Part II In patients with gastric ulcer

EDITORIAL SYNOPSIS The electrophoretic patterns of the proteins of the gastric juice of a series of patients with gastric ulcer, a control group, and a group of patients with miscellaneous gastric and systemic diseases were studied, autodigestion being prevented by maintaining the *p*H of the gastric contents above 7.

A slow moving anodal band (band 2) was present in 50% of the observations on gastric ulcer patients, whereas this band was present in only 10% of the patients who did not have a gastric ulcer.

Studies of gastric acid secretion in patients with gastric ulcer have not demonstrated any secretory abnormality in this group of patients. Compared with normals, the output of acid found in gastric ulcer patients is usually either normal or lower than normal (Card, 1952). However, while studying the protein fractions in gastric juice by electrophoresis (Piper, Stiel, and Builder, 1962) we observed an electrophoretic band commonly in patients with gastric ulcer that was rarely present in patients who were not suffering from gastric ulceration.

The present study compares the frequency and quantitative aspect of an electrophoretic fraction in the proteins of the gastric juice of a series of patients with gastric ulcer and a series of patients not suffering from gastric ulceration, including some free of gastrointestinal disease and a group with other gastroduodenal lesions.

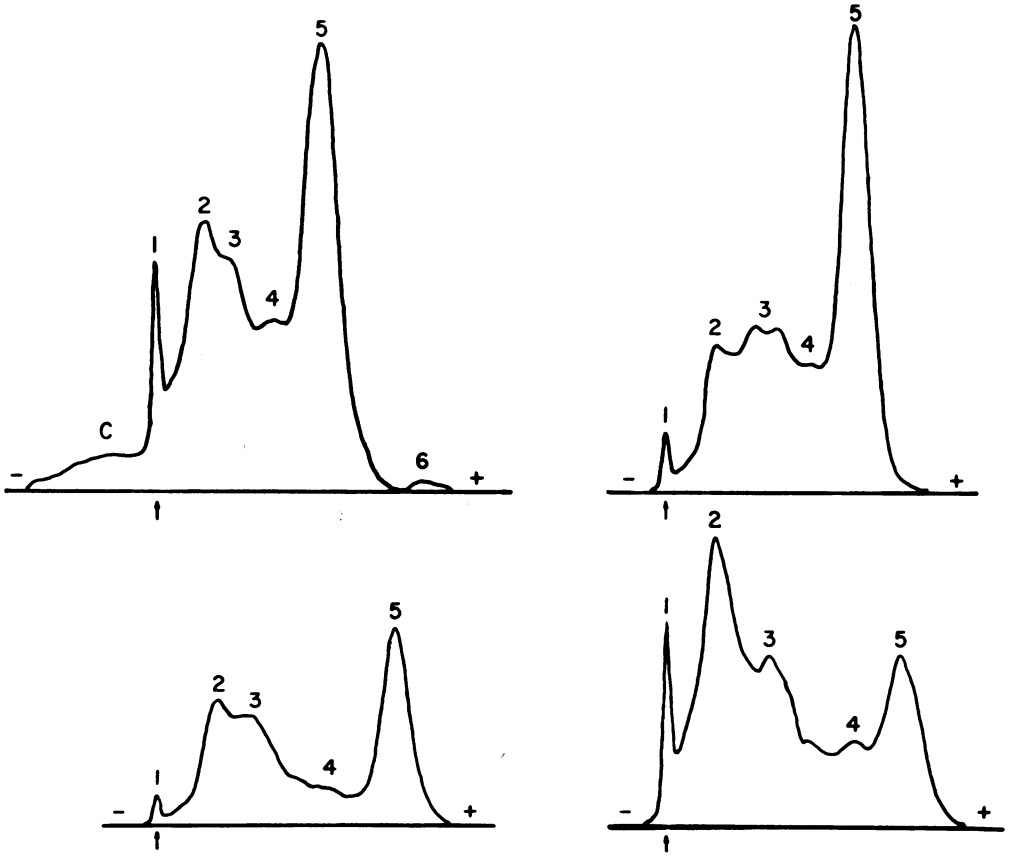

FIG. 5. *Electrophoretic pattern of gastric juice found in patients with gastric ulcer.*

METHOD

The controls were those patients described in Part I, 23 patients with gastric ulcer, 19 patients with carcinoma of the stomach, five patients with duodenal ulcer, five patients with pernicious anaemia, and a group of 14 patients with miscellaneous non-gastrointestinal diseases. Some of the gastric ulcer patients were studied on more than one occasion, 33 observations being made on the 23 gastric ulcer patients.

The method used is described in Part I.

RESULTS

The patterns obtained in normal patients are shown in Fig. 1. Some typical examples of the pattern found in gastric ulcer patients are given in Fig. 5.

It is not proposed in this study to present a detailed analysis of the qualitative and quantitative aspects of the electrophoretic pattern of protein components of the gastric juice in the several groups studied. We wish to demonstrate an increased frequency of band 2 in the gastric ulcer group; compared with the non-ulcer group, this difference is highly significant ($P<0.001$). Also, when band 2 was present in the non-ulcer group, it was small; this quantitative difference is also highly significant ($P<0.001$). If the results obtained in the first observation only on each patient are considered, similarly significant differences are present.

Of 23 gastric ulcer patients studied, 14 showed band 2 on at least one occasion. In the first study done on each of the 23 patients, this band was present in 13. In the 14 patients who showed this band on at least one occasion, 22 studies were made and of these 16 showed band 2, and of the 33 studies made on the 23 gastric ulcer patients band 2 was present on 16 occasions.

TABLE I

FREQUENCY AND QUANTITATIVE ASPECT OF ELECTROPHORETIC BANDS IN CONTROLS AND PATIENTS WITH GASTRIC ULCER AND OTHER DISEASES OF THE STOMACH

Band	*C*	*1*	*2*	*3*	*4*	*5*	*6*
Controls (24)[1]							
Frequency	13	24	2	24	23	24	7
Size-mean	4·7	4·4	7	48·1	15·2	26·7	5·7
S.E.	0·9	0·5	1·4	3·3	1·8	2·2	1·7
Duodenal Ulcer (5)							
Frequency	1	5	1	5	4	5	2
Size-mean	4·0	3·0	9·0	40·6	18·8	34·8	4
S.E.	0	0·4	0	3	5·9	2·8	0·7
Pernicious Anaemia (5)							
Frequency	0	4	0	5	5	5	0
Size-mean	0	3·8	0	4·7	6·2	44·2	0
S.E.	0	1·2	0	4·8	0·5	4·9	0
Carcinoma (19)							
Frequency	4	19	2	19	18	19	0
Size-mean	1·3	2·8	6	44·2	14·6	35·5	0
S.E.	0·5	0·4	0	2·5	1·4	2·3	0
Miscellaneous Group (14)							
Frequency	4	14	3	14	11	14	1
Size-mean	2·3	4·7	9·7	52·7	13·1	24·4	5
S.E.	0·4	0·6	3·8	1·3	1·6	1·6	0
Total Non-gastric Ulcer Group (67)							
Frequency	22	66	8	67	61	67	10
Size-mean	3·6	3·9	8	47·3	14·2	30·6	5·3
S.E.	0·6	0·3	1·6	1·6	1	1·4	1·2
Gastric Ulcer Group (33)							
Frequency	10	33	16	32	26	33	2
Size-mean	3	3·2	23·2	45·4	11·4	33	1·5
S.E.	1·1	0·4	5·1	2·5	0·9	2·3	0·4

[1]The number in brackets after each group represents the number of observations made in this group and not necessarily the number of patients studied.

DISCUSSION

The demonstration of an abnormality in the gastric juice of gastric ulcer patients could be of value from many points of view. First, this abnormality could be directly related to ulcer formation, and secondly it could provide a means of differentiating a simple from a malignant gastric ulcer. If this band is related to ulcer formation, it is not unexpected that it was found in only a proportion of those studied. It is likely that gastric ulceration is of multifactorial origin, *i.e.*, it is a common response to a group of different aetiological factors.

There are several possible explanations for the occurrence of this band in gastric ulcer patients: (*a*) it may be a technical artefact arising from inadequate neutralization, alkali denaturation, freeze drying, etc., but would not, however, account for its presence predominantly in one group of the series studied when the same technique was used for the whole series; (*b*) it may be due to some ulcerogenic factor present in gastric juice. If this were so, the presence of gastric ulceration in approximately 50% of those studied would be accounted for. There is no evidence to refute or confirm this concept; the group of controls who showed this band could yet develop a gastric ulcer. It is interesting that the incidence of band 2 in the non-ulcer group was approximately equal to the incidence of peptic ulcer in the community (Doll, Avery Jones, and Buckatzsch, 1951); (*c*) it may be the result of digestion of the normal gastric juice proteins by some enzyme present in gastric juice of gastric ulcer patients that is active at a *p*H above 7. This enzyme could continue the digestion of the protein fractions present normally in gastric juice and the presence of band 2 be an end-result of this activity.

This enzymatic activity at high *p*H levels may appear to be negated by the observation that peptic ulceration will not occur or will heal if the *p*H is

kept above the upper limit of the *p*H level at which pepsin exerts proteolytic activity. However, both enzymes could act at different *p*H levels and pepsin may maintain and perpetuate the ulcer-producing process which may have been initiated by another enzyme. As regards the last mentioned explanation for the presence of band 2, it is theoretically possible that it could result from tryptic digestion from duodenal reflux. This enzyme could be active at the *p*H of the neutralized gastric contents. This, we feel, is unlikely because amongst the many specimens collected some showed slight to marked biliary reflux (these were excluded from the analysis) and the incidence of band 2 in this group was no higher than in the group that showed no evidence of biliary reflux.

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Part III In pernicious anaemia patients

EDITORIAL SYNOPSIS The electrophoretic pattern of the proteins in the gastric juice of patients with pernicious anaemia is compared with the pattern obtained in a group of controls in whom intragastric digestion of proteins has been prevented by intragastric neutralization of the gastric juice.

In patients with pernicious anaemia, band 5, which represents albumin, is increased, and band 4 and band C are decreased. The decrease in band 4 may be related to deficiency of intrinsic factor.

Though the manifestations of pernicious anaemia are predominantly haematological or neurological, it basically is a disease involving the gastric mucosa. The inability of pernicious anaemia patients to secrete acid was demonstrated initially by Cahn and Mehring (1886) and since then this observation has been adequately confirmed (Helmer, Fouts, and Zerfas, 1932; Kirsner, Nutter, and Palmer, 1940; Shay, Komarov, and Beck, 1950; Card, Marks, and Sircus, 1955; Callender, Retief, and Witts, 1960). As a result of the work of Castle and his colleagues (Castle and Townsend, 1929; Castle, Townsend, and Heath, 1930; Castle, Heath, and Strauss, 1931), it was demonstrated that the essential secretory abnormality in pernicious anaemia was not in acid secretion but involved the defective secretion of another substance essential for the absorption of vitamin B12, which they termed intrinsic factor.

It was felt to be of interest to compare the protein fractions in the gastric juice of a group of pernicious anaemia patients with a group of control patients. In this study, efforts were made to prevent changes in the juice of the control group consequent upon *p*H levels that made autodigestion possible. Previous studies have not taken this latter precaution and consequently the protein pattern observed in pernicious anaemia patients may have been more a reflection of the acid and or pepsin secretory failure than an inherently different protein pattern.

METHOD

The 24 controls were the same patients described in Part II. The five patients with pernicious anaemia were diagnosed on the basis of a macrocytic megaloblastic anaemia with histamine-fast achlorhydria to Kay's augmented histamine test (Kay, 1953), and a complete response to vitamin B12 by injection. In three patients a Schilling's test confirmed the presence of vitamin B12 malabsorption corrected by the administration of intrinsic factor; two of the patients with pernicious anaemia were being treated when the study was carried out.

The gastric juice was collected and electrophoresed according to the method described above. The patients were requested to expectorate all saliva and all specimens that showed evidence of biliary reflux were discarded. To standardize the technique both in the control and pernicious anaemia groups, frequent gastric lavage with sodium bicarbonate solution was performed in the pernicious anaemia patients, though this was not necessary to maintain the *p*H above 7 in this group.