pH of the contents of the duodenal bulb in relation to duodenal ulcer

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EDITORIAL SYNOPSIS Wide fluctuations of pH were found in the duodenal bulb for at least six hours after a meal. There was a clear correlation between pain and duodenal acidity.

To test the hypothesis that duodenal ulcer is caused by abnormal acidity, it is necessary to measure acidity in the ulcer-bearing part of the duodenum. Previous investigators have attempted to do this, either by aspirating duodenal contents (Morton, 1929; Berk, Rehfuß, and Thomas 1942a; 1942b; Atkinson and Henley, 1955) or by measuring pH *in situ* with a glass electrode (Eyerley, 1940; Tomenius and Williams, 1960; Rovelstad and Maher, 1962; Bircher, Mann, Carlson, Code, and Rovelstad, 1965). The results in general are not very satisfactory

because it is difficult to keep a tube in the short duodenal bulb. Using two glass electrodes we have been able to control the position of the tube continuously and to measure pH in the duodenal bulb for long periods.

METHODS

SUBJECTS Three groups of subjects were studied (Table I).

(a) Six normal subjects.

TABLE I

Patient No.	Diagnosis	Evidence for Diagnosis	Age	Sex	Number of Electrodes	Histamine Infusion Test (mEq.HCl/hr.)	Total Hours of Observation	Time (hours) during which pH Recorded in		
								Antrum Alone	Bulb Alone	Antrum and Bulb
1	Normal	No symptoms	32	M	1	—	20	7	12	—
2	Normal	No + radiograph	45	M	1	31	18	5	12	—
3	Normal	No + radiograph	21	M	2	—	11	—	—	4
4	Normal	Indigestion								
		Normal radiograph	18	M	2	—	18	1	15	1
5	Normal	No symptoms	41	M	1	—	9	—	9	—
6	Normal	No symptoms	21	M	1	24	9	—	9	—
7	Duodenal ulcer	Radiograph	34	M	1	36	20	—	17	—
8	Duodenal ulcer	Radiograph	45	M	1	58	19	1	17	—
9	Duodenal ulcer	Radiograph	24	M	2	69	16	—	6	10
10	Duodenal ulcer	Radiograph	72	M	2	—	14	1	9	4
11	Duodenal ulcer	Radiograph	18	F	2	35	16	—	2	14
12	Duodenal ulcer	Radiograph	34	M	2	51	11	—	5	6
13	Duodenal ulcer	Radiograph	50	M	2	41	13	—	1	6
14	Duodenal ulcer	Operation	21	M	2	18	16	1	8	6
15	Duodenal ulcer	Radiograph	62	M	2	30	19	—	6	12
16a	Large duodenal mucosal folds	Radiograph	19	M	1	55	19	3	13	—
16b	Large duodenal mucosal folds	Radiograph			2			1	6	11
17	Large duodenal mucosal folds	Radiograph	25	M	2	65	12	—	10	2
18	Large duodenal mucosal folds	Radiograph	55	M	2	44	13	—	2	4
19	Large duodenal mucosal folds	Radiograph	42	M	1	60	21	6	14	—

¹This value has been calculated from the result of a Kay test (53 mEq./hr.).

²In subject 16 the duodenal bulb pH was first measured with a single electrode and later with two electrodes.

(b) Nine patients with active duodenal ulcer: barium meals on these patients were examined independently by two radiologists who agreed in all cases that there was either a deformity of the duodenal bulb or an ulcer.

(c) Four patients, who had coarse duodenal mucosal folds, had ulcer-like symptoms but no ulcer could be demonstrated radiologically. Instead the duodenal mucosa had a coarse or 'cobble stone' appearance. They were members of a group of patients described recently by Fraser, Pitman, Lawrie, Smith, Forrest, and Rhodes (1964). The output of gastric acid after histamine stimulation was high in this group of patients, the range of values being similar to that in subjects with duodenal ulcer.

APPARATUS A composite tube system was used (Fig. 1), consisting initially of one, and later two, intestinal glass electrodes (Cambridge Instrument Co. Ltd.), a reference lead from the calomel electrode and a tube which opened close to the electrodes, down which Gastrografin could be injected. Twenty-five centimetres distal to the electrodes was a small bag containing mercury. When two electrodes were used they were 4 cm. apart. The proximal electrode was attached to the main tube in such a way that it tended to protrude laterally.

PROCEDURE The tube was passed after the nasal cavity had been anaesthetized with cocaine. When two electrodes were used the position of the tube was adjusted so that the proximal electrode was in the antrum of the stomach and the distal in the middle of the duodenal bulb. The proximal electrode which protruded laterally often lodged in the fornix of the pylorus and kept the tube in position; this, however, did not always happen. When only one electrode was used it was placed in the bulb. This position was checked radiologically three or four times during the investigation after 2 ml. of Gastrografin had been injected into the bulb (Fig. 2).

Early in the investigation it was found that in the gastric antrum the pH was fairly constant about 2, where-

FIG. 1. The tube, with two glass electrodes, and a terminal bag containing mercury.

FIG. 2. A radiograph which shows the two electrodes in position; the distal electrode is in the duodenal bulb and Gastrografin outlines the base of the bulb.

FIG. 3. Normal subject: simultaneous records of pH from the antrum and duodenal bulb. The antral pH is steady; the duodenal pH fluctuates (time scale in minutes).

as in the duodenal bulb it either fluctuated widely or was about neutral (Fig. 3). This difference between the records of pH from the antrum and duodenum enabled us to localize the position of the tube. Thus when the pH record from the proximal electrode was steady, and that from the distal electrode fluctuating, it was inferred that the distal electrode was in the first 4 cm. of the duodenum. When both records were fluctuating it was inferred that both electrodes were in the duodenum, and the tube was withdrawn until the proximal electrode gave a steady antral pH. This technique made it possible to control the position of the tube continuously.

MEALS All subjects were given similar meals at the same time of day. The evening meal was given at 6.15 p.m. and followed at 9.30 p.m. by a milk drink and biscuits. A large meal alters the length of the stomach, making it difficult to control the position of the electrodes; for this reason

the volume of the meals was kept small. The subjects remained in bed during the investigations and were not allowed to smoke or take alkali.

pH RECORDS Duodenal pH was measured continuously for between 12 and 18 hours. In all patients this included the period between midnight and 8.0 a.m. Duodenal pH was recorded with a potentiometric recorder (Honeywell Controls Ltd., Model 153 × 11, chart speed 25.5 cm. per hour) and a second recorder (Control Instr. Ltd., model H, chart speed 10.2 cm. per hour) was used for antral pH. In patients 3, 13, and 18, duodenal and antral pH were recorded with a Sanborn recorder (model 64 A, chart speed 91 cm. per hour). In patients 3 and 18, pH was only recorded for the first quarter of each hour at night. At the beginning and the end of the investigation the electrodes were calibrated in two buffered solutions of pH 8 and 4. The two calibrations did not differ by more than 0.2 pH units.

HISTAMINE TESTS Thirteen subjects had a histamine infusion test (Lawrie, Smith, and Forrest, 1964). One had a Kay test (Kay, 1953) and five patients had neither.

ANALYSIS OF THE pH RECORDS The records were first examined to check the position of the electrodes (as previously explained). The following observations were then made.

- The length of time between midnight and 6 a.m. in which fluctuations were present was noted: the record was said to fluctuate if the pH altered by more than 0.5 more often than once every 10 minutes.
- The frequencies for each hour of pH swings lower than 2.5 and 2.0 were measured.
- The lowest duodenal pH in each hour was noted.
- The average antral pH for each hour and the time taken for the antral contents to become acid after a meal were measured.

The results from normal subjects, patients with

duodenal ulcer and coarse duodenal mucosal folds were compared.

RESULTS

DUODENAL BULB pH Results in the duodenal bulb are recorded first.

Fluctuations of pH Immediately after food, when the antral contents were almost neutral, fluctuations in the duodenal pH were small and irregular. About one hour later, when the antral contents had usually been acidified, the fluctuations were irregular and of greater amplitude. These regular fluctuations continued for about six hours, but were then broken up by periods in which the pH was neutral (Fig. 4). The

FIG. 5. The percentage of time between midnight and 6 a.m. for which fluctuations of pH were present is given for each patient.

FIG. 4. Patient with a duodenal ulcer: at night there are fluctuations of pH in the duodenal bulb separated by long periods of neutral pH (time scale in hours).

TABLE II

FLUCTUATIONS IN DUODENAL BULB pH BETWEEN MIDNIGHT AND 6 A.M.

Patient	Diagnosis	Time (min.) for which Records Available	Time (min.) Fluctuations Present	% Time pH Fluctuates	Mean and S.E.
1	Normal	295	85	29	31.8 ± 5
2	Normal	260	70	27	
3	Normal	110	60	54	
4	Normal	360	60	17	
5	Normal	360	108	30	
6	Normal	360	122	34	
7	Duodenal ulcer	360	70	19	50.8 ± 7.2
8	Duodenal ulcer	360	90	25	
9	Duodenal ulcer	360	295	85	
10	Duodenal ulcer	360	205	58	
11	Duodenal ulcer	360	145	41	
12	Duodenal ulcer	360	185	53	
13	Duodenal ulcer	85	35	42	
14	Duodenal ulcer	315	190	60	
15	Duodenal ulcer	360	265	74	
16a	Coarse duodenal mucosa	360	300	83	72.4 ± 4.4
16b	Coarse duodenal mucosa	342	210	62	
17	Coarse duodenal mucosa	360	255	71	
18	Coarse duodenal mucosa	70	45	64	
19	Coarse duodenal mucosa	360	245	84	

Significance of difference between means:—

Normal and duodenal ulcer 0.2 > p > 0.1
 Normal and coarse mucosa 0.01 > p > 0.001
 Duodenal ulcer and coarse mucosa 0.05 > p > 0.02

percentage of time for which the pH fluctuated between midnight and 6 a.m. is given in Fig. 5 and the results on which these percentages are based are given in Table II. The number of patients in each group is small but the results suggest that fluctuations in the duodenal pH continued for longer in patients with duodenal ulcer than in normal subjects and longest in the patients with coarse duodenal mucosa. The mean for normal subjects was 31.8%; for subjects with duodenal ulcer 50.8%, and for subjects with coarse duodenal mucosal folds 72.4%.

The lowest duodenal pH The lowest duodenal pH reached during each hour is recorded in Figure 6. Most of the values are between 1.5 and 2.5 but in patients with coarse duodenal mucosa the pH was often less than 1.5.

The frequency of low levels of duodenal bulb pH The frequencies with which the duodenal pH fell below 2 and 2.5 are given in Figure 7. The duodenal pH often fell below 2.5 without reaching 2. (The pH fell below 2.5 with a frequency greater than 40 times per hour on 46 occasions and below 2 at a frequency greater than 40 times per hour on 19 occasions.) In the subjects with coarse mucosal folds, all of whom had a high output of gastric acid with histamine stimulation, the pH fell below 2.5 more often than in other subjects.

THE ANTRAL pH Variations of antral pH over a short time were seldom greater than 0.3 pH units. The antral contents, which are neutral after a meal, are

gradually acidified reaching a steady level within one hour after the meal.

THE HISTAMINE INFUSION TEST The results of the histamine infusion test are given in Table I. Only one of the patients with duodenal ulcer secreted less than 30 mEq. HCl per hour. The four patients with coarse duodenal mucosal folds had a high acid output. When histamine stimulation is by continuous intravenous infusion the results are 30% higher than those from the Kay test (Lawrie *et al.*, 1964).

In Fig. 8 the secretion of acid after histamine is plotted against the percentage of time between midnight and 6 a.m. that the duodenal pH fluctuated. The relationship is linear (significance of correlation 0.05 > p > 0.02).

The relationship between the secretion of acid after histamine and the duodenal pH was examined. Allowing for considerable scatter, the lowest pH levels and the greater frequencies of pH swings below 2.5 and 2.0 were seen in subjects with the highest levels of acid secretion.

There was no relationship between the antral pH and the secretion of acid after histamine. Neither was there any relation between the antral pH and any of the duodenal values analysed.

In some of the patients with duodenal ulcer, fluctuations of duodenal pH were accompanied by pain. The pain began about an hour after food when the lowest limits of the duodenal pH were between 1 and 2. At night, pain was associated with a fluctuat-

FIG. 6. The lowest duodenal pH for each hour between 5 p.m. and 6 p.m. is given for each patient.

FIG. 7. The frequencies with which the duodenal pH fell below 2 and 2.5 are given for each hour in each patient.

FIG. 8. The percentage of time the pH fluctuates between midnight and 6 a.m. is plotted against the subject's secretion of gastric acid during histamine stimulation.

ing duodenal pH and did not occur when the pH was neutral.

DISCUSSION

Previous investigators who have tried to measure pH in the duodenal bulb have faced two main technical difficulties. First, those who have aspirated duodenal samples may have caused gastric contents to move into the duodenum and contaminate the sample. Secondly, it is difficult to keep a tube in the very short duodenal bulb because peristaltic waves in the stomach and duodenum tend to move it. Furthermore, there has been no convenient method for localizing the position of the electrode for any length of time.

Atkinson and Henley (1955) attempted to aspirate samples from the duodenal bulb for between 12 and 24 hours. The position of their tube was checked radiologically at least every three hours during the day, but not at all at night. They found that the pH was less than 2 for 32% and 47% of the time in normal and duodenal ulcer subjects respectively. They had no method of localizing the pylorus continuously and, because of this, one cannot accept that their samples were always taken from the bulb. Eyerley (1940), Tomenius and Williams (1960), and Rovelstad and Maher (1962) used a glass electrode to record pH in the duodenal bulb, but had difficulty in keeping the electrode in position. Rovelstad and Maher made records for only short periods in the bulb. Bircher *et al.* (1965) have recently recorded pH in the proximal part of the duodenum with two electrodes. They recorded pH simultaneously from

the bulb and immediately distal to the apex of the bulb for short periods. During some of their experiments they used cine-radiography to correlate changes in pH with the movement of duodenal contents. In the present studies the pH has been recorded on both sides of the pylorus using two electrodes so that we knew that the distal electrode was always in the duodenal bulb.

One objection to the use of intestinal electrodes is that each gastric or duodenal contraction may cause the electrode to be buried transiently in the duodenal mucosa. This may change the recorded pH without any change occurring in the pH of the duodenal contents. To examine the possibility Bircher *et al.* (1965) recorded duodenal pH with bare and guarded (the guard was a simple wire cage) electrodes. Records of pH from the two electrodes were different. In the duodenal bulb a guarded electrode recorded a steady pH about 2, whereas a bare electrode recorded a fluctuating pH. They interpret the difference to be due to the bare electrode rubbing against the mucosa, but do not consider the possibility that a guard may prevent the electrode from recording rapid fluctuations of pH. Eyerley (1940) and Tomenius and Williams (1960) also used guarded electrodes and recorded a steady pH in the duodenal bulb. In our experience any attachments around the electrode become clogged with mucus and prevent the electrode recording wide fluctuations of pH.

In the present investigation wide fluctuations of pH (between about 1.5 and 7) were recorded in the duodenal bulb. The fluctuations in pH at night continued for longer in patients with duodenal ulcer and with coarse duodenal mucosal folds than in normal subjects (Fig. 5). The total length of time during which there were fluctuations at night was related to the subject's acid output during histamine stimulation. Moreover, the lowest pH recorded in the duodenum, and the frequency with which the pH fell below 2 and 2.5 were all related to the acid output after histamine stimulation.

Although one can keep the intestinal electrode in the duodenal bulb, its position within the bulb cannot be controlled. The electrode may move between the base of the bulb and the apex, and if there is a gradient of pH across the bulb, the pH records would depend on the position of the electrode. For this reason a more detailed analysis of the results is not justified.

The results show that the mucosa in the duodenal bulb is exposed to wide fluctuations in acidity. In patients with high levels of acid secretion the fluctuations continue for longer, and reach lower levels than in normal people. These results support the hypothesis that peptic ulceration occurs at sites where acidity alternates with neutrality. Similarly, gastric

ulcer usually occurs on the lesser curve at the junction of acid-secreting and mucus-secreting mucosa (Oi, Oshida, and Sugimura, 1959; Capper, Laidlaw, Buckler, and Richards 1962), a site which is probably exposed alternately to acid and neutral contents. Furthermore the changes in acidity at night at the site of ulceration are similar in both groups since many patients with gastric ulcer have neutral gastric contents at night (James and Pickering, 1949; Watkinson, 1951; Ball and James, 1961).

Many patients with coarse duodenal mucosal folds do not have a duodenal ulcer in spite of high secretion of gastric acid. Extensive areas of gastric epithelium were found in five of six biopsies of duodenal mucosa in these patients (Fraser *et al.*, 1964); such epithelium may protect the mucosa against ulceration. Gastric epithelium has been produced in the duodenum of animals by exposing the mucosa to abnormal amounts of acid (Florey, Jennings, Jennings, and O'Connor, 1939; Rhodes, 1964). Florey *et al.* (1939) constructed a duodenal fistula between a Pavlov pouch and the jejunum in seven pigs. Five of these were killed eight to ten and a half months later, when it was found that the duodenal mucosa was not ulcerated and the villi were covered with gastric epithelium. Gastric epithelium in the duodenum is common but not extensive in patients with duodenal ulcer (James, 1964).

In those patients who had pain during the investigation there was a clear relationship between pain and duodenal acidity. Pain did not occur when the duodenal contents were neutral but when the duodenal contents were intermittently acid during gastric emptying.

SUMMARY

The pH of the duodenal bulb was measured for long periods in normal subjects, in patients with duodenal ulcer, and in patients with coarse duodenal mucosal folds. With two intestinal electrodes it was possible to control the position of the electrode in the bulb continuously.

In the duodenal bulb wide fluctuations of pH were observed for at least six hours after a meal. At night, when gastric emptying was intermittent, the fluctuations were interrupted by intervals of neutral pH, and persisted for longer periods than normal in patients with duodenal ulcer and patients with coarse

duodenal mucosal folds. The duration of these fluctuations at night was related to the maximal secretion of acid after histamine.

The significance of these observations in relation to the aetiology of peptic ulceration is discussed.

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