Clinical and laboratory study of postvagotomy diarrhoea

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SUMMARY Thirty-two patients with diarrhoea, on average four years following truncal vagotomy and drainage, were studied. A comparison was made with 24 patients without postvagotomy diarrhoea. The incidence of bacterial colonization of the upper small intestine was no different in the two groups, though patients with a gastroenterostomy had a significantly higher incidence than those with a pyloroplasty. There was a higher incidence of 'anaerobic colonization' in patients with diarrhoea, but statistical significance was not reached.

Colonization was associated with significantly lower levels of gastric acid secretion.

Though 13 patients with diarrhoea had an abnormal faecal fat excretion, no correlation could be found between this and the severity of the diarrhoea or bacterial colonization, either with an anaerobic or a coliform type flora.

In patients with diarrhoea, no small intestinal mucosal abnormality was detected, the mean haematological and serum biochemistry values were within normal limits, and the body weight was similar to that before operation.

Two patients with diarrhoea had abnormal haematological values five years following vagotomy and gastroenterostomy in association with 'anaerobic colonization' of the upper small intestine. As the incidence of haematological abnormalities after gastric surgery increases with time, colonized patients might merit particularly close clinical observation.

Diarrhoea is known to occur in some patients following surgery for duodenal ulcer (Dragstedt and Woodward, 1951). Truncal vagotomy has been particularly implicated, but when combined with drainage or antrectomy the incidence of diarrhoea is generally held to be in the region of 25% of which only 1-3% find the symptom troublesome (Cox and Bond, 1964; Goligher, Pulvertaft, DeDombal, Conyers, Duthie, Feather, Latchmore, Shoesmith, Smiddy, and Willson-Pepper, 1968). This reported incidence has caused some workers concern (Burge and Clark, 1960), but controlled clinical trials will help to differentiate between the alternative forms of vagotomy, with or without drainage. Selective vagotomy in this respect has been shown to be superior to truncal vagotomy when combined with a Finney-type pyloroplasty (Kennedy, Connell, Love, MacRae, and Spencer, 1973) and there are promising results for the future from highly selective vagotomy without drainage (Johnston, Humphrey, Walker, Pulvertaft, and Goligher, 1972).

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Despite clinical interest, the aetiology of post-vagotomy diarrhoea is unresolved. Dragstedt and Woodward (1951) and others have suggested that its occurrence might be related to bacterial colonization of the upper small intestine. The upper small bowel normally contains few microorganisms (Cregan and Hayward, 1953; Donaldson, 1964; Drasar, Shiner, and McLeod, 1969), but it has been shown that in some patients, studied on average 18 months following truncal vagotomy and drainage, colonization occurs (Browning, Buchan, and MacKay, 1972).

Colonization, particularly with anaerobic organisms, has been implicated in the causation of steatorrhoea in patients with the 'blind loop syndrome' (Tabaqchali, 1970). Though steatorrhoea does not commonly occur following truncal vagotomy, the daily faecal fat excretion is known to be raised compared with preoperative levels (Cox and Bond, 1964) and this rise could also be associated with an altered bowel flora.

The aim of this investigation was to study the upper small bowel flora, small bowel function, and

bowel habit in patients with and without diarrhoea following truncal vagotomy and drainage.

Methods

Diarrhoea was defined as the daily or episodic passage of loose, frequent bowel motions associated with a degree of urgency. Thirty-two patients who had diarrhoea following elective surgery for chronic duodenal ulcer were studied: in eight (25%) the diarrhoea was a daily occurrence, and in 24 (75%) it was episodic in nature. Each patient had had a bilateral truncal vagotomy; in 16 patients (13 male, three female, mean age 44.6 years) this was combined with a Heineke-Mikulicz pyloroplasty, and in the other 16 patients (11 male, five female, mean age 45.8 years) with a retrocolic gastroenterostomy. Surgery had been performed on average 4.1 years (range 0.75 to 13 years) previously.

Twenty-four patients, who also had had elective surgery for chronic duodenal ulceration but in whom the symptom of diarrhoea was not elicited, were also studied. Each patient had had a bilateral truncal vagotomy, and in 12 patients (all male, mean age 47 years) this was combined with a Heineke-Mikulicz pyloroplasty, and in the other 12 patients (11 male, one female, mean age 48 years) with a retrocolic gastroenterostomy. Surgery had been performed on average 1.5 years (range 0.75 to 2.4 years) previously.

The following investigations were performed in all patients: (1) The bacterial flora of the upper small intestine was assessed by the culture of contents aspirated via an orally passed polyethylene tube which had been guided into the upper small intestine under radiological control. Samples were aspirated from the patient in the fasting state, and at half an hour and at one hour following the ingestion of a cup of tea and a slice of buttered toast. No patient was on antibiotic therapy at the time of the study. (2) The bowel habit had been recorded before operation, and regularly on follow up at the routine outpatient attendances. Patients with diarrhoea were classified according to the severity of the diarrhoea using a modified Visick grading (Visick, 1948). Patients without diarrhoea were graded Visick I; patients with mild diarrhoea, Visick II; patients with poorly controlled diarrhoea, Visick III; and patients with diarrhoea which interfered with work or the enjoyment of life were graded as Visick IV. (3) The body weight had been recorded before surgery and at the regular follow-up attendances. (4) The haemoglobin, serum iron, and total iron-binding capacity, serum vitamin B₁₂, and the serum folate or red blood cell folate were estimated at the time of culture of the intestinal contents. (5) The maximal acid response to

pentagastrin had been measured seven to 10 days postoperatively. (6) An insulin test, interpreted according to Hollander's criteria (Hollander, 1948), had been performed seven to 10 days postoperatively.

The following additional investigations were performed on the patients complaining of diarrhoea. A biopsy of the small intestine was taken at the time of intestinal intubation and examined under the dissecting microscope and subsequently under the light microscope. The serum calcium, phosphate, and proteins were estimated. The faecal fat excretion was estimated from a three-day total collection while the patient was on a normal diet at home (van de Kamer, 1958).

BACTERIOLOGICAL CULTURES

The samples of intestinal content were cultured within one hour of aspiration. A ten-fold dilution of the aspirate was made in distilled water reducing the viscosity of the fluid to enable more accurate plating. An estimate of the viable colony count was obtained using a standard plating technique (Urquhart and Gould, 1965) after at least four days' incubation under aerobic and strict anaerobic conditions. Anaerobiosis was achieved either by vacuum extraction and hydrogen flushing of a BTL (Baird and Tatlock Limited, Chadwell Heath, Essex, Great Britain) modification of a McIntosh-Fildes jar, or by the 'Gas pack system' (Becton, Dickinson UK Limited, York House, Empire Way, Wembley, Middlesex, Great Britain). The media employed were brain-heart infusion blood agar (Oxoid), MacConkey no. 2 agar (Oxoid), mannitol salt agar (Oxoid), boiled blood nutrient agar (Cruikshank, 1968), Sabouraud's 4% glucose agar (Cruikshank, 1968), and phenyl ethyl alcohol tomato juice boiled blood agar (Buchan and Gould, 1967). Identification of the isolates was confirmed according to Bergey's 'Manual of determinative bacteriology' (Bergey, 1957).

The aspirates were classified into four groups as follows: (I) 'sterile', ie, < 10⁴ organisms/ml aspirate; (II) upper respiratory tract flora in concentrations of ≥ 10⁴/ml aspirate, and included the aerobic genera *Staphylococcus*, *Streptococcus*, *Corynebacterium*, *Haemophilus*, *Neisseria*, *Lactobacillus*, and *Nocardia*, and also yeasts and fungi; (III) 'coliform colonization', ie, members of the Enterobacteriaceae in concentrations of ≥ 10⁵/ml aspirate; (IV) 'anaerobic colonization', ie, as for III with the addition of the anaerobic genera *Veillonella*, *Bacteroides*, *Lactobacillus*, and *Clostridium*.

Aspirates classified as III or IV, 'faecal type' organisms, were considered to be indicative of significant colonization of the upper small bowel. Significant colonization was therefore defined as 'the presence in the upper jejunum of "faecal type"

organisms in a concentration of at least 10^5 per ml. of aspirate'. In the subsequent text the term 'colonization' denotes significant colonization while 'coliform colonization' denotes classification III and 'anaerobic colonization' denotes classification IV.

Results

BACTERIAL FLORA

Figures 1 and 2 show the bacterial flora of the fasting and the one hour postprandial samples from the upper small intestine of both the control and post-vagotomy diarrhoea patients recorded qualitatively and quantitatively according to the drainage procedure. The flora was no different in the fasting or in any of the postprandial samples.

The coliform type organisms (III) were mainly *E. coli* and *Klebsiella aerogenes*. The anaerobic organisms (IV) were *Veillonella* with, in addition, an anaerobic *Lactobacillus* in one patient without diarrhoea following vagotomy and gastroenterostomy. *Bacteroides* was not isolated.

In the 32 patients with diarrhoea there was no feature to distinguish the eight with daily diarrhoea (fig 3).

INCIDENCE OF COLONIZATION

The incidence of colonization in patients with diarrhoea was 31% (ten of 32), which was similar to that of 33% (eight of 24) in those without diarrhoea. More of the patients with diarrhoea (three of ten) were colonized with anaerobic organisms than those without diarrhoea (one of eight), but the difference did not reach statistical significance. Three of eight (38%) patients with daily diarrhoea were colonized, which was essentially similar to the incidence of colonization of seven of 24 (29%) with episodic diarrhoea.

Although the mean time since operation was 4.1 years in those with diarrhoea compared with 1.5 years in those without, there was no evidence to suggest that the incidence of colonization was related to the length of time since operation, as the mean time since operation of 3.5 ± 0.7 years (mean $\pm$ 1 standard error) in patients from both groups who

were colonized was similar to 3.2 ± 0.5 years in those who were not.

Table I shows the incidence analysed according to the drainage procedure, as this has been shown to influence the incidence of colonization (Browning, MacKay, and Buchan, 1969). In patients without diarrhoea there was a significant difference ($P < 0.05$) in the incidence of colonization in that 58% (seven of 12) of those with a gastroenterostomy were colonized compared with only 8% (one of 12) of those with a pyloroplasty. In patients with diarrhoea, 44% (seven of 16) of patients with a gastroenterostomy were colonized compared with 19% (three of 16) of those with a pyloroplasty ($P < 0.1$). There was a higher frequency of colonization with anaerobic organisms in diarrhoea patients, and this was seen to be more often associated with a gastroenterostomy.

CORRELATION OF COLONIZATION AND VISICK GRADING OF DIARRHOEA

Of the 32 patients with diarrhoea, in 17 (53%) the symptoms were graded Visick II, in 13 (41%) patients Visick III, and in two (6%) patients Visick IV. Those with daily diarrhoea were more inconvenienced, in that of the eight patients, four were graded Visick III, and one graded Visick IV. Table II shows that there was no correlation between the severity of the symptoms and colonization in general, or 'coliform' or 'anaerobic' colonization in particular.

Visick Grade	Total No.	No. with Coliform Colonization	No. with Anaerobic Colonization	No. Colonized
II	17	5	1	6
III	13	2	2	4
IV	2	0	0	0

Table II Visick grading of diarrhoea analysed according to colonization

FAECAL FAT EXCRETION IN DIARRHOEA PATIENTS

Table III shows the faecal fat excretion in diarrhoea patients according to the drainage procedure and

Group	Total No.	No. with Coliform Colonization	No. with Anaerobic Colonization	No. Colonized
<i>Gastroenterostomy</i>				
Diarrhoea	16	4	3	7 (44%)
No diarrhoea	12	6	1	7 (58%)
<i>Pyloroplasty</i>				
Diarrhoea	16	3	0	3 (19%)
No diarrhoea	12	1	0	1 (8%)

Table I Incidence of colonization analysed by drainage procedure

Logarithm of the quantitative bacterial count

Qualitative Bacterial Groups

II = upper respiratory type, III = coliform type, IV = anaerobic

Fig 1 The bacterial flora of the fasting and postprandial contents of the upper small intestine assessed qualitatively and quantitatively in patients with and without diarrhoea following vagotomy and pyloroplasty

Fig 2 The bacterial flora of the fasting and postprandial contents of the upper small intestine assessed qualitatively and quantitatively in patients with and without diarrhoea following vagotomy and gastroenterostomy

Fig 3 The bacterial flora of the fasting and postprandial contents of the upper small intestine assessed qualitatively and quantitatively in patients with daily diarrhoea following vagotomy and either pyloroplasty or gastroenterostomy

Group	Total No.	Faecal Fat Excretion ¹
Total	32	6.5 ± 0.9
Pyloroplasty	16	5.0 ± 1.7
Gastroenterostomy	16	8.0 ± 1.4
Non-colonized	22	7.2 ± 1.3
Colonized	10	5.2 ± 1.2
Coliform	6	4.6 ± 1.1
Anaerobic	4	6.0 ± 2.7

Table III Correlation of drainage procedure and colonization with faecal fat excretion in diarrhoea patients¹

Mean grams/day ± 1 standard error

colonization. The faecal fat excretion in the 32 diarrhoea patients was 6.5 ± 0.9 g per day (mean ± 1 standard error). The faecal fat excretion was 4.6 ± 1.2 g per day in the eight patients with daily diarrhoea compared with the level of 7.2 ± 1.2 g per day in the 24 patients with episodic diarrhoea. The drainage procedure did not significantly influence the level, which was 8.0 ± 1.4 g per day in the 16 patients with a gastroenterostomy, and 5.0 ± 1.7 g per day in the 16 with a pyloroplasty. The 22 non-colonized patients had a level of 7.2 ± 1.3 g per day, and the 10 colonized patients 5.2 ± 1.2 g per day. Of the colonized patients, six with 'coliform colonization' had a level of 4.6 ± 1.1 g per day, and four with 'anaerobic colonization' 6.0 ± 2.7 g per day. None of these differences achieved statistical significance.

Although the mean daily faecal fat excretion for the 32 patients with diarrhoea was within normal limits, 13 patients had levels exceeding 7 g per day, which was the upper limit of our accepted normal range. In eight patients the level was between 7 and 14 g per day, in four between 7 and 21 g per day, and in one patient it was over 21 g per day. In the 17 patients graded Visick II the level was 6.6 ± 1.2 g per day, in the 13 graded Visick III, 6.0 ± 1.5 g per day, and in the two graded Visick IV it was 11.3 g per day. There was, however, no correlation between the grade of severity of the diarrhoea and the mean faecal fat excretion.

BODY WEIGHT

Despite the diarrhoea there was no significant weight change in patients with diarrhoea whose body weight of 63.2 ± 1.9 kg (mean ± 1 standard error) was no different from their preoperative weight of 62.9 ± 2.7 kg. This was also similar to the weight of the control patients of 62.1 ± 2.5 kg postoperatively and 61.2 ± 2.1 kg preoperatively. In addition, the patients with daily diarrhoea had a postoperative weight of 61.8 ± 6.6 kg compared with 64.3 ± 9.1 kg preoperatively.

HAEMATOLOGY

The mean values of the haematological investigations of the 32 patients with diarrhoea, shown in table IV, were within normal limits. In particular, the mean values of the patients who were colonized, either with coliform or anaerobic organisms, showed no departure from normal values.

Although these mean values fell within normal limits, two postmenopausal female patients had a hypochromic microcytic anaemia. In the first patient the haemoglobin level was 7.9 g%, the serum iron saturation 5%, and the serum vitamin B₁₂ and red cell folate levels normal. In the second, the haemoglobin level was 10.3 g%, the serum iron saturation 12%, the serum vitamin B₁₂ low normal, and the red cell folate normal. Neither had a history of gastrointestinal bleeding or salicylate ingestion. Their levels of faecal fat excretion were 5.3 and 9 g per day respectively. Both patients had diarrhoea following truncal vagotomy and gastroenterostomy five years previously and in each patient the upper small intestine was colonized with anaerobic organisms.

BIOCHEMICAL INVESTIGATIONS

The results (mean ± 1 standard error) of the biochemical investigations in the patients with diarrhoea were:

Serum calcium	..	..	9.2 ± 0.1 g/100 ml
Serum phosphate	..	..	3.0 ± 0.1 mg/100 ml
Serum albumin	..	..	4.2 ± 0.1 g/100 ml
Serum globulin	..	..	2.4 ± 0.1 g/100 ml

No patient had abnormal values.

Haematology	Total	Not Colonized	Colonized	With Coliform Colonization	With Anaerobic Colonization
Hb (g %)	14.4 ± 0.3	16.6 ± 2.0	13.6 ± 0.8	14.3 ± 0.8	12.4 ± 1.53
B ₁₂ (pg/ml)	251.0 ± 22.7	262.0 ± 29.0	219.0 ± 37.3	240.0 ± 50.8	119.0 ± 29.4
Folate	Normal	Normal	Normal	Normal	Normal
TIBC (μg/100 ml)	357.0 ± 8.9	351.0 ± 11.9	344.0 ± 16.7	340.0 ± 15.9	354.0 ± 63.0
Fo (μg/100 ml)	108.0 ± 9.1	109.0 ± 10.7	98.0 ± 18.0	108.0 ± 19.4	66.0 ± 46.0
% saturation	3.00 ± 2.7	31.0 ± 3.1	0.30 ± 5.6	33.0 ± 5.8	22.0 ± 17.0

Table IV Haematological investigations in diarrhoea patients analysed according to colonization

¹Values are for means ± 1 standard error.

SMALL INTESTINAL BIOPSY

All small intestinal biopsies were normal both under the dissecting and light microscopes, with no evidence of villous atrophy. The villi were in 56% mainly finger-shaped, in 36% equally finger and leaf-shaped, and in 8% ridged.

Histological examination showed essentially normal jejunal architecture, with no mucosal abnormality and no increase in chronic inflammatory infiltrate of the submucosal stroma.

MAXIMAL ACID OUTPUT

The patients with diarrhoea had a peak half-hour acid secretion similar to those without diarrhoea (table V). When analysed in relation to colonization, those patients who were colonized had a significantly lower level of acid secretion than those who were not ($P < 0.05$).

Group	Total No.	All Patients	Non-colonized Patients	Colonized Patients
Diarrhoea	32	6.1 $\pm$ 1.8	8.1 $\pm$ 2.1	2.7 $\pm$ 2.7
No diarrhoea	24	5.3 $\pm$ 1.0	6.2 $\pm$ 1.5	4.0 $\pm$ 1.5
Total	56	5.2 $\pm$ 0.9	6.7 $\pm$ 1.2	3.5 $\pm$ 1.3

Table V Maximal acid output in mequiv/peak half hour analysed according to colonization¹

¹Values are for means $\pm$ 1 standard error.

INSULIN RESPONSE

Two patients with diarrhoea had an early positive insulin response. One patient with a gastroenterostomy was colonized with anaerobic organisms, the other with a pyloroplasty was colonized with coliform type organisms. Neither patient had any other abnormality on investigation. No patient without diarrhoea had an early positive insulin response.

BOWEL HABIT

The bowel habit in the 32 patients with diarrhoea was no different in those who had had a pyloroplasty compared with those with a gastroenterostomy. The diarrhoea was a daily occurrence in eight (25%) and in 24 (75%) it was of an episodic nature; in three of the latter diarrhoea alternated with periods of relative constipation. In the patients with daily diarrhoea the mean number of motions was 4.1 per day (29 per week). In the others, between the attacks of diarrhoea, the mean number of motions was 8.7 per week.

The 24 patients without diarrhoea had a mean number of 6.8 bowel motions per week which was similar to their preoperative habit of 6.9 bowel motions per week.

Discussion

The upper small intestine normally contains few microorganisms (Cregan and Hayward, 1953; Donaldson, 1964; Drasar *et al*, 1969). Following vagotomy and drainage there is an anatomical disturbance, a changed pattern of gastric emptying, and reduction in acid secretion (Gillespie, Clark, Kay, and Tankel, 1960); each, or all, of these changes may allow an overgrowth of faecal type organisms (Donaldson, 1964; Tabaqchali, 1970). This is particularly liable to occur when the drainage procedure is gastroenterostomy, presumably due to the production of a potential 'blind loop'. It might be expected that patients with postvagotomy diarrhoea would have a higher incidence of colonization with faecal type organisms, but the incidence of colonization in such patients was no higher than in controls and, although 'anaerobic colonization' was more common, statistical significance was not reached. This confirms previous reports on small numbers of patients (Dellipiani and Girdwood, 1967; Tinker, Hoffbrand, Mitchison, Tabaqchali, and Cox, 1971). In the first two postoperative weeks, *Clostridium welchii* has been particularly implicated (Howie, Duncan, and Mackie, 1953), but a more recent quantitative study has not confirmed this (Browning *et al*, 1969), and in the present study, on average four years following surgery no single pathogenic organism could be isolated.

The presence of a faecal type flora in association with steatorrhoea following gastric surgery was first reported by Goldstein, Wirts, and Kramer (1961). Subsequent quantitative studies following gastrectomy have not confirmed this finding (Wirts and Goldstein, 1964; Tabaqchali and Booth, 1966; Dellipiani and Girdwood, 1967; Gorbach and Tabaqchali, 1969) nor was it confirmed after vagotomy and gastroenterostomy (Dellipiani and Girdwood, 1967). The present study has sought, for the first time, to correlate the faecal fat excretion and the small intestinal flora in patients with diarrhoea following gastric surgery. Though 13 of the 32 patients in this study with diarrhoea had a faecal fat excretion above 7 g per day, no simple correlation could be made between this and the small intestinal flora.

'Anaerobic colonization', in particular with *Bacteroides*, has been implicated in the causation of steatorrhoea (Gorbach and Tabaqchali, 1969), and it has been suggested that this is due to the ability of this organism to deconjugate bile salts (Drasar, Hill, and Shiner, 1966). In our patients a mean faecal fat excretion of 6.0 $\pm$ 2.7 g per day in patients with an anaerobic flora was essentially similar to the level of 7.2 $\pm$ 1.3 g per day in the non-colonized

patients. Despite strict anaerobic conditions we did not isolate *Bacteroides*. This would support the work of others (Gorbach and Tabaqchali, 1969; Drasar and Shiner, 1969) who have particularly sought for these organisms in related conditions and found no close correlation. In addition Tinker *et al* (1971) could not detect free bile salts in patients with postvagotomy diarrhoea.

The patients with postvagotomy diarrhoea had a mean faecal fat excretion at the upper limit of normal, almost half of the patients having raised levels. A similar incidence has been reported following truncal vagotomy and either a gastroenterostomy (Cox, Bond, Podmore, and Rose, 1964) or a pyloroplasty (Wastell and Ellis, 1966). The associated increase in the bulk of these stool motions might be expected to be reflected symptomatically in the severity of the diarrhoea, but no correlation was found between the level of steatorrhoea and this symptom. Other workers (Wastell and Ellis, 1966; Williams and Irvine, 1966) similarly found no correlation between those patients with an altered bowel habit but no diarrhoea, and the level of faecal fat excretion. Tinker *et al* (1971), however, showed that the mean faecal fat excretion in seven patients with diarrhoea was statistically significantly higher than in 13 patients without diarrhoea; only one of the group with diarrhoea had a normal level.

Investigation of postvagotomy diarrhoea has occasionally brought to light associated small intestinal mucosal disease (Franklin, 1970) but investigation of patients with self-limiting diarrhoea in the first six postoperative weeks has not revealed any mucosal abnormalities (Bejar, Breitman, and Zamcheck, 1968). In this study no mucosal abnormalities were detected in patients with diarrhoea, on average four years following surgery.

We have found a significant correlation ($P < 0.05$) to exist between the mean maximal acid output and colonization of the upper small intestine. This must be qualified by the fact that not all the patients with low levels of acid secretion were colonized, and *vice versa*. This latter finding is in agreement with the work of Greenlee, Vivit, Paez, and Dietz (1971) two months following truncal vagotomy and antrectomy. A reduced gastric acid secretion may therefore, it would seem, require to be associated with some additional factor such as local stasis before colonization ensues.

So far, any long-term effect of colonization in patients with vagotomy and drainage has not been shown. Haematological abnormalities develop with increasing frequency and severity with the passage of time in patients following gastric surgery (Booth, 1967). No patient in this study, with or without diarrhoea following vagotomy and drainage, had

low serum vitamin B₁₂ values, but investigation was perhaps too soon after operation for deficiency to develop (Wintrobe, 1967). Two patients were noted to have a hypochromic microcytic anaemia, associated with a gastroenterostomy five years previously. In both, the upper small intestine was colonized with anaerobic organisms. An iron-deficiency anaemia is well recognized to occur following vagotomy and drainage and Wastell (1969) has shown that gastroenterostomy was more frequently implicated than pyloroplasty. Achlorhydria is known to reduce the amount of dietary iron available for absorption (Wintrobe, 1967) but neither of our patients was achlorhydric. The role of bacteria in the causation of iron malabsorption has not yet been clearly documented (Tabaqchali, 1970; Gracey, 1971), but clearly merits further investigation. A clinical follow up of other colonized patients would appear justified.

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