Liver biopsy under ultrasound control

Editor,—I read the recent occasional viewpoint by Shah et al (Gut 1999;45:628–629) with much interest. The authors describe their regional practice of mandatory real time ultrasound guidance for percutaneous liver biopsy in all cases of suspected diffuse liver disease. However, the published literature does not convincingly randomised the universal adoption of such a policy.

The only prospective randomised study cited in support of their protocol, by Lindor and colleagues,1 is open to a number of methodological criticisms. In particular, in an unspecified proportion of the patients randomised to ultrasound guidance, the procedure was not actually performed under direct guidance and was instead immediately pre-ceded by a “biopsy room” ultrasound scan. The net result of this may have been to selectively raise the pre-biopsy scanning rates in the “ultrasound” cohort who were already more likely to have been previously scanned rather than the “blind” patients (76–78% v 67–68% in the respective groups).

In terms of the reduction in post-biopsy complications claimed by Lindor et al, the major impact was a reduction in hospitalisation due to pain. There was no statistically significant difference in the rates of bleeding or hypotension. The reduction in pain, in a non-blinded study, could have been due to several factors such as the patients’ perceptions of a “safer” guided scan or the potential for the physicians to more readily hospitalise patients with abdominal pain in the “blind” group.

There is considerable published data available regarding the safety of percutaneous liver biopsy without real time ultrasound guidance.2 3 Indeed, the British Society of Gastroenterology’s recent guidelines do not advocate changing from the practice of pre-procedural ultrasound scanning which will be part of the routine investigation of most patients with suspected hepatic disorders anyway) to biopsies performed exclusively by radiologists under imaging control1 and it is difficult to see how adopting such a policy nationally could be justified.

Finally, I would urge that too much gravity falls so readily from the pen that it is easy to forget that two distinct processes are involved: firstly, providing appropriate information and then obtaining consent from the patient. In attempting to combine these two steps, Shepherd and colleagues (Gut 1996;47:37–39) remove some of the patients’ essential safeguards. As stated in our paper, a similar situation is probably relevant in the failure of studies to detect significant differences in mortality due to the large numbers required. Clinical procedures are now the subject of appropriate monitoring. When clinicians fall below standard and imperil the safety of the patient, questions of competence are raised. The current concern about the safety of cardiac surgery has raised public awareness of the need for adequate training in all clinical procedures. The GMC and other professional bodies are looking at all aspects of day to day clinical practices and the moves towards structured training of junior doctors is part of these developments. Clearly there is a need to train gastroenterologists in endoscopic techniques—the need is no less for the practice of liver biopsy. “See one, do one, teach one” is an aphorism that will not stand up to scrutiny.

R J ASPINALL
Digestive Disorders Foundation Fellow, ICRF Molecular Oncology Unit, Imperial College School Of Medicine, Hammersmith Hospital, London W12 0NN, UK


Reply

Editor,—The technique used in the Lindor paper was somewhat of a hybrid between the “X marks the spot” (site usually marked in ultrasound department, and the patient transferred to the ward for the procedure) and real time ultrasonography performed in the department under continuous visualisation. In their paper, Lindor and colleagues performed an ultrasound immediately before performing the procedure within the department. Using Lindor’s method, the patient may move prior to biopsy, and intrahepatic vessels cannot be avoided. It is therefore an inferior technique compared with using the “real time ultrasound guided biopsy” method recommended by us. Nevertheless, the relevant statistical analyses from their study were as follows: two patients required hospitalisation in the ultrasound group compared with nine in the blind biopsy group (p=0.04), pain being the reason for admission in seven patients and pain plus hypotension in four. Bleeding occurred in nine patients in the ultrasound group versus 18 in the blind biopsy group (p=0.07). Simply stating that this last finding, which had a twofold difference, could have been due to insu-lar II error). As stated in our paper, a similar situation is probably relevant in the failure of studies to detect significant differences in mortality due to the large numbers required.

Clinical procedures are now the subject of appropriate monitoring. When clinicians fall below standard and imperil the safety of the patient, questions of competence are raised. The current concern about the safety of cardiac surgery has raised public awareness of the need for adequate training in all clinical procedures. The GMC and other professional bodies are looking at all aspects of day to day clinical practice and the moves towards structured training of junior doctors is part of these developments. Clearly there is a need to train gastroenterologists in endoscopic techniques—the need is no less for the practice of liver biopsy. “See one, do one, teach one” is an aphorism that will not stand up in the 21st century.

Dr Aspinall fails to mention what we consider to be one of the key results in the paper by Lindor et al; one of the patients in the blind biopsy group had to have emergency surgery for a damaged gall bladder. As stated in our paper, this situation can be virtually completely avoided by using real time ultrasonography. In the current climate, patients in whom a blind biopsy has led to perforation of the gall bladder, pleural cavity, or colon will seek legal redress for such blun-
EDITOR,—Shepherd and colleagues (Gut 2000;46:37–39) offer a timely and thoughtful contribution to the increasingly loud debate surrounding the practicalities surrounding the delivery of open access procedures, especially radiology. Their booklet is the first to openly address this problem that endoscopy is required for a particular procedure. It was foreseen many years ago that once an open access endoscopy service was made available it would become a high volume service, which can leave both endoscopists and patients vulnerable. Protocols for endoscopy have been in existence for some time but they are not always available. We think it must be regarded as a minimum standard of care that the consent obtained for these procedures is as informed as it can possibly be made, within the practicalities surrounding the delivery of service. Furthermore, we suggest that this booklet is the first to openly address this problem and that, judging by the response the authorship has had, many other colleagues throughout the country agree with our approach.

H A SHEPHERD
Winchester Gastrointestinal Units, Royal Hampshire County Hospital, Romsey Road, Winchester, Hampshire SO22 5DG, UK

Increased prevalence of methylenetetrahydrofolate reductase C677T variant in patients with IBD

EDITORS,—We read with interest the paper by Mahmud et al (Gut 1999;45:389–394). The study showed an increased prevalence of methylenetetrahydrofolate reductase (MTHFR) C677T variant in patients with inflammatory bowel disease (IBD). The C677T polymorphism is a known genetic cause of mild hyperhomocysteinemia (hyper-hcy) and may be associated with a variable degree of risk for thromboembolic disease in patients with IBD.1

To confirm a higher prevalence of the C677T polymorphism, we investigated 99 patients with established IBD for this polymorphism compared with 1084 unselected newborns. DNA samples were genotyped for the MTHFR (C677T) mutation. Patients were categorised as homozygous for the thermolabile variant (TT), heterozygous for the wild-type variant (CT), or homozygous for the wild-type (CC).

In difference prevalence between IBD patients and controls was compared using the $\chi^2$ test. Differences in onset of disease between patients with Crohn’s disease (CD) and...
and those with ulcerative colitis (UC) were compared using the Mann-Whitney test. A total of 16.2% (16/99) of IBD patients were homozygous for the C677T variant compared with 8.3% (90/1084) in the control group. This difference was statistically significant (p<0.009). When patients were stratified according to CD and UC, we found that homozygosity for the MTHFR C677T variant (TT) was present in 14.0% (7/50) of patients with CD and 18.4% (9/49) of those with UC. Both results were independently significantly higher than in the background population.

Onset of disease in carriers of the (TT) variant in CD and UC patients was 33.8 and 40.6, respectively, compared with 34.4 and 43.3 in non-carriers. This difference was not statistically significant. There was no correlation between disease activity indices of the IBD patients (Crohn’s disease activity index for CD and clinic activity index for UC) and carriers of the (TT) variants. Also, C reactive protein levels in IBD patients was independent of MTHFR gene prevalence.

Genome wide linkage screen of a large population of IBD patients found evidence of linkage of IBD to the short arm of chromosome 1 in all families investigated. It is interesting that the MTHFR gene is located on chromosome 1 (1p36.3). Additional loci on chromosomes 3, 7, and 16 are linked to IBD. The genetic basis of IBD is non-mendelian in nature and very complex. Unrecognised factors may therefore be important in the aetiology of IBD. Further investigation of other factors is being carried out in our laboratory at present.

J NIELSEN
T B LARSEN
I FREDHOLM
IBDCC and ISDND
Department of Clinical Laboratory, Vibe County Hospital, 7100 Vibe, University of Southern Denmark, Denmark

P MUNKHOLM
Department of Gastroenterology, Hvidovre Hospital, 2800 Hvidovre, University of Copenhagen, Copenhagen Denmark

H HEY
Department of Gastroenterology, Vibe County Hospital, 7100 Vibe, University of Southern Denmark, Denmark

Correspondence to: J Nielsen. (Email: JNN@vs.vejle amt.dk)


Reply

Editor,—Thank you for the opportunity to comment on the letter of Dr Nielsen and colleagues. We are pleased that their data have confirmed our findings, as previously recorded (Gut 1999;48:389-94). We agree with their comment that the genetic basis of inflammatory bowel disease (IBD) is very complex. One point needs to be emphasised, namely that serum homocysteine levels were increased in our patients compared with controls, even when those patients who were homozygous for C677T polymorphism were excluded. This elevated level was present even when the effect of folate deficiency was excluded. This suggests that other polymorphisms as yet undiscovered may be present in one or other of the three enzymes responsible for removal of homocysteine in internal metabolism, namely methylenetetrahydrofolate reductase, methionine synthase, and cystathionine synthase. Accordingly, it is important to emphasise that all patients with IBD should receive regular therapy with 400 µg of folic acid daily.

D G WEIR
N MAHMUD
A MOLLOY
J SCOTT
Department of Clinical Medicine, Trinity Centre for Health Sciences, St James’s Hospital, James’s Street, Dublin 8, Republic of Ireland

BOOK REVIEWS


Pediatric gastroenterology, and our knowledge about diseases of the small intestine in children, has grown rapidly over the last few years, owing to advances in the basic sciences, such as molecular genetics and, particularly, gut immunology. The purpose of this book is to provide the consultant paediatrician, as well as the trainees, with a review of the diseases of the small intestine in children. There are two major sections in the book: the first, more general, is focused on structure and mechanisms; the second, more specific, in which attention is given not only to the commoner and more important specific disease entities. This fourth edition of a book published in the past by John Walker Smith, and now coauthored by Simon Murch, reflects the long clinical experience of the first author. At the same time, it offers a thorough review of the most recent literature. The long clinical experience of the senior author, which is particularly evident in the chapter dedicated to necrotising enterocolitis, is now integrated by the strong clinical and research interest of Dr Murch in mucosal immunology. The value of the chapters dedicated to matrix (a topic to which Dr Murch has significantly contributed with his own research), and to the immune system of the small intestine in the first section of the book, and to coeliac disease and Crohn’s disease in the second one, is a proof of this special competence. Also very good is the chapter on laboratory assessment, although less convincing is the part of the same chapter that discusses the chief symptoms of the child with gastrointestinal problems (diarrhoea, vomiting). The appendix on special milks is especially useful. Overall, the editorial quality of the book is high.

In conclusion, this book is a very valuable reference not only for paediatric gastroenterologists, but also for general practitioners, medical students, and dieticians.

R TRONCONE


I enjoyed looking at this book. The editors’ intention is that “a moment’s notice, a surgeon may open it and consult an authority on a particular topic related to IBD surgery”. They have assembled an international group of contributors and there are excellent sections on history, surgical pathology, pouches, and Crohn’s surgery. There are some surprising omissions, however. A chapter on revision surgery for pouches that have gone wrong would have been timely, and a thorough review of balloon dilatation and stents would have provided a look to the future. I think the sections on septic complications of pouches and Crohn’s disease should have been kept separate.

I was irritated by the lack of uniformity in the illustrations and drawings of procedures, and in places the text is very dense, for example, in the section on ileostomy.

A final point: there is only one chapter on medical management just when there is an explosion of new medical therapy. Joint physician/surgeon management is seen by many as the ideal, and surgical treatment cannot be viewed in isolation: in my opinion, this is a comprehensive and well illustrated book that will be a welcome addition to the shelves of specialists in IBD surgery.

N MORTENSEN


This is a substantial book edited by Dr Michael Wolfe with six of his colleagues acting as section editors. Many of the hundred or so contributors are members of the Boston home team. The others are from the key centres in North America with a smattering of contributors from Canada, Europe, Israel, and South America. This is in effect a GI textbook, but stripped largely of pathogenesis, pathophysiology, diagnosis, and differential diagnosis. Five main sections consider treatment of oesophageal, gastroduodenal, pancreatic or biliary, hepatic, and intestinal diseases.

The two column black and white presentation is relieved by good summary tables, with small clear diagrams and figures within the two column format. No flashy colour or bullet points here, but good solid information.

Clear instructions to the contributors and careful editing has produced consistent and well balanced chapters. In fact, the excellent contribution from Stephen Hanson deals briefly with an approach to history taking, physical examination, diagnostic studies, and laboratory investigation in patients with inflammatory bowel disease. This is followed by an overview of individual patient
management and then the “meat” of the chapter reviews therapeutic options for ulcerative colitis and Crohn’s disease. The approaches to treatment in North America and in Europe were remarkably similar. International journals and meetings have moved the focus from the Atlantic Ocean to a trickle.

The chapter on non-variceal GI bleeding by Lichtenstein also provides remarkably consistent intercontinental advice, which is practical and appropriate and wherever possible evidence based. The detail is remarkable—for example, he has researched the history of iced saline lavage and concludes that water at room temperature is preferable.

I particularly liked the section on therapeutic endoscopy, which is a model of clarity and brevity.

Whichever chapter is selected, the information is consistent, reliable, and well researched. The chapter by Nicholas La Russo on primary sclerosing cholangitis opens with an excellent and brief review of the genetics, pathogenesis, clinical features, diagnosis, and natural history, and then considers potential therapy of cupruresis, immunosuppressant agents, antifibrogenesis, cholestatic agents, surgery, and transplantation.

Even in complex areas such as the contribution by John Del Valle, concerned with the treatment of neuro endocrine tumours, for each specific syndrome there is a crisp, clear summary of recommended treatment.

In summary, this is a remarkable, formidable achievement with consistent structure and advice, which is reliable and well based. Inevitably for a book of this size, the turnaround time results in the latest references not being included.