

LETTERS TO THE EDITOR

Helicobacter pylori eradication, duodenal ulcer healing, and gastric secretory state

EDITOR,—There is little doubt that *H pylori* is an important factor in the pathogenesis of duodenal ulcer disease. The mechanism for this is probably multifactorial, and may include changes in gastric secretory state consequent upon *H pylori* associated hypergastrinaemia. The study by El-Omar *et al* (*Gut* 1993; 34: 1060–5) attempts to examine the effect of *H pylori* eradication on acid secretory state in 'patients with duodenal ulcer'. The authors show a significant fall in both basal and gastrin mediated acid output after *H pylori* eradication, and infer that this fall is, simply, because of elimination of the *H pylori* infection.

These results seem to be at variance with two previous studies carried out by the same group.^{1,2} No differences in basal and pentagastrin stimulated acid output after *H pylori* eradication were noted in the first, while parietal cell sensitivity to pentagastrin remained unchanged after eradication in the second. Both studies, importantly, were carried out in patients with inactive duodenal ulcer disease. The findings in the study by El-Omar *et al*, however, are in keeping with those reported by Moss and Calam³ in a group of patients with active duodenal ulcer studied before and after *H pylori* eradication and successful ulcer healing. One can but speculate as to whether the patients studied by El-Omar *et al* had active ulceration on entry and, if so, whether ulcer healing was achieved after three weeks' bismuth containing triple therapy. Or was a mixed group of both active and healed duodenal ulcer subjects entered into their study?

The belief that *H pylori* eradication is strategic in the reduction of gastric secretion seems to have been so seductive that El-Omar *et al* have chosen to overlook the reported effect of duodenal ulcer healing in itself on gastric secretory states. There is good evidence that basal,^{4,6} nocturnal,⁷ and stimulated acid secretion,⁸ fall significantly after duodenal ulcer healing with sucralfate, the mucosal protective agent with but a modest suppressive effect on *H pylori*. There are only scant data on the possible effect of duodenal ulcer healing by colloidal bismuth on gastric secretion, but one small study⁹ showed a numerical but insignificant fall in acid secretion and a significant reduction in basal and pentagastrin stimulated pepsin output.

We believe that any conclusion regarding the effect of *H pylori* eradication in itself on acid and pepsin secretion must await the outcome of suitably designed studies that discriminate between the effects of healing on the one hand, and eradication on the other. At the very least, readers should be unequivocally informed of the ulcer activity state in any study considering this controversial issue.

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Reply

EDITOR,—We are grateful for the opportunity to respond to the points raised by Dr Louw and Professor Marks. They wonder if the changes in acid secretion might be secondary to some effect of ulcer healing rather than to the eradication of *H pylori* infection. We can reassure them that the changes could not be explained by ulcer healing as none of the patients had active ulceration when recruited into the study. All of them had an endoscopy before entering the study and any patient with an active ulcer had treatment with an H₂ antagonist for six weeks and then repeat endoscopy performed to ensure healing before the start of the study. We apologise for not mentioning this point in the paper.

Further evidence that the fall in acid secretion is not a consequence of ulcer healing is our more recent finding that the increased acid output noted in the non-ulcer subjects also resolves after eradication of the *H pylori* infection.¹

We should also like the opportunity to emphasise that our present findings of appreciable changes in gastrin releasing peptide (GRP) stimulated acid secretion are in no way inconsistent with our earlier studies in which we noted no change in pentagastrin stimulated acid secretion at one month after eradication of *H pylori* in duodenal ulcer patients. GRP stimulated acid secretion differs from maximal acid output to pentagastrin in the following ways: (1) GRP stimulated acid secretion provides an assessment of the combined function response of the antrum and body of the stomach, whereas pentagastrin only assesses body function; (2) At the doses of GRP that we use, we can assess acid secretion in response to physiological concentrations of gastrin that contrasts with the supraphysiological concentrations during assessment of maximal acid output to pentagastrin; (3) GRP activates not only the stimulatory pathway of acid secretion mediated by gastrin but also the inhibitory

pathways mediated by other hormones such as cholecystokinin and somatostatin.

For these three reasons, GRP stimulated acid secretion provides a far more comprehensive assessment of gastric secretion and is thus more able to identify defects in its regulation.

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- 1 El Omar E, Penman I, Dorrian CA, Ardill JES, McColl KEL. Eradicating *H pylori* lowers gastrin-mediated acid secretion by 70% in DU patients and by 50% in healthy volunteers. *Gastroenterology* 1983; 104 (suppl 4): A75.

Food intolerance and Crohn's disease

EDITOR,—We were delighted to read the paper from Northwick Park by Pearson *et al* (*Gut* 1993; 34: 783–7) confirming our previous reports of food intolerance in Crohn's disease. It is possible, however, that the way this study was conducted has led to an underestimation of the importance of this phenomenon.

The dietary studies did not follow the methods that we have shown to be successful. Patients were given elemental diet for four to eight weeks. In our view this is far too long. Food reintroductions should start as soon as the patient is in clinical remission, which occurs on average after nine days.¹ If elemental diet is continued for longer periods, it is more difficult to show food intolerances as food challenges must be extended for several days to provoke symptoms.

This leads to mistakes in the detection of food intolerances. We have consistently reported that wheat, milk, and yeast are the foods most likely to cause problems. In a recent survey of 114 patients successfully treated in Cambridge by diet, 39 (34%) were upset by wheat, 22 (19%) by yeast, and 35 (31%) by milk. It is therefore very surprising that among the 42 patients studied at Northwick Park, only five were upset by milk, two by wheat, and none at all by yeast. We therefore believe that the dietary studies were not carried out correctly.

We were also concerned by the claim that there was no significant difference in the duration of remission after elemental diet between patients who did identify food sensitivities and those who did not. The Northwick Park study was not a controlled trial and no evidence is presented to suggest that the Crohn's disease in those patients with food intolerances was similar in extent and severity to those without. These results contrast sharply with the much larger study that we have recently concluded.² One hundred and thirty six patients were treated with elemental diet for up to two weeks and 78 achieved remission. These were randomised to our standard food testing programme or to oral corticosteroids. Patients receiving steroids were advised on healthy eating and diet patients received identical placebo tablets. The median survival in the diet group was 12 months compared with three in the steroid group and after two years the overall relapse rate was 59% in the diet group compared with 82% of patients receiving steroids ($p < 0.05$).

Food intolerance is an important factor in the pathophysiology of Crohn's disease. The management of these patients by diet is not easy, demanding determination from the patients and skill and experience from their medical and dietetic advisors. Nevertheless,

the benefits when dietary treatment succeeds are well worth the effort involved.

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- 1 Hunter JO. Inflammatory bowel disease. In: Hunter JO, Alun Jones V, eds. *Food and the gut*. London: Baillière Tindall, 1985.
- 2 Riordan AM, Hunter JO. Multicentre controlled trial of diet in the treatment of active Crohn's disease. *Gastroenterology* 1992; 102: A612.

Reply

EDITOR,—We are grateful for this letter from the Cambridge group that brings to light a number of inaccuracies and misconceptions regarding the significance of food intolerance in the treatment and pathophysiology of Crohn's disease.

We are aware of three reports dealing with this issue.^{1-3,4,5} The first series,¹⁻³ from Cambridge concludes that most patients with Crohn's disease have food intolerances and that remissions may be 'significantly prolonged if specific food intolerances are discovered'.

Curiously a more recent report from the same unit does not support these findings.⁴ Fotherby shows clearly that such food intolerances cannot be identified by double blind food challenge. A Sheffield group also used double blind food challenges and had similar findings.⁵ Our study confirms the last two studies and refutes the former series. We have merely clarified the issue of food intolerance and not underestimated it.

It is correct that we did not follow the methods used in the earlier Cambridge studies. Rather we followed the standard and widely accepted methods for identifying food intolerance by initial open food introduction followed by repeat open challenge and then double blind challenge.⁶ It is therefore flying in the face of science to suggest that our 'studies were not carried out correctly'.

We accept that the length of time that the patient is in remission may change the occurrence of food sensitivities, a feature that has been suggested by other groups.⁷ This is precisely why all of our open challenges were performed over a period of five days. In addition it is of note that the double blind challenges carried out in the Cambridge unit were performed both early and late in the remission period and yet failed to confirm their earlier findings.⁴

We have recently had the opportunity to study the abstract quoted⁸ in full.⁹ Unfortunately this study was not a controlled trial of exclusion diet because the control group was, for some reason, treated with steroids. In addition no attempt was made to confirm the food intolerances identified. The study simply shows that gradual reintroduction of normal food is important after diet induced remission and this has been suggested by other groups.¹⁰

In conclusion our study, that of the Sheffield group, and the double blind study from the Cambridge unit itself show that although food

intolerances may occur in Crohn's disease they are not as common as previously suggested, are of insufficient importance to warrant putting all patients through elimination diets, do not change the length of remission for most patients, and are unlikely to be of prime importance in the pathophysiology of Crohn's disease.

Yes, our work confirms previous reports from the Cambridge Unit but not those reports quoted in their letter.

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- 1 Hunter JO. Inflammatory bowel disease. In: Hunter JO, Alun Jones V, eds. *Food and the gut*. London: Baillière Tindall, 1985.
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Non-penetrance and late appearance of polyps in families with familial adenomatous polyposis

EDITOR,—The paper by Evans *et al* is indeed of interest (*Gut* 1993; 34: 1389-93).

We reported a similar case in which the polyps presented at the age of 58. The patient had had abdominoperineal excision of the rectum for a carcinoma when aged 35. A barium enema performed by the stoma at the age of 53 was entirely normal with no evidence of polyposis. She then presented at the age of 58 with polyps on the stoma and a further barium enema performed by the stoma showed thousands of polyps throughout the colon. More than 1000 tubuloadenomas were confirmed on the histology specimen when the remaining colon was removed.¹

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- 1 Law NW, Gilbert JM. Adenomatous polyposis arising after the age of 53. *J R Soc Med* 1987; 80: 383-4.

Bowel dysfunction in young women

EDITOR,—Bowel dysfunction in young women with urinary retention (*Gut* 1993; 34: 1397-9) may result from inefficient cortical circuits and dopamine abnormalities lateralised to the right hemisphere in which the metabolic rate is higher in women. This hypothesis is supported by reports of dopaminergic neurotransmission subserving gastrointestinal protection and genitourinary and immune functions.¹⁻³ It is also supported by the onset of bowel and bladder symptoms after a flu like illness in an 18 year old nulliparous woman, and by infectious insult blocking neostriatal dopamine receptor, producing a Parkinsonian syndrome after 'mild' influenza in a 14 year old boy.⁴ The role of a change in dopamine pathways in a shared smooth muscle disorder between the bladder and the bowel is suggested by neurovascular complications of cocaine abuse.⁵

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NOTES

Digestive endoscopy, ultrasonography, and radiology

The 5th International Workshop of Digestive Endoscopy, Ultrasonography, and Radiology will be held in Marseille on 5-6 May 1994. Further details from: Professor J Sahel, Service d'Hépatogastroentérologie, Hôpital Sainte-Marguerite, 270 Bld de Ste Marguerite, BP 29, 13274 Marseille Cédex 9, France. Tel: 91 74 40 55, 91 75 48 41; fax: 91 75 23 04.

Digestive Disease Week

The Digestive Disease Week will be held on 14-20 May 1994 at New Orleans, Louisiana, USA. Further details from: Slack Incorporated, 6900 Grove Road, Thorofare, NJ 08086-9447, USA. Tel: 609 848 1000; fax: 609 853-5991.