PostScript

LETTERS

Food elimination in IBS: the case for IgG testing remains doubtful

I read with interest the study of a diet for irritable bowel syndrome (IBS) based on serum IgG levels to foods (*Gut* 2004;**53**: 1459–64).

In rigorous elimination diet studies, about one third of IBS patients are found not to have food intolerance.[1–3] Yet it appears that everyone tested for food specific IgG in this study had some positive reactions and was therefore subjected to dietary recommendations. This does not in itself suggest that serum IgG is a particularly useful test.

One notable finding of this study appears to be that 87% of patients gave a high level of IgG to yeast. In two large scale studies of IBS using diagnostic elimination diets, the percentages who had a symptomatic reaction to yeast when challenged were 5.5% (out of 73 unselected IBS patients)[1] and 12% (out of 122 unselected IBS patients).[2] It seems unlikely that yeast causes IBS symptoms in 87% of patients in Manchester but in only 5–12% of patients in Oxfordshire and Cambridgeshire. A logical implication is that high levels of IgG against yeast do not, in themselves, reveal anything significant in relation to IBS symptoms.

The same, in my view, would follow for several other foods. The numbers of patients with positive responses to eggs, cow's milk, and cashew nuts, as judged by IgG levels, are much higher than one would expect from empirical dietary studies,[1 2] while the numbers testing positive to chocolate and oranges appear far too low. Again, it seems doubtful that IgG can reveal sensitivities accurately in IBS.

The percentage of patients showing substantial benefit from this diet is disappointing. In studies using a well conducted and rigorous elimination diet, the "number needed to treat" is between 1.5 and 2.2.[1–4] The "number needed to treat" in this study was 9. (The value of 2.5, calculated on the basis of those who fully complied with the diet, abrogates the intention to treat principle.)

This seemingly poor response to an IgG based diet confirms the widely held view to date that IgG testing for food intolerance is not of value.[5–7] These results suggest that if IgG testing identifies food intolerances at all, it does so fortuitously and with an apparent low degree of accuracy.

I conclude that the difference in outcome between the "true diet" and the "sham diet" groups can largely be explained, not by specific identification of food reactions, but by the gross differences between the two diets. The "true diet" excluded milk products for 84% of patients and wheat for 49% (both foods are known to be common offenders in IBS) while the total number of foods avoided by the group was 498 (value calculated from table 2). For the "sham diet" group, 1.3% avoided milk, 8% avoided wheat, and the total number of foods avoided was only 453. These overall differences between the diets could easily explain the modest difference in outcome between the two diet groups. The same diet sheets, distributed randomly to the patients in each group, regardless of IgG levels, would probably have produced the same overall result.

Similarly, I consider that the effectiveness of the blinding in this trial is questionable. The "nutritional advisor" giving support by telephone may have become aware of which patients were receiving the "sham diet" as this regularly excluded potatoes and rice, while the "true diet" rarely did so—the reverse being true for wheat, milk, and yeast. The views of the nutritional advisor on the likely effectiveness of the diets could inadvertently have been communicated to the patients, and unintentionally influenced their assessment of the outcome.

Before this trial was begun, in my view it would have made sense to try to answer the more basic research question: do high levels of IgG against a food predict an adverse reaction to that food? Only one very small trial has so far done this.[8] It measured food specific serum IgG in individual IBS patients and compared the results with those from food challenges (following a period of avoidance): there was no correspondence between the foods identified. Such work needs to be repeated with larger sample sizes.

Despite the inconclusive results of this study, it has regrettably already been the subject of a press release and other publicity by the company that provided the IgG testing for this study, in order to promote IgG tests to the general public. On the company's website, IgG testing is now described as "clinically proven" by the British Allergy Foundation on the basis of this study (The UK YorkTest website: www.yorktest.com). This blurring of the boundaries between what should be a disinterested scientific enquiry and the promotion of a commercial venture is regrettable.

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Author's reply

John Hunter states that the generally held view is that IgG testing for food intolerance is not of value and gives references in support of this contention.[1] However, the consensus of these papers and others is that the research is of poor quality and better designed studies are needed to resolve this question. Designing trials in this field, which meet all of the criticisms that can be levelled at them, is always going to be difficult. However, we believe that we have conducted a pretty robust trial, which is the first in the field.

In his letter, Hunter also implies that irritable bowel syndrome (IBS) and food intolerance have the same basis. However, it is entirely possible that IgG antibodies may be important in IBS, where we now know that there is an inflammatory component in some cases, whereas they may not be relevant in food intolerance in general. Furthermore, it is likely that only a subset of patients are likely to have an immuno-inflammatory basis to their condition and these might be the very individuals who respond to dietary exclusion based on IgG antibodies. This would fit with our results where only a proportion of patients responded despite all having antibodies. This, of course, limits the specificity and usefulness of the test unless such subgroups can be identified beforehand. We should also bear in mind that an immunological reaction in the gut, as opposed to other forms of food intolerance, may make the gut more susceptible to other perturbing stimuli, such as stress, rather than necessarily causing symptoms directly.

It is of interest that Hunter singles out the level of IgG to cashew nuts, among other foods, as an anomaly. Since undertaking this study, we have been asking patients about cashew nut consumption and found an extraordinary high intake of this item. Of course, we do not know what the level of consumption is in the general population.

This study was undertaken independently, the data are the data, they are not overstated, and just because they challenge current dogma is not enough reason to reject them without further research. Progress in unravelling the pathophysiology of IBS will only be made if we continue to explore new avenues of research as well as re-examining issues that may have been regarded as unimportant in the past.

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Conflict of interest: declared (the declaration can be viewed on the Gut website at http://www.gutjnl.com/supplemental)

IgG antibodies to foods in IBS

Mawdsley *et al* raise the important question as to whether patients with irritable bowel syndrome (IBS) would gain as much symptomatic improvement if recommended to exclude the top four foods (yeast, milk, whole egg, and wheat) compared with an IgG antibody test based diet.[1] In other words, does the test add specificity? This requires a trial which compares patients receiving an IgG antibody test based diet to those advised to eliminate some or all of the top four foods. We are currently seeking funding for such a trial.

There is some evidence however from our trial that the IgG antibody test based diet may provide a better response than simply eliminating a standard set of foods. When the change in IBS symptom severity score was compared for fully adherent true and sham diet patients who were advised to eliminate one or more of the top four foods, it was found that the true diet patients experienced a significantly greater reduction than the sham diet patients (difference = 94; 95% confidence interval 18, 170; p = 0.017).

We agree with Sewell's comment that the food elimination diets in the true and sham groups were not similar in terms of content,[2] although they were for numbers of food types excluded. This was to some extent inevitable given the high prevalence of IgG antibodies to certain foods, such as yeast (86.7%) and milk (84.3%). However, exclusion was not quite as unbalanced as implied as the so-called sugar foods were allowed in the ''yeast positive'' patients. While we accept that a more balanced comparison would have been desirable, the principal point of the sham diet was to control for placebo effect. In future, more care needs to be taken to match diets not just for number of food types excluded but also for types of food. We are still confident, however, that the difference in symptom improvement observed in our study for the true and sham diet groups is a real one. This is evidenced by the highly significant difference in worsening of symptoms between the true and sham groups when patients reintroduced foods they had been asked to exclude (p = 0.003).

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Two models better than one

The study by Shaheen and colleagues (*Gut* 2004;**53**:1736–44) is the results of a decision analysis model which determined the cost effectiveness of various management strategies for high grade dysplasia in Barrett's oesophagus. We were surprised to note that the authors of this article did not reference our analysis which was published in July 2003.[1] Our model and analysis had conclusions that were identical to those published by Shaheen *et al*. Similarities included the finding that endoscopic ablation (photodynamic therapy in our model) results in the greatest number of quality adjusted life years with similar incremental cost effectiveness ratios (ICER) compared with endoscopic surveillance. Also, both of our analyses found that endoscopic surveillance was less expensive than endoscopic ablation but associated with shorter survival.

The authors state in their discussion that their model has several strengths that distinguish it from previously published decision models of Barrett's oesophagus, including the possibility of histological misdiagnosis of specimens as well as a non-linear progression to cancer, including the possibility of pathological regression. Our model also incorporated these strengths.

This congruency in the results of two independently constructed models only serves to strengthen and validate the findings of both models.

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Competing interest: none declared

Reference

1 **Hur C**, Nishioka NS, Gazelle GS. Cost-effectiveness of photodynamic therapy for treatment of Barrett's esophagus with high grade dysplasia. *Dig Dis Sci* 2003;**48**:1273–83.

Author's reply

I thank Hur *et al* for their interest in our article. I agree that his article,[1] which appeared after the initial iterations of our article (*Gut* 2004;**53**:1736–44) had been written but prior to the acceptance of our revised manuscript, is highly pertinent to our work as it models the same clinical scenario.

There are clearly some differences in the models, which are likely due in part to the estimates used to construct it. For instance, average quality adjusted life expectancy when going from surgery to photodynamic therapy (PDT) in our model was increased by approximately 0.5 years whereas in the model by Hur *et al* the increase was 2.2 years, or four times our estimate. Also, some of our estimated lifetime costs for various therapies varied by as much as 25% from those estimated by Hur *et al*.

However, considering the number of assumptions and estimates inherent in modelling a complex clinical decision such as Barrett's with high grade dysplasia (HGD), the model of Hur *et al* reports remarkably similar results to ours. An ablative approach with PDT yielded an increased quality adjusted life expectancy at a reasonable cost.

I agree with Hur *et al* that the similar findings of the models strengthens and validates the findings. More generally speaking, I feel that any model that features an intervention with some efficacy in the setting of HGD is likely to demonstrate that this intervention will be cost effective. The frequent progression of HGD to cancer, the high cost associated with caring for subjects with cancer, and the poor prognosis associated with cancer all suggest that any intervention keeping even a small fraction of patients with HGD from developing cancer is likely to be cost effective. This is true even if the intervention itself is costly (such as PDT). It probably does not matter whether the intervention is chemoprevention (as elegantly modelled recently by Sonnenberg and colleagues[2]) or ablative therapy, as modelled by Hur *et al* and ourselves.

Of course, there is a possibility that both models share the same flaws, leading them to come to similar, but erroneous, conclusions. After all, these models are only as good as the data used to create them, and good data on the natural history of various subsets of Barrett's patients are hard to obtain, given the current state of the literature. However, until good randomised data comparing the treatment modalities for HGD are available with which to make these clinical decisions, the models are superior to expert opinion, intuition, or just plain guessing, as to the most appropriate path.

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When acquired thrombophilia mattered

A 52 year old previously healthy Afro-Caribbean woman was admitted as an emergency with a 12 hour history of epigastric pain. She was a non-smoker, denied alcohol use, and had no significant comorbidity. Heart rate, respiratory rate, and temperature were normal at presentation. Abdominal examination revealed mild epigastric tenderness with guarding. Baseline investigations (full blood count, clotting, urea and electrolytes, and liver function tests) were within normal limits, except for a raised white cell count (12.1 (normal range 4–11)$\times 10^9$/l (neutrophilia)) and a raised amylase level (2409 (normal <220) U/l). Abdominal and chest *x* rays were also normal. She was diagnosed with acute pancreatitis and treated supportively with intravenous fluids, analgesia, and thromboprophylaxis.

Twelve hours after admission the patient deteriorated significantly, with signs of abdominal peritonitis and a marked metabolic acidosis. She underwent an emergency laparotomy where she was found to have a

perforated necrotic gall bladder with biliary peritonitis. The common bile duct was dilated but no gall stones were identified. In addition, two segments of her liver were noted to be dusky. Her spleen was normal. The abdomen was washed out and a cholecystectomy performed. Histology confirmed that the gall bladder was necrotic. Several of the arteries were occluded by thrombus but there was no evidence of atheroma or vasculitis.

Following surgery she ran a prolonged septic course requiring ventilatory and renal support, and on day 13 had a large upper gastrointestinal bleed secondary to intestinal ischaemia. Serial computed tomography scans to identify the source of sepsis were normal until day 21 when a large right subphrenic collection was identified. In addition, an area of low attenuation at the site of the spleen and a cystic mass in the pancreatic tail, consistent with a pseudocyst, were noted. Radiological drainage of the abscess was performed and over the next week the patient was successfully weaned and withdrawn from circulatory and renal support. At this stage her blood film demonstrated the presence of Howell-Jolly bodies, which were consistent with the splenic changes identified on computed tomography.

Recurrent intrabdominal sepsis at day 42, not amenable to radiological drainage, necessitated a further laparotomy. The collection was drained and the remnants of her autolysed spleen and pancreatic tail removed. At this point the possibility of a thrombotic disorder was raised. Histology showed no evidence of vasculitis and she was antineutrophilic cytoplasmic antibody and autoantibody negative. Her thrombophillia screen revealed low levels of protein C (functional: 45 (65–250) u/dl; antigen: 52 (65–130) u/dl) and antithrombin III. (functional: 59 (80–120) IU/l, antigen: 70 (80–120) u/dl). Free protein S levels were normal (73 (55–120) iu/dl). She was negative for lupus anticoagulant, APC resistance ratio was normal 2.05 (1.8–4), and neither factor V Leiden nor prothrombin gene 20210 allele was detected. Her antithrombin level was not suggestive of an inherited defect and levels in first degree family members were within normal limits. A presumptive diagnosis of acquired antithrombin deficiency was made, her low molecular weight heparin was increased to therapeutic doses, and she was commenced on warfarin.

Two months after discharge her antithrombin levels had returned to normal and her warfarin was stopped. She had developed no further problems on follow up at 12 months.

This case illustrates how the systemic inflammatory response can be complicated by a series of thrombotic events. Antithrombin is a natural anticoagulant that plays a pivotal role in coagulation and haemostasis. In addition, it has potent anti-inflammatory properties, and is protective in animal models of sepsis.[1–5] Acquired antithrombin III deficiency is commonly present in severe sepsis and levels can be predictive of outcome.[6–8] It should therefore be considered in patients with severe sepsis when the clinical course is complicated by arterial or venous thrombosis.

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No association of the *NFKB1* promoter polymorphism with ulcerative colitis in a British case control cohort

Recently, Karban and colleagues[1] reported an association of a common *NFKB1* gene polymorphism, −94ins/delATTG, with ulcerative colitis (UC) in a non-Hispanic, non-Jewish North American population. The deletion was significantly associated with disease in both family based and case control studies: in the combined case control cohort, the allele frequency of −94delATTG (D) was significantly increased in 350 non-Jewish UC cases (45.3%) compared with 802 non-Jewish controls (38.8%, $p = 0.002$). In a recessive model of inheritance, the homozygous (DD) genotype was significantly increased in UC cases (21.4%) compared with controls (14.8%) ($p = 0.0043$), giving an odds ratio of 1.57 for the DD genotype (95% confidence interval 1.14–2.16).

Nuclear factor κB (NFκB) is an important transcription factor implicated in the inflammatory response.[2] The *NFKB1*gene, which encodes the p105/p50 subunit of the NFκB family of proteins, maps to chromosome 4q24, in a region showing linkage to inflammatory bowel disease[3–5]; a mouse locus for colitis, *cdcs1*, maps near the mouse homologue of human *NFKB1*. The −94ins/delATTG polymorphism in the promoter region of *NFKB1* near transcription factor binding motifs may regulate expression of the gene. As *NFKB1* is a plausible inflammatory bowel disease candidate gene, we sought to replicate the findings of Karban and colleagues.[1]

We genotyped the −94ins/delATTG polymorphism in 472 independent British UC cases (for ascertainment and diagnosis see Cuthbert and colleagues[6]) and 657 ethnically matched healthy controls. This compares with 350 cases and 802 controls in the Karban study. Case control studies have increased power to detect association compared with family based tests (for example, the transmission disequilibrium test).[7] The χ^2 test was used to analyse differences in allele and genotype frequencies between cases and controls, and to test for Hardy-Weinberg equilibrium. Our study was well powered to replicate this association, with 86% power to detect a significant difference in D allele frequency (significance level 5%) based on the allele frequencies of allele D observed by Karban *et al*, and 79% power to detect a significant difference in DD genotype frequency (significance level 5%) in a recessive model of inheritance.

The *NFKB1* promoter region was amplified by polymerase chain reaction (PCR) using the primers *promoter e forward* (labelled with FAM fluorescent dye) and *promoter f reverse* described by Karban and colleagues,[1] and PCR products sized by electrophoresis on an ABI 3100 Prism Genetic Analyser. The size of the product determined the presence or absence of the −94ATTG deletion: 286/286 bp = WW, 282/282 bp = DD, and 286/282 bp = WD.

Both case and control genotypes were in Hardy-Weinberg equilibrium ($p>0.2$). There was no significant difference in allele D frequency (40.1% *v* 39.7%, $\chi^2 = 0.04$, $p>0.5$, 1 df) or in the frequency of the DD genotype (16.3% *v* 14.6%, $\chi^2 = 0.62$, $p>0.5$, 1 df) (see table 1) between UC cases and controls. The odds ratio (OR) for the DD genotype in our sample was 1.14 (95% confidence interval 0.822–1.579) compared with an OR of 1.57 (95% confidence interval 1.14–2.16) in the Karban study. The confidence intervals for the two studies overlap, with the OR estimate of Karban *et al* lying at the upper end of the range for our study.

There are several possible reasons for non-replication of association studies.[8] There could be phenotypic differences in the case population from the two studies, such as different proportions of patients with limited or extensive disease. Data on site of disease were available from 251 patients in our study; the frequency of allele D was very similar in patients with distal (n = 92, f = 40.8%) or extensive (n = 159, f = 39.9%) disease. There

Table 1 −94delATTG allele and genotype frequencies in British ulcerative colitis (UC) cases and controls

	n	WW (%)	WD (%)	DD (%)	Frequency of D allele (%)
Controls	657	231 (35.2)	330 (50.2)	96 (14.6)	39.7
UC	472	170 (36.0)	225 (47.7)	77 (16.3)	40.1

WW, wild insertion homozygote; WD, heterozygote; DD, deletion homozygote; D, −94 del ATTG allele

may also be population specific differences in the contribution of this variant to UC susceptibility although other loci such as *CARD15* and *IBD5* have been widely replicated in North American and British populations.[9] Alternatively, the original report may be a false positive: it involved multiple testing against various phenotypes and Jewish versus non-Jewish populations that has not been corrected for. However, the UC association was detected in both family based and case control study designs. Lastly, the size of the effect may be much smaller than indicated by the Karban study, requiring a very large sample size to replicate.[10]

In summary, we found no evidence for association of the −94ins/delATTG *NFKB1* polymorphism with ulcerative colitis in the British population. A more detailed survey of the NFκB activation pathway is in progress to assess its contribution to susceptibility to inflammatory bowel disease.

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Primary intestinal autoimmune disease as a cause of chronic intestinal pseudo-obstruction

The purpose of this letter is to elucidate on the pathophysiology of a disease that is often considered to be idiopathic. Chronic intestinal pseudo-obstruction (CIPO) is a clinical syndrome characterised by ineffective intestinal propulsion in the absence of organic intestinal obstruction. It is a common cause of intestinal failure requiring total parenteral nutrition (TPN). It can be either a primary/idiopathic (neurogenic or myogenic) disorder or secondary to another recognised underlying disease. Most cases of childhood CIPO are congenital enteral neuromuscular diseases; however, neuropathy due to Hirschprung's disease, Chagas disease, infections, and toxins occur in later childhood. In adults, most cases of CIPO are secondary to progressive systemic sclerosis, dermatomyositis, systemic lupus erythematosus, rheumatoid arthritis, and Sjogren's syndrome.[1 2]

We report a case of an adult onset of CIPO secondary to an autoimmune process affecting exclusively the small intestine without any other systemic organ involvement. A 53 year old Black man with an unremarkable past medical history experienced symptoms of "mechanical obstruction" (nausea/vomiting). After three abdominal explorations, including small bowel resections, he failed enteral feeding rendering him fully TPN dependent. Antroduodenal manometry demonstrated low amplitude contractions in the distal duodenum, and gastrointestinal scintigraphy revealed normal stomach emptying and colonic transit, but delayed small bowel transit. Trypanosoma cruzi antibodies and an extensive serological work up for collagen-vascular disease were negative, except for antinuclear antibody (ANA 1/1280). During five years on TPN, the patient developed multiple episodes of line sepsis and progressive liver disease. He then successfully underwent isolated intestinal transplantation.

Intraoperatively, the small bowel was dilated only in the proximal 270 cm (18 cm circumference). Microscopic examination showed marked degeneration of the muscularis propria with pronounced atrophy of muscle fibres (fig 1). Eosinophilic hyaline globular inclusions were detected within smooth muscle cells, predominantly in the perinuclear regions. Masson-trichrome stain revealed fibrous tissue deposition around atrophic muscle bundles. The neuronal plexus was entirely preserved. Histological findings were compatible with an idiopathic visceral myopathy.[3] Positive immunofluorescence staining for anti-IgG and anti-IgA was found in degenerated muscle fibres but not in areas of intact musculature (fig 1). Nine months post transplant, a full thickness biopsy of the intestine showed no evidence of recurrent disease in the graft. The patient's ANA became negative one month after transplant and remained undetectable after 15 months of follow up.

Only one similar case of a two year old boy who developed intestinal pseudo-obstruction following an episode of gastroenteritis has been reported.[4] In that case, ANA, anti-neutrophil cytoplasmic, and antismooth muscle antibodies became negative on

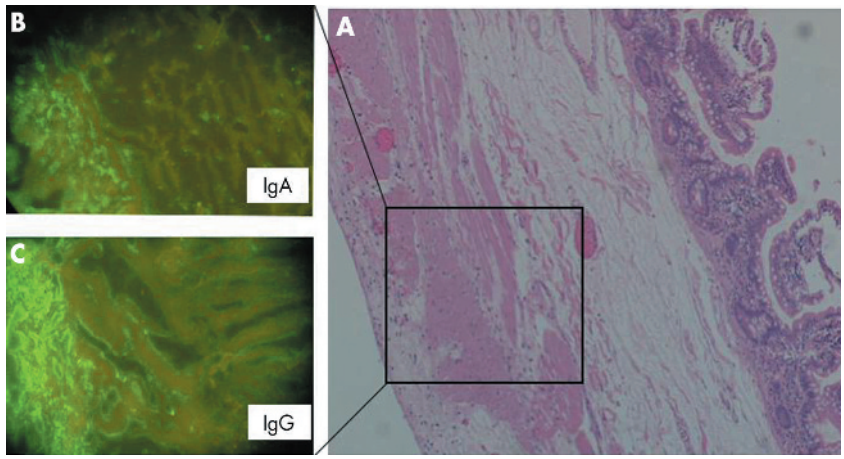

Figure 1 (A) Thinning of the small bowel wall with normal appearing mucosa and inner circular muscular layer. The outer longitudinal layer is severely thinned and some muscle fibres contain cytoplasmic globules. (B, C) Immunofluorescent study using anti-IgA (B) and anti-IgG (C). Positive green fluorescent staining is seen along the edges of degenerated muscle fibres of the outer longitudinal layer.

immunosuppressive therapy. Histology after two years of treatment showed profound loss of myocytes in the outermost circular muscle layer with T lymphocyte infiltration. Deposition of (auto)antibodies was not mentioned. Other cases of CIPO and systemic autoimmune disorders have been published.[5–7]

Our report is the first to describe an adult without previous gastrointestinal symptoms or other signs of systemic autoimmune disease who developed subacute ANA positive CIPO, resulting in myocytolysis of the intestinal muscularis propria. Documentation of IgG and IgA deposits in the areas of muscle degeneration and fibrosis is suggestive of an autoimmune-type disease involving the humoral immune system. The findings however do not exclude a role for cell mediated cytotoxicity at the beginning of the disease and may only represent a late stage of a complex autoimmune disorder.

In summary, some patients with idiopathic CIPO may suffer from a primary intestinal autoimmune disease, an autoimmune process exclusively directed towards the intestine. An early full thickness intestinal biopsy may indicate the need for immunosuppression. At late stages, timely intestinal transplantation is an acceptable option before patients develop irreversible liver disease.[8–10]

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HCV genotype 2 as a risk factor for reactivation of chronic HCV infection

Little information is available in the literature on acute exacerbation of chronic hepatitis C (r-CHC).[1–5] In Taiwan, Sheen *et al* estimated an annual incidence rate of 11.9%.[3] In this study, 40.2% of 78 patients experienced at least one episode of reactivation during a mean observation period of six years and a total of 151 episodes of reactivation were observed, 45% of them symptomatic. The paper by Rumi *et al* from Milan (*Gut* 2005;**54**:402–6) on r-CHC in relation to hepatitis C virus (HCV) genotyping described it as frequent in patients with genotype 2c (39% of 100 patients) and infrequent in those with genotype 1b (7.5% of 106 patients), with a rate×1000 persons/year of 55.6 and 15.0, respectively. From January 2002 to the present, we have enrolled 49 consecutive patients with acute hepatitis C (AHC group) and 57 consecutive patients with r-CHC (r-CHC group) in a prospective follow up study. All patients were hospitalised at our ward because the illness was symptomatic.

The criteria for a diagnosis of AHC were: (a) negative serum anti-HCV and normal serum alanine aminotransferase (ALT) levels in the four months preceding the onset of symptoms; and (b) positive anti-HCV/HCV-RNA and increased ALT (>5 times the highest value of normal) during the acute stage of the illness. The diagnosis of r-CHC was made for patients with: (a) positive serum anti-HCV and plasma HCV-RNA during the six months before the onset of symptoms and on admission; and (b) ALT increase >5 times the mean of the ALT values observed during the previous six months. As a control group for patients in the r-CHC group, 57 hepatitis B virus surface antigen (HBsAg) negative, symptom free, untreated patients with chronic hepatitis C (CHC group), hospitalised in the same period for their first liver biopsy, were pair matched by age (±5 years), sex, and risk factors for acquisition of parenteral infection.

All patients in the AHC and r-CHC groups lacked serum HBsAg, antibodies to hepatitis B core antigen (anti-HBc) IgM, anti-hepatitis D virus (HDV) and anti-hepatitis A virus IgM, and IgM to the herpes viruses. Excluded were patients treated with interferon and ribavirin in the last 24 months, anti-human immunodeficiency virus (HIV) positive subjects, those with a history of alcohol abuse, and those treated with potentially hepatotoxic drugs. Plasma HCV-RNA was determined by qualitative reverse transcriptase-polymerase chain reaction (HEPA-Check-C; Nuclear Laser Medicine) and HCV genotyping by Line-Probe- Assay (INNO-LIPA HCV II; Innogenetics). Anti-HCV, anti-HIV, HBV, and HDV serum markers were determined using a commercial immunoenzymatic assay. Statistical analysis of the results was made applying the χ^2 test with Yates' correction. A p value <0.05 was considered statistically significant.

HCV genotype 2 was found more frequently in patients in the r-CHC group (35.1%) than in those in the AHC group (8.2%, p<0.005) or the CHC group (14%, p<0.05). Conversely, HCV genotype 1 was detected less frequently in the r-CHC group (49.1%) than in the AHC (67.3%) or CHC (65%) group (p>0.1). The observation that patients with symptomatic acute exacerbation of chronic hepatitis C harbour HCV genotype 2 more frequently than asymptomatic chronic hepatitis patients and patients with acute hepatitis C is in good agreement with the more frequent occurrence described by Rumi *et al* of r-CHC (mostly asymptomatic) in patients with HCV genotype 2c compared with those with HCV genotype 1b. The available data seem to indicate that whether the clinical presentation is symptomatic or asymptomatic, acute exacerbation of chronic hepatitis C is associated with HCV genotype 2 chronic infection. However, a multicentre prospective study is needed to obtain more conclusive data.

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Management of acute pancreatitis

No account of the complications of acute pancreatitis (*Gut* 2005;**54**:426–36) would be complete without mention of diabetic ketoacidosis as an association, which is either fortuitous or one which exists as a complication in its own right. Recognition of this association has been inhibited by the complicated relationship between diabetic ketoacidosis, acute abdominal pain, and hyperamylassaemia, notwithstanding the

fact that, as long ago as 1961, a patient with subsequent post mortem validation of acute pancreatitis did present with sudden deterioration of diabetic status, the latter being characterised by unequivocal diabetic ketoacidosis.[1]

Subsequently, it was also recognised that diabetic ketoacidosis could present with acute abdominal pain and elevation in serum amylase (even beyond four times the upper limit) without necessarily signifying acute pancreatitis.[2] The relationship between the two disorders was clarified by a recent study comprising 100 consecutive episodes of diabetic ketoacidosis in which all patients with either abdominal pain or elevation in serum amylase to ''more than three times normal'' had an abdominal computerised tomography (CT) scan.[3] Eleven per cent of patients had CT evidence of acute pancreatitis, and this was associated with abdominal pain in eight. Among the three without abdominal pain was one who was comatose on admission. Accordingly, although in the context of diabetic ketoacidosis and abdominal pain the presence of ''pancreatitis levels'' of serum amylase does not necessarily signify acute pancreatitis,[2] it is nevertheless also true that unequivocal acute pancreatitis can be associated with diabetic ketoacidosis,[3] the latter being either a complication or a coincidence. Either way, this is an association which has to be acknowledged rather than ignored, given the prevalence of the association (11% of 100 consecutive cases),[3] the potential lethality of either of the two disorders, and the fact that, at least one of the complications of diabetic ketoacidosis, namely, acute respiratory distress syndrome,[4] can be identical in its presentation with its counterpart in acute pancreatitis.[5]

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BOOK REVIEW

Kirsner's Inflammatory Bowel Disease, 6th edn

Edited by R B Sartor, W Sandborn. Philadelphia: W B Saunders Co, 2003, £105.00, pp 768. ISBN 0721600018

This single volume comprehensive reference tome on inflammatory bowel disease (IBD) is now in its sixth edition, having been regenerated five yearly for the past 30 years. Balfour Sartor and William Sandborn have extensively revised it, with a greater focus on basic science and translational areas. Indeed, the first third of the book covering basic science issues is exceptionally good, and would make a superb background primer for investigators setting out in the IBD research field. The clinical sections thoroughly cover the expected areas: diagnosis, including endoscopy, imaging and laboratory investigations; medical and surgical therapy; and complications/associated diseases. The medical therapy section is particularly strong, as one would hope given the authors are some of the leading study investigators, with first rate sections on somewhat neglected areas such as clinical trial design, clinical pharmacology, and pharmacoeconomics. There are numerous diagnostic and therapeutic algorithms throughout.

The entire book has a nice feel—very clear layout, compact text (and even more compact references), clear figures, and comprehensive tables. The latter often provide a rapid guide to the key studies—for example trials of nutritional therapy and strictureplasty in Crohn's disease. Unfortunately, a few of the tables have been poorly edited, with unreferenced citations or poor layout, but these are the minority. There are also a few areas of overlap between chapters (50 in all)—for example, two chapters covering different aspects of the genetic advances in IBD pathogenesis. Use of colour is a little sparse; in a book of this cost I was disappointed to find some histology slides reproduced in black and white. Although the editors are proud of the short seven month final submission to publication timeline, this nevertheless means today's purchaser of the book (perhaps having read this review) is getting a text written in mid-2003. I still like the book format however and find it quick and easy to use. To research a topic I would happily look first in *Kirsner's Inflammatory Bowel Disease* and obtain more recent papers with a PubMed search. A personal copy is a luxury but the book would be a good buy for a department or institutional library.

How does it compare to the competition? To my surprise, an Amazon search generated a list of over a hundred books on inflammatory bowel disease. While most of these were monographs, or covering highly specific topics, there were several other comprehensive general IBD textbooks. Those with a recent edition (last three years) included hardbacks edited by Satsangi and Sutherland (Churchill Livingstone) and Cohen (Humana Press). The Satsangi and Sutherland text was described by a recent *Gut* reviewer as the ''Ferrari'' of IBD books (*Gut* 2004;**53**:1880) and has a predominantly European outlook. Sartor and Sandborn differs in its mainly North American viewpoint (three quarters of the 87 contributors) but the books have more similarities than differences, are both good, and which to buy comes down to a matter of personal preference. If pushed to choose, I would probably go for Sartor and Sandborn, based on the more attractive cover, easier to read text and tables, and lighter weight.

D A van Heel

NOTICE

First Beijing International GI Summit: call for papers

Researchers, academics, and technology companies are all encouraged to submit their posters for consideration by this unique international collaborative conference organised by the Digestive Disease Research Center of the University of Peking, China Medical Tribune, and Journal Watch Gastroenterology, with support from the *New England Journal of Medicine*.

Poster space is limited and gastroenterologists interested in submitting a poster should send a scientific abstract of not more than 250 words (English) or 500 characters (Chinese), full contact information, and a US$50 non-refundable application fee to The Goodwin Group, 79 Broadway, Suite 1, Arlington, MA 02474, USA. Electronic submissions can be sent via email to goodwingroup@comcast.net. Submissions are due no later than 15 August 2005.

The summit is scheduled to take place on 5–6 November 2005 at the Golden Resources Hotel, Beijing. For more information about the first International GI Summit in Beijing, please visit the conference web site at http://www.gisummit.com.

CORRECTION

Abstract 420 of supplement II, BSG Annual Meeting Abstracts, April 2005, is incorrect (A prospective audit to establish if infliximab is safe to be administered by a nurse specialist in a district general hospital. Thomson *et al*, p A111). The two letter abbreviation of CD was mistakenly changed to Coeliac disease rather than Crohn's disease throughout the abstract.