showing the "typical" coeliac sprue lesion, a clinical response to gluten withdrawal is required to diagnose the disorder unequivocally.

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Reply

EDITOR,—I thank Dr Yarze for his interest and kind comments. He is of course correct that small bowel biopsy is not 100% specific for coeliac disease taken in isolation. (Very few tests reach 100% specificity.) However, I hope he would agree that, in conjunction with a positive anti-gliaden antibody used as the intial screening test, the specificity is high. Another way of looking at this would be the positive predictive value of a small bowel biopsy, which depends upon the prevalence of the disease in the population being studied. As coeliac disease is relatively common among the Caucasian population affected by primary biliary cirrhosis, whereas the other cases of villous atrophy are rare among this group, small bowel biopsy would have a high positive predictive value.

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Prevalence of the factor V Leiden mutation in portal and hepatic vein thrombosis

EDITOR,—We read with great interest the article by Mahmoud *et al* (*Gut* 1997;**40**:798–800) on the prevalence of factor V Leiden (FVL) mutation in hepatic and portal vein thrombosis. In the past few years the FVL mutation has emerged as the commonest genetic risk factor for venous thrombosis.[1] The FVL mutation seems to be most prevalent in Europe, extending to northern India in the east and Saudi Arabia in the south.[2] The two striking features of the population genetics of the FVL mutation are the confined racial distribution and the high prevalence in European peoples (allele frequencies ranging from 1.4 to 7%). We have found an allele frequency of 1.9% for the FVL mutation in 130 unrelated subjects from northern India who had no predisposing cause or family history of thrombosis.[3]

In India portal vein thrombosis (PVT) and hepatic vein thrombosis (Budd-Chiari syndrome) are frequently encountered hepatic disorders causing portal hypertension. In a series of patients with PVT from our institute the cause of disease could be elucidated in only 17 of the 213 cases.[4] Umbilical sepsis led to PVT in 13 patients and congenital heart disease was responsible in four. Budd-Chiari syndrome represents a spectrum of disease primarily caused by a hypercoagulable state. Analysis of our cases of Budd-Chiari syndrome revealed the aetiology in 65 of the 177 patients.[5] In four patients Budd-Chiari syndrome was associated with polycythaemia vera and in three with paroxysmal nocturnal haemoglobinuria. It has been well recognised that the clinical course, outcome and aetiopathogenic factors leading to PVT and Budd-Chiari syndrome are substantially different in the East and West.

As the FVL mutation has recently been detected in our population we attempted to study cases of PVT and Budd-Chiari syndrome to evaluate the role of this mutation in the aetiopathogenesis of these two conditions. Twenty three cases of PVT and nine cases of Budd-Chiari syndrome, including the five reported in our previous study,[3] constituted the study group. The FVL mutation was detected as described by Bertina and colleagues.[6] Genomic DNA was extracted from leucocytes by chloroform-phenol extraction, amplified using the polymerase chain reaction using specific primers, and the product was digested with the Mnl1 restriction enzyme. One of the 23 patients with PVT and two of the nine patients with Budd-Chiari syndrome were heterozygous for the FVL mutation. None of the patients was homozygous for the mutation. Another case of Budd-Chiari syndrome was associated with polycythaemia vera.

The prevalence of FVL mutation in our small series seems to be higher in patients with Budd-Chiari syndrome than in those with PVT or in controls. Therefore we concur with Mahmoud *et al*'s observation that screening for the FVL mutation is important in patients with Budd-Chiari syndrome. However, in cases of idiopathic PVT this mutation does not seem to have a major pathogenic role.

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Steatorrhoea and pancreatic disease in HIV infected patients

EDITOR,—The study by Carbonnel *et al* (*Gut* 1997;**41**:805–10) on macronutrient intake and steatorrhoea in HIV infected patients tackles one important clinical feature of HIV infection. On admission to hospital up to 60% of patients with AIDS are underweight (>10% weight loss).[1] Even asymptomatic patients at an early stage of disease have changes in body composition as shown by a reduction in body cell mass, which is associated with an increased mortality and morbidity.[2] HIV associated malnutrition has a multifactorial origin but as shown by Carbonnel *et al* and other authors steatorrhoea is a common problem in HIV infected patients, especially in those with opportunistic infections of the gastrointestinal tract.[3] Inadequate energy intake is a major determinant of malnutrition in these patients, which is confirmed by the fact that enteral refeeding can improve their nutritional status.[4]

Unfortunately Carbonnel *et al*'s study missed one important aspect of steatorrhoea—next to decreased fat absorption, exocrine pancreatic insufficiency may also result in lipid malassimilation. Raised pancreatic serum enzyme concentrations are frequently seen in patients with AIDS and also to a lower extent in asymptomatic HIV infected patients, suggesting the presence of pancreatic inflammation.[5] A recently published study reported that 54% of patients with suspected AIDS related cholangitis who underwent endoscopic retrograde cholangiopancreaticography (ERCP) had a pathological pancreaticography (I°, 26%; II°, 47%; III°, 27% classified according to the Cambridge classification).[6] Pathological pancreatographies were associated with opportunistic infections (candida, cytomegalovirus, cryptosporidia, microsporidia, and mycobacteria) and a CD4 count of less than 60/mm^2. In the study by Carbonnel *et al* 60% of the patients with diarrhoea were infected with cryptosporidia or microsporidia and the mean CD4 count was 16/mm^3, therefore these patients have an increased risk of pancreatic involvement. To our knowledge no studies have been published on exocrine pancreatic function in HIV infected adult patients. In a small preliminary study in HIV infected children five of 17 patients had pancreatic dysfunction and three of five had significant steatorrhoea.[7]

Further investigations of lipid malabsorption and weight loss in HIV infected patients, especially in those with advanced disease and cryptosporidial or microsporidial infection, should include a diagnostic work up of the exocrine pancreas. This is important because these patients may benefit from pancreatic enzyme supplementation.

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Reply

EDITOR,—We appreciate Ockenga *et al*'s comments on our study. Although we did not assess pancreatic function in our patients, we would like to discuss the hypothesis that exocrine pancreatic insufficiency may contribute to steatorrhoea in malnourished HIV infected patients. As pointed out by Ockenga and colleagues, HIV infected patients frequently have elevated pancreatic serum enzymes and this can be due to several causes.[1] Furthermore, a recent study has shown that pancreatic abnormalities are frequently found on ERCP of HIV infected patients with cholangitis.[2] However, these biochemical or morphological abnormalities do not necessarily imply that exocrine pancreatic insufficiency is present. Indeed, roughly 90% of the secretory capacity must be lost before fat malabsorption occurs.[3] In addition, previous studies have shown that faecal fat concentration is higher in patients with pancreatic insufficiency than in those with gastrointestinal diseases.[4] In the paper by Bo-Linn and colleagues, all patients with pancreatic steatorrhoea had faecal fat concentrations of more than 9.5%. In our study, the faecal fat concentration was significantly lower in HIV infected patients than in patients with small bowel disease or short bowel syndrome, suggesting higher intestinal secretion; a faecal fat concentration of more than 9.5% was found in only one of 79 patients. Intestinal involvement is sufficient to explain faecal weight and steatorrhoea in HIV infected patients. Yet, these data do not exclude that, in some patients, particularly the severely malnourished ones, some degree of exocrine pancreatic insufficiency may aggravate malabsorption.

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Treatment of *Helicobacter pylori* infection

EDITOR,—Apart from validating the reversibility of the pathogenic processes mediated by *Helicobacter pylori* in the causation of duodenal ulcer, the study by Lam *et al* (*Gut* 1997;**41**:43–8) also served as a reminder that, even in *H pylori* associated ulcer disease, other mechanisms have a reversible aetiopathogenic role, exemplified by the spontaneous remission documented through the use of placebo. There is a danger of underestimating these unknown mechanisms if, as the authors unfortunately did, like is not compared with like, an example being the reporting of the 100% 12 week healing rate achieved through adherence to the antibiotic protocol as a comparison with the 53.1% healing rate for placebo on the intention to treat analysis in the Results section (page 45). Strictly speaking, the former should have been compared with patients on placebo in the protocol group, yielding a comparison of 100% *v* 63.4%. Finally, the penultimate line in table 3, dealing with the healing rate for *H pylori* positive patients allocated to placebo, did not make sense. These are minor criticisms in an otherwise good paper.

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Reply

EDITOR,—We are pleased that Dr Jolobe hit the nail on its head by pointing out that placebo can heal duodenal ulcers. In fact, placebo has been shown to heal up to 70% of duodenal ulcers.[1] Factors other than eradication of *H pylori* are clearly operating in the pathophysiology of ulcer healing. Our study does help to reassure us that as long as we can get rid of *H pylori*, whether temporarily or permanently, duodenal ulcers heal.

Dr Jolobe's two criticisms are valid. The first one represents a slip of the pen when writing the text, as the comparisons were done head for head, tail for tail in table 2. The second is a slip in proof reading, as there should be an absolute number, 14, in front of the percentage 37.8 in table 3. Our apologies.

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One week triple therapy for *Helicobacter pylori*

EDITOR,—The paper by Misiewicz *et al* (*Gut* 1997;**41**:735–9) is an important contribution which demonstrates the usefulness of lansoprazole and clarithromycin combined with either amoxycillin or metronidazole in the treatment of *Helicobacter pylori* infection.

However, there are some questions which arise:

(1) Only half the patients had duodenal ulcers. There is good evidence that the response rate to eradication therapy is inferior in other patients and it is hard to justify grouping ulcer and non-ulcer patients together in the study.
(2) Why use lansoprazole 30 mg twice daily? Optimal acid reduction should be achievable with 30 mg daily, and doubling the dose merely reduces the cost effectiveness of this drug. The balance of evidence suggests that omeprazole 40 mg daily, lansoprazole 30 mg daily and pantoprazole 40 mg daily should be equivalent in these regimens.
(3) It is amazing to read that the combination of lansoprazole or omeprazole with twice daily amoxycillin and metronidazole was judged to be "effective". The success rates achieved were 66 to 83% depending upon the method of analysis. These sorts of incomplete success rates rightly led to the abandoning of dual therapy with omeprazole and amoxycillin or clarithromycin, and are no better than the old triple therapy with bismuth, tetracycline and metronidazole, which has now been superseded.

If success rates of 90% cannot be achieved there are better treatments available.

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Reply

EDITOR,—We thank Dr Bateson for his interesting comments. We should like to reply to each of his questions in turn.

(1) The success of *H pylori* eradication therapy depends on the patients' compliance with treatment and the sensitivity of the bacterium to antimicrobials.[1] We are unaware of studies reporting significantly greater efficacy in patients with duodenal ulcer disease, compared with patients with non-ulcer dyspepsia.
(2) When combined with clarithromycin and a nitroimidazole, we agree that at present there seems to be no therapeutic advantage in increasing the dose of lansoprazole above 30 mg,[2] omeprazole above 20 mg,[3] or pantoprazole above 40 mg[4] daily. However, no such comparative data exist for the combination of a proton pump inhibitor (PPI) with clarithromycin and amoxycillin. When we planned the study, the data available supported the twice daily use of a PPI with antimicrobials, and also the patients' compliance seems to be better.
(3) A PPI together with amoxycillin and metronidazole was "judged to be effective" as this combination produced eradication of *H pylori* in 88 to 94% of patients with metronidazole sensitive strains, according to intention to treat analysis. In such circumstances, these regimens were as effective as the other treatment arms. However, these regimens are significantly less effective in the presence of metronidazole resistant strains, with eradication between 46 and 62%. As discussed in the paper, these regimens are not recommended where antimicrobial sensitivities of *H pylori* are unknown or in areas where the prevalence of such strains is at least 30%, where a PPI in combination with amoxycillin and clarithromycin should be the first choice of treatment.

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