LETTERS TO THE EDITOR

Co-screening for primary biliary cirrhosis and coeliac disease

Association between primary biliary cirrhosis and coeliac disease

EDITOR,—We were interested to read the paper by Kingham and Parker (*Gut* 1998;**42**:120–2) as we have recently reported a study exploring the association between primary biliary cirrhosis (PBC) and coeliac disease.[1]

We tested serum samples from 57 patients with biopsy proved PBC for IgA class endomysial antibody. Six (11%) had endomysial antibody though only four agreed to undergo small bowel biopsy, which confirmed coeliac disease in all cases. As we have found endomysial antibody to have 100% specificity for coeliac disease,[2] 11% is likely to be the true prevalence of coeliac disease among our patients with PBC, which is over 15 times that of the general population in Northern Ireland.[3] None of the four patients with biopsy proved coeliac disease showed improvement in liver biochemistry after exclusion of dietary gluten.

Our experience of screening patients with coeliac disease for PBC was less productive.[4] Of the 129 patients with coeliac disease screened prospectively for liver disease at the time of diagnosis, none had serum antimitochondrial antibodies. The commonest abnormality in our coeliac patients was a rise in aspartate or alanine aminotransferase, or both, (15%) which was not associated with serum antinuclear or smooth muscle antibodies and which resolved following gluten exclusion.

We agree that patients with PBC should be routinely screened for coeliac disease, though endomysial antibody is likely to be superior to antigliadin antibody for this.[2] Apart from the possibility of preventing long term consequences like malignancy and osteoporosis, non-specific symptoms conventionally attributed to PBC, such as fatigue and abdominal pain, may be actually due to coeliac disease and respond to a gluten-free diet.

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1 Dickey W, McMillan SA, Callender ME. High prevalence of celiac sprue among patients with primary biliary cirrhosis. *J Clin Gastroenterol* 1997;**25**:328–9.
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Primary biliary cirrhosis and coeliac disease: a study of relative prevalences

EDITOR,—We read with interest the study from Swansea (*Gut* 1998;**42**:120–2) reporting that the prevalence of coeliac disease in patients with primary biliary cirrhosis (PBC) is 6%. The diagnosis of coeliac disease in this group can easily be missed as some of the clinical features may be attributed to cholestasis. This is important in a population where nutrition may be critical, such as those who may eventually undergo liver transplantation for end stage liver disease.

One non-invasive screening strategy is to use the highly specific and sensitive IgA endomysial antibody assay to screen all new patients with PBC, and to perform duodenal biopsies on positive patients for confirmation. We recently investigated whether this yielded occult cases in our population of patients with PBC.

We studied 87 antimitochondrial antibody positive patients with PBC for the presence of endomysial antibody on indirect immunofluorescence. We also included 24 non-PBC cholestatic controls (13 with extrahepatic obstruction, 11 with primary sclerosing cholangitis) and four coeliac serum samples from newly diagnosed patients in a blinded fashion as methodological controls. None of the cholestatic control serum samples showed staining whereas two of the 87 PBC samples stained positively for endomysial antibody: all four coeliac samples were positive.

On review of the records, both of the patients with PBC positive for endomysial antibody had been screened for coeliac disease already on the basis of symptoms alone, and the diagnosis confirmed by duodenal biopsy. None of the remaining 85 patients with PBC had any suggestion of occult coeliac disease. Thus it seems that no new cases were detected by screening with endomysial antibody alone, and the prevalence of coeliac disease in our population was 2.3%. We do not therefore routinely screen all patients with PBC for coeliac disease, but if there is clinical suspicion we measure endomysial antibody in addition to the IgA and IgG gliadin antibodies suggested by Kingham and Parker.

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Reply

EDITOR,—We thank Drs Dickey and McMillan, and Fidler *et al* for their interest in our paper and note the higher prevalence of coeliac disease among patients with PBC in Northern Ireland but lower in London than that found in Swansea. The precise methods used for case ascertainment in these other populations are not given so the results are not directly comparable with ours. However the very high incidence of coeliac disease in Ireland is well described and a higher than average incidence in the largely Celtic population of South West Wales would not be unexpected. These regional variations in the incidence of coeliac disease in the general population might account for differences in relative prevalences of the two conditions.

If Dickey and McMillan were to repeat their search for PBC among their patients with coeliac disease they should now of course identify those four whom they have shown to have both conditions provided the surveys cover the same patient population.

Whether or not to screen patients with PBC for coeliac disease will depend on clinicians' perceptions of published figures and their own experience. However, we know that a proportion of coeliac patients have no specific symptoms, so reliance on symptoms alone is inadequate for detecting all cases.

We agree that endomysial antibody now looks to be a more specific marker for coeliac disease than anti-gliadin antibody though the latter assay is more widely available, can be automated and is cheaper.

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Helicobacter pylori: the African enigma

EDITOR,—A major advance in gastroenterology was the discovery that *Helicobacter pylori* causes chronic active gastritis, and is associated with duodenal ulcers and with gastric cancer. In an international study on 17 populations from 13 countries, it was concluded that there is a roughly six-fold risk of gastric cancer in populations with 100% *H pylori* infection.[1 2] In Africa, a puzzling feature is that although there is a very high prevalence of the infection, associated complications are very uncommon. In unpublished investigations carried out in the Soweto environs, it was found that at the age of 1 year, 46% of African infants were infected with *H pylori*, and that this proportion reaches 100% by the age of 12 years. Accordingly, it would be expected that stomach cancer should be common. However, Baragwanath hospital records from 1940 show a low occurrence of the disease. From 1948 to 1964 gastric cancer accounted for 2.2% of all cancers diagnosed,[3] and in 1992 the figure was 2.8%, an average of 40 cases annually (National Cancer Registry, unpublished data). The hospital mentioned serves Soweto, which has grown from half a million people in 1940 to 3–4 million in 1995. Between 1990 and 1996, 280 cases of gastric cancer were diagnosed. It should be noted that endoscopy has been available at Baragwanath Hospital since 1975.

The problem becomes more puzzling because vitamin C status another risk for stomach cancer—the former is very low in Sowetans.[4] Thus the milieu for a high incidence of stomach cancer seems propitious, but other factors must be present preventing this from happening. Although age of acquisition was found to be an important risk factor for gastric cancer in developed

countries, one hypothesis is that in Africa, acquisition of *H pylori* at an early age leads to immunological tolerance, resulting in a low grade gastritis which has little or no clinical relevance.

Inexplicable behaviour in Africa respecting health/ill-health is not unusual. In Soweto, coronary heart disease is very uncommon, in spite of high levels of plasma homocysteine.[5] Hip fracture in elderly African women is very uncommon despite, inter alia, a habitually low intake of calcium and losses of the element from high parity and long lactations.[6] In brief, an outwardly unfavourable parameter can have a widely varying degree of noxiousness.

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6-Mercaptopurine metabolism in Crohn's disease

EDITOR,—I have read with interest the article by Cuffari *et al* (*Gut* 1996;**39**:401–6) and do not feel that the conclusions of their study are supported by the results. The major aim of their study was to determine whether erythrocyte 6 mercaptopurine metabolite (6-TG) concentrations correlated with disease activity in patients with Crohn's disease. The authors state that their results show an inverse correlation ($r = -0.457$, $p < 0.05$) between 6-mercaptopurine nucleotide concentrations and the Harvey-Bradshaw index of disease activity. They conclude that these results support the immunosuppressive role of 6-TG metabolites and that measurement of concentrations are useful in the treatment of patients with inflammatory bowel disease (IBD). However, using the same statistical test as the authors, I could find no such correlation (0.322, $p > 0.05$) when I analysed the data presented in figure 4. The original data may not be represented accurately in graphical form and I would welcome the authors' comments clarifying this. I do not think that the study provides any evidence that measurement of 6-TG metabolites are useful in the management of patients with IBD.

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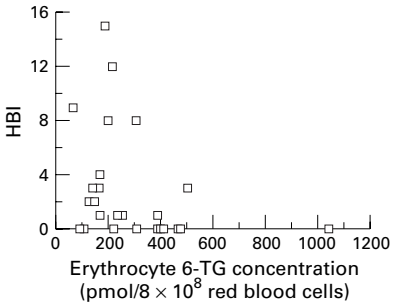
Reply

EDITOR,—We appreciate Dr Ballinger's interest in our study, and for her astutely pointing out that figure 4 from our paper inaccurately displayed our original data. Hence any results calculated directly from the graph would be erroneous. A corrected version of the graph is shown. The significant inverse correlation ($r = -0.457$, $p < 0.05$) between erythrocyte 6-TG concentrations and the patients' Harvey-Bradshaw index (HBI) of disease was obtained using a matrix calculation of the Spearman correlation coefficient, with Systat software. The parameters included in our matrix analysis were neutrophil, lymphocyte and total leucocyte counts, haemoglobin, serum albumin, erythrocyte 6-TG and 6-methylmercaptopurine concentrations. The only significant correlation to the HBI was observed for 6-TG concentrations. The level of significance ($p < 0.05$) was maintained even when the analysis did not compensate for the ties in HBI values.



Furthermore, we have re-calculated the Spearman correlation coefficient between HBI values and erythrocyte 6-TG values alone, using SPSS, Sigma Stat and Systat software programs. The r value obtained was −0.409, which yields a p value of 0.04 using a two tailed analysis. The r value obtained was the same when manually calculated for ties using the formula $\sum_{y2} = (N^3 - N)/12 - \sum T_y$, as described in a reference textbook on non-parametric statistics.[1]

Therefore, despite the limitation of interpreting data from 25 paediatric patients, our initial conclusion that 6-TG metabolite measurements are useful in the management of patients with IBD is firmly held. This conclusion is furthermore sustained by our analysis of almost 200 samples collected prospectively from adult and paediatric patients with IBD on long term 6-mercaptopurine. Using these metabolite studies, we have been able to identify clearly non-complying patients as well as those whose concentrations were in the toxic range, resulting in haematological and biochemical abnormalities.

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BOOK REVIEWS

Imaging of Abdominal and Pelvic Anatomy. Edited by Weill FS, Manco-Johnson ML. (Pp 384; illustrated; £99.00.) Edinburgh: Churchill Livingstone, 1997. ISBN 0-443-05238-7.

During the past 20 years the newer imaging techniques of ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI) have significantly advanced the diagnosis and management of disorders of the abdomen and pelvis. It is essential to recognise normal anatomical structures when performing these techniques and interpreting the images that they provide. Details of normal anatomy are mostly provided in books and publications describing the different imaging techniques and in system related publications.

There is a place for a textbook devoted to detailed descriptions of the normal anatomical appearances as shown by all imaging methods used for investigating the abdomen and pelvis. The authors of this book have aimed to do this and in my opinion they have succeeded.

This book provides a detailed description of the anatomy and normal variations of abdominal and pelvic structures as shown by angiography, barium studies, CT, MRI, radionuclide imaging, and ultrasound, including endoluminal ultrasound. The lymph system is also demonstrated and lymphography is used, whenever possible, to show the detailed anatomy. The text is comprehensively illustrated and 24 pages of colour plates are included. Most of these are from *Gray's Anatomy* but there are also examples of colour Doppler.

This is an excellent textbook and in my opinion should become essential reading for anyone learning to perform or interpret abdominal imaging procedures.

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Gastrointestinal Infections. Edited by LaMont JT. (Pp 533; illustrated; US$125.00.) New York: Marcel Dekker Inc., 1997. ISBN 0-8247-0055-4.

Gastrointestinal Infections is a new multi-authored text which is aimed at a wide audience and is highly informative with regard to the biology of the microbes responsible for infection in the alimentary tract, the pathogenetic mechanisms by which they cause disease and the current recommendations for management. The book is unashamedly American, 22 of the 27 contributors coming from Boston or Baltimore.

Devising an overall structure for a book on gastrointestinal infection presents the editor with certain dilemmas. Should the book be organism based, organ based, or problem