

Histological and functional study of gastric mucosa in tropical sprue

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In patients with tropical sprue studied both in Puerto Rico and South India, histological changes in gastric mucosa were noted in 67% and 90% of patients respectively (Floch, Thomassen, Cox, and Sheehy, 1963; Vaish, Sampathkumar, Jacob, and Baker, 1965). Besides histological abnormalities, a significant reduction in gastric acid output was also observed. However, these studies did not exclude the possibility that the two conditions might be separate entities coexisting in the same population. To exclude or confirm this possibility, the incidence of chronic gastritis in patients with tropical sprue should be compared with its incidence in general hospital patients with non-specific symptoms.

The purpose of this communication was to study the histology and secretory function of the gastric mucosa in healthy control subjects, patients with 'vague' gastrointestinal symptoms showing normal jejunal mucosa and absorption tests, and patients with tropical sprue from Bombay. The results showed that the incidence of chronic gastritis in patients with tropical sprue was higher than in healthy control subjects but was comparable to that in patients with vague gastrointestinal symptoms. These results suggest that chronic gastritis and tropical sprue are perhaps two unrelated conditions coexisting in the same population.

MATERIAL AND METHODS

CONTROL SUBJECTS (GROUP I) Thirty-six healthy adult subjects without gastrointestinal symptoms were selected for study. The subjects (who agreed to the procedure) were selected from the outpatient department and had minor symptoms which were not related to the gastrointestinal system.

VAGUE GASTROINTESTINAL SYMPTOMS (GROUP II) Twenty-two adult patients with symptoms such as distension or heaviness in the abdomen after food, dull, aching or colicky abdominal pain, vomiting, anorexia, belching, or excessive flatulence were included in this group. A detailed clinical history, physical examination and barium meal study did not show any obvious organic cause for these symptoms. In a few patients, the symptoms were probably

functional. All patients had a haemoglobin level of above 10 g./100 ml. Jejunal mucosa, ⁵⁸Co vitamin B₁₂ absorption, and d-xylose and faecal fat excretion were normal in all of them.

TROPICAL SPRUE (GROUP III) Thirty-four adult patients with tropical sprue showing histological and/or functional abnormalities of the small intestinal mucosa were selected for study and conformed to those described previously (Jeejeebhoy, Desai, Noronha, Antia, and Parekh, 1966).

GASTRIC BIOPSY The gastric biopsy was performed in 24 control subjects, in 30 patients with tropical sprue, and in all patients (22) with vague gastrointestinal symptoms. Gastric mucosa was obtained from the body of the stomach with a Crosby capsule (Crosby and Kugler, 1957). The specimen was fixed in 10% formalin and sections were stained with haematoxylin and eosin. The diagnosis of chronic gastritis was based on histology and the histological changes were classified according to Williams, Edwards, Lewis, and Coghill (1957).

AUGMENTED HISTAMINE TEST In fasting subjects, the tip of a 14-18 Fr. Levine tube was placed with the aid of fluoroscopy in the most dependent part of stomach. After aspirating the fasting gastric contents, an intramuscular injection of 50 mg. of mepyramine maleate was given and the basal secretion was collected for half an hour. Histamine acid phosphate was then injected subcutaneously and the gastric secretion was subsequently collected by continuous hand suction, in 15-minute pooled samples for one hour. The total acidity in gastric samples was titrated with 0.1 N NaOH using phenolphthalein as an indicator. The maximal acid output (M.A.O.) was measured in mEq./hr. by multiplying the volume (in litres) and concentration (mEq./litre) of acid in the gastric secretion.

The test was done in 20 control subjects, in 13 patients with vague gastrointestinal symptoms, and in 22 patients with tropical sprue using a dose of 0.04 mg./kg. body weight dose of histamine acid phosphate. In eight control subjects and patients with tropical sprue, the test was repeated with a 0.06 mg./kg. body weight dose of histamine acid phosphate.

JEJUNAL BIOPSY AND ABSORPTION TESTS These were performed in patients of groups II and III, using methods

described in a previous study (Jeejeebhoy *et al.*, 1966). The dissecting microscope appearances of the jejunal mucosa were also classified in the same way as in the previous study (Jeejeebhoy *et al.*, 1966).

RESULTS

SEX, AGE, AND WEIGHT In the control subjects the mean age and weight of 30 males and six females were 35.0 years and 49.5 kg respectively. There were 17 males and five females in group II, and their mean age and weight were 36.3 years and 49 kg. respectively. In group III there were 26 males and eight females, and their mean age and weight were 36 years and 45.5 kg. respectively.

GASTRIC BIOPSY (TABLE I) In the controls the gastric mucosa was normal in 18 (75%) subjects; chronic gastritis was observed in six (25%) and superficial gastritis in four, and mild to moderate atrophic gastritis in two subjects. In patients with vague gastrointestinal symptoms, the gastric mucosa was normal in only nine (41%). In the remaining 13 (59%) patients, superficial gastritis was observed in three, mild to moderate atrophic gastritis in six, and severe atrophic gastritis in four patients. In group III, 15 (50%) patients had normal mucosa, the incidence being the same as in the last group. The remaining 15 patients had gastritis and the distribution of the different forms of gastritis was also similar to that in patients in group II, namely, superficial gastritis in four, mild to moderate atrophic gastritis in five, and severe atrophic gastritis in six patients.

AUGMENTED HISTAMINE TEST The mean and standard deviation (S.D.) of the M.A.O. on the augmented histamine test using the conventional dose of histamine (0.04 mg./kg. body weight) was 15.62 ± 6.72 mEq./hr. in 20 control subjects, 9.82 ± 4.93 mEq./hr. in 13 patients with vague gastrointestinal symptoms, and 7.32 ± 6.47 mEq./hr. in

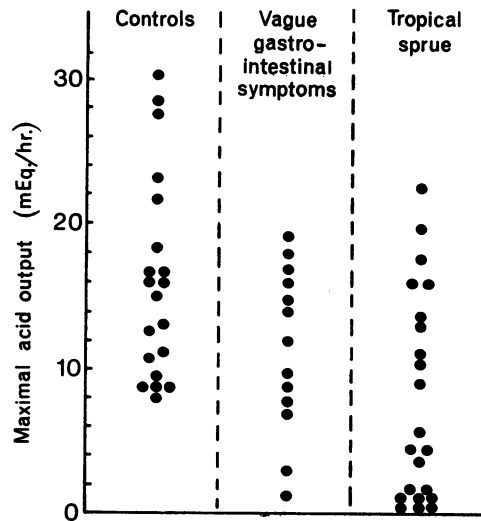


FIG. 1. The maximal acid output on the augmented histamine test.

22 patients with tropical sprue (Fig. 1). The differences in acid output between control subjects and patients with tropical sprue ($P = 0.0005$) or patients with vague gastrointestinal symptoms were significant ($P = 0.005$). However, the differences in acid output between patients with tropical sprue and those with vague gastrointestinal symptoms were not significant ($P = 0.15$).

The comparison of the results of the M.A.O. on the augmented histamine test with 0.04 and 0.06 mg./kg. body weight of histamine acid phosphate showed significantly higher values with the higher dose (Fig. 2). The mean and S.D. of the differences between the two tests in the same patient were 4.34 ± 1.71 mEq./hr. ($P = 0.0005$).

TABLE I

GASTRIC BIOPSY FINDINGS IN 24 HEALTHY CONTROL SUBJECTS, 22 PATIENTS WITH VAGUE GASTROINTESTINAL SYMPTOMS, AND 30 PATIENTS WITH TROPICAL SPRUE

Group	Diagnosis	Gastric Biopsy				Correlation between	
		Normal	Superficial Gastritis	Atrophic Gastritis		Normal and Abnormal Biopsy	Normal Biopsy and Atrophic Gastritis
				Mild to Moderate	Severe		
I	Healthy control subjects (24)	18	4	2	0	} $P < 0.025$	} $P < 0.01$
II	Vague gastrointestinal symptoms (22)	9	3	6	4		
III	Tropical sprue (30)	15	4	5	6	} $P = 0.5$	} $P = 0.4$

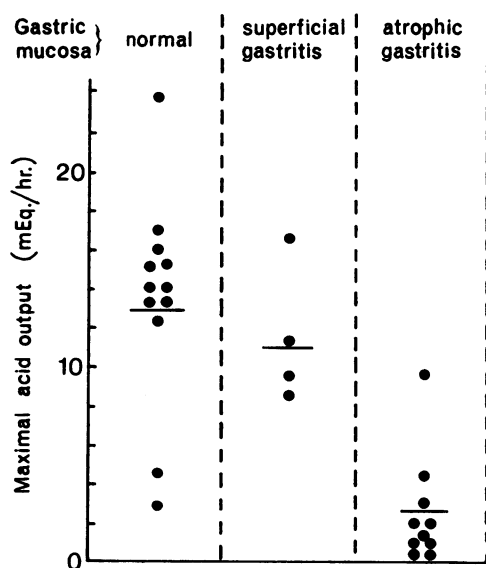


FIG. 2. The maximal acid output on the augmented histamine test with 0.04 and 0.06 mg./kg. body weight doses of histamine acid phosphate.

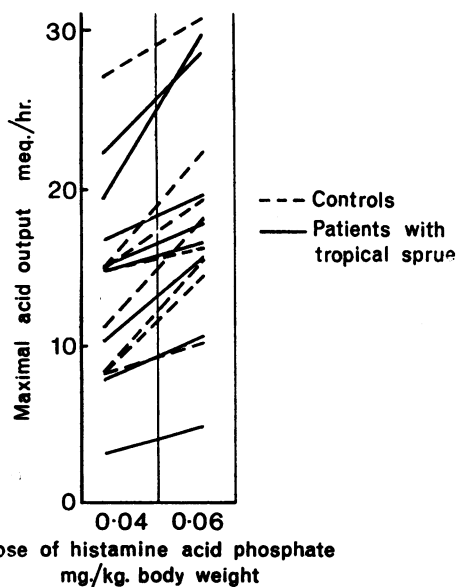


FIG. 3. Correlation between gastric mucosa and maximal acid output on the augmented histamine test.

CORRELATION BETWEEN GASTRIC MUCOSA AND ACID OUTPUT IN PATIENTS WITH TROPICAL SPRUE AND VAGUE GASTROINTESTINAL SYMPTOMS The results are shown in Figure 3. There was good correlation between the histology of the gastric mucosa and acid output on the augmented histamine test.

CORRELATION ON ABSORPTION TESTS BETWEEN GASTRIC MUCOSA OF PATIENTS WITH TROPICAL SPRUE AND JEJUNAL MUCOSA No correlation was observed between the histology of gastric mucosa and dissecting microscope appearances of jejunal mucosa ($P > 0.05$) or d-xylose ($P = 0.1$) or faecal fat excretion ($P > 0.05$). Furthermore, no correlation was observed between the histology of the gastric mucosa and haemoglobin levels ($P = 0.6$), or serum iron ($P = 0.6$), or serum B_{12} ($P = 0.5$), or serum folic acid ($P = 0.5$), or serum albumin ($P = 0.06$), or weight loss ($P = 0.6$), or duration of symptoms ($P = 0.02$).

TABLE II

COMPARISON OF DISSECTING MICROSCOPE APPEARANCES OF JEJUNAL MUCOSA WITH HISTOLOGICAL APPEARANCES OF GASTRIC MUCOSA IN 29 PATIENTS WITH TROPICAL SPRUE

Jejunal Biopsy	Gastric Biopsy		
	Normal	Superficial Gastritis	Atrophic Gastritis
Dissecting Microscope Appearances			
Leaves ± fingers (7) ¹	21.4% (3)	25% (1)	27.3% (3)
Leaves + convolution (6)	14.3% (2)	50% (2)	18.2% (2)
Convolution (16)	64.3% (9)	25% (1)	54.5% (6)

¹The figures in brackets refers to the number of patients.

DISCUSSION

The results of the present study showed that the incidence of chronic atrophic gastritis in patients with tropical sprue was significantly higher than in healthy control subjects ('hypernormal' Indians) ($P < 0.025$) but was not significantly different from patients with vague gastrointestinal symptoms showing neither histological nor functional abnormalities of the small intestinal mucosa ($P = 0.5$) nor with the latter group and control subjects combined ($P = 0.4$). The findings suggested that chronic gastritis in patients with tropical sprue might be an incidental finding and not directly related to this disease. It was apparent from the results that the incidence of chronic gastritis in patients with tropical sprue probably reflected the incidence in an unselected general hospital population.

The results of the augmented histamine test showed a diminished acid output in patients with tropical sprue as has been observed by others (Floch *et al.*, 1963; Vaish *et al.*, 1965). In our patients, the significantly raised acid output observed with a

higher dose of histamine (0.06 mg./kg. body weight) suggested that low values for acid output on the augmented histamine test might at least partly be due to the lower doses of histamine administered, calculated in relation to their reduced body weights. It is of interest to note that Vaish *et al.* (1965) reported a marked increase in acid output in a patient with tropical sprue whose weight had increased by about 15 kg. between the two tests but the finding was unexplained.

The chronic gastritis reported in tropical sprue was believed to be due to (1) extension of the mucosal damage from the small intestine (Delamore and Shearman, 1965) or (2) nutritional deficiencies resulting from malabsorption of substances from the small bowel (Cowan, Joseph, and Satija, 1966), or (3) deficiency of iron, or (4) anaemia. However, no correlation was observed between the histology of the gastric mucosa and jejunal mucosa or absorption tests and comparable findings were noted by Floch *et al.* (1963) and Vaish *et al.* (1965). Lack of correlation between gastric and small intestine mucosal diseases supported the contention that chronic gastritis and tropical sprue were two independent pathological conditions which were associated because of their wide prevalence in India and Puerto Rico. The high incidence of chronic gastritis in our subjects with vague gastrointestinal symptoms showing neither histological nor functional abnormalities of the small bowel mucosa, and the observation that four of eight non-anaemic Puerto-Rican control subjects showed changes of gastritis (Floch, Meroney, and Martinez de Jesus, 1962) supports the above hypothesis.

The changes in gastric mucosa may be secondary to nutritional deficiencies resulting from malabsorption of substances such as vitamin B₁₂ or folic acid or proteins from the small intestine. However, no correlation was observed between gastric mucosal changes and serum B₁₂ or folic acid or serum albumin or weight loss. Furthermore, in several of our severely ill elderly subjects both gastric mucosa and

acid output were found to be normal, showing that nutritional deficiencies alone did not affect gastric mucosa, an observation also reported earlier (Floch *et al.*, 1963).

The role of anaemia in causing gastritis is questionable. Lees and Rosenthal (1958) studied gastric biopsies in 19 patients with hypochromic anaemia, before and after correction of the anaemia, and noted no improvement; if anything, gastritis progressed. Similarly, Vaish *et al.* (1965) found no improvement of acid output after the correction of an anaemia. In megaloblastic anaemia, except Addisonian pernicious anaemia, gastric mucosa was normal in western subjects (Coghill, 1960) but was abnormal in 43% and 41.6% of patients from Puerto Rico and India respectively (Floch *et al.*, 1962; Cowan *et al.*, 1966). The latter observation again emphasized that great caution should be exercised in relating gastric mucosal changes in subjects from tropical countries to such other abnormalities as might be found.

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