LETTERS TO THE EDITOR

Small bowel biopsies in patients with iron deficiency anaemia

EDITOR,—We noted in the guidelines for the management of iron deficiency anaemia (*Gut* 2000;**46**(suppl IV):iv1–iv5) that it is recommended that small bowel biopsies should be taken in all patients presenting with iron deficiency anaemia. This has been the subject of much discussion between the pathology department and ours recently.

Antiendomysial antibodies (EMAs) give at best close to 100% sensitivity and specificity[1 2] although other studies suggest around 95% sensitivity with much lower values for specificity depending on the exact criteria for gluten sensitive enteropathy adopted.[3 4] This has been discussed at both the recent British Society of Gastroenterology (BSG) meeting (Ciclitira PJ. State of the Art Lecture: *Coeliac Disease—pathogenesis and prevention*. BSG Annual Meeting, March 2000) and the American Gastroenterology Association (AGA) meeting (Schuppan D. *Sprue: new insights into pathogenesis and management*. AGA Postgraduate Course, May 2000).

A possible reason for these differences in sensitivity and specificity in the literature is that standards vary between different pathology departments in the techniques of anti-EMA assessment.[5] Most hospital biochemistry departments perform the tests using monkey oesophagus tissue bought from commercial suppliers; on the market at present there are 19 different suppliers of monkey oesophagus and 23 different suppliers of the enzyme immunoassay (EIA) (United Kingdom External Quality Assessment Services for Autoimmune Serology (NEQAS)). These tissue samples will be of varying quality, and the EIAs will vary in their accuracy. To compound the problems the immunofluorescent technique is essentially subjective, and results will vary between different observers. Our laboratory automatically measures total IgA levels, patients deficient in IgA will have negative IgA EMA, and laboratories need to have the resources to measure IgG EMA in these patients.

Our biochemistry laboratory is evaluating antitissue transglutaminase antibody (AtTGA) assays to replace the monkey oesophagus immunofluorescence system, which should be more automated and therefore more cost effective. Initial sensitivity and specificity for AtTGA assays are promising.[6]

There is some evidence that endoscopic markers are useful in detecting villous abnormality in coeliac disease[7] and we await the development of high resolution endoscopy.[8] It seems that although duodenal biopsy is traditionally regarded as the gold standard, there is still the possibility that false negatives in patients with patchy villous changes will occur with these screening methods. A recent abstract from the AGA from Columbia University, New York, found that fewer than half of duodenal biopsy samples in their study were orientated sufficiently to allow evaluation of villous atrophy, and 39% of patients had patchy disease.[9]

The implications in terms of resources for the histology departments in handling multiple duodenal biopsies in all patients with iron deficiency anaemia are considerable and this is currently the subject of an internal audit at our hospital. Although for the reasons stated anti-EMA has varying sensitivity and specificity, there is potential for considerable improvement in this area, with close to 100% values for both being possible, particularly with newer assays that will be automated and more efficient. Paradoxically, when these tests become more widely available there may be many more referrals to gastroenterology departments due to positive serological tests and this may in fact increase further the number of duodenal biopsy specimens reaching histopathology departments even if duodenal biopsy were a second line test. We wonder if the guidelines for duodenal biopsy and anti-EMA in iron deficiency anaemia should be the subject of further discussion.

C B PEARCE
H D DUNCAN
D SINCLAIR
D N POLLER
Department of Gastroenterology, Queen Alexandra Hospital, Portsmouth, UK

Correspondence to: C B pearce, Department of Medicine, Queen Alexandra Hospital, Cosham, Portsmouth PO6 3LY, UK.
callum@pearcey.screaming.net

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Reply

EDITOR,—Pearce *et al* raise the possibility of using the endomysial antibody (EMA) test instead of histology of small bowel biopsies as a test for coeliac disease in the investigation of iron deficiency anaemia (IDA). They wish to consider this because of the considerable resource implications for histology departments.

The EMA test is excellent but its value is dependent on the prevalence of coeliac disease in the population being tested (the pre-test probability). Based on all peer reviewed published studies from 1985 to 1999, we have calculated specificity to be 98.4 % (95% confidence interval (CI) 98.0–98.8) and sensitivity to be 93.8% (95% CI 92.7–94.9).[1] These give a likelihood ratio for a positive test of 59 and for a negative test of 0.06. We have found that the prevalence of coeliac disease in IDA is 4%. Thus using the Fagan nomogram, if the EMA test is positive, the post-test probability of coeliac disease is 75%—that is, one in four patients with IDA who have a positive EMA test will have normal histology on small bowel biopsy. If the EMA test is negative, the post-test probability is 0.2%, which effectively excludes coeliac disease.

We therefore agree that the EMA test could be used instead of small bowel biopsy to exclude coeliac disease in patients with IDA. However, as most of the cost of obtaining a histological diagnosis may be in the endoscopic examination (during which small bowel biopsies are taken by most gastroenterologists since we validated the technique in 1981[2]) and as most patients will be having an endoscopy anyway, it seemed reasonable to us to apply the definitive test (that is, histology) in all those undergoing endoscopy. For those not undergoing endoscopy, such as menstruating women under 45 years, we recommend the EMA test in our guidelines.

We agree that patchiness of mucosal abnormality, which we formally documented in 1976,[3] needs to be taken into consideration and we routinely take at least four endoscopic biopsies. We realise that this may increase the cost of histology. If after a proper cost benefit study histology is found to be excessively expensive, consideration could be given to immediate stereomicroscopic assessment of biopsies which was popular in the 1960s and early 1970s,[4 5] and which we still apply when time allows. This is a very simple technique which allows visualisation at a glance of the whole surface of biopsies as well as helping to unfold and correctly orientate the specimens before fixation if histology is still deemed necessary. However, both this and high resolution endoscopy need experience for correct interpretation and would also need good quality photography for a permanent record if fixed biopsies were not stored.

In conclusion, we agree that the EMA test is a reasonable alternative to exclude coeliac disease in IDA but until we have a proper cost benefit study indicating otherwise, we recommend histology of endoscopic small bowel biopsies when endoscopy is already being undertaken.

B B SCOTT
Lincoln County Hospital, Lincoln LN2 4BJ, UK
drbbscott@aol.com

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Is coeliac disease a confounding factor in the diagnosis of NASH?

EDITOR,—We read with great interest the paper by Wigg *et al* (*Gut* 2001;**48**:206–11) concerning the role of small intestinal bacterial overgrowth in the pathogenesis of non-alcoholic steatohepatitis (NASH) but we would like to comment on the enrolment criteria used for their study. We agree with Farrell (*Gut* 2001;**48**:148–9) that the Adelaide group's failure to characterise the variables of obesity and diabetes in their population might result in selection bias. Moreover, they made no attempt to exclude the possibility of coeliac disease (CD) which can also be associated with altered intestinal permeability even when the disease is subclinical.[1]

In approximately 40% of all adults with this disease, increased serum transaminase levels are found at diagnosis,[2] and such elevations may be the only abnormality in cases of "occult" CD.[3] In fact, in a study by Bardella *et al*, 9.3% of cases of unexplained chronic hypertransaminasaemia were ultimately diagnosed as CD.[4]

From December 1997 to December 1999, we observed 30 subjects (22 males, eight females; mean age 40 (9.3) years; mean weight 71.6 (7.9) kg) with clinical and laboratory pictures fully compatible with a diagnosis of NASH—that is, AST 56.3 (13.6) IU/l (normal 7–45); ALT 102 (36.8) IU/l (normal 7–45); histological findings of macrovesicular steatosis, inflammation, hepatic fibrosis, and Mallory's bodies; no history of alcohol consumption; and no other significant liver disease. All 30 patients had serum assays of IgG and IgA antibodies against gliadin and endomysium antibody (EMA), and duodenal biopsies were collected from those who were EMA positive. Four of these patients (one male and three females; mean age 30.6 (5.5) years) were thus diagnosed as having occult CD. The only clinical abnormalities were elevations in serum transaminase and sonographic evidence of fatty infiltration of the liver. All four were placed on a gluten free diet and followed with clinical examination and blood chemistry studies every three months. After three months on the prescribed diet, all patients presented decreases in serum transaminase levels (AST 30.2 (8.6) IU/l and ALT 45.2 (9.3) IU/l) and reduced steatosis on ultrasound. At one year from diagnosis, transaminase levels have normalised (AST 29.6 (9.7) IU/l and ALT 23.6 (2.5) IU/l), duodenal histology has improved considerably, and there is no sign of steatosis on sonography.

CD may cause increased intestinal permeability,[5] and its clinical, biochemical, and histological findings are similar to those of NASH.[6] The fact that elevated transaminase levels and EMA positivity can be documented even in the subclinical stages of CD suggests that the inflammatory process in this disease may be triggered by the same oxidative stress cited by Farrell as a cause of tissue damage in NASH. In a recent study, Lahat *et al* showed that CD is also associated with increased expression of inflammatory cytokines, including tumour necrosis factor α.[7]

In light of the findings reviewed here, we feel that all patients with unexplained hypertransaminasaemia should be screened for CD, and that CD must be excluded before the diagnosis of NASH is made.

A GRIECO
L MIELE
G PIGNATARO
M POMPILI
G L RAPACCINI
G GASBARRINI
Institute of Internal Medicine, Policlinico Universitario A Gemelli, Catholic University of Sacred Heart, Rome, Italy

Correspondence to: Dr A Grieco, Institute of Internal Medicine, Catholic University of Sacred Heart, Largo Gemelli 8—00168 Rome, Italy.
antgrieco@katamail.com

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Reply

EDITOR,—We thank Grieco *et al* for their important observation that NASH may be associated with occult coeliac disease (13% in their series). We have also been interested in the possibility of this association. Coeliac disease, like small intestinal bacterial overgrowth, can be associated with increased intestinal permeability. It is plausible therefore that they could also share a similar pathogenetic mechanism resulting in non-alcoholic steatohepatitis (NASH) (that is, translocation of gut bacteria, Kupffer cell stimulation, and production of tumour necrosis factor α (TNF-α), proinflammatory cytokine, and reactive oxygen species, resulting in liver inflammation).

In our series of 22 NASH patients, none had a prior diagnosis of coeliac disease or suggestive symptoms. We also tested for antigliadin IgA and IgG antibodies (unpublished data). Three patients had positive antibodies (one positive for both antibodies, and two positive for the antigliadin IgG antibody only). One of these patients has been further investigated and coeliac disease has been confirmed histologically.

Although further investigation is required in the remaining two patients to exclude coeliac disease, it is possible that three patients (14%) in our NASH series could have occult coeliac disease (a value similar to that reported by Grieco *et al*).

None of the possible coeliac disease patients however had positive breath tests and their mean TNF-α levels did not differ significantly from the mean of the other NASH patients. Coeliac disease is therefore unlikely to be a confounding factor in our important observation of a high prevalence of small intestinal bacterial overgrowth and elevated serum TNF-α levels in NASH patients.

In our study, small intestinal bacterial overgrowth was present in 50% of patients. We have always considered that the pathogenesis of NASH is likely to be multifactorial. Coeliac disease, with perhaps a similar pathogenetic mechanism to small intestinal bacterial overgrowth, could be another important contributing factor in the development of NASH.

A WIGG
Unit of Gastroenterology and Hepatology, Flinders Medical Centre, Bedford Park, Adelaide, SA, 5042, Australia

A CUMMINS
Department of Gastroenterology, Queen Elizabeth Hospital, 28 Woodville Road, Woodville South, Adelaide, SA, 5011, Australia

Correspondence to: A Wigg.
alan.wigg@flinders.edu.au

Induction of multiple autoantibodies to islet cell antigens during treatment with interferon alpha for chronic hepatitis C

EDITOR,—Induction or augmentation of autoimmunity during the treatment of chronic hepatitis C with interferon alpha is a well known phenomenon and a matter of great concern to physicians involved in the field of viral hepatitis. In recent years there have been a number of reports suggesting a link between the antiviral therapy and the development of antibodies to multiple autoantigens. In a recent issue of *Gut*, Wesche *et al* (*Gut* 2001;**48**:378–83) described the appearance of antibodies to 21-hydroxylase, an autoantigen of the adrenal cortex, and autoantibodies to glutamate decarboxylase 65 (GAD65) and the tyrosine phosphatase IA2 (IA2), both important autoantigens with respect to the pathogenesis of autoimmune (type 1) diabetes. Autoantibodies to GAD65 and IA2 appeared during or after therapy with alpha interferon for chronic hepatitis C in 5/62 and 1/62 patients, respectively. However, none of these patients was positive for both antibodies.

Type 1 diabetes is regarded as a chronic autoimmune disease caused by selective destruction of the insulin producing β cells. The disease is mediated by T cells but autoantibodies are well established markers for an ongoing autoimmune process within the islets.[1] As these autoantibodies usually appear prior to the clinical onset of the disease, they may be used to predict type 1 diabetes in predisposed individuals. In recent studies it has been shown that only those individuals in whom more than one diabetes related autoantibody could be determined are at considerable risk of developing type 1 diabetes.[2] Overall, the risk increases with the number of positive autoantibodies.[3] Therefore, combined screening for diabetes related autoantibodies is suggested to increase the specificity and the positive predictive value of the autoantibody tests.

We studied 56 patients with chronic hepatitis C (defined by positive anti-HCV and positive HCV-RNA) for the appearance of diabetes related autoantibodies after interferon therapy. We first screened for islet cell antibodies (indirect immunofluorescene) and if positive additionally determined autoantibodies to GAD 65, IA2, and insulin (radioimmunoassay and ELISA, respectively). In case of positivity for any antibody we analysed a pretreatment serum sample to

Table 1 Characteristics of patients with diabetes related autoantibodies after interferon alpha therapy for chronic hepatitis C infection

Patient No/sex/age	Mode of infection/genotype of HCV	Date of interferon therapy	Diabetes related autoantibodies	Estimated risk for type 1 diabetes
No 1/male/52 y	Unknown/genotype 1	8/98–8/99	IAA, GAD 65	Moderate
No 2 /male/49 y	IV drug use/genotype 1	9/98–3/99	ICA, GAD, IA2	High
No 3/female/48 y	Blood transfusion/genotype 1	7/98–7/99	IAA	Low
No 4/male/41 y	Unknown/genotype 3	11/98–5/99	IAA	Low

ICA, islet cell antibodies; GAD65, autoantiodies to glutamate decarboxylase 65; IA2, autoantibodies to tyrosine phosphatase IA2; IAA, insulin autoantibodies.

exclude the existence of any of these autoantibodies prior to interferon alpha therapy.

We identified four patients with diabetes related autoantibodies after cessation of therapy with interferon alpha (table 1). None of the patients had any of these antibodies prior to antiviral therapy nor had they a positive family history for autoimmune diabetes. Patient Nos 3 and 4 only developed insulin autoantibodies at a low titre. Induction of antibodies to insulin is a known phenomenon during therapy with interferon alpha and is described in a frequent number of cases.[4] Overall, these patients seem to have a low risk of progressing to clinically overt diabetes. Patient No 1 was found to be positive for insulin and GAD65 autoantibodies. Based on prospective clinical studies, this patient has an intermediate risk of developing diabetes.[5] We have now followed the patient for 16 months after interferon therapy and he has not developed an abnormal fasting glucose so far. The most striking example for induction of diabetes related autoantibodies was found in patient No 2. He developed three major autoantibodies during interferon therapy (GAD65, IA2, and ICA). Based on the predictive value of three positive autoantibody tests, this patient has a considerable risk of developing clinical overt diabetes over the next years. To date (follow up for 12 months) he has not developed an abnormal fasting glucose or an abnormal glucose tolerance test. The situation in this patient is further complicated as he did not respond to the antiviral therapy and another course of interferon might further increase his risk of developing autoimmune diabetes.

In summary, different diabetes related autoantibodies can be induced during interferon therapy for chronic HCV infection. However, we propose that only those patients with more than one autoantibody are at a considerable risk of progressing to clinically overt disease. Therefore, if one autoantibody appears during antiviral therapy, follow up should include screening for all other diabetes related autoantibodies. Furthermore, the question of whether patients with multiple autoantibodies should be retreated with interferon remains unsolved. Here the physician has to weigh possible progression of liver disease against the possibility of inducing autoimmune diabetes.

H E WASMUTH
C STOLTE
A GEIER
C GARTUNG
S MATERN
Medical Department III,
Technical University of Aachen, Germany

Correspondence to: H E Wasmuth, Medical Department III, Technical University of Aachen, Pauwelsstraβe 30, D-52074 Aachen, Germany. hwasmuth@hotmail.com

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ERCP training

EDITOR,—The leading article "ERCP training —time for change" by Hellier and Morris (*Gut* 2000;**47**:459–60) addresses important issues. Views as to how endoscopic retrograde cholangiopancreatography (ERCP) training should change may vary considerably between those in the average district general hospital (DGH) serving 220 000–250 000, and those in larger units, frequently serving populations of around 500 000.

Firstly, those without ERCP training but additional skills elsewhere will soon find themselves a favoured species. What price a skilled ultrasonographer? Advertising recently for a third consultant gastroenterologist to join two who undertook ERCP, we specified that ERCP was a skill *not* required. We felt an additional ERCP practitioner would dilute experience and eventually skill. Many DGH trusts are in a similar position with two consultants already in post who can provide sufficient ERCP cover and they do not want a third.

Secondly, the quality of training is largely dependent on two factors: the skill of the trainer, both in relation to ERCP and as an educationalist, and the case exposure available to the trainee. Frequently in a DGH there is only one trainee and case exposure is high. In a larger centre, while the number of ERCPs undertaken may be twice as great, there are frequently 3–5 trainees wanting to gain experience and "hands on" case experience is unavoidably less.

I am sure that I am not alone in finding that some attached SpRs have improved rapidly when exposed to a regular weekly list, an exposure that they were unable to achieve at their main teaching centre where teaching was otherwise excellent, simply because of pressure of the number of trainees on lists.

If the final decision is that units undertaking less than an arbitrary number of procedures (currently 250) are not to train SpRs, there are obvious consequences for training beyond further loading of the teaching centres which are already overstretched. It means that if an SpR is attached to a DGH at a late stage of training, when she is competent to undertake procedures independently, as judged by the main teaching centre, she will be unable to consolidate her skill at the DGH during the attachment. This is because it would be unwise from the clinical governance and medicolegal standpoint for a consultant or trust to allow anyone still defined as being a "trainee" near an ERCP if the unit is not a Joint Advisory Group (JAG) approved training centre.

The top centres in the country have practitioners the skill of which we all admire but few of us working elsewhere could ever approach. They provide excellent live demonstration teaching days and at times informal and friendly one to one advice from which we greatly benefit. Attendance at such live demonstration days should be a required component of all trainees' training and regularly considered for CPD by trainers.

Finally, my recent experience of SpR applicants for a consultant post had its illuminating aspects. The stated experience of some was such that they had apparently undertaken ERCPs independently on the equivalent entire average clinical load for a DGH for a three year period and this was for a post where ERCP was not required. I did wonder how trainers were maintaining any skill at all.

D BULLIMORE
Barnsley DGH Trust, Gawber Road,
Barnsley, South Yorkshire S75 2EP, UK
dwwbullimore@compuserve.com

Reinnervation after childbirth—a new paradigm for sensory bowel symptoms?

Visceral hypersensitivity has been identified as a significant feature in a proportion of patients with irritable bowel syndrome.[1] Reinnervation following a difficult intrapartum episode may be an important contributory factor. Many benign pelvic symptoms may be interpreted as pain or discomfort in response to touch (allodyniae or hyperalgesiae), including chronic pelvic pain, deep dyspareunia, urinary urgency, tampon discomfort, dysmenorrhoea, etc. Premature and prolonged maternal voluntary efforts in the second stage of labour appear to be significant aetiological features in women presenting with these clusters of sensory pelvic symptoms that include laparoscopically-negative pelvic pain.[1] Malpresentations, big babies, operative vaginal delivery, and excessive uterine activity may also contribute to the primary visceral denervation. Reinnervation has been demonstrated in the uterus, though an interval of five to ten years precedes the onset of sensory pelvic symptoms.[2] Similar patterns of reinnervation have been demonstrated in the vulva[3] and may occur in other pelvic viscera.

Anecdotal reports suggest that women treated with tolterodine tartrate (Detrusitol, Pharmacia, New Jersey) for irritative bladder symptoms, experience some improvement in sensory bowel symptoms—for example, faecal urgency and incomplete emptying. Precise questions about a woman's intrapartum history, medium term reinnervation, and different receptor systems may help to account for the neuropathic hypersensitivity that is such a feature of some forms of irritable bowel syndrome.

MARTIN QUINN
Department of Obstetrics & Gynaecology,
Hinchingbrooke Hospital,
Huntingdon, PE29 6NT, UK
martin.quinn@hbhc-tr.anglox.nhs.uk

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BOOK REVIEWS

Challenges in Colorectal Cancer. Edited by J H Scholefield (Pp230; illustrated; £69.50). Oxford, UK: Blackwell Science, 2000. ISBN 0 63205 116 7.

If asked to supply a subtitle for this excellent eminently readable book, I would suggest "All you ever wanted to know about the basics of colorectal cancer but were afraid to ask because you assumed that people would expect you to know already". The chapters are written by experts renowned in their field and each topic is dealt with comprehensively and clearly with the reader being led from one line of argument to the next in a satisfyingly logical way. Although aimed at the clinician rather than the scientist, where necessary the scientific evidence is given in sufficient detail without overwhelming the non-expert with technical jargon. Similarly, in this era of evidence based medicine, the authors are to be congratulated on choosing judiciously the most relevant clinical trials which help explain the development of currently accepted clinical practice. Areas of controversy (such as the use of total mesorectal excision (TME) in rectal cancer) are presented in a fair and (largely) unbiased way.

Perhaps a few more figures or diagrams might have been useful, although the easily readable text makes this less of a problem than it might have been (I assume the labelling of the first two figures in the chapter on adjuvant chemotherapy which does not correspond with the text will have been corrected by the time the book is published).

There are a few minor quibbles concerning details of individual chapters. The statement that in rectal cancer the use of TME to reduce local recurrence rates to less than 10% precludes the need for adjuvant therapy should have read adjuvant *radio*therapy—adjuvant chemotherapy is still indicated in these patients. The chapter on surgery for recurrent and metastatic disease deals mainly with local recurrence: it would have been interesting to have greater discussion of the role of surgery for hepatic and pulmonary metastases. A short historical introduction to the Dukes' staging system (although well known) and its modifications (perhaps not so well known) would have been appreciated in the chapter on pathology. Some readers may find a little too much technical detail in the otherwise excellent chapter on radiotherapy.

The authors of the chapter on adjuvant chemotherapy may have changed their emphasis on radiotherapy as the "prime adjuvant weapon" in rectal cancer if they had known the results of the recently published NSABP-R02 trial which showed that radiotherapy seems to be more useful at reducing local recurrence rates (which is probably more of a problem in the subgroup of patients with positive circumferential margins or who undergo suboptimal surgery) rather than improving overall survival: the clinical choice for adjuvant treatment in these patients is probably between chemotherapy alone or combined chemoradiation.

The chapter on future directions misses the opportunity to discuss in greater detail the potential of the new drugs irinotecan, oxaliplatin, and the oral fluoropyrimidines. A separate chapter on imaging techniques might be considered for the next edition, considering the increasing interest in virtual colonoscopy and the value of MRI in helping to determine the resectability of rectal tumours.

I am somewhat loath to mention these points as they are probably a reflection of individual opinion and certainly should not detract from this valuable book, which would be an excellent introduction for a registrar or SHO plunged into the field and expected to be a knowledgeable expert from the outset. Likewise, as the relevance of a multidisciplinary approach to colorectal cancer becomes increasingly important, it is essential that the specialist in one discipline keeps up to date with the current thinking in related specialties: a function which this books serves admirably.

M ALLEN

Surgery of the Anus, Rectum, and Colon, 2nd edn, vols 1 and 2. Edited by M R B Keighley, N S Williams (Pp 2702; illustrated; £285). UK: Harcourt Publishers Ltd, 2000. ISBN 0702023353.

This is a monumental effort and the editors, who have written much of this textbook themselves, are to be congratulated on a terrific job. They have taken on the task of reworking the iconic textbook first started by the late and great John Goligher. His was a very personal style, with repeated references to his own practice and results, and then a weighing of the evidence and a firm opinion, an approach which was much loved. With the growing emphasis on a larger body of evidence, the editors have widened their search in the world's literature and updated it for the now established specialty of coloproctology which tends to be surgical but spans the many disciplines looking after patients with diseases of the lower gastrointestinal tract. And here, despite the view that electronic publishing will consign many textbooks to history, is a second edition, tribute to its success and what Vie Fazio in his foreword calls the perspective "thing". There must still be a place for one or two prominent and authoritative reference textbooks in any specialty provided they are kept up to date, and I have no doubt this will continue to be just such a tome.

There is much here which will be of interest to gastroenterologists as well as surgeons. If you want to argue the point with your local surgeon, give a talk which includes some surgical outcomes, write a medicolegal report, or find a reference, it is all there. The style of the previous edition has been retained, with clear text, excellent line drawings, and helpful tables. The bibliography arranged at the end of each section is exhaustive and comprehensive. New sections have been added on medical management of anal fissure, newer treatments for incontinence, and the combined management of pelvic floor disorders. In inflammatory bowel disease, the place of newer therapies have been discussed, and pouch salvage procedures are reviewed. Cancer has been updated with additions to the whole area of biology, natural history, and hereditary and polyposis syndromes, as well as adjuvant therapy, The chapter on laparoscopy in colorectal cancer which includes length of stay and cost issues, anticipates the recent pronouncement of the NICE in concluding that open surgery still has room for improvement, and until specialisation and quality improve these results and there are clear advantages, laparoscopic resection must remain in abeyance outside clinical trials. A good examination of the place of local excision includes transanal endoscopic microsurgery but with so many surgical staff carrying out colonoscopy, the section on technique was rather short and the newer approaches to polypectomy, including endoscopic mucosal resection, and placement of clips and ligatures, and tattooing was disappointing.

Inevitably there are some gaps. Although the place of nitrites is reviewed for the treatment of fissure, the more recent introduction of calcium channel blockers and a growing disenchantment with GTN are missed. In the management of Crohn's fistulae, anti-tumour necrosis factor may have a profound impact on surgical practice but this too did not reach the cut. And the controversial new stapling procedure for haemorrhoids arrived too recently for inclusion.

These are minor criticisms however. Although it comes in two hefty volumes and at a similarly weighty price, this is a must have. It is in my view the finest reference textbook on the subject on both sides of the Atlantic, and will be taken frequently and enjoyably from the bookshelves in offices and studies of those who really care deeply about the management, medical and surgical, of these embarrassing, distressing, and challenging conditions. The owners will just have to make sure the books are returned.

N MORTENSEN

Practical Management of Oesophageal Disease. Edited by A Adam, R Mason, W Owen (£69.95). UK: Isis Medical Media Ltd, 2000. ISBN 1-899066-94-2.

The choice of title for a book can make or break its sales. Despite any caution or maturity of judgement we may claim, it seems we are all at risk of being seduced by books with titles such as " Improve your golf", or "Make the stock market work for you". Read the book and find the success/wealth/glamorous lifestyle or whatever that has eluded you up to now. *Practical management of oesophageal disease* is in this mould—the title hints not at a glamorous lifestyle admittedly, but at delivering the easy answers gastroenterologists would like to find for all oesophageal problems. And of course it does not deliver them. However, if expectations are tempered to the real world rather than fantasy, this is a useful book, written by people who know their subject, describing what they do and why.

In 12 chapters, the 20 authors give their own perspectives on the major topics in oesophageal disease. There is a surgical bias (for example, medical management of gastro-oesophageal reflux disease is covered in two

pages, surgical management in 12) which is not altogether unexpected with a mainly surgical authorship but it is not a problem once the reader appreciates that the book is a vehicle in which the authors explain their own approach to topics on which they are expert without necessarily dealing with every topic or every viewpoint. All topics considered are important in clinical practice. Approximately a third of the book is on oesophageal cancer, which is covered in breadth and depth, and in a way that offers something of real value for everyone.

In fact, this quality is the essence of the book—it has something in it of value to almost every gastroenterologist. For example, even physicians professing a major interest in the gullet may be just a little vague about the surgical technicalities of an Ivor Lewis oesophagectomy, and if they need the detail they will find it here. Upper gastrointestinal surgeons may welcome information about the otolarnygologists' views on modern management of pharyngeal pouch and hypopharyngeal carcinoma, and the explanation of a physiologist's approach to use of the oesophageal laboratory. Both medical and surgical gastroenterologists are likely to value clear expositions of the place of chemotherapy, radiotherapy, and multimodality treatments for patients with oesophageal cancer. For clinicians whose interest in the oesophagus ends with onward referral of patients who do not get better with a proton pump inhibitor, there is still something of value—they will at least be helped to interpret the clinical history.

The editors and publishers have done well—the book is easy to hold, easy to use, and easy to read. Reality being as it is, you will not find answers to all of your questions or solutions to all oesophageal problems, but it deals with many of them clearly and with evident expertise.

PS. If anyone knows of a short book entitled "Get yourself a perfect golf swing" or one on "How to make £££millions from derivatives", please let me know.

R C HEADING

Celiac Disease: Methods and Protocols. Edited by M N Marsh (Pp 300; US$99.50). Totowa, New Jersey, USA: Humana Press, 2000.

Michael Marsh's latest book on coeliac disease started out at a distinct disadvantage as I took it with a pile of novels to read while on a summer holiday in Provence. However, he need not have worried; this is a distinctive book and, to someone interested in coeliac disease, it came as a refreshing approach to the subject.

Marsh was charged with editing a volume in a new series on "*Methods in Molecular Medicine*". He was a good choice as he has spent virtually the whole of his professional life working on coeliac disease and, in particular, on the morphology of the intestinal mucosa. He has dedicated the volume to the late Anne Ferguson, who did so much to further our understanding of mucosal immunity, particularly in respect of coeliac disease.

The book starts with a good introductory chapter that clearly states the modern understanding of gluten sensitivity and clinically apparent coeliac disease. Then follow three chapters outlining genetic methods, ranging from DNA extraction through positional cloning to complex family studies. These describe the techniques, as used in Richard Houlston's laboratory, and are comprehensive with informative notes. However, they are not for the uninitiated in this area.

Tatham and colleagues have produced a good and easily accessible description of the modern classification of cereal proteins, as well as a detailed account of extraction, separation, and purification processes. Koning's group has written three excellent complementary chapters on characterising gluten peptides using mass spectrometry, on producing synthetic peptides for T cell recognition, and on identifying specific peptide binding regions on HLA-DQ molecules. Ludvig Sollid's group follows this with another excellent chapter on the establishment and use of gliadin specific T cell lines and clones. This is written by obvious leaders in this field and the accompanying notes reveal a wealth of useful technical detail for the budding researcher.

Marsh's group is responsible for two chapters on morphometry. The first is probably the best account yet that they have produced on their methods of morphometric analysis of small intestinal mucosa. The second chapter describes their methods for detecting changes in gluten sensitive rectal mucosa. These chapters are didactic and reflect the many years of careful observations made by Marsh and his coworkers. One wonders whether there is anything further to be measured in the small intestinal mucosa, but it is useful to have such a comprehensive account of these methods.

Riccardo Troncone and his colleagues describe the use of in vitro rectal gluten challenge as a means of studying immunological phenomena in coeliac disease. These are interesting observations but of limited usefulness. It is disappointing that the immune morphometric methods of Marsh are not used in these studies. I was sorry not to see a description of organ culture of small intestinal mucosa and the possibilities arising from it.

Paul Ciclitira's laboratory has a longstanding interest in in situ hybridisation techniques and there is a good account of these from workers with first hand knowledge of the problems and pitfalls, as well as the usefulness. Per Brandtzaeg is the acknowledged guru of gastrointestinal mucosal immunohistochemistry. His group provide two chapters, one on quantitative polymerase chain reaction for the assessment of cytokine mRNA expression, and a comprehensive one on immunohistochemistry. These chapters are extensive and detailed, with useful practical notes from an expert. Dieterich (on an ELISA for tissue transglutaminase antibodies) and Unsworth (on routine serological tests) provide two practically useful chapters for more routine diagnostic laboratories. Finally, the Edinburgh group, founded by Anne Ferguson, describes the technique and uses of whole gut lavage fluid analysis.

Marsh has assembled a group of international authorities on the various aspects he has chosen. The book achieves the aim of providing good working methods for many of the research techniques currently used in coeliac disease. One wonders about the readership of such a volume. I suspect it will be quite specialised but for those who, as Marsh says (page 8) want to "plunge into this complex pool of intrigue, this book should provide good introductory exposure". Ah well! From the wizardry of Marsh and colleagues, I return to the witchcraft of Harry Potter.

P D HOWDLE

NOTES

Sir Francis Avery Jones British Society of Gastroenterology Research Award 2002

Applications are invited by the Education Committee of the British Society of Gastroenterology who will recommend to Council the recipient of the 2002 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 or less on 31 December 2001 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 Birmingham in March 2002. Applications (TWENTY COPIES) should be made to the Honorary Secretary, British Society of Gastroenterology, 3 St Andrews Place, London NW1 4LB by 1 December 2001.

Hopkins Endscopy Prize 2002

Applications are invited by the Endoscopy Committee of the British Society of Gastroenterology who will recommend to Council the recipient of the 2002 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 2002. Applications (TEN COPIES) should be made to the Honorary Secretary, British Society of Gastroenterology, 3 St Andrews Place, London NW1 4LB by 1 December 2001.

Falk Symposium No 126: Hepatocyte Transplantation

This Falk Symposium will be held on 2–3 October 2001 in Hannover, Germany.Further information: Falk Foundation e.V. - Congress Division, Leinenweberstr. 5, PO Box 6529, D-79041 Freiburg, Germany. Tel: +49 761 15 14 0; fax: +49 761 15 14 359; email: symposia@falkfoundation.de

EASL Single Topic Conference

The EASL Single Topic Conference "Liver fibrosis: from basic science to clinical targets" will be held on 12–13 October 2001 in Florence, Italy. Organisers: Massimo Pinzani (University of Florence) and Detlef Schuppan (University of Erlangen-Nuernberg). The aim of the conference is to provide the latest information on this key area of hepatology and to translate the current knowledge into clinical terms. It is directed at both the expert in the field and the general hepatologist. Further information: Massimo Pinzani, Dipartimento di Medicina Interna, Università degli Studi di Firenze, Viale GB Morgagni, 85, I-50134 Firenze, Italy. Tel: +39 055 4277845; fax: +44 39 055 417123; email: m.pinzani@dfc.unifi.it

Lecture Course in Coloproctology

This course will be held on 15–17 October 2001 in Harrow, UK. Professor Russell Stitz from Australia will be the Sir Alan Parks Visiting Professor and, for the first time, there will be a Sir Francis Avery Jones Visiting Professor, which will be Professor Paul Rutgeerts from Belgium. Further information: The Administrator, St Mark's Academic Institute, St Mark's Hospital, Northwick Park, Harrow, Middx, HA1 3UJ, UK. Tel: +44 (0)20 8235 4046/8; fax: +44 (0)20 8235 4039; email: stmarks@ic.ac.uk; website: www.stmarkshospital.org.uk

International Symposium on Hyperammonemia, Liver Failure and Hepatic Encephalopathy

This symposium will be held on 20–22 October 2001 in Valencia, Spain. Further information: Cátedra Santiago Grisolía, Fundación Museu de les Ciències Príncipe Felipe, Ciutat de les Arts i les Ciències, Avda. Instituto Obrero, s/n, 46013 Valencia, Spain. Tel: +34 96 197 44 66; fax: +34 96 197 44 70; email: catedrasg@cac.es. **Deadline for receipt of abstracts is 15 July 2001.**

ICGH-2: The Second Iranian Congress of Gastroenterology and Hepatology

The main Iranian meeting of gastroenterologists and researchers in this field will be held on 27 October to 1 November 2001 in Tehran, Iran. Further information: Dr Shahin Merat, Digestive Diseases Research Center, Shariati Hospital, N. Kargar Street, Tehran 14114, Iran. Tel: +98 911 717 3966; fax: +98 21 225 3635; email: merat@ams.ac.ir; website: www.ams.ac.ir/icgh. **Deadline for submission of abstracts is 31 May 2001.**

Falk Symposium No 127: Autoimmune Diseases in Pediatric Gastroenterology

This Falk Symposium will be held on 8–9 November 2001 in Basel, Switzerland. Further information: see Falk Symposium No 126 above.

42nd Annual Conference of the Indian Society of Gastroenterology

This conference will be held on 23–29 November 2001 in Lucknow, India. The programme includes two pre-conference symposia (on gastrointestinal motility and scientific communication, on 23 November), a one day postgraduate course or CME (24 November), and an endoscopy workshop (28–29 November). Further information: Dr S R Naik, Department of Gastroenterology, SGPGI, Lucknow 226014, India. Tel: +91 522 440700 or 440800, ext 2400; fax: +91 522 440078 or 440017; website: www.sgpgi.ac.in/conf/isg2001.html

41st St Andrew's Day Festival Symposium on Therapeutics

This will be held on 6–7 December 2001 in Edinburgh, UK. Further information: Ms Eileen Strawn, Syposium Co-ordinator. Tel: +44 (0)131 225 7324; fax: +44 (0)131 220 4393; email: e.strawn@rcpe.ac.uk; website: www.rcpe.ac.uk

14th Intensive European Course of Digestive Endoscopy

This course will be held on 17–18 December 2001 in Strasbourg, France. Further information: Michele Centonze Conseil, 6 bis rue des Cendriers, 75020 Paris, France. Tel: +33 1 44 62 68 80; fax: +33 1 43 49 68 58; email: mail@m-centonze-conseil.com