TPMT in the treatment of inflammatory bowel disease with azathioprine

We read with interest the recent article by Lennard on the role of thiopurine methyltransferase (TPMT) enzyme in predicting azathioprine related toxicity in patients with inflammatory bowel disease (IBD) (Gut 2002;51:143–6). He concludes that measurement of TPMT activity has no specific role in identifying the risk of significant bone marrow toxicity in long term users of azathioprine. This conclusion is in agreement with other published work and emphasises the importance of ongoing haematological monitoring of TPMT activity has no specific role in predicting azathioprine related toxicity in patients with inflammatory bowel disease (IBD) (mean duration 101 weeks/patient, range 2 weeks to 5 years). In our practice, we feel that significant toxicity during the early (<3 months) period of therapy could have been missed by strictly following existing guidelines.

Early detection of abnormalities in asymptomatic patients helped in dose adjustment with resolution of side effects. In addition, early detection of azathioprine related bone marrow suppression is likely to save lives. We recommend that gastroenterologists employ an extended (three month) period of intensive haematological monitoring after initiation of azathioprine therapy in IBD. Although neutropenia is occasionally observed beyond this point, intensive monitoring for the duration of treatment, which may continue for years, is clearly not practical from a patient or service perspective. However, this serves to emphasise the importance of continuous patient education concerning “alarm symptoms” throughout the duration of azathioprine therapy.

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References

Author’s reply
Measurement of thiopurine methyltransferase (TPMT) status, prior to the start of azathioprine therapy, has a role in identifying the TPMT deficient patient at risk of severe myelosuppression and TPMT heterozygous individuals who are prone to early myelosuppression.

The risk of azathioprine toxicity is well recognised but, as the authors state, the duration of early monitoring is a matter of controversy. The matter for debate is the time of onset of potentially life threatening myelosuppression.
Quasim et al state that this information is not available for inflammatory bowel disease (IBD). However, data can be derived from observations in other patient groups which may serve as useful guidelines for this time interval.

Reports of azathioprine induced severe myelosuppression in the TPMT deficient patient indicate that bone marrow toxicity is recorded after 3–10 weeks (median 4) of azathioprine therapy.1,2 In these reports the drug dosage varied from 1 to 2.9 mg/kg (median 1.7). One patient taking azathioprine at a dosage of 1 mg/kg developed myelosuppression (white blood cell count (WBC) 1.6x10^9/L, platelets 25x10^9/L) at 10 weeks’ while another dosed at 1 mg/kg developed myelosuppression (WBC 3.8x10^9/L, platelets 40x10^9/L) in the second week of therapy. The patient indicated that bone marrow toxicity is precipitated by the use of aminosalicylate derivatives for severe inflammatory bowel disease (IBD). However, data can be derived from observations in other patient groups which may serve as useful guidelines for this time interval.

Appendectomy and ulcerative colitis

Cosnes et al demonstrated that previous appendectomy is not only associated with a lower incidence of ulcerative colitis, but also with a less severe course of the disease. Although we can fully agree with this result, we disagree with the recommendation that appendectomy should not be considered a therapeutic option for patients with inflammatory bowel disease.


Screening and surveillance for asymptomatic colorectal cancer in IB

We would like to voice our concerns about some of the recommendations in the guidelines recently published by the British Society of Gastroenterology and Association of Coloproctology for screening and surveillance for asymptomatic colorectal cancer in patients with inflammatory bowel disease (Gut 2002;48:526–35).

(1) In the present medico-legal environment, failure to comply with guidelines which carry the imprimatur of respected national bodies will require vigorous defence should mishap occur. We do not believe the evidence is strong enough to justify the recommendation that every patient with extensive colitis of duration greater than 8–10 years should undergo regular colonoscopy. Firstly, it must be determined at each hospital whether it is feasible and considered sufficient cost effective to offer such a service within the constraint of local resources available. Secondly, if regular colonoscopy can be offered, then each patient should decide whether or not to accept regular colonoscopy after full discussion of its possible advantages and limitations.

(2) The success of colonoscopic surveillance programmes is disputed. Although some centres (including our own) have been protagonists for this approach, others have argued that it is not only labour intensive but also ineffective. Before imposing global national guidelines we should have firm evidence of a scheme’s efficacy or, failing this, we should have multicentre consensus. The guidelines, as published, appear to be the sincerely held opinions of a single consultant team based on their own research and assessment of the literature, followed by approval of a committee, but no indication is given of widespread consultation.

(3) The recommendations for patients with extensive colitis of surveillance every third year during the second decade of disease, every second year during the third decade, and annual colonoscopy thereafter are complex. The evidence for an increasing risk of cancer in the second, third, and succeeding decades of disease duration is controversial, and is not borne out by the unstratified figures for patients with severe disease based on 26 reported studies in the meta-analysis reported by the authors of the guidelines, although an increase was observed in stratified data.

(4) We have concerns about the benefits of routine colonoscopic examinations of taking two to four random biopsy specimens every 10 cm. This approach is time consuming for both the colonoscopist and the pathology department, and adds a considerable financial burden to the programme (which is not included in Eaden and Mayberry’s cost analysis).

In theory, the risk of a false negative examination is reduced as more biopsies are taken in practice the additional yield is very low indeed. During a recent study at St Mark’s Hospital, almost 3000 random surveillance biopsies from such patients yielded no dysplasia (unpublished data).

(5) Considering the disputed efficacy of current colonoscopic surveillance programmes for patients with extensive ulcerative colitis, it is inappropriate at present to extend this to default to patients with left sided colitis or (by implication) those with Crohn’s disease.

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Reference


Authors’ reply

We would like to thank Dr Forbes et al for their response to the guidelines published by the British Society of Gastroenterology (BSG) and the Association of Coloproctology of Great Britain and Ireland on screening and surveillance for asymptomatic colorectal cancer in patients with inflammatory bowel disease (Gut 2002;48:526–35). These comments raise a number of points which will be answered in turn.

(1) There are medico-legal implications of failing to comply with recommendations from a respected body but a guideline is precisely that—a guideline. They are not etched in stone and may need to be amended at future dates to continue to reflect best practice. The case of Wilsher v Essex Area Health Authority demonstrates how guidelines can now be made to practice to the highest standards. However, the courts (Early v Newham Health Authority) will consider local guidelines. This will be of particular importance in units that are unable to deliver standards that have been identified nationally, provided the local practice has been formulated into a local guide-

line. There is a wealth of data supporting the increased cancer risk in patients with ulcerative colitis and although evidence of the effectiveness of surveillance as practiced in expert centres is uncertain, such an approach is widespread. The purpose of guidelines is to identify good practice and lead to a uniform approach throughout the country. The alternatives are to abandon surveillance or to offer haphazard and unstructured (and ineffective) service. The acceptance of surveillance for both colitis and Crohn’s patients is estimated to be £9600 per annum.

Hopefully, as resources become available this cost but we realise funds may not be available initially which is one of the reasons for suggesting the guidelines are audited in five years. It is clearly stated in the guidelines that a discussion should take place between the doctor and patient informing them of their individual risk so that the patient can make an informed decision before embarking on a surveillance programme. Gone are the days of a paternalistic attitude, as patients should now accept some responsibility for their illness.

(2) Forbes et al raise the point that before any guidelines are imposed we should have firm evidence of a scheme’s efficacy. There are no randomised studies comparing different surveillance protocols or for that matter even surveillance and no guidelines are “evidence based”. Forbes et al are well aware, it will never be possible to provide grade A recommendations on this issue and the best we can do is to assess surveillance programmes retrospectively. Data are accumulating that surveillance participants have reduced morbidity and mortality, as outlined in the guidelines, and one of the signatories to your letter has stated that surveillance improves survival.

A national review of surveillance programmes from the Leeds group did not show any benefit from surveillance but the group had very stringent criteria. They felt inclusion of dysplasia alone as a measure of success was of debatable value. Therefore, they limited their audit to those eventually found to have cancer. They also decided to exclude patients in whom cancer was found at an initial colonoscopy undertaken at least 12 years after the onset of symptoms. We feel that finding dysplasia is the very aim of surveillance and because it is found on the first colonoscopy in a surveillance programme it should not be deemed a failure of surveillance.

As far as evidence that was possible as obtained before the guidelines were published. A national audit of the surveillance practices of gastroenterologists was conducted which revealed that although 94% of gastroenterologists performed surveillance, there was wide variation in practice. This alone suggests there would be little chance of a consensus opinion across the UK. Once the guidelines had been formulated, the Clinical Services and Standards Committee comprising of 40 individuals reviewed them. They then went through the usual guidelines process after being seen by the Clinical Services Committee and approved by the IBD section of the BSG. After this they were posted on the BSG website for six weeks to attract comments from other members of the society. The guidelines then went back to the Clinical Services Committee after amendments were made on the basis of comments from the wide range of consultants. Finally, the guidelines went before the Executive Committee of the BSG for a further review and signing off. Thus the guidelines evolved and accepted and published. They are not simply the opinions of two consultant gastroenterologists.
(3) We appreciate that increasing the colonoscopy frequency with increasing duration of disease is more complicated than 1–2 yearly surveillance. However, we are sure that it is not too difficult to calculate and it actually reduces the number of colonoscopies being performed initially, so this must be regarded as an increase in patient well-being and not a decrease in the present routine practice of some gastroenterologists.

The meta-analysis does show an increasing cancer risk in the second and third decades of disease. It is only stratified data that can be used in this way. Such data will give the most accurate estimate as it is only these data that included studies which reported cancer incidence stratified by decade and duration of patient follow up (19 studies). The decade specific incidence rates correspond to a cumulative risk of 1.6% (95% confidence interval (CI) 1.2–2.2%) by 10 years, 8.3% (95% CI 4.8–11.7%) by 20 years, and 18.4% (95% CI 15.3–21.5%) by 30 years.

The 26 studies Forbes et al refer to also included more serious studies which reported cancer incidence where only duration of patient follow up was reported—that is, the incidence rates were not broken down for each decade. Even when the cumulative stratified data were examined the cancer incidence still increased by decade of disease! The unstratified cumulative probabilites give a risk of 4.4% (95% CI 2.0–6.8%) at 10 years, 8.6% (95% CI 4.0–13.3%) at 20 years, and 12.7% (95% CI 6.0–19.3%) at 30 years.

Therefore, the strategy suggested is based on firm data. Of course the numbers of patients by the third decade are few but this is the nature of the beast. The use of a meta-analysis of cancer risk in ulcerative colitis overcomes the inadequacies of any reliance on smaller studies from single specialist centres.

(4) We accept that the cost of biopsies was not included in the cost analysis. There are numerous articles debating the number of biopsies which should be taken during a surveil lance colonoscopy. ‘Yes it is time consuming and we all know that to stand any chance of detecting dysplasia, the more biopsies taken the better. What is the point in surveillance at all if it is not conducted to the best standard. ’ Investigating the data from the unpublished STMark’s data how many biopsies were taken per colonoscopy. If for example only 10 biopsies were being taken at each examination, we would expect the chance of detecting dysplasia to be low.

(5) As patients with Crohn’s colitis have been shown to have the same cancer risk as patients with extensive ulcerative colitis, it would be doing them a disservice to exclude them from a surveillance programme. 3 4 Left sided colitis also carries an intermediate risk for colorectal cancer and as such our guideline lines reflect this. Indeed, one of the signatories to the Forbes et al letter has himself advocated a similar approach after discussion with the patients. 5

The guidelines were formulated on the best evidence available at present. Surveillance was being conducted in an extremely dissimilar environment. We appreciate that such a guideline is not acceptable in the current climate of clinical governance. The BSG has properly encouraged a national approach to cancer surveillance in a rapidly changing discipline. The principles, which underlie such an approach, are that of best practice throughout the country. The law no longer relies on the Bolam principle; rather we are now expected to practice to the best standards. 6 If we are to offer long term care to patients with inflammatory bowel disease we must discuss with them the nature of surveillance and its inadequacies. If patients then choose to have surveillance we are obligated to provide a service which reaches the highest standards—standardising practice is similar to those in other screening services.

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References
1 Wilsher v Essex Area Health Authority. (1986) 3 All ER 80.

Crohn’s disease: ethnic variation in CARD15 genotypes

Crohn’s disease shows significant variability in incidence between different world populations. For example, patients with inflammatory bowel disease we studied the annual incidence of Crohn’s disease in Caucasian, African, Asian, and Hispanic individuals, with an observed range from 4.6 per 100 000 population for Caucasian, 29.8 for African, 5.6 for Asian, and 4.1 for Hispanics. Recently, a genetic basis for Crohn’s disease has been described. 7 The CARD15 gene (NOD2, MIM 605956) acts as a sensor for bacterial products. When functioning correctly, this would lead to activation of nuclear factor κB1. Sixty-seven variations in the CARD15 gene sequence have been reported. 8 Of these 67, three variations (2104 6–8, 357 3–5, and 603 2–3) have been extensively assessed in patients of European, African, and Asian descent. The principles, which underlie such an approach, are that of best practice throughout the country. The law no longer relies on the Bolam principle; rather we are now expected to practice to the best standards. 9 If we are to offer long term care to patients with inflammatory bowel disease we must discuss with them the nature of surveillance and its inadequacies. If patients then choose to have surveillance we are obligated to provide a service which reaches the highest standards—standardising practice is similar to those in other screening services.

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References

Doctor or technician

In 1984, Sir Christopher Booth (President British Society of Gastroenterology (BSG) 1979) gave a lecture in Berlin on the effect of technology on clinical practice. He lauded the rapidly expanding benefits of diagnostic and interventional gastrointestinal endoscopy but was led to ask “Will the gastroenterologist simply become a technician who carries out a technical index but personally satisfying techniques?”

Most gastroenterologists remain general physicians but in talking with specialist...
An elderly man taking diclofenac for osteoarthritis and the patient recouperating, multiple diverticulae were found in the case. No 1, he was listed for OGD and colonoscopy. MCV 105, WCC 10.3, and platelets 240. As in melaena. After the weekend he was admitted. He felt faint, vomited black fluid, and passed faeces, described feeling a hard liver edge. A blood cell count (WCC) 6.6, and platelets 63. The patient was transfused and without further investigation the physician/gastroenterologist arranged for oesophageo-gastro-duodenoscopy (OGD) and colonoscopy.

At OGD the stomach was described as showing a moderate erythematous/exudative gastritis. At colonoscopy no abnormality was seen apart from a little fresh bleeding, the cause of which was not apparent. The patient was discharged to return the gold only to be admitted 36 hours later with faecal peritonitis. The colon had been perforated at the rectosigmoid junction. The patient recovered well from reparative surgery but died six weeks later of multorgan failure. At necropsy he was found to have cirrhosis of the liver. In retrospect, photographs of the gastric mucosa were consistent with portal gastropathy.

Case No 2

An elderly man taking diclofenac for osteoarthritis of the hip began drinking heavily after the death of his wife. One Saturday he felt faint, vomited black fluid, and passed melena. After the weekend he was admitted to hospital. His blood count showed HB 9.7, MCV 105, WCC 10.3, and platelets 240. As in case No 1, he was listed for OGD and colonoscopy. At OGD he was found to have a marked antral gastritis and multiple duodenal erosions in a deformed duodenal cap. At colonoscopy, multiple diverticulae were found in the sigmoid, one of which was thought to be an instrumental perforation occurred. The patient was referred promptly for surgery. There was little faecal contamination and the patient recovered well after resection of a short length of colon.

In both of these cases the physician-gastroenterologists appeared to be working to the dictum: bleeding from the gut requires OGD and colonoscopy. Yet in neither case was the need for colonoscopy clearly indicated. So was Chris Booth right to be concerned about what technology has done to gastroenterology? Or is it just fortuitous that I should be asked about these two cases so close to one another?

In the USA, many health care organisations suggest that this sort of issue should be addressed by paying more attention to the balance between underuse, overuse, and misuse of medical interventions. So perhaps the programmes for meetings of the BSG should not be just sectionalled by organ and disease processes. A section devoted to efficiency, care and safety in gastroenterological practice could gather together contributions having a direct and immediate bearing on clinical care. For as Sir Cyril Chantler said, when he was President of the Institute of Health Services Research in the USA, “Medicine used to be simple, ineffective and relatively safe. Now it is complex, effective and potentially dangerous.” And we should all remain aware of this.

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References

1 Booth CC. What has technology done to gastroenterology? Gut 1982;26:1088–94.

Which 5-ASA?

I read Dr Travis’ therapy update (Gut 2002;51:548–9) with interest; the topic is timely in a sector about to be challenged by new generic mesalazine brands. I note the choice of time dependent mesalazine (Pentasa) but, if mesalazine is to be relied upon to improve this situation. My interpretation of recent trials on UC treatment with 5-ASA does balsalazide (1.5 g twice daily) and mesalazine (0.5 g three times daily) maintained remission of ulcerative colitis but high dose balsalazide (3 g twice daily) was superior in preventing relapses. Gut 2001;49:73–9.

TIPS for gastric varices

We recently read with interest the study by Tripathi and colleagues investigating the outcome of TIPS in patients with gastric (GV) compared to oesophageal varices (OV). This study confirmed the previous finding of lower mean portosystemic pressure gradient (PPG) in patients with GV bleeding relative to those with a history of OV bleeding. Indeed in this study 35% (14/40) of GV patients compared to only 8% (20/232) of OV patients had a PPG <12 mm Hg. The group of patients who bled at PPG <12 mm Hg (group 1) is particularly intriguing. As mentioned by the authors, low PPG in GV patients has been associated with the presence and size of a spontaneous gastrorenal shunt (GRS) which is present in up to 85% of GV patients but present in only about 20% of OV patients. Previously, Sanyal et al. found that 50% (6/12) of patients who underwent TIPS for prevention of GV rebleeding failed to decompress the varices as documented by endoscopy. In 6 of these patients had a large GRS and a PPG <12 mm Hg. Thus, based on the presence of GRS in their patient population, perhaps documented by portogram taken at the time of TIPS? Also, did they document decompression of varices post-TIPS as an indicator of the clinical efficacy of the procedure? For example, it would be interesting to know if patients in group 1 failed to decompress varices post-TIPS more often than patients in group 2. Alternatively, we have experience of a number of patients with large GV who had a baseline PPG of <12 mm Hg and a large GRS. Following TIPS in these patients, there was a minimal or no reduction in PPG and filling of the GRS was not shown to be reduced on post-TIPS portogram.

Finally the authors noted in group 2 (baseline PPG >12 mm Hg) that lower PPG post-TIPS was associated with a lower risk of bleeding. Thus based on probability, the group 1 patients in the current study (both GV and OV) are likely to have had a spontaneous GRS already decompressing the portal system. It would be valuable to know if the authors have any data on the presence of GRS in their patient population, perhaps documented by portogram taken at the time of TIPS? Also, did they document decompression of varices post-TIPS as an indicator of the clinical efficacy of the procedure? For example, it would be interesting to know if patients in group 1 failed to decompress varices post-TIPS more often than patients in group 2. Alternatively, we have experience of a number of patients with large GV who had a baseline PPG of <12 mm Hg and a large GRS. Following TIPS in these patients, there was a minimal or no reduction in PPG and filling of the GRS was not shown to be reduced on post-TIPS portogram.

We agree that the presence of gastrorenal shunts (GRS) is likely to explain the low portal pressure gradient (PPG) post-transjugular intrahepatic portosystemic stent shunt (TIPS). Portography at the time of index TIPS insertion was primarily performed to identify varices and not specifically to look for the presence of GRS, although the splenic vein was visualised if not always in its entirety. Given these limitations, we have looked at the portograms of over 400 patients who have had TIPS for any cause, and identified shunts in 18.3%. A wider portographic review and a prospective magnetic resonance angiography study will be required to answer the questions raised. For the interim, we used a post-TIPS PPG <12 mm Hg as an indicator of the efficacy of the TIPS procedure for patients with both gastric and oesophageal variceal bleeding. In light of our findings we have revised our target PPG post-TIPS to <7 mm Hg.

Our finding of a lack of a statistical difference in the post-TIPS PPG of those patients who did or did not rebleed may be due to the small numbers in group 1. It may be that factors other than portal pressure such as variceal size and variceal wall tension play an important part in the risk of variceal bleeding in patients with a PPG of <12 mm Hg. It is also true that portal pressure directly affects the variceal wall tension, and attempts to reduce the portal pressure by a TIPS will be beneficial. We strongly believe that TIPS has a significant role in patients who have refractory gastric variceal bleeding, as mirrored by studies from others. At the present time it is the most effective non-surgical method of treating gastric variceal haemorrhage and preventing rebleeding. Other therapeutic options are promising, and we have previously reported on the effective use of human thrombin in the treatment of acute gastric variceal haemorrhage. However, controlled studies are required before universal recommendation for endoscopic therapies for gastric variceal haemorrhage.

References

Authors’ reply

ABC of Liver, Pancreas and Gall Bladder


The ABC Series are well established as handy reference guides but they sometimes struggle from not being clear about their target readership. Midway between a textbook and an update, this publication follows the usual format. The topic is covered from investigations used in liver and biliary disease to the clinical conditions themselves, ranging from gall stones to liver and pancreatic transplantation. Because of the nature of the clinical area, the book will probably appeal more to the hospital clinician than the general practitioner although the latter will gain much in having a source of reference for unusual and awkward clinical situations.

Although the list of topics is complete, there are still problems in interpreting some of the information for use in the pragmatic clinical setting. The section on gall stones, for example, while full of detail of anatomy and presentation does not make it any easier for the clinician trying to decide whether to refer the patient with stones or when cholecytectomy is indicated. It may well be that in some areas, such as gall stone management, clinical judgement still outdistances evidence but it would have been useful to have had
available evidence about different management approaches.

The book also has a feel of having been compiled by an upstream vineyard. Apart from a hepatologist, the other five contributors are all surgeons—it might have been useful to have had the perspectives of a general physician and a general practitioner, even if only to raise the pragmatic queries that arise at the earlier stage of management of hepatobilary problems. An example is the potential prophylactic management of patients with varices. As it stands, variceal management in this publication commences essentially after the bleed with only a few lines on prophylactic management, and even those largely dismissive of possible measures apart from the global use of beta blockers. So what should a primary care practitioner dealing with a patient who might have varices actually do, and at what stage of abnormal liver tests or clinical findings is referral likely? I have no doubt at all that my blood pressure is likely to rise with the knowledge that there is a liver problem. Many of them will rely on such publications as a ready source of information. Ease of care. Many of them will rely on such publications as a ready source of information. Ease of Care. Many of them will rely on such publications as a ready source of information.

Inhibitors

Therapeutic Roles of Selective COX-2 Inhibitors


The review editor sent me a book to review for Gut with holidays looming. He left a week before Christmas, and is currently observing whales off the east coast of the USA where I hope he will encounter the albino whale. I, on the other hand, am in a more peaceful location surrounded by the truly magnificent lochs, standing stones, stone circles, chambered cairns, duns, and crannogs on the Outer Hebridean island of North Uist.

The book Therapeutic Roles of Selective COX-2 Inhibitors is the latest in a series of similar books edited by Vane and Botling, and I have found it in many ways as interesting and extraordinary as my surroundings. It exceeded all expectations, bringing together some of the people that have driven the COX-2 story through from birth of a concept to a marketable drug.

Vane and Botling set the pace with an authoritative introduction, elegantly outlining the history, biochemistry, and physiology of COX and its clinical potential. In this book they gracefully allow etodolac and nimesulide into the privileged COX-2 selective club or, as they call it, the “COX-1 sparing drug” club. Then follow high quality chapters on the discovery and studies on rofecoxib and celecoxib along with discussions on the various test systems to assess selectivity. The exquisiteness of the first two chapters should not be missed. In the chapter on COX-2 in inflammation in experimental models kept me awake for the whole night. This is a true masterpiece at work.

At last (Ballou et al) a detailed and intelligent account of the lessons that we should have learned from the study of COX-1 and -2 deficient animals. Indeed, four, the knee jerk response, if not silence, to “unexpected” data obtained from these animals, such as the lack of gastrointestinal damage in COX-1 knock outs, simply allows prevailing simplistic theories on the role of the two enzymes to be maintained a bit longer. The following chapters on enzymes in nocioception, Alzheimer’s disease, neurodegeneration, and reflect the scope of the book. Whittle, Hawkey and Rodriguez could have combined their three chapters on the gastro-intestinal toxicity of NSAIDs as their knowledge is complementary. They invade each others “intellectual” territory which gives the impression of conflict and confusion where none exists. The chapter by DuBois on COX-2 in colorectal cancer is only disappointing because of its brevity; the man has so much more knowledge to share! However, this is partially compensated by an excellent review of the role of COX-2 in other cancers. The book ends with rather biased accounts on the virtues of each of the COX-2 selective agents.

This book is currently the best available reference source on a subject that is growing in importance and complexity. The only irritations are some unnecessary self-congratulatory comments and unashamed pleas for financial support that will raise the eyebrows of the purchaser of this book in Hay-on-Wye bookshops at the end of this century. I can thoroughly recommend it for all established prostaglandin and COX researchers, and PhD students. Gastroenterologists will find something new of interest. Those with time, concentration, and a biochemical background will surely enjoy this book as much as I did.

Aah! Catherine my lifelong companion has just brought me a wee dram (Talisker single malt whisky with 10% v/v local water). Life just does not get much better than this. My empathy is however marred by the knowledge that the COX-2 selective drugs are not available to the citizens of Cuba as a result of the USA’s embargo. Aah! Catherine my lifelong companion has just brought me a wee dram (Talisker single malt whisky with 10% v/v local water). Life just does not get much better than this. My empathy is however marred by the knowledge that the COX-2 selective drugs are not available to the citizens of Cuba as a result of the USA’s embargo. Aah! Catherine my lifelong companion has just brought me a wee dram (Talisker single malt whisky with 10% v/v local water). Life just does not get much better than this. My empathy is however marred by the knowledge that the COX-2 selective drugs are not available to the citizens of Cuba as a result of the USA’s embargo.

I Bjarnason

Drug-Induced Liver Disease


On the face of it, this hardback does not sound like a very good bedtime read and splashing out £195 might seem a little extravagant for what might appear to be some dry tome that would readily gather dust on a shelf. It was therefore with some trepidation that I received this ostensibly unwitting 773-page brick and green covered book, and turning the pages quickly, the casual reader might still be deceived into casting it into the nether regions of a desk drawer or the dimmer corners of an office. However, I am pleased to say that these were all poorly ground misapprehensions. Because of the expertise and very large casts of experts, covering the mechanisms of drug induced liver injury in an easily readable format (who cannot stand up and say that paracetamol/acetaminophen poisoning is a mystery to most mere mortals, despite the fact we all know the antidote?). The book also contains a comprehensive set of chapters on the hepatotoxicity of specific drugs for quick and easy reference, which is set firmly in clinical context, and for the generalist, a very useful clinical section on diagnosis and management of drug induced liver disease.

Another reason not to look at such a book might be that many of those emanating from the USA have an American perspective only, but this is a real exception as at least one third of the chapters are written by authors from countries as far apart as Switzerland and India and the book as a whole develops a truly international theme. It is well referenced in a very authoritative and up to date way, and sheds light on a whole host of topics that are both to gastroenterologists and to the generalist practitioner dealing with a patient who might have varices.
Prague Hepatology Meeting
To be held on 5–7 June 2003 in Prague, Czech Republic. Leading speakers from Europe and the USA will present new ideas and suggestions on pathophysiology, diagnostics, and therapy of liver diseases in ten programmes blocks. Further details: Ms Veronica Revicka. Tel: +420 241 445 759; fax: +420 241 445 806; email: veronika@congressprague.cz

Falk Symposia—New Findings on Pathogenesis and Progress in Management of IBD
Two symposia and a workshop will be held on 10–14 June 2003 in Berlin, Germany. Further details: Falk Foundation e.V., Congress Division, PO Box 6529, Leinenweberstr. 5, 79041 Freiburg/Br, Germany. Tel: +49 761 15 14 39; fax: +49 761 15 14 359; email: symposia@falkfoundation.de; website: www.falkfoundation.de

Gastroenterology and Endotherapy: XXIst European Workshop
This will be held on 16–18 June 2003 in Brussels, Belgium. Further details: Nancy Beauprez, Administrative Secretariat of the Workshop, Gastroenterology Department, Erasme Hospital, Route de Lennik 808, B-1070 Brussels, Belgium. Tel: +32 (0)2 555 49 00; fax:+32 (0)2 555 49 01; email: beauprez@ulb.ac.be

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 - see Falk Symposia above.

The Association of Coloproctology of Great Britain & Ireland
This annual meeting will be held on 7–10 July 2003 in Edinburgh, UK. Further details: Conference Secretariat, The ACGBI at the Royal College of Surgeons of England, 35–43 Lincoln’s Inn Fields, London WC2A 3PE. Tel: +44 (0)20 7973 0307; fax: +44 (0)20 7430 9235; email: acpgbi@asgbi.org.uk; website: www.acpgbi.org.uk

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: strae@asmb@proximedia.be; website: www.strae-asmb.com

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

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