

LETTERS TO THE EDITOR

Osteopenia in adult coeliac disease

EDITOR,—We wish to comment on the paper by Valdimarsson *et al* (*Gut* 1996; **38**: 322–7) regarding osteopenia in adult coeliac disease. Their results agree with ours^{1,2} with regard to the frequency, the severity of the derangement of bone and mineral metabolism, and the effect of gluten free diet. There are, however, some significant discrepancies between their results and ours. The first and most evident discrepancy concerns coeliac patients without malabsorption symptoms who currently represent the majority of all diagnosed adult patients.³ In this group they did not find a lower degree of osteopenia compared with those complaining of diarrhoea or weight loss. We have now examined 57 consecutive untreated coeliac patients (median age 30 years, range 17–68), of whom 23 presented the classic symptoms of malabsorption and 34 were subclinical or had been identified during the serological screening of coeliac relatives, patients with iron deficiency anaemia, recurrent aphthous stomatitis or alopecia areata. Unlike Valdimarsson, subclinical patients showed a significantly higher age adjusted bone mineral density ($p < 0.0005$) with respect to the coeliac patients with the classic disease, both at lumbar (-1.21 (0.97) v -2.32 (1.0) and femoral level (-1.31 (0.96) v -2.14 (0.92)). Moreover, the changes of the biochemical indices of bone metabolism and remodelling (strangely enough, these results were not provided by Valdimarsson) were significantly lower in our patients without diarrhoea or weight loss. The distinction between patients with and without malabsorption was made according to the same criteria adopted by Valdimarsson – that is, the presence or absence of diarrhoea or weight loss. It is in fact difficult to explain his results. Although there is no doubt that osteopenia may also be present in patients without diarrhoea, it is difficult to believe that it could be present to the same extent as in patients with a significant degree of malabsorption. This is confirmed by the fact that their seven patients with dermatitis herpetiformis, a condition characterised by a less extensive enteropathy and consequently by mild or no symptoms of malabsorption, had normal bone mass. Mazure *et al*,⁴ who divided their patients in a similar way, obtained results that were the same as ours.

Another important discrepancy concerns the relation between bone mass and age at diagnosis, which was lower in our patients (median 30 years, range 17–68) than in the study by Valdimarsson (median 53, range 17–79), but this merely accentuates the extent of this discrepancy. Valdimarsson, in fact, concludes that osteopenia represents a late complication of coeliac disease, occurring only after the third decade. This is not so in our experience nor in that of authors who have demonstrated osteopenia also in coeliac children.^{5,6} Our results show that 85% of patients diagnosed in their third decade fail to reach a normal peak bone mass and that other parameters such as the degree of physical activity and exposure to sunlight, the possible presence of amenorrhoea and, above all,

nutritional status and the presence of malabsorption symptoms are more important than age in conditioning the presence of osteopenia.

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Reply

EDITOR,—Di Stefano *et al* are correct to note that our untreated patients with coeliac disease who did not have symptoms of malabsorption (diarrhoea or weight loss) had osteopenia of the same degree as patients with these symptoms (*Gut* 1996; **38**: 322–7). In contrast with the asymptomatic patients of Di Stefano *et al* and that of Mazure *et al*¹ all of our patients had clinical symptoms of coeliac disease and none of them had been identified during serological screening. All our patients had clinical suspicion of coeliac disease, although 34 of 63 did 'only' have dyspepsia or biochemical abnormalities. Di Stefano *et al* do not report the degree of mucosal changes in their patients. All our patients had severe mucosal changes in the proximal small bowel of grade III or IV on the basis of Alexander's classification.²

This difference in patient selection may explain the discrepancy in the degree of osteopenia in our studies.

Di Stefano *et al* report that '85% of their patients diagnosed in their third decade fail to reach a normal peak bone mass'. Does this mean T score -1 or -2 ? Mora *et al*³ did report low bone mass in 33 children with untreated coeliac disease (mean age 8.95 years). Our eight patients who were 17–25 years old when diagnosed did not (as a group) have reduced bone mineral density, but five of them had Z score slightly below zero (Fig 1, *Gut* 1996; **38**: 322–7). Maybe the patients reported by Mora *et al* had a greater degree of malabsorptive state than our patients as they were diagnosed at a lower age. Molteni *et al*⁴ did not report osteopenia in coeliac children (as cited) but found normal bone mineral density in patients with coeliac disease treated since childhood.

Our patients younger than the age of 25 did not have reduced bone mineral density but if

left untreated they would probably be at risk of osteopenia. Dietary treatment is therefore important for coeliac patients of all ages.

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Acute idiopathic pancreatitis

EDITOR,—We have read with great interest the article by Ballinger and colleagues. The authors conclude that the prognosis is good after a first episode of acute 'idiopathic' pancreatitis and that specialised investigation is unnecessary (*Gut* 1996; **38**: 293–5). We entirely disagree with their conclusions.

We performed recently¹ a study of the aetiology of acute pancreatitis in the region of Nice. During one year, we included prospectively 121 cases of acute pancreatitis. In 19 cases, no cause was found at admission (patients without history of alcohol abuse, without gall bladder or common bile duct calculi on ultrasound examination and with normal computed tomograms except signs of acute pancreatitis). These patients were re-investigated two months later: calcaemia, phosphoraemia, triglycerides, echoendoscopy, and ERCP searching for biliary cholesterol crystals. Finally, a definite cause of acute pancreatitis was found for 10 patients giving a percentage of 'idiopathic pancreatitis' changing from 15.7 to 7.4%. The diagnoses found were four cases of 'occult lithiasis' (two patients with biliary cholesterol crystals, one patient with microlithiasis in the common bile duct at ERCP and without stones in the gall bladder, one patient with microlithiasis occurring in the gall bladder during the follow up), one drug induced pancreatitis (proved by unintentional rechallenge), one patient with hyperparathyroid adenoma (with normal calcaemia at the time of the first episode), three patients with acute pancreatitis revealing a carcinoma (two pancreatic carcinoma, and one antral carcinoma involving the main pancreatic duct) and one cryptosporidial infection of the biliary tract resulting from HIV. For one of the cancers, ERCP after the first episode showed only the presence of a pancreas divisum, and a sphincterotomy of the minor papilla was performed. After a second episode, a plastic stent was put in the santorini duct but we note at the time of writing a stenosis at the corporeocaudal junction (the scanner showed only the presence of a small pseudocyst of the pancreatic tail). So we decided to perform surgery that finally revealed a small carcinoma. There was 20% of recurrence during the follow up (median 111 days) but only one recurrence after the correct diagnosis was made.

The important point is that these 19 cases were labelled 'idiopathic' at admission and

that it is only with subsequent investigations that we could find definite aetiology in 10 cases. Perhaps prognosis is good and special investigations unnecessary in 'true idiopathic pancreatitis' but how to know if it is a 'true idiopathic pancreatitis' without doing investigations? In the study of Ballinger *et al*, the pancreatitis was labelled idiopathic retrospectively and patients with rare causes of acute pancreatitis were excluded from the study. We think that prospectively, it is often difficult to distinguish between 'true idiopathic' and rare causes of acute pancreatitis at the time of admission and that specialised investigations are often needed to separate them. 'Idiopathic pancreatitis' is a rare diagnosis that can be accepted only after specialised investigations. We outline that three of our patients had acute pancreatitis revealing a carcinoma and that hyperparathyroidism is sometimes caused by a cancer.²

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Reply

EDITOR,—We have read the comments of Dr Maes and co-authors and also referred to their article that has been published in abstract form.¹ They have reported on 121 consecutive cases of acute pancreatitis and the abstract includes the first 62 of these patients. In the 19 patients in whom no cause of acute pancreatitis was found on initial investigation, the authors do not state if these were first or recurrent episodes of pancreatitis. This is obviously important if comparisons are to be made with our study in which we clearly state that we have only studied patients with a first attack of acute idiopathic pancreatitis and thus our conclusions are only applicable to this group of patients. As Maes *et al* recruited consecutive patients with acute pancreatitis it is probable that a proportion were presenting with recurrent episodes.

On subsequent investigation a possible cause for acute pancreatitis was found in 10 of 19 patients in the authors' series. We are surprised that some of these aetiological factors were not identified on the first hospital admission; for instance, we would expect an antral carcinoma invading the pancreatic duct to be easily seen on the abdominal computed tomogram. The authors do not state which drug was implicated in causation of acute pancreatitis but a clinical history taken on the first admission should have identified this as a possible causative factor.

Finally, the authors state that there was a 20% recurrence rate during the follow up period but only one recurrence after the correct diagnosis was made. We are not told what specific treatment, if any, those patients with a diagnosis received and therefore it is impossible to determine if the treatment changed the natural history. It is probably only worth searching for a cause if the treatment changes the longterm outcome.

In summary, the data presented in the authors' letter and their original abstract do not change our conclusions and recommendations for the treatment of first attacks of acute idiopathic pancreatitis.

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Screening for familial colorectal cancer

EDITOR,—Based upon their findings using an immunological faecal occult blood test, Cripps and Heald (*Gut* 1996; 38: 421-5) make recommendations for screening of colorectal cancer (CRC) on the basis of a positive family history. However, current knowledge calls for a more targeted and scientifically founded approach.

Their recommendations are intended for subjects who do not have a family history suggestive of an autosomal dominant condition predisposing to CRC. How is the distinction to be made between a 'dominant pedigree' and a less than dominant pedigree? For example, one of their patients was found to have familial adenomatous polyposis (FAP). This patient was originally assigned with a low lifetime risk by virtue of the single affected first degree relative, yet the patient's true original risk was 1:2 not 1:17. Single case hereditary non-polyposis colorectal cancer (HNPCC) families have now been identified through the demonstration of germline mutations in a DNA mismatch repair gene. The affected subjects were ascertained exclusively on the basis of young age at onset of CRC.¹ These examples illustrate the inadequacy of attributing lifetime risk on the basis of family history alone.² Indeed such estimates are both crude and misleading.

The alternative approach is to offer targeted screening on the basis of the underlying genetic disorder. An approach to the correct diagnosis is achieved through the ascertainment of detailed and extended family pedigrees for which all cancer diagnoses are verified with respect to location, age at onset, and histological type. The presence of DNA microsatellite instability is an important biomarker for HNPCC, particularly when found within early onset cancers,¹ two or more cancers from the same patient or in cancers from two or more members of the same family.³ Once classic FAP, attenuated FAP,⁴ and HNPCC have been excluded, what is left? Apart from various rare forms of precancerous polyposis the literature hints at least one additional important autosomal dominant disorder. This has been described 'late onset familial CRC'⁵ or 'adenoma families'.⁶ Still poorly understood, this syndrome features cancers of the left colon and rectum, a modest increase in the number of adenomas, and an increased tendency for adenomas to become large and villous.^{5,7} No reliable marker for this putative autosomal dominant syndrome exists at this time.

A weak family history of colorectal cancer with no distinguishing clinical, pathological or

molecular features is likely to be a chance event, associated with a low lifetime risk for family members. CRC is common and affected subjects are likely to have multiple first degree relatives. Might not these relatives, perhaps representing an estimated 20% of the total population, be served through a conventional population based screening approach? Obviously this would depend on correctly assigning high risk families to particular autosomal dominant disorders. Although we currently lack full diagnostic capability in this respect, the way forward is to establish cancer family clinics that would facilitate integration of clinical, genetic, and pathological data and coordinate longterm management strategies. One shudders at the prospect of local enthusiasms linked to unlicensed gene testing outfits.⁸

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Screening for colorectal cancer

EDITOR,—The article by Cripps and Heald made for interesting and informative reading (*Gut* 1996; 38: 421-5). Their compliance rate of 60% was indeed impressive, comparing it with most other screening studies for detecting colorectal cancer. In this context, we would like to draw attention to some additional data relevant to this subject.

Hobbs and coworkers found significant difference in compliance among patients aged between 50-69 (683; 61.6%), 70 or over (343; 54.3%), and 40-49 (204; 43.8%), ($p < 0.001$). They report that patients from the inner city practice were less likely to comply (55; 3.5% versus 78; 12.5%; $p < 0.001$).¹ Powe found that fatalism, in a study among 192 elderly African Americans, was the only significant predictor of faecal occult blood testing (FOBT), even when factors such as age, poverty, and education were controlled.² Another study found significantly higher compliance (72.8% versus 51.8%; $p < 0.01$) among 153 patients when dietary restrictions were