

PostScript

LETTERS

Platelet count/spleen diameter ratio as a predictor of oesophageal varices in alcoholic cirrhosis

We read with great interest the article by Giannini *et al* (*Gut* 2003;52:1200-5) regarding platelet count/spleen diameter ratio as a non-invasive parameter to predict the presence of oesophageal varices in patients with liver cirrhosis.¹ In patients with liver disease due to alcohol, platelet count is reduced due to the myelotoxic effect of alcohol. In the study, only 16.55% (24/145) of patients had liver cirrhosis due to alcohol. In the UK, alcohol is the commonest cause of liver cirrhosis.

We retrospectively studied endoscopy, haematology, and radiology reports of 40 patients who had been treated for alcohol induced cirrhosis at Homerton Hospital, London. Of these, 30 had oesophageal varices at endoscopy and 10 did not. The platelet count/spleen diameter ratio was calculated within two months of endoscopy.

The median platelet count/spleen diameter ratio in patients with varices was 537 (range 371-670) and with no varices 2229 (range 1542-3174). A platelet count/spleen diameter ratio of <909 had 100% sensitivity and specificity for the prediction of oesophageal varices in patients.

We have shown that this non-invasive method of predicting the presence of oesophageal varices through platelet count/spleen diameter ratio is reproducible in alcoholic cirrhotic patients.

T A Zimbwa, C Blanshard, A Subramaniam
Homerton University Hospital, London, UK

Correspondence to: Dr T A Zimbwa, Homerton University Hospital, Homerton Row, London E9 6SR, UK; TrmnZimbwa@aol.com

Reference

- 1 Peck-Radosavljevic M. Thrombocytopenia in liver disease. *Can J Gastroenterol* 2000;14(suppl D):60-6D.

Diagnosis of hereditary non-polyposis colorectal cancer (HNPCC)

The paper addressing the role of monogenic inheritance in the aetiology of colorectal cancer highlights the importance of achieving a meaningful working diagnosis of hereditary non-polyposis colorectal cancer (HNPCC) (*Gut* 2004;53:115-22). The diagnosis of HNPCC may be achieved in two ways:

- (1) by equating the Amsterdam criteria with a clinical diagnosis,
- (2) by compiling a comprehensive set of clinical, pathological, and molecular features that would together support the diagnosis of a specific condition caused by a germline mutation in a DNA mismatch repair gene such as hMLH1 or hMSH2.

It is clear that there is potential for considerable confusion if the label HNPCC is used in these very different ways.

The original Amsterdam criteria were not developed to serve as the diagnostic criteria for HNPCC but merely to introduce a uniform approach to the selection of families for collaborative studies.¹ It was originally considered that the criteria would be relatively specific rather than sensitive. However, colorectal cancer is a common disease, and the finding of three close relatives affected by bowel cancer within a single large family would not necessarily equate with a specific autosomal dominant disorder, even if one of the subjects happened to be aged below 50 years. Ponz de Leon and colleagues (*Gut* 2004;53:115-22) show in table 3 that families meeting the Amsterdam criteria but having cancers that are DNA microsatellite stable do not display the clinical features of HNPCC (see below). This is not altogether surprising. In fact it was shown nearly 10 years ago that colorectal cancers in such Amsterdam criteria positive kindreds were frequently DNA microsatellite stable and that the clinical and pathological features of these families were unlike HNPCC (see below).² Of course, the latter findings do not preclude a genetic basis for such clustering of colorectal cancer within a family.

The diagnostic features of HNPCC have accumulated and been refined over time. HNPCC is now defined by a set of clinical, pathological, and molecular features that encompass: a family history of colorectal cancer, a particular spectrum of extracolonic neoplasms, multiple colorectal neoplasia, early onset neoplasia, particular histological features among colorectal cancers, the presence of DNA microsatellite instability, loss of expression of DNA mismatch repair proteins as shown by immunohistochemistry, and a germline mutation in a DNA mismatch repair gene.³ It may not be possible to identify the germline mutation in all families, even when cancers show evidence of deficient DNA mismatch repair. This is merely the result of technical limitations which should not preclude a diagnosis when the other features are met. Close mimicry of HNPCC may occur when hMLH1 has been methylated, perhaps through a familial predisposition to this chemical modification of DNA.⁴ In the latter instance colorectal cancers may develop in a background of multiple hyperplastic polyps.⁵

Now that there is international agreement that the term HNPCC equates to a specific clinicopathological entity,³ there would seem to be little merit in applying the diagnosis when only the limited set of clinical features encompassed by the Amsterdam criteria is met. Reporting of a family history of colorectal cancer has been shown to be unreliable.⁶ What would we think of a judge who chose to base his verdict only on hearsay and rumour and to ignore all evidence of a scientific nature? Why should a family be burdened unnecessarily with the label HNPCC and all its ramifications and how may epidemiological research be advanced by the application of a vague and unreliable diagnostic label?

J R Jass

Correspondence to: Professor J R Jass, Department of Pathology, Duff Medical Building, 3775 University st, Montreal, Quebec, Canada H3A 2B4; jeremy.jass@mcgill.ca

References

- 1 Vasen HFA, Mecklin J-P, Khan PM, *et al*. The international collaborative group on hereditary non-polyposis colorectal cancer (ICG-HNPCC). *Dis Colon Rectum* 1991;34:424-5.
- 2 Jass JR, Cottier DS, Jeevaratnam P, *et al*. Diagnostic use of microsatellite instability in hereditary non-polyposis colorectal cancer. *Lancet* 1995;346:1200-1.
- 3 Vasen HF, Watson P, Mecklin J-P, *et al*. New clinical criteria for hereditary nonpolyposis colorectal cancer (HNPCC, Lynch syndrome) proposed by the International Collaborative Group on HNPCC. *Gastroenterology* 1999;116:1453-6.
- 4 Frazier ML, Xi L, Zong J, *et al*. Association of the CpG island methylator phenotype with family history of cancer in patients with colorectal cancer. *Cancer Res* 2003;63:4805-8.
- 5 Jass JR, Cottier DS, Pokos V, *et al*. Mixed epithelial polyps in association with hereditary non-polyposis colorectal cancer providing an alternative pathway of cancer histogenesis. *Pathology* 1997;29:28-33.
- 6 Mitchell RJ, Brewster D, Campbell H, *et al*. Accuracy of reporting of familial history of colorectal cancer. *Gut* 2004;53:291-5.

Author's reply

In reply to the letter of Dr Jass we would like to make the following points.

We agree with Dr Jass that since the new discoveries and advances in our knowledge of hereditary non-polyposis colorectal cancer (HNPCC), the diagnosis of the syndrome has become a matter of conscience. The Amsterdam clinical criteria are useful but not definitive in the diagnosis of the disease, and other parameters (pathological, biological, molecular) must be taken into account. Besides, family history is not reliable in every case. So, what should we do?

We believe that, as a first step, the classical clinical approach of tracing a genealogical tree focused on malignancies in the family should be pursued for each proband, to attempt to estimate the probability of disclosing an hereditary form of colorectal cancer. In doing this, we do not label a family as HNPCC on clinical grounds alone, but we think that such families should be studied and followed with particular attention to obtain other clues and proof of the syndrome and to provide appropriate counselling measures.

From an epidemiological point of view, we agree that estimation of the frequency of the syndrome based on clinical criteria should be considered with caution, but it is the only practical way. When a population approach was used, defining the microsatellite status of all registered tumours in a period and then searching for constitutional mutations in patients with unstable tumours, as high as 2.7% of patients with colorectal tumours were labelled as HNPCC. These values are similar to those obtained with clinical criteria (*Gut* 2004;53:115-22) although not confirmed in other settings.² Therefore, we believe that it is not a burden for the family if we choose to follow them with special care. Moreover, it has been demonstrated that active follow up can reduce the number of newly developed carcinomas in families with HNPCC (not all with a molecular diagnosis) and reduce cancer mortality.³

L Roncucci, M Ponz de Leon, P Benatti,
F Borghi, M Pedroni, A Scarselli,
C di Gregorio, L Losi, A Viel, M Genuardi,
G Abbati, G Rossi, M Menigatti, G Ponti
University of Modena and Reggio Emilia, Modena,
Italy

Correspondence to: Professor L Roncucci, Department
of Internal Medicine, University of Modena and
Reggio Emilia, Via Del Pozzo, 71 Modena 41100,
Italy; roncucci@unimo.it

References

- 1 Salovaara R, Loukola AA, Kristo P, *et al*. Population-based molecular detection of hereditary nonpolyposis colorectal cancer. *J Clin Oncol* 2000;**18**:2193–200.
- 2 Percepe A, Borghi F, Menigatti M, *et al*. Molecular screening for hereditary nonpolyposis colorectal cancer: a prospective, population-based study. *J Clin Oncol* 2001;**19**:3944–50.
- 3 Jarvinen HJ, Aarnio M, Mustonen H, *et al*. Controlled 15-year trial on screening for colorectal cancer in families with hereditary nonpolyposis colorectal cancer. *Gastroenterology* 2000;**116**:829–34.

Bone density loss in Crohn's disease: role of TNF and potential for prevention by bupropion

We note with interest the demonstration by Card *et al* that the increased hip fracture rate in Crohn's disease (CD), and by inference the diminished bone density commonly noted in CD, is only to a minor degree secondary to iatrogenic corticosteroid use (*Gut* 2004;**53**:251–5). The subject of bone mineral density loss in CD has been recently reviewed; tumour necrosis factor α (TNF- α) is suspected of being an important mediator of this loss.^{1,2} Evidence has been published for localised overproduction of TNF- α being largely responsible for the bone loss seen in rheumatoid arthritis,^{3,4} psoriatic arthritis,⁵ multiple myeloma,⁶ hip prosthesis loosening,⁷ periodontal disease,⁸ and spondyloarthropathies.⁹ Anti-TNF- α antibody has been shown to slow the bone loss of spondyloarthropathy⁹ and rheumatoid arthritis.^{3,10}

We have found that the commonly used antidepressant bupropion can induce remission in CD^{11,12} and have found that bupropion can lower TNF- α levels.¹³ If bupropion is found to be effective in CD and to lower TNF- α levels in large trials, it might be considered for use in bone loss and osteoporosis, in CD or otherwise.

R E Kast, E L Altschuler

Department of Psychiatry, University of Vermont,
Vermont, USA

Correspondence to: Dr R E Kast, Department of
Psychiatry College of Medicine, University of Vermont,
2 Church St, Burlington, Vermont 05401, USA;
rekast@email.com

References

- 1 Lichtenstein GR. Evaluation of bone mineral density in IBD: current safety focus. *Am J Gastroenterol* 2003;**98**(suppl 12): S24–30.
- 2 Nanes MS. TNF- α : molecular and cellular mechanisms in skeletal pathology. *Gene* 2003;**321**:1–15.
- 3 Bingham CO iii. The pathogenesis of rheumatoid arthritis: pivotal cytokines involved in bone degradation and inflammation. *J Rheumatol Suppl* 2002;**65**:39.

- 4 Goldring SR. Pathogenesis of bone and cartilage destruction in rheumatoid arthritis. *Rheumatology* 2003;**42**(suppl 2):ii11–6.
- 5 Ritchlin CT, Haas-Smith SA, Li P, *et al*. Mechanism of TNF- α and RANKL mediated osteoclastogenesis and bone resorption in psoriatic arthritis. *J Clin Invest* 2003;**111**:821–31.
- 6 Jurisic V, Colovic M. Correlation of sera TNF- α with percentage of bone marrow plasma cells, LDH, beta 2 micro globulin, and clinical stage in multiple myeloma. *Med Oncol* 2002;**19**:133–9.
- 7 Campbell PA, Wang M, Amstutz HC, *et al*. Positive cytokine production in failed metal on metal total hip replacements. *Acta Orthop Scand* 2002;**73**:506–12.
- 8 Graves DT, Cochran DN. The contribution of IL-1 and TNF- α to periodontal tissue destruction. *J Periodont* 2003;**74**:391–401.
- 9 Allali F, Breban M, Porcher R, *et al*. Increase in bone mineral density in patients with spondyloarthropathy treated with anti-TNF- α . *Ann Rheum Dis* 2003;**62**:347–9.
- 10 Geimold AM. New indications for treatment of chronic inflammation by TNF- α blockade. *Am J Med Sci* 2003;**325**:75–92.
- 11 Kast RE, Altschuler EL. Remission of Crohn's disease on bupropion. *Gastroenterology* 2001;**121**:1260–1.
- 12 Kane S, Altschuler EL, Kast RE. Crohn's disease remission on bupropion. *Gastroenterology* 2003;**125**:1290.
- 13 Kast RE, Altschuler EL. TNF in hepatitis B: potential role for bupropion. *J Hepatol* 2003;**39**:131–3.

Poor bowel preparation: a poor excuse

In the article by Bowles *et al* (*Gut* 2004;**53**: 277–83), poor bowel preparation is cited as the cause of 19.6% of failures to achieve complete colonoscopy. Similarly high values of up to 35% have been quoted elsewhere.

In a personal series of 1195 procedures, only 19 of 197 (9.6%) failures were attributed to this cause. This difference was highly significant ($p < 0.001$).

As choice of laxative agent and population demographics are similar, one could conclude that either Guernsey patients are more compliant with or responsive to bowel preparation or that minimal faecal residue present in a difficult colon is used as a non-operator dependent reason (excuse?) for what is basically a technique failure.

I suspect the same applies to "patient discomfort" which, at 34.7%, is also significantly higher ($p < 0.001$) than my own values of 31/197 (15.7%). My typical sedation is 5 mg midazolam and 10 mg nalbuphine.

I confess that my usage of these excuses has declined over the years as my success rate has climbed! It is time to get training and be honest.

P J Mullen

Correspondence to: Dr P J Mullen; The Princess
Elizabeth Hospital, Guernsey GY2 4AP, UK;
chateau@guernsey.net

Sporadic duodenal adenoma and colorectal neoplasia

We read with great interest Murray *et al*'s article concerning the association between sporadic duodenal adenoma and colorectal neoplasia (*Gut* 2004;**53**:261–5).

We have also noted a lack of published literature regarding sporadic duodenal adenomas, with the exception of the two reports identified by the authors,^{1,2} as well as a more recent case series,³ and therefore welcome the addition of their large case series and comparison

group. Although there is the potential for bias in the detection of colorectal neoplasia in their duodenal adenoma cases, as the indications for colonoscopy were somewhat different between cases and controls (with almost one third of cases of duodenal adenomas being endoscoped for investigation of anaemia or melaena), overall their data support a clinically relevant association between duodenal and colonic adenomas.

These results are corroborated by our own recent experience at Leeds General Infirmary where we have studied the natural history of duodenal adenoma. We also examined histopathology records and case notes for patients with sporadic duodenal adenomas between 1990 and 2002 (excluding familial adenomatous polyposis and hereditary non-polyposis colorectal cancer). We identified 35 cases; 16 males and 19 females (mean age 65 years). The majority of these were noted incidentally at upper gastrointestinal endoscopy or endoscopic retrograde cholangiopancreatography, with a similar range of indications for examination as those noted by Murray *et al*. Using the criteria stipulated by the authors, 25 (71%) of the adenomas were advanced. Of the 35 patients in our series, 11 underwent colonoscopic examination. This revealed a synchronous colonic adenoma in four patients (36%), three of which were tubulovillous adenomas and therefore advanced according to the aforementioned criteria, and the fourth a tubular adenoma. This compares with a reported rate of colonic neoplasia of 25.5% in a series of 1000 consecutive unselected patients attending the Leeds General Infirmary for colonoscopy.⁴ Unlike Murray *et al*, we did not find any colonic carcinomas in our patients. This discrepancy presumably relates to the fact that both series are relatively small and the confidence intervals are likely to be wide, much as they found.

Unfortunately, Murray *et al* provide no follow up data relating to the duodenal adenomas in their series. We have clinical data for all our cases, with a median duration of follow up of four years. Seventeen of the 35 adenomas were removed (six surgically, four by endoscopic mucosal resection (EMR), three snared, three during biopsy, and one by argon photocoagulation), and of these, two patients had a recurrence (one treated by EMR, the other kept under surveillance), and all were alive at the time of review (median time from diagnosis 58 months). Among the 18 patients who had no therapy for their polyp, 10 died (median length of follow up 43 months). One patient who had a tubulovillous adenoma with high grade dysplasia developed a 3 cm adenocarcinoma of the first part of the duodenum five months after initial diagnosis and underwent a Whipple's procedure but died 12 months later from metastatic disease. The other patients died from unrelated causes.

Despite published literature that suggests duodenal polyps have no prognostic importance,⁵ we believe that the optimal management of duodenal adenomas is early excision and follow up. We also concur that there is an association between sporadic duodenal adenomas and colonic neoplasia, and agree entirely that all patients found to have sporadic duodenal adenomas should undergo colonoscopy. However, owing to reasons of study size and bias in the comparison groups, the magnitude of this association cannot be accurately determined. Furthermore, the reasons for this association are as yet unclear, and

molecular studies are required to further investigate.

A C Ford, O Rotimi, S M Everett

Centre for Digestive Diseases, Leeds General Infirmary, Leeds, UK

Correspondence to: Dr A C Ford, Centre for Digestive Diseases, Leeds General Infirmary, Great George St, Leeds LS1 3EX, UK; alexf12399@yahoo.com

References

- Hochter W, Weingart J, Seib HJ, *et al*. Duodenal polyps. Incidence, histologic substrate, and significance. *Dtsch Med Wochenschr* 1984;**109**:1183–6.
- Jepsen JM, Persson M, Jakobsen NO, *et al*. Prospective study of prevalence and endoscopic and histopathologic characteristics of duodenal polyps in patients submitted to upper endoscopy. *Scand J Gastroenterol* 1994;**29**:483–7.
- Chong KC, Cheah WK, Lenzi JE, *et al*. Benign duodenal tumors. *Hepatogastroenterology* 2000;**47**:1298–300.
- Rembacken BJ, Fujii T, Cairns A, *et al*. Flat and depressed colonic neoplasms: a prospective study of 1000 colonoscopies in the UK. *Lancet* 2000;**35**:1211–14.
- Burke CA, van Stolk RU. Diagnosis and management of gastroduodenal polyps. *Surg Oncol Clin North Am* 1996;**5**:589–607.

Dysbiosis as a prerequisite for IBD

We thank Dr Szilagyi for his very interesting comments in his letter regarding dysbiosis in inflammatory bowel disease (IBD).¹

The main question remains as to why beneficial bacteria such as bifidobacteria might be lacking in IBD (*Gut* 2004;**53**:1–4). Dr Szilagyi describes an interesting hypothesis of colonic prebiotic deficiency as a possible mechanism for dysbiosis. A suggestion is made that this deficiency could be linked to increased proximal small intestinal permeability with enhanced absorption of prebiotic substrate, causing a relative deficit of prebiotics distally. Certainly, the phenomenon of increased small bowel permeability has been documented in Crohn's disease; its importance in ulcerative colitis is less clear however. As lactulose is not a major component of the normal human diet, long term epidemiological dietary trends should also have to be consistent with a significantly decreased intake of common prebiotic substrates, if this hypothesis is correct. Unfortunately, there is currently little clinical evidence to support or refute this theory, as dietary studies in IBD have been subject to many biases inherent in their study design.

Bifidobacteria are strongly glucidolytic and show nearly no growth in the absence of fermentable sugars or polysaccharides. One group of good substrates are mucins, which are often increased in Crohn's disease. Perhaps differences in ease of glycosylation between some substrates affect the ability of the flora to metabolise them. This has not been well studied in IBD. There are also likely to be other influences on the host's dominant flora, including genetic factors. Observations among some of our healthy cohorts with low levels of bifidobacteria have revealed highly variable responses of bifidobacterial counts to prebiotic treatments. Whether a poor response might represent a risk factor for IBD is also an interesting question.

C P Tamboli

Division of Gastroenterology, Department of Internal Medicine, University of Iowa Hospitals and Clinics, Iowa City, USA

C Neut

Laboratoire de Bacteriologie, Faculté de Pharmacie, Lille, France, and INSERM EPIO114, CHU Lille, France

P Desreumaux, J F Colombel

Service d'Hépatogastroentérologie, Hôpital Huriez, and INSERM EPIO114, CHU Lille, France

Correspondence to: Dr C P Tamboli, Division of Gastroenterology, University of Iowa Hospitals and Clinics, 200 Haskins Dr, Iowa City 52242, USA; cyrus-tamboli@uiowa.edu

Reference

- Szilagyi A. Dysbiosis as a prerequisite for IBD (electronic response to Tamboli *et al*. Dysbiosis in inflammatory bowel disease. *Gut* 2004;**53**: 1–4), <http://gut.bmjournals.com/cgi/eletters/53/1/1#244>.

Remarkable difference in the mode of HCV transmission among haemodialysis patients and IVDAs

We read with great interest the letter by Saxena *et al* (*Gut* 2003;**52**:1656–7). We would however take issue with their hypothesis, as we indeed believe in the remarkable differences in the mode of hepatitis C virus (HCV) transmission in these two high risk groups. Studies have reported a value of 70–90% for the prevalence rate of HCV infection among intravenous drug abusers (IVDAs).¹ The main source of HCV infection in this population is sharing contaminated needles. The incidence of rapid acquisition of HCV infection following initial intravenous drug use within the first year has been reported to be as high as 80%.² Moreover, syringe exchange programmes have been shown in some studies to reduce the risk of infection.³ In the study in India,⁴ as also mentioned by Saxena *et al*, although the syringe exchange programme was not effective in the prevention of HCV infection, it was effective in controlling hepatitis B virus (HBV) and human immunodeficiency virus (HIV) infection. Moreover, in these types of studies and programmes, consideration should be given to the fact that IVDAs are a special population with particular behaviour patterns. As they often have no strong motivation to be educated, they may deny their high risk behaviour, even within an instructive programme.

On the other hand, the main route of HCV transmission in haemodialysis (HD) patients seems to be transfusion, as the HCV infection incidence in haemodialysis units has been declining following implementation of blood product screening in developed countries.⁵ The Centers for Disease Control and Prevention (CDC, Atlanta, Georgia, USA) reported a nationwide prevalence of HCV infection in HD patients of 8.9% in a recent update.⁶ Thus the prevalence and incidence of HCV infection in HD patients appear not to be as high as that for IVDAs. However, we are in agreement with Saxena *et al* that nosocomial transmission should not be neglected in HD sites. The study by Okuda *et al* showed that education of staff members and application of adhesive pads at the time of needle withdrawal in HD sites resulted in a decrease in the incidence of HCV infection to zero, and no new HCV infected cases were reported for over a year in 730 patients on maintenance HD.⁶

The other point to note is the fact that coinfection with HCV and HBV is common in IVDAs⁷ but less prevalent in HD patients. This interesting point may highlight evidence of another difference in the main transmission route of infection in these two populations.

S M Alavian, B Hajarzadeh

Tehran Hepatitis Center, Tehran, Iran

Correspondence to: Dr S M Alavian, PO Box 14155-3651, Tehran, Iran; manager@iranhepgroup.info

References

- MacDonald M, Crofts N, Kaldor J. Transmission of hepatitis C virus: rates, routes and cofactors. *Epidemiol Rev* 1996;**18**:137–48.
- Garfein RS, Vlahov D, Galai N, *et al*. Viral infections in short-term injection drug users: the prevalence of the hepatitis C, hepatitis B, human immunodeficiency, and human T-lymphocyte viruses. *Am J Public Health* 1996;**86**:655–61.
- Hagan H, Des Jarlais DC, Friedman SR, *et al*. Reduced risk of hepatitis B and C among participants in a syringe exchange program. *Am J Public Health* 1995;**85**:1531–7.
- Sarkar K, Mitra S, Bal B, *et al*. Rapid spread of hepatitis C virus and needle exchange programme in Kolkata, India. *Lancet* 2003;**361**:1301–2.
- Centers for Disease Control and Prevention. Recommendations for preventing transmission of infections among chronic hemodialysis patients. *MMWR Morb Mortal Wkly Rep*, 2001;**50**(RR-5):1–43.
- Okuda KH, Hayashi H, Kobayashi S, Irie Y. Mode of hepatitis C infection not associated with blood transfusions among chronic hemodialysis patients. *J Hepatol* 1995;**23**:28–31.
- Sterling RK. Triple infection with human immunodeficiency virus, hepatitis C virus, and hepatitis B virus: A clinical challenge. *Am J Gastroenterol* 2003;**98**:2130–4.

COX 2 inhibition and bowel strictures

The letter by Mir *et al* (*Gut* 2004;**53**:154) caught our attention and seems to have caught the editorial staff dozing.

Mir *et al* present a patient who had been regularly taking conventional non-steroidal anti-inflammatory drugs (NSAIDs) for 26 years for axial spondylarthropathy and ascribe the presence of distal ileal stricturing and ulceration solely to the use of a cyclooxygenase 2 (COX 2) selective inhibitor that had been taken for two years. The differential diagnosis of ileal lesions in spondylarthropathy is quite clear. Firstly, as the authors themselves stated, strictures are associated with long term use of conventional NSAIDs.¹ The 26 year use of NSAIDs by the patient is most significant. While such lesions are usually more proximal, slow release formulations of NSAIDs can give rise to distal disease such as in this circumstance. The authors do not specify if this is the case. NSAID induced ulcers, when established, may take years to heal, such that the two year time lag between stopping NSAIDs and clinical symptoms is not unexpected.

Secondly, spondylarthropathy is itself associated with ileitis in 30–70% of cases, irrespective of NSAID intake. Most cases are asymptomatic but some cases proceed to stricturing disease.² De Keyser *et al*, in particular, have made a case for spondylarthropathic ileitis being a form of subclinical Crohn's disease.³ Finally, axial spondylarthropathy may be an extraintestinal manifestation of 5–10% of cases of inflammatory bowel disease.² It is difficult to exclude this as the cause of both the recent ulceration and

stricturing because histology does not always show typical (for example, granulomatous) changes. To date, the only small bowel pathology reported from selective COX 2 inhibition (or absence) is of ileocaecal inflammation and perforation (not stricturing) in animal studies.⁴ Hence, while it is a remote possibility that COX 2 inhibition may have given rise to the lesions in this patient, these are far more likely to be due to other factors.

L P Maiden

King's College Hospital, London, UK

I Bjarnason

Department of Medicine, Guy's, King's, and St Thomas' School of Medicine, Bessemer Rd, London, UK

Correspondence to: Dr L P Maiden; lpmaiden@doctors.net.uk

References

- 1 **Bjarnason I**, Hayllar J, Macpherson A, *et al*. Side effects of nonsteroidal anti-inflammatory drugs on the small and large intestine in humans. *Gastroenterology*, 1993;**104**:1832–47.
- 2 **Smale S**, Natt RS, Orchard T, *et al*. Spondylarthropathy and inflammatory bowel disease. *Arthritis Rheum* 2001;**44**:2728–36.
- 3 **De Keyser F**, Baeten D, Van den Bosch F, *et al*. Gut inflammation and spondylarthropathies. *Curr Rheumatol Rep* 2002;**4**:525–32.
- 4 **Sigthorsson G**, Simpson RJ, Walley M, *et al*. COX-1 and 2, intestinal integrity and pathogenesis of NSAID-enteropathy in mice. *Gastroenterology* 2002;**122**:1913–23.

Intravenous pulse cyclophosphamide therapy in Crohn's disease and ulcerative colitis

The management of refractory severe inflammatory bowel disease (IBD) is still unresolved. We read with interest the article by Stallmach *et al* on the safety and efficacy of intravenous pulse cyclophosphamide in acute steroid refractory IBD (*Gut* 2003;**52**:377–82).

In common with other disease, the aims of therapy in IBD fall into three categories:

- (a) induction of remission;
- (b) maintenance of remission; and
- (c) prevention of relapse, all of which should be undertaken with minimal mortality and morbidity either from the disease itself or from therapy.

Based on previous observations of improvement in autoimmune diseases (that is, vasculitides), cyclophosphamide can be a primary cytotoxic drug: pulse intravenous cyclophosphamide is probably equally effective as oral cyclophosphamide in inducing remission and this remission is usually maintained by continuing cyclophosphamide for 3–6 months before changing to a combination of other oral therapies. Therapy must be continued to prevent relapse and for maintenance.¹

We would like to report on some other cases. In our cohort, we included patients with Crohn's disease (CD) and ulcerative colitis (UC). Four patients with CD and four with UC were diagnosed according to standard criteria. They did not respond to conventional therapy and therefore we administered pulse cyclophosphamide therapy monthly (for six months, 800 mg each time). Most patients went into remission after the second/third cyclophosphamide pulse. Disease activity

decreased, there were no side effects, no toxicity, and all patients achieved long lasting remission. For maintenance, patients with CD were treated with methotrexate (10 mg/week) and patients with UC were given azathioprine (100 mg/day). Remission appears to be stable.

These findings suggest that aggressive immunosuppressive therapy may be useful in some refractory patients, and further controlled study should be considered in order to fully evaluate this type of treatment as a potential therapy in IBD.

IBD continue to pose a challenge to clinicians. Over the past few years there have been significant advances in our understanding of pathogenesis and treatment. These advances will hopefully lead to more specific and targeted treatments, with consequent improvement in clinical outcomes. Intravenous pulse cyclophosphamide may be a safe and effective treatment in patients with severe IBD unresponsive to "conventional" treatment. It is also recommended as a firstline adjunct to, or replacement for, systemic corticosteroids in the treatment of IBD.

Z Barta, L Toth, G G Szabo, G Szegedi, M Zeher

University of Debrecen, Debrecen, Hungary

Correspondence to: Z Barta, 3rd Department of Medicine, University of Debrecen, Moricz Zs krt, 22 Debrecen, Hungary; barta@iibel.dote.hu

Reference

- 1 **Watts RA**, Scott DG, Pusey CD, *et al*. Vasculitis—aims of therapy. An overview. *Rheumatology (Oxford)* 2000;**39**:229–32.

CORRECTION

In the paper by Finotto *et al* (*Gut* 2004;**53**:392–400), one of the author name's appeared incorrectly. The author name which was printed as R Khosravi-Fahr should have appeared as R Khosravi-Far.

NOTICES

British Society of Gastroenterology Paul Brown Travel Fellowships

The Paul Brown Travel Fellowships are awarded by the Endoscopy Committee of the BSG. They are intended to assist trainee gastroenterologists and established consultants in visits to units outside the United Kingdom for specialist experience and training in endoscopy.

Specialist registrars who have not achieved their CCST are expected to have the approval of their Postgraduate Dean and their Regional Training Director when they apply for a Travel Fellowship. Applicants are expected to provide confirmation that they have been accepted for training in the unit that they wish to visit.

Successful applicants will be expected to provide a brief written report to the Endoscopy Committee of the outcome of their visit.

Application forms are available from the British Society of Gastroenterology Office, 3 St Andrew's Place, London NW1 4LB. Email: bsg@mailbox.ulcc.ac.uk

8th Southeast European Symposium of Paediatric Surgery

The 8th Southeast European Symposium of Paediatric Surgery will focus upon 'Infectious Problems in Paediatric Surgery.' The event will be held between 24–25 September 2004, at the University of Graz, Austria. For further information, please contact: Professor M E Höllwarth, Department of Paediatric Surgery, Medical University of Graz, Austria, Auenbruggerplatz 34, 8036 Graz; tel: + 43 316 385 3762; fax: tel: + 43 316 385 3775; e-mail: kinderchirurgie@uni-graz.at

World Congress on Gastrointestinal Cancer

The World Congress on Gastrointestinal Cancer will be held in Barcelona, Spain, on 16–19 June 2004. For further information, please contact Coleson Chase (tel: +1 770 751 7332; fax: +1 770 751 7334; e-mail: c.chase@imedex.com; website: www.worldgicancer.com).

Advances in the Inflammatory Bowel Diseases

The conference for advances in the inflammatory bowel diseases will be held in Chicago, Illinois, USA on 8–9 October 2004. For further information, please contact: Coleson Chase (tel: +1 770 751 7332; fax: +1 770 751 7334; e-mail: c.chase@imedex.com; website: www.imedex.com/calendars/therapeutic.htm).

12th European Symposium on Neurogastroenterology and Motility

The 12th European Symposium on Neurogastroenterology and Motility will be taking place at Robinson College, Cambridge, UK. The symposium will be taking place on 15–18 September 2004.

On Wednesday 15 September, there will be a postgraduate teaching day. This will cover established and evolving assessments of esophageal, gastric and intestinal function, visceral sensitivity and brain responses. Basic science techniques including electrophysiology, imaging of gut movements and neural activation will be covered in the afternoon. Finally there will be a session on GI pharmacology covering cytokines, capsaicin and tachykinins.

On Thursday 16 September through to Saturday 18 September midday, the main meeting will be held. This will include symposia, oral free papers and poster rounds. The symposia will be designed to move from basic science to clinical practice and will include sessions on stress and the gut, appetite and obesity, serotonin and inflammation, and inflammation and GI motility. There will also be state of the art lectures and prize presentations.

For registration and further information, please see the website www.neurogastro.org and follow links for '12th European Symposium on Neurogastroenterology and Motility.' Please contact the conference organizers at: Confrex, PO Box 21, Rottingdean, East Sussex, BN2 8WZ (tel: +44(0)1273 302200; fax: +44(0)1273 302334; e-mail: confrex@easynet.co.uk).