

PostScript

LETTERS

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To perform or not to perform liver biopsy: an alternative view

I would like to thank Joy and Scott for their comments in their letter in response to my review (*Gut* 2002;51:9-10).¹ I entirely agree with their view that ultrasound is highly specific and sensitive for the diagnosis of fatty liver. However, I do not feel that the presence or absence of fatty liver is the issue here. It is established that approximately 30% of patients with fatty liver who have significant fibrosis will go on to develop chronic liver disease and cirrhosis, with all its complications, including hepatoma.² The purpose of histological sampling is not to confirm the presence of fatty liver but to see whether fibrosis and other abnormalities are present, putting the patient at risk of developing chronic liver disease.

This issue was addressed in a recent article by Saadeh and colleagues³ who compared patients with non-alcoholic steatohepatitis (NASH) and those with steatosis (non-alcoholic fatty liver disease (NAFLD)) alone. The authors evaluated the role of various radiological modalities, including ultrasound, computed tomography, and magnetic resonance imaging, in the role of distinguishing between NASH and the less aggressive forms of NAFLD. Their conclusion was that none of the radiological modalities detected the presence of hepatocyte ballooning, Mallory's hyaline, or fibrosis, which are the important features in the diagnosis of NASH. The study showed that ultrasound had high sensitivity and specificity for the diagnosis of severe steatosis but it confirmed that ultrasound had no predictive value in the diagnosis of fibrosis or cirrhosis.

On the basis of this article together with earlier studies, I can find no basis for the conclusion reached by Joy and Scott that ultrasound is a reasonable alternative to liver biopsy for patients who have abnormal liver function tests with no diagnostic serology.

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Non-medical treatment of GORD

The interesting comment of Heading (*Gut* 2002;50:592-3) on the work by Fibbe *et al* needs to be completed by considering the anatomical factor in the study of gastro-oesophageal reflux disease (GORD) before advocating any non-medical appropriate treatment (fundoplicator, Stratten procedure, Gastropexie, etc).

The multiple controversies arising from all non-medical proposed treatments, with contradictory results, are due to the complete neglect of delimitating the cardio-oesophageal junction (CEJ) and the shape of the angle of HIS, and the role of the anatomical factor in selecting the correct candidate for successful non-medical treatment.

The new generation of gastrointestinal specialists, who come after the endoscopy era, are not aware of the radiology of the gastrointestinal tract, particularly when we need to have the anatomical configuration of the CEJ.

Gastric physiology and junction motility are the next step in evaluating any case of GORD. Ignoring the anatomical shape of the CEJ is behind the various conflicting results that we are hearing at medical meetings devoted to GORD.

Imposing the study of the anatomical feature of the junction, which is very variable from person to person, is the first step in evaluating any proposed treatment of GORD, medically or surgically.

Applying the devices (Plicator, Stratten procedure, etc) without studying the anatomy of the junction is behind any side effects of these proposed procedures.

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Association between K469E allele of intercellular adhesion molecule 1 gene and inflammatory bowel disease in different populations

We read with interest the article by Matsuzawa *et al* showing an association between the

K469E allele of intercellular adhesion molecule (ICAM)-1 gene and inflammatory bowel disease (IBD) in a Japanese population (*Gut* 2003;52:75-8). The ICAM-1 gene lies on chromosome 19p13, previously implicated in determining susceptibility to IBD,¹ and codifies for a surface glycoprotein that belongs to the immunoglobulin superfamily. ICAM-1 plays an important role in the trafficking and activation of leucocytes and is upregulated in the inflamed mucosa of IBD patients. Matsuzawa *et al* found that the allelic frequency of K469 was significantly higher in both Crohn's disease (CD) and ulcerative colitis (UC) patients than controls (*Gut* 2003;52:75-8). These data are in contrast with the results of two previous studies from the USA² and Germany³ which showed no significant difference in K469 allele frequency between IBD patients and healthy controls. The G241R polymorphism of the ICAM-1 gene was also investigated in these studies, and IBD patients were stratified by antineutrophil cytoplasmic antibody (ANCA) status. In particular, Yang *et al* found a significantly increased frequency of the G241R polymorphism both in ANCA negative UC and ANCA positive CD patients² while Braun *et al* showed an association between R241 allele and UC, independently of ANCA status.³

We also searched for the K469E mutation in 42 consecutive Italian IBD patients (31 males, mean age 36 (14) years), 17 with CD and 25 with UC, and 227 ethnically matched controls. Our preliminary results (see table 1), although obtained in a limited number of patients, are in contrast with the findings of Matsuzawa *et al* (*Gut* 2003;52:75-8) and confirm those obtained in Caucasians patients.^{2,3} The possible explanation for such a discrepancy in results is the influence of the different geographic distribution of the genetic mutation. Japanese patients with IBD have a genetic background that differs from Western patients, as also demonstrated recently for the NOD2/CARD15 gene polymorphisms. Indeed, several studies have reported an association between CD and NOD2/CARD15 mutations in Caucasians⁴⁻⁶ but not in Japanese cohorts.^{7,8} These data indicate that there may be significant genetic heterogeneity between different ethnic and racial IBD populations and environmental factors may play a leading role in the pathogenesis of IBD. Thus gene-environment interactions represent a crucial event in the pathogenesis of IBD and they cannot be considered as distinct entities.

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Table 1 Allelic frequencies of the E/K469 ICAM-1 polymorphism in Italian patients affected by IBD, and in controls

	Controls (n=227)	IBD (n=42)	UC (n=25)	CD (n=17)
Allelic frequency (%)				
E469	45	45	46	44
K469	55	55	54	56

IBD, inflammatory bowel disease; UC, ulcerative colitis; CD, Crohn's disease; ICAM, intercellular adhesion molecule.

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Authors' reply

We would like to address the possible cause of the inconsistency of the *ICAM1* alleles, which associated with inflammatory bowel disease (IBD), between Japanese (K469) (*Gut* 2003;**52**:75–8) and German White populations (R241).¹

Inconsistency of the associated alleles with a certain complex genetic disease among ethnic groups has been repeatedly described in the long term history of the association studies between inflammatory bowel disease (IBD) and HLA alleles. For example, the positive association between ulcerative colitis and DRB1*0103 in a Caucasian population but with DRB1*1502 in the Japanese has been reported in many studies. Such allelic inconsistencies were also observed in the HLA-B, HLA-DQA, and DQB genes.²

Three explanations have been considered for these inconsistencies.³ Firstly, the marker genes (HLA genes) themselves may not be the primary disease predisposing genes in this region but are in linkage disequilibrium with one or more primary responsible genes located in this region. Also, in different populations there may be different linkage disequilibria. This explanation seems to fit with the inconsistencies of *ICAM1* allele association.

The second explanation is that there may be genetic heterogeneity in the allele associations in a certain gene. Recently, the existence of a population specific disease predisposing mutation (DPM) in *NOD2* to Crohn's disease (CD) has been proposed,^{4,7} suggesting the genetic heterogeneity of CD in the *NOD2* region. However, if a certain DPM allele of *NOD2* exists in a certain population, the

increasing frequency of that DPM allele in CD should be observed consistently in all ethnic groups.⁷ In contrast, *ICAM1* K469 frequency, which is increased in Japanese patients with IBD, is not increased in German patients. This observation could argue that the *ICAM1* K469 polymorphism does not have a pathological effect directly but more likely occurs in strong linkage disequilibrium with a causative factor in both populations—that is, the time is not ripe enough to discuss the existence of genetic heterogeneity in this region (chromosome 19p13).

The third explanation is that these inconsistencies may be due to sample size and/or inappropriate control populations. As the *ICAM1* polymorphism consists of only two SNPs and these polymorphisms are less informative, a considerable volume of sample size and simple composition of haplotype in the ethnic group would be required to detect the increase in the predisposing haplotype.

In conclusion, this inconsistency of the associated *ICAM1* allele is most likely due to the difference in linkage disequilibria of the *ICAM1* allele to the DPM in 19p13 among ethnic groups. However, the positive associations between the *ICAM1* polymorphism and IBD in these ethnic groups highlights the potential importance of this region in the search for the predisposing gene(s) to IBD.^{1,8}

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Eosinophilic oesophagitis: treatment using Montelukast

I read with interest the paper by Attwood and colleagues (*Gut* 2003;**52**:181–5) on eosinophilic oesophagitis (EO). According to the authors, the distinct clinical syndrome of EO is not usually seen either as a component of gastro-oesophageal reflux disease or as a variant of eosinophilic gastroenteritis (EG).

The diagnostic hallmark of EO is odynophagia and the diagnosis is always histology dependent (>20 eosinophils/high power field) (*Gut* 2003;**52**:181–5). In the paediatric setting, the condition is widely recognised but the adult EO may escape diagnosis due to general lack of awareness of the condition. In this respect, the paper by Attwood and colleagues (*Gut* 2003;**52**:181–5) is a valuable contribution towards understanding the complex oesophageal condition of EO.

The pathophysiology of EG or EO may be similar to that of asthma. Asthmatic patients demonstrate increased production of cysteinyl leukotrienes during acute asthma attacks.¹ Cysteinyl leukotrienes have potent chemo-attractant properties for eosinophils and play an important role in the pathophysiology of asthma.

In EG, accumulated eosinophils cause severe tissue damage characteristic of EG. Cysteinyl leukotrienes, along with cytokines interleukin 3 and 5 and granulocyte macrophage-colony stimulating factor play a role in the recruitment of eosinophils into the tissue causing the damage.²

No controlled treatment trial for EG or EO exist. Limited results have been achieved with oral cromolyn, ketotifen, and other antihistamines. Oral corticosteroids are effective but long term use is complicated by side effects.

Montelukast is a leukotriene receptor antagonist (LTRA) which actively and selectively blocks the leukotriene D4 (LTD4) receptor. Because LTD4 is both produced by and a chemotactic factor for eosinophils, this may provide the rationale for treating a patient with EG or EO with a LTRA. The first reported case of successful Montelukast treatment for an young EG patient was published in 1999.³

Montelukast was originally licensed in the UK for use in asthma.⁴ There has been some concern regarding association between the use of LTRA and Churg-Strauss syndrome (CSS) in asthma.⁵ CSS is a rare form of eosinophilic vasculitis associated with asthma. This syndrome has previously been associated with the use of Zafirlukast.⁶ The Committee on Safety of Medicines has received 12 reports of CSS and pulmonary eosinophilia possibly associated with Montelukast.⁷ There are other reports of Montelukast induced CSS in asthma patients⁸ in the literature.

Attwood and colleagues (*Gut* 2003;**52**:181–5) observed nausea in four patients and myalgia in one in the Montelukast group but there was no mention of CSS. In the previous report of Montelukast therapy in EG, it was shown that Montelukast did not affect tissue eosinophilia (TE) or symptoms in a patient with severe EG complicated by oesophageal stricture.⁹ In another report, Montelukast reduced peripheral eosinophilia but there was no mention of whether TE was reduced.³ In Attwood *et al's* paper (*Gut* 2003;**52**:181–5), treatment with Montelukast for a median

period of 14 months in eight patients out of a cohort of 12 patients with EO did not change the density of TE. However, subjective improvements were seen in seven patients with swallowing difficulties in Attwood's series, one of eight patients on Montelukast.

LTRAs are a useful therapy for EO. While anti-leukotriene drugs are generally safe and effective for most patients, from the asthma experience I conclude that clinicians need to be vigilant of any development of CSS in all patients with eosinophilic oesophagitis undergoing treatment with Montelukast. I agree with the authors that further randomised control trials are required to assess the full benefits of Montelukast therapy in EO.

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Effect of a rapid access flexible sigmoidoscopy clinic on the yield of early stage rectal cancer

We read with interest the debate on population based endoscopic screening for colorectal cancer (*Gut* 2003;**52**:323–6). While we agree that the case for population screening is compelling, we believe that Macafee and Scholefield's statement that "earlier diagnosis is unlikely to occur through increased awareness or patient education alone" is unnecessarily pessimistic.

We have recently had the opportunity to audit the impact of a dedicated rapid access flexible sigmoidoscopy clinic established in the endoscopy department of Dewsbury and District Hospital in January 1997. General practitioners were invited to use a proforma to refer patients to the clinic who were over 40 years old and had presented with a history of a recent change in bowel habit, rectal bleeding, or iron deficiency anaemia. Following initial consultation using a structured history form and clinical examination, flexible sigmoidoscopy was carried out by a consultant surgeon or a nurse endoscopist. If significant pathology was encountered, biopsy material was obtained and further investigations and management were planned as appropriate.

During the period January 1993 to December 1999, 167 patients underwent surgery for

Table 1 Association between treatment before (clinic period 1; 1993–96) and after (clinic period 2; 1997–99) the introduction of a dedicated rapid access flexible sigmoidoscopy clinic and the clinicopathological characteristics of resected rectal adenocarcinomas

	Clinic period 1 (n=87)	Clinic period 2 (n=80)	p Value
Age (y)	69.9	69.0	NS
ASA			
1	2	3	NS
2	36	38	
3	31	24	
4	18	15	
Admission			
Emergency	15	10	NS
Elective	72	70	
Treatment			
Curative	59	65	<0.05*
Palliative	28	15	
CRM			
Clear	56	66	<0.05*
Positive	18	8	
Dukes'			
A	10	21	<0.02*
B-D	77	59	

CRM, circumferential resection margin. Not all patients had their tumours resected.
* χ^2 .

histologically confirmed adenocarcinoma of the rectum. Introduction of the dedicated rapid access flexible sigmoidoscopy clinic occurred 48 months into this audit period, with 87 patients treated before the introduction (clinic period 1) and 80 patients after (clinic period 2). Comparison of the groups of patients treated before and after reorganisation of the colorectal service demonstrated significant differences in several important clinical variables, with early stage tumour resection, complete circumferential margin clearance, and absence of visible residual tumour following excision all commoner in the later period (table 1).

There are several possible factors that may have contributed to the observed clinicopathological differences in the two time periods, including increased public awareness of suspicious symptoms, decreased embarrassment about reporting these symptoms, and increased GP education. Creation of a fast track flexible sigmoidoscopy clinic may also have contributed to the improved patient outcomes observed in our institution, and we believe that the debate around screening for colorectal cancer should take into account the improving results of the investigation of symptomatic colorectal disease. Not to do so may prevent the improvement of service provision in the hospital sector and is unnecessarily nihilistic.

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Detecting the risks of osteoporotic fractures in coeliac disease

The recent report by Thomason and colleagues (*Gut* 2003;**52**:518–22) which failed to

detect a significant increase in fractures experienced by treated coeliacs might reassure many patients and physicians. However, this study, and the accompanying commentary by Compton (*Gut* 2003;**52**:459), need full and critical assessment before changes in practice are adopted and coeliacs are no longer targeted to be screened for osteoporosis.

It is not surprising that no significant increase in fracture could be detected in this population of well treated coeliacs, given previous findings. The American Gastroenterology Association recently reviewed studies of osteoporosis in gastrointestinal diseases, including coeliac disease, according to standard levels of evidence.¹ All such studies have shown low mean bone mineral density (BMD) around the time of diagnosis of untreated coeliac disease, with a pooled analysis showing very low bone mass (age and sex adjusted z scores below –2) in 40% in the spine and 15% at the hip. However, many reports, including our own,² have shown normal or near normal mean values after treatment. This reflects the great improvement in BMD³ and calcium absorption⁴ which occurs when enteropathy is reversed with a gluten free diet. The real issues are how to recognise previously undiagnosed cases, and how to identify potential patient subgroups who might still be at risk due to suboptimal treatment.²

The study also did not have sufficient power to detect any increase in those fractures most typical of osteoporosis which have a high prevalence late in life.⁵ Such fractures typically include vertebral collapse and deformity, causing significant morbidity, but which commonly are undiagnosed unless looked for radiologically. In a 50 year old woman, there is a 32% life time risk of subsequent vertebral fractures.⁶ However, these were not recorded in either coeliacs or controls in this study, indicating that the questionnaire method employed led to marked under reporting. Femoral neck (hip) fractures, the most serious complication of osteoporosis, have a population incidence of less than 1% by the age of 65 years but approaching 20% by the age of 90 years. In this study, only about one third of coeliacs were aged over 65 years and only

one-tenth (n=20) over 75 years. Approximately 400 cases and controls would be needed in a prospective study to detect a 50% increase in risk from 20% to 30% with 90% power. Hence the ability of this study to detect a significant life time increase in fracture risk in the minority of coeliacs who are suboptimally treated is clearly limited. Much larger groups are needed in a prospective study which includes radiological ascertainment of vertebral fractures.

A relevant comparison can be made with the large US Study of Osteoporotic Fractures Research Group where over 9000 women older than 65 years of age were studied. In 1814 subjects with a daily calcium intake less than 400 mg, those below the median for fractional calcium absorption (so resembling untreated coeliacs) experienced an incidence of hip fractures of about 9 per 1000 person years—2.5-fold greater than those with absorption above the median.⁷

The absolute life time risk of osteoporotic fractures is reasonably large in the ageing population, even if the relative risk in coeliacs is not that great. Patients will be reassured by the knowledge that BMD has improved with dietary treatment and that individual risk has decreased. We hold that as the true risk of fracture in treated and untreated elderly coeliacs is unknown at present, judicious use of DXA measurements, following appropriate guidelines, to monitor calcium homeostasis and the benefits of treatment should continue.

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Collagenous colitis: constipation or diarrhoea?

As an axiom, collagenous colitis is characterized by diarrhoea, lymphocytic inflammation,

and a thickened subepithelial collagen layer in the colorectal mucosa.¹ Various case presentations in the literature have reported that frequent watery diarrhoea introduces the clinical picture of collagenous colitis and intermittent or continuous diarrhoea can remain.² On the other hand, numerous cases never suffer from episodes of watery diarrhoea but suffer from chronic constipation. Can we call into question the "incontestable" definition? Bonderup *et al* investigated the clinical and histological effect of oral budesonide in the treatment of collagenous colitis in 20 patients and concluded that budesonide is a highly effective and well tolerated treatment. The histological inflammation grade in the sigmoid mucosa and the thickness of the collagen layer were significantly reduced. A correlation between the grade of inflammation as well as collagen layer thickness and stool weight was found (*Gut* 2003;**52**:248–51).

In our recent study, we investigated 32 patients with histologically identified collagenous colitis. In contrast with the literature, 18 had chronic constipation and only 14 had the well known diarrhoea. We also treated all of them with budesonide (Budenofalk; Dr Falk Pharma) and all patients receiving budesonide had a clinical response: stool frequency and weight. These conflicting results suggest a role for additional factors other than the thickened collagen table. For example, allergy (food allergy), a great mimic, can cause both diarrhoea and constipation. Diseases or symptoms (that is, food protein induced enterocolitis, diarrhoea, or constipation) involving the gastrointestinal system have been attributed to hypersensitivity reactions to food.^{3–6} Many of these symptoms reflect the concept of "delayed" reactions. This notion presumes that certain clinical symptoms reflect allergies to food which develop over a period of hours or days (or longer) and are caused by immunological mechanisms other than immediate type hypersensitivity. For example, cow's milk protein allergy should be considered as a cause of chronic refractory constipation in children although the underlying mechanisms still require further investigation. Albeit the aetiology of collagenous colitis is still unknown, the subepithelial band-like collagenous deposit may be produced by fibroblasts after immune stimulation. Our hypothesis was to test whether collagenous colitis might be related to food allergy.

Patient sera were analysed for common food antigens. Our data support the hypothesis that patients with collagenous colitis have laboratory and/or clinical evidence of food allergy: the high frequency of specific antibodies to food antigens and the increased total IgE levels imply a possible connection between collagenous colitis and food allergy and suggest a possible reason for the paradox of diarrhoea-constipation. Corticosteroids are the most effective drugs available for the treatment of allergic diseases and are very useful in treatment because they have potent anti-inflammatory effects.⁷ Topical corticosteroids work by reducing the effects of histamine and other inflammatory mediators involved in the allergic response and repeated dosing inhibits both the early and late phase allergic reactions, including priming and hyper-responsiveness. These observations suggest further investigations in other groups of patients with collagenous colitis are needed to prove this hypothesis.

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BOOK REVIEWS



Hepatology: a Textbook of Liver Disease, 4th edition

Edited by Zakim, Boyer. Philadelphia: Saunders, 2003, £230.00, pp 1765. ISBN 0-7216-9051-3

The fourth edition of Zakim and Boyer's *Hepatology: a Textbook of Liver Disease* is published this year and significantly updates the previous edition published in 1996. The work once again comes in two volumes with exactly 100 contributing authors, the majority of whom are from the USA. The book is arranged into four sections. Sections 1–3 are in volume 1 and cover cell biology, biochemistry, and physiology (section 1); the systemic effects of liver disease (section 2); and laboratory methods for evaluating liver disease (section 3). The whole of volume 2 is taken up by section IV covering aetiology, clinical features, diagnosis, and treatment of specific liver diseases subdivided into toxic injury, infection, chronic liver disease, tumours, childhood liver disease, diseases of the biliary tree, and special topics.

The approach works well and all the relevant areas are comprehensively covered. There is inevitably some duplication between sections but this is kept to a minimum. Placing most of the basic science in the first volume allows readers who want to concentrate on specific diseases to do so easily and then to refer to the first volume if they need further background. There are some inconsistencies in this approach, for instance immunology is included under section IV "Diagnosis and management of chronic forms of liver disease". Given the major physiological role of the liver as an immune organ and

the fact that many acute liver diseases have an immunological basis, it might have been appropriate to highlight immunology in volume 1 where it would fit very well with the excellent chapters on hepatic regeneration and fibrosis. Section 3 contains an informative chapter on laparoscopy but only a four page section on hepatic imaging. Imaging is subsequently covered in the individual chapters in section IV but given the major advances in interventional radiology and imaging it would have been appropriate to give this subject a chapter of its own. For example, there are only two brief references to positive emission tomography in the whole book.

Individual chapters are extremely well referenced although it might help to highlight the most significant references or those that provide an in depth review. One minor criticism is the quality of some of the figures. The chapters are richly illustrated but there is an irritating variation in the quality and style of the line drawings. It would have improved the overall appearance of the book if figures had been redrawn in a uniform style, and for some of the figures this would also have improved their clarity. The reluctance to use colour is presumably based on cost considerations. However, the recently published *Comprehensive Clinical Hepatology* edited by O'Grady, Lake, and Howdell (Mosby), provides an example of how the use of modern technology can provide outstanding illustrations that enhance the readability of the book.

How does Zakim and Boyer compare with other similar volumes? The two main rivals are the *Oxford Textbook of Clinical Hepatology* and Schiff's *Diseases of the Liver*, both of which were last updated in 1999. All three works are excellent. There are some differences in emphasis and presentation between them but all three are highly readable and cover the field comprehensively. I have greatly enjoyed having access to Zakim and Boyer over the last few weeks and would recommend the fourth edition unreservedly to anyone with an interest in liver disease, whether research scientists, specialist hepatologists, or gastroenterologists. The editors are to be congratulated for managing to improve an already outstanding reference work.

D H Adams

Genetic Disorders of the Exocrine Pancreas

Edited by P Durie, *et al.* Basle: Karger, 2002, b/w, pp 155. ISBN 3-8055-7411 8

This multiauthor work, derived from a symposium held in April 2001, summarises our current knowledge of the genetics of exocrine pancreatic disease. As is usual with such publications, the individual chapters have been written as free standing presentations which results in a degree of repetition. The editors have grouped the chapters into sections; a "consensus conference" dealing with ethical issues and with guidelines for prevention, screening, and treatment is followed by sections on hereditary pancreatitis (HP), pancreatic cancer, and cystic fibrosis. Finally, there is a conference report and a monograph celebrating the work of Henry Lynch of the eponymous cancer syndromes.

The first section will be of the most practical interest to general gastroenterologists. Gastrointestinal physicians and surgeons

should already be aware of the ethics of screening from more common conditions such as colon cancer. A brief overview of these issues is followed by clear advice on whom to test, appropriate pre-test information, post-test information, and acting on the results. The algorithm looks forbidding but is straightforward and logical. Both service and research testing are covered. Screening for cancer in HP is a more difficult issue. The advice that patients over 40 years should have annual screening at a specialist centre however may build a knowledge base for future patients but will not necessarily help our current population.

The HP section suffers from its symposium origins. In the six years since David Whitcombe and his colleagues identified a mutation of the PRSS1 (cationic trypsinogen) gene in a kindred with HP, a new understanding of the relationship between the three entities of acute and chronic pancreatitis and pancreatic cancer has developed. It is a pity that the format of this book has not allowed this to be made explicit. It starts well with a two page overview neatly logging the known PRSS1 and SPINK mutations. Unfortunately, the chapters dealing with the mechanisms by which these mutations might translate into clinical disease, which logically should follow, are instead towards the end of the section (although an earlier chapter on gene mutations in children does cover some of this ground). The general reader might well find the intervening chapters on national experiences superfluous. The review of inborn errors of metabolism is useful but surely belongs at the end of the section rather than in the middle.

The pancreatic cancer section is better organised and provides a comprehensive review of the contribution of genes to disease. In contrast with HP, there are no defined single gene mutations identified for pancreatic cancer. Families with two or more affected members have been reported: whether this simply represents random clustering is discussed. The risk of pancreatic cancer in accepted cancer syndromes such as FAMM, Lynch syndrome II, BRCA2 mutation, and Peutz-Jehgers syndrome is also considered. The chapters on surveillance and molecular diagnosis will be of particular interest as they offer the first glimpse of hope for early detection and treatment. Non-pancreatologists may not be aware that premalignant ductal lesions termed PanINs have now been described and classified. Ways in which this discovery and molecular markers such as K-ras mutations may be exploited in screening strategies are reviewed, as are the practical difficulties of assessing the pancreas even with the benefit of EUS and CT. Ultimately however, all strategies being considered or tried will lead to a prophylactic pancreatectomy: the practicalities of the timing and extent of pancreatectomy are covered in the final chapter.

The final section covering cystic fibrosis and the Shwachman-Diamond syndrome is limited in its scope and appears to reflect one centre's interests and research.

Currently, pancreatic disease is either self limiting or incurable. Effective treatments for pancreatitis and pancreatic cancer will come from molecular and genetic research of the type described here. The presentation of this book is not perfect but the information it contains should be available to anyone dealing with pancreatic disease. Ask your library to buy it.

D Fine

CORRECTIONS

In the BSG Abstracts supplement, there was an error in abstract 175 by Li *et al* (*Gut* 2003;52 Suppl 1:A48). In the results section, the sentence after the table should read "1 year survival for all patients with and without pre-existing Barrett's was 51.5% and 31% respectively, and for those undergoing potential curative resection, was 72.6% and 52.7%, respectively". The authors apologise for the error.

In the author index of the BSG Abstracts supplement, J E Crabtree should have been listed as an author on abstract 126 by Jeremy *et al* (*Gut* 2003;52 Suppl 1:A34). This was due to a technical error for which the journal apologises.

NOTICES

British Society of Gastroenterology Sir Francis Avery Jones Research Award 2004

Applications are invited by the Education Committee of the British Society of Gastroenterology who will recommend to Council the recipient of the 2004 Award. Applications (TWENTY COPIES) should include:

- A manuscript (2 A4 pages ONLY) describing the work conducted
- A bibliography of relevant personal publications
- An outline of the proposed content of the lecture, including title
- A written statement confirming that all or a substantial part of the work has been personally conducted in the UK or Eire.

Entrants must be 40 years old or less on 31 December 2004 but need not be a member of the Society. The recipient will be required to deliver a 30 minute lecture at the Annual meeting of the Society in Glasgow in March 2004. Applications (TWENTY COPIES) should be made to the Honorary Secretary, British Society of Gastroenterology, 3 St Andrews Place, London NW1 4LB by 1 December 2003.

British Society of Gastroenterology Hopkins Endoscopy Prize 2004

Applications are invited by the Endoscopy Committee of the British Society of Gastroenterology who will recommend to the Council the recipient of the 2004 Award. Applications (TEN COPIES) should include:

- A manuscript (2 A4 pages ONLY) describing the work conducted
- A bibliography of relevant personal publications
- An outline of the proposed content of the lecture, including title
- A written statement confirming that all or a substantial part of the work has been personally conducted in the UK or Eire.

An applicant need not be a member of the Society. The recipient will be required to deliver a 20 minute lecture at the Annual meeting of the Society in Glasgow in March 2004. Applications (TEN COPIES) should be made to the Honorary Secretary, British Society of Gastroenterology, 3 St Andrews Place, London NW1 4LB by 1 December 2003.

European Helicobacter Study Group (EHSG)

This meeting, on Helicobacter infections and gastroduodenal pathology, will be held on 3–6 September 2003 in Stockholm, Sweden. Further details: Professor Torkel Wadstrom, President-EHSG, Lund University, Department of Infectious Diseases & Medical Microbiology, Division of Bacteriology, Solvegatan 23, SE-223 62 Lund, Sweden. Tel: +46 46 173 241; fax: +46 46 152 564; email: Torkel.Wadstrom@mmb.lu.se; website: www.helicobacter.org

Falk Symposium 135—Immunological Diseases of Liver and Gut

This symposium will be held on 12–13 September 2003 in Prague, Czech Republic. Further details: Falk Foundation e.V., Congress Division, PO Box 6529, Leinenweberstr. 5, 79041 Freiburg/Br, Germany. Tel: +49 761 15 140; fax: +49 761 15 14 359; email: symposia@falkfoundation.de; website: www.falkfoundation.de

The European Society of Parenteral and Enteral Nutrition (ESPEN)

ESPEN will celebrate its silver anniversary at the time of the annual congress, which is to be held on 20–23 September 2003 in Cannes, France. Further details: www.espen.org

XII Falk Liver Week

The XII Falk Liver Week, in honour of Hans Popper's 100th birthday, will be held on 15–22 October 2003 in Freiburg, Germany. Further details - see Falk Symposia above.

European Course on Laparoscopic Endoscopy

This course will be held on 18–21 November 2003 in Brussels, Belgium. Further details: Secretary to Professor Cadière, Service de Chirurgie Digestive, Rue Haute 322, Brussels 1000, Belgium. Tel: +32 (0)2 648 07 60; fax: +32 (0)2 647 86 94; email: straeb.asmb@proximedia.be; website: www.straeb-asmb.com

4th Nutrition and Health Conference

A multidisciplinary event will be held on 21–22 November 2003 in London, UK. This year's topics include cancer, obesity, exercise on prescription, menopause, ageing, motivation skills, and coronary heart disease. Further details: Tanya Carr, 16 Brownlow Court, Lyttelton Road, London N2 0EA. Tel/fax: +44 (0)208 455 2126 or 6570; website: www.nutritionandhealth.co.uk

Hong Kong-Shanghai International Liver Congress 2004

This conference will be held on 14–17 February 2004 in Hong Kong. The topic of the conference is "Liver Diseases in the Post-Genomic Era". Further details: Ms Kristie Leung, Room 102–105 School of General Nursing, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong. Tel: +852 2818 4300/8101 2442; fax: +852 2818 4030; email: kristieleung@hepa2004.org; website: www.hepa2004.org