></td>
<td>146</td>
</tr>
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<td>2</td>
<td>75</td>
<td>F</td>
<td>Atrophic gastritis</td>
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<td>6</td>
<td>4.2</td>
<td>5.4</td>
<td></td>
<td>131</td>
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<tr>
<td>3</td>
<td>64</td>
<td>F</td>
<td>Pernicious anaemia</td>
<td>0</td>
<td>10</td>
<td>2.4</td>
<td>4.3</td>
<td>8.1</td>
<td>108</td>
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<td>4</td>
<td>61</td>
<td>M</td>
<td>Gastric ulcer</td>
<td>1</td>
<td>3</td>
<td>5.0</td>
<td>5.0</td>
<td>8.0</td>
<td>84.5</td>
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<tr>
<td>5</td>
<td>67</td>
<td>F</td>
<td>Gastric ulcer</td>
<td>27</td>
<td>3</td>
<td>11.1</td>
<td>14.8</td>
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<td>67.0</td>
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<td>6</td>
<td>59</td>
<td>M</td>
<td>Duodenal ulcer</td>
<td>31.5</td>
<td>3</td>
<td>15.8</td>
<td>17.5</td>
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<td>64.0</td>
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<td>21.0</td>
<td>8.2</td>
<td>61.0</td>
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<td>8</td>
<td>63</td>
<td>M</td>
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<td>8</td>
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<td>11.5</td>
<td>7.8</td>
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<td>9</td>
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<td>F</td>
<td>Pernicious anaemia</td>
<td>4</td>
<td>4</td>
<td>7.0</td>
<td>9.3</td>
<td>7.4</td>
<td>55.8</td>
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<td>10</td>
<td>72</td>
<td>F</td>
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<td>3.0</td>
<td>14.9</td>
<td>7.9</td>
<td>51.0</td>
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<tr>
<td>11</td>
<td>64</td>
<td>F</td>
<td>Pernicious anaemia</td>
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<td>12</td>
<td>0.5</td>
<td>3.4</td>
<td>7.3</td>
<td>48.0</td>
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<tr>
<td>Mean values</td>
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<td></td>
<td></td>
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<td>79.5</td>
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</table>

* Negative response to histamine during previous test.
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Fig. 1. Regression of sodium and chloride concentrations in alkaline gastric aspirate (solid lines), compared with a hypothetical mixture (interrupted line) between pure alkaline component of gastric juice and pure saliva in varying proportions.

Fig. 2. Regression of alkali and chloride concentrations, compared with a hypothetical mixture of alkaline component and saliva.
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Fig. 3. Regression of alkali and sodium concentrations, compared with a hypothetical mixture of alkaline component and saliva.

Fig. 4. Regression of potassium and chloride concentrations, compared with a hypothetical mixture of alkaline component and saliva.

**Saliva**

The composition of saliva expectorated during the test was measured in subjects Nos. 3, 8, 9, and 11. The mean concentrations were as follows:

- Na⁺ : 10.7 mEq/l (Range 3.6–28.4)
- K⁺ : 26.0 mEq/l (Range 21.8–31.0)
- Cl⁻ : 29.7 mEq/l (Range 20–37)
- Alkali : 4.5 mEq/l (Range 4–5)
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These values are compatible with other reports of salivary composition at low rates of flow (Thaysen, Thorn & Schwartz, 1954), and confirm the high potassium content of saliva.

![Graph showing regression of potassium and sodium concentrations, compared with a hypothetical alkaline component and saliva.]

**DISCUSSION**

The electrolyte concentrations in alkaline gastric contents varied from one subject to another, and were different from those of saliva. A pattern of interrelation between the electrolytes emerged in the six regression equations. It will be shown that this pattern closely resembled that which would be expected if a pure alkaline gastric juice of constant composition were mixed in varying proportions with saliva.

Before discussing the results in detail, it is necessary to comment on possible inaccuracies in the measurements of titratable alkali and of volume. Specimens were collected in aerobic conditions which allowed evolution of CO₂. Any evolution of CO₂ leaves in solution a corresponding amount of hydroxyl ions, so that the measurement of titratable alkali corresponds with bicarbonate in the original fluid. The volumes available for titration were often very small (e.g. 0.5 ml) and the measurement of titratable alkali was probably less accurate than that of the other electrolytes. This lack of accuracy may be reflected in the lesser values for those correlations involving alkali.

The volume of stomach contents aspirated is likely to be incomplete (Hobsley & Silen, 1969). For this reason the phenol red marker dye technique was used to correct the volume of aspirate to the true volume of gastric secretion. There is doubt as to whether phenol red is an adequate marker in these circumstances. It has been shown (Bloom, Jacobson & Grossman, 1967), that in an alkaline medium recovery of phenol red is not complete, but the proportion recovered in their experiments was 90–95%. Therefore the error from this source is probably not gross. In addition, adequate mixing may not have occurred in the very small volumes of gastric juice in some of these tests.
For these reasons, and because in some tests a very large correction for incomplete recovery was necessary, there must be some doubt about the validity of the corrected volume results.

Correlations interpreted as the effect of saliva

The subjects were allowed to swallow saliva, because it was judged to be impracticable entirely to prevent this. The most effective method of preventing salivary contamination is probably that used by Makhlouf et al. (1966), namely the use of frequently changed dental pledgets in the floor of the mouth. Whilst this procedure was suitable for Makhlouf et al.'s two practised subjects, it was considered to be too arduous for elderly subjects in this study. Other methods, such as expectoration, or use of a dental sucker, have been ineffective in our hands. Comparison of our results with those of Lambling, Bernier, Badoz-Lambling & Dives, (1956) supports the conclusion that such methods are not effective. Lambling and his colleagues studied seven patients with pernicious anaemia and attempted to exclude saliva by expectoration, or by a dental sucker. They found the electrolyte concentration of the aspirates to be variable, and concluded that alkaline gastric juice was not constant in composition. However our findings were similar to those of Lambling et al. (1956) (Table 2) and this suggests that their precautions against swallowing of saliva were not effective.

| TABLE 2. Mean electrolyte concentrations in alkaline gastric juice. (The ranges of observed values are given in parentheses for this series and for Lambling et al., 1956) |
|---------------------------------|----------------|----------------|------------------------|------------------------|-----------------|----------------|
| 1 | 2 | 3 | 4 | 5 | 6 |
| Na⁺ | 80 (48-146) | 94 (64-135) | 137 | 138 | 133 | 151 |
| K⁺ | 17 (11-27) | 20 (14-24) | 6 | 4 | 4 | 9 |
| Cl⁻ | 92 (56-147) | 83 (50-113) | 117 | 117 | 120 | 145 |
| HCO₃⁻ | 8 (3-18) | 18 (16-22) | (25*) | 23 | 13 | 8 |

Concentrations in mEq/l (to nearest mEq). * Assumed value.

The varying electrolyte concentrations in the aspirate might be explained on the hypothesis that the pure alkaline gastric juice was diluted by varying quantities of saliva in different subjects. This hypothesis can be examined with reference to Figs. 1-5. In each of the figures the two solid lines are the regression lines from our data. Two lines have been reproduced for each pair of electrolytes because there was no reason to select one electrolyte as the independent variable. In addition a hypothetical mixture of saliva and alkaline gastric juice is also represen-
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Fig. 6. Comparison of the electrolyte concentrations in the alkaline component of acid gastric juice (Makhlouf et al., 1966) with the mean of the measured concentrations in subjects 1, 2 and 3 of this series.

secreted at low rates is reasonable (Thaysen et al., 1954). So, despite the variety of pathological states in the subjects studied, it appears that a characteristic alkaline gastric juice was present in all subjects.

The exact electrolyte concentrations in pure alkaline gastric juice cannot be determined from our results. In Table 2 the data from the present series are compared with other data from the literature. In our series and that of Lambling et al. (1956) salivary contamination probably lowered the mean sodium and chloride concentrations, and raised the potassium concentration. The third column of Table 2 shows the alkaline component calculated by Makhlouf et al.
(1966) for one normal subject tested repeatedly with strict exclusion of saliva. There is a close resemblance between this estimate and those of our samples which appeared to be least contaminated with saliva (Fig. 6). Makhlouf and his colleagues based their calculations on an assumed bicarbonate concentration of 25 mEq/l. The difference between this assumption and the maximum titratable alkali of 18 mEq/l in our series accounts for the divergence from the predicted regressions in Figs. 2 and 3. The possibility that samples were contaminated with minute amounts of acid cannot be denied.

Three authors (Altamirano, 1963; Hollander, 1963; Grossman, 1959) have published results from dogs, and these results are also reproduced in Table 2. In each instance the method ensured that the alkaline gastric juice was entirely free of saliva.

**Alkaline component or diffusion**

Do these observations indicate whether the two component hypothesis or the diffusion theory is the correct physiological concept of gastric secretion? In favour of the two component hypothesis is the finding that, after allowing for salivary contamination, the aspirated alkaline gastric juice appeared to be of constant composition, and resembled the alkaline component which has been predicted from a theoretical basis. The alkaline gastric juice from our subjects, like that from dog pouches, resembled extracellular fluid, and may have been a simple transudate, as suggested by Hollander (1963). Alternatively this fluid might have been the result of back-diffusion of a primary acid secretion in exchange for sodium. Space does not allow a detailed discussion of the theory of Teorell (1947), but his paper indicated that a number of factors would influence the diffusion process.

These factors include the primary acid concentration, the rate of secretion, the area of diffusion and the thickness of the membrane. Chapman *et al.* (1968) have recently shown that 200 ml of acid instilled via a nasogastric tube into the stomachs of four subjects with pernicious anaemia resulted in diffusion exchange for sodium of approximately 10% of the instilled acid within 15 min. If diffusion in exchange for acid had been the main factor in our subjects, it would be necessary to postulate that the interaction of several variable factors combined in each subject to produce the same composition in the alkaline juice. Therefore, if a primary acid secretion did occur at very low rates, the results could be explained if diffusion proceeded to equilibrium in all cases.

In seven of our subjects the pH of the aspirate never fell below 7.0, and in these subjects there was no overt evidence of ability to produce a primary acid secretion. Teorell also considered the possibility of absence of primary acid secretion and derived an equation for simple diffusion of NaCl. In the situation of total anacidity this concept does not differ from that of Hollander (1963).

Therefore, the possible alternatives are either that back-diffusion to the same equilibrium occurred in each subject, or that the results were due to simple diffusion, or secretion, of an alkaline juice of fixed composition. It has already been indicated that back diffusion would depend on the rate of secretion of acid. Calculations of the apparent alkaline component at various rates of acid secretion (Makhlouf *et al.*, 1966; Hobsley & Silen, 1970) may be considered in conjunction with the present data. The similar compositions of the observed alkaline juice in the absence of acid, and the derived alkaline component in the presence of acid secreted at different rates, support the concept of an alkaline component which is not dependent on the rate of acid secretion.
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REFERENCES


