LETTERS TO
THE EDITOR

Coeliac disease and birth defects in offspring

EDITOR,—I read with interest the paper by Martinelli et al (Gut 2000;46:332–335) and letter by Unsworth et al (Gut 2000;47:598) which stress the high prevalence of coeliac disease in anaemic pregnant women. Untreated coeliac disease can adversely affect the reproductive system and result in infertility, multiple abortions, low birth weight babies, and short breast feeding periods. 1 A low plasma level of folic acid is a common finding in newly diagnosed patients:2 there are good theoretical reasons for hypothesising that coeliac disease could also be a maternal risk factor for birth defects. 3 There were coeliac women identified in the study of Martinelli et al 4 that a further pregnancy and reached term. One of them had a boy with a maternal heart defects, and 24 mothers of coeliac disease at endomysium antibody screening, one of whom was con- firmed by biopsy. Both of these women were very short in stature but unfortunately no data on their folate status were reported. How much do these isolated numbers of women indicate a special risk of untreated coeliac women? Not very much: if we had to compare the data of Hozyasz with the mean expected prevalence rate among a cohort of women (with or without an unfavourable outcome of pregnancy), their values would be well within the 95% confidence interval of a rate of 1%. We reported a rate of 1:70 among fathers and mothers of children with and without folate dietary supplements. 4 Five additional cases were identified in the Blum trial, as randomisation was not performed and the presence of an incentive for categorisation positive was exploratory. In the Blum trial, the statistical analysis was not significant. In the pooled data from the BOND and OPERA studies, there was also an association between symptom relief and positive 

Reply

EDITOR,—Women affected by untreated coe- liac disease have indeed a considerable risk of having low birth weight babies and unfavourable outcome of pregnancy. Very recently in Sweden it was suggested that offspring of coeliac fathers are also at risk of low birth weight. 5 The mean birth weight of offspring of mothers and fathers affected by other autoimmune dis- eases. The authors of the large population based Swedish study suggest that there are “coeliac“ familial defects in children born to women using multivitamins containing folic acid periconceptionally. Lancet 1995;346:393– 6. 6 Shaw GM, O’Mally CD, Wasserman CR, et al. Maternal periconceptional use of vitamins and reduced risk for conotruncal heart defects and limb deficiencies among offspring. Am J Med Genet 1995;58:436–45.

of 12 trials reporting that the risk reduction with \( H \) \( pylori \) eradication therapy from the pooled data was 9% (95% confidence interval (CI) 4–14%). However, these results are in conflict with a similarly high quality meta-analysis of 10 trials which failed to detect a significant benefit of \( H \) \( pylori \) eradication (odds ratio for success 1.3, 95% CI 0.89–1.189). The positive and negative trial results in non-ulcer dyspepsia may be reconcileable if \( H \) \( pylori \) eradication only benefits those with hidden peptic ulcer disease or those predisposed to subsequently develop peptic ulceration which in turn is likely to vary across different populations. If this hypothesis is correct, then eradication therapy in a subset of patients with non-ulcer dyspepsia would be indicated (as the benefits should then outweigh the risks). In the absence of predictors which usefully identify a subset who will achieve symptom relief with eradication therapy, the decision to treat the infection is by necessity on a case by case basis.

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Conflict of interest: Professor Talley is a consultant for Astra Zeneca, Janssen, TAP, Pharmacia, Lederle, and GlaxoSmithKline.

Reply

Editor,—I am very confused by Professor Talley’s comments regarding the symptomatic benefit from omeprazole in \( Helicobacter \) \( pylori \) positive and negative subjects with functional dyspepsia. In his original paper, he states in the results section that “resolution of dyspepsia in the active treatment arms was not significantly different in the \( H \) \( pylori \) infected and uninfected patients” and in the abstract that “symptom relief was similar in \( H \) \( pylori \) positive and negative cases”. I was therefore very surprised to read Professor Talley’s letter in which referring to the same paper he states that “there was a small therapeutic gain observed in \( H \) \( pylori \) positive patients versus those who were \( H \) \( pylori \) negative”. He goes on to state that “in the \( H \) \( pylori \) positive group, 43% on omeprazole 20 mg had complete resolution of dyspepsia symptoms compared with 35% in \( H \) \( pylori \) negative patients”. However, therapeutic gain compares the benefit of the active treatment versus the placebo treatment. The therapeutic gain in the \( H \) \( pylori \) positive group on omeprazole is 9% and the therapeutic gain in the \( H \) \( pylori \) negative patients is 11% (fig 1). Therefore, contrary to the comments made in his above letter, Professor Talley’s original study showed that the therapeutic gain for omeprazole is similar or less in \( H \) \( pylori \) positive versus negative patients with functional dyspepsia.

Professor Talley also challenges the therapeutic gain achieved with eradication of \( H \) \( pylori \) infection in functional dyspepsia. There are only two recent high quality meta-analyses of \( H \) \( pylori \) eradication in functional dyspepsia published as full papers. These both showed unequivocal benefit of the active treatment over placebo. The other meta-analysis Professor Talley refers to has only appeared in abstract form and it is therefore difficult to comment on its quality. In addition, it did not include the most recent studies. None the less, even this study showed a strong trend in favour of eradication therapy over placebo (odds ratio for success 1.95 CI 0.98–1.6). Hence all of the studies and meta-analyses indicate that eradication of \( H \) \( pylori \) infection is superior to placebo in non-ulcer dyspepsia producing a therapeutic gain of about 10%. Although the magnitude of the benefit may not be large, it is equivalent to the only other treatment which is effective for this common disorder, namely proton pump inhibitor therapy. \( H \) \( pylori \) eradication treatment however has the advantage of producing this benefit by a one off course of treatment rather than requiring long term maintenance treatment.

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The future of ERCP training in the UK

Editor,—We read with great interest the leading article by Heller and Morris (Gut 2000;47:459–60) regarding the future of endoscopic retrograde cholangiopancreatography (ERCP) training in the UK. They discuss the importance of restricting training in ERCP to some trainees and training only in centres that are accredited for training by the Joint Advisory Group (JAG) in Endoscopy. JAG, at the request of the Royal Colleges, produced endoscopy training guidelines. For ERCP training, these state that a centre should be performing a minimum of 250 procedures per annum (with specialist centres performing 500 per annum). They should also have regular meetings to discuss radiological findings with a radiologist with special interest in ERCP. While we certainly agree with the importance of ensuring satisfactory training, we are concerned that the guidelines base competence for training in ERCP solely on the number of procedures carried out in individual centres. We have noted that larger centres often have several practitioners performing ERCP and several trainees learning. To determine the likely impact of the JAG recommendations on ERCP training and whether trainees were likely to have individual exposure to procedures in larger units, we performed a questionnaire based study, which was mailed to all acute UK hospitals. A total of 178 of 292 units replied (61%) to a single mailout (mailing list anonymous), of whom 151 (84.8%) were performing ERCPs. Forty teaching hospitals (THs 75.5%) and 74 district general hospitals (DGHs 61.2%) offered ERCPs per annum.

The service was mainly consultant based (92.1% of lists being consultant led). Gastroenterologists (68.0%), surgeons (29.2%), and radiologists (2.8%) performed ERCPs. The number of procedures performed per annum in DGHs was 40–800 (mean 228) and in THs 60–2000 (mean 336), 57.2% of which were therapeutic. Of those performing more than 250 procedures per annum, 82.1% of DGHs and 77.3% of THs held regular radiology meetings to discuss findings of those performing less than 250 procedures per annum, 72.9% of DGHs and 75.0% of THs held regular radiology meetings.

Each centre trained up to six trainees per annum, most training one or two. The average number of procedures which trainees could perform per annum was 176 (48–431) in DGHs and 144 (range 54–311) in THs. This was dependent more on the number of trainees per centre than on the type of hospital in which the training was performed with

I might as well get it off my chest first! This is not a good book and I did not enjoy reading it. I would not recommend that you read it or advise your library to purchase it.

In the first instance, the title of the book is wrong. It should be called ‘The John Hopkins’ Version of Evidence Based Surgery’: 90% of the multitude of authors involved come from that institution. One hesitates to say that the judgement of some of the authors seems to be clouded by institutional bias but words such as ‘prejudice’ and phrases such as ‘tunnel vision’ spring to mind. Like any North American textbook, the rest of the world largely does not exist: 90% of the quoted references are from North American texts with the token British author being a surgeon who wandered between the old fashioned ‘R’ and the newer ‘D’ notation to describe the extent of gastrectomy.


Reply

Editor.—We read with interest the letter and enclosed results of a survey on endoscopic retrograde cholangiopancreatography (ERCP) training. We, like the authors, have been concerned since the initial Joint Advisory Group (JAG) document that to a large extent competence is judged by numbers rather than other measures of endoscopy skills. Indeed, reliance on numbers has been the cause of most of the correspondence that JAG has received following the publication of the initial training document. However, at that time and to a large extent at present, there are few satisfactory measures of competence to replace numbers and time. The authors state in their letter ‘that only centres that are accredited for training by JAG will be permitted to continue endoscopy training’. Strictly speaking this is not true. Lack of recognition of a unit for training would mean that any training that takes place in that unit would not be recognised by the statutory bodies but this would not prohibit the units from training. They also state that ‘the guidelines base competence for training in ERCP solely on the number of procedures carried out in the individual centres’. The training does actually require a little more than numbers, for example the training document states that ‘endoscopists cannot be considered competent in ERCP until they are able to cannulate the desired duct in over 90% of cases and provide biliary drainage. Trainees should carry out at least 100 procedures under supervision and be achieving a high percentage of success before performing the procedure independently’. Nevertheless, the general message is accepted that we must be looking at quality rather than quantity.

Although it is clear that good opportunities do exist for gaining training in units undertaking smaller numbers of procedures, it is difficult to define a precise number that takes into account the needs of the individual trainee in getting the required experience and the numbers required for the trainer to maintain competence.

In the new JAG document, which we hope to publish in the next month, the emphasis has moved away from numbers to other measures of assessing competence. We are still of the opinion that those units with lower throughputs should combine with larger units to provide training as part of a regionally organised training scheme. Trainees are already organised regionally and decisions as to who will undertake ERCP training will be made in consultation with the regional training director. Several hospitals have already applied for, and been granted, ERCP training status on the basis of a combined training unit. A total of 747 units have now registered with JAG, of whom 115 have been approved for ERCP training.

The new JAG document makes it clear that trainees should undergo training on endoscopy specific skills. The first 250 pages have already been piloted by the Raven Department of Education at the RCS. In future, it will be essential for re-accreditation of units that trainees will have gone on such courses.

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Chairman—Joint Advisory Group in Endoscopy (JAG)

BOOK REVIEWS


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To be honest, some chapters were so stupefyingly boring that I just could not finish them, notably ‘Administrative Data and Evidence-Based Surgery’, although ‘Literating Information Technology’ ran it a close second! In the chapter on ‘Patient Reported Outcome Measures’, we are told thatause cause surgery is primarily palliative for oesophageal malignancies, quality of life assessment may be less important. While it is disappointing to see such nonsense in print, it does hearten me that we have nothing to fear on intellectual grounds from the so-called leaders of American surgery.

Turning to the second half of the book which is described as the ‘Practice of Evidence-Based Surgery’, individual chapters are given up to the recognised surgical specialties. The first six of these cover various aspects of gastrointestinal surgery. One of them, the chapter on colon surgery, is well written and should have been given to the other authors as an example of how to write a good chapter on an evidence based element of surgery. The chapter on oesophageal surgery is a classic example of, ‘what we do at Hopkins and why’. Of the 29 references quoted, only one was from a non-USA publication. The chapter on gastric surgery wanders between the old fashioned ‘R’ and the newer ‘D’ notation to describe the extent of gastrectomy. The author’s appraisal of the two European trials which compared D versus D2 gastrectomy is particularly superficial and appears to me as if he has only read the abstract or is content to make the same type of uncritical appraisal perpetuated by individuals who do not wish to see the major flaws in both of these trials.

The chapter on pancreatic surgery contains one of the best examples of institutional bias in the entire book. The author quotes his own prospective, randomised, placebo controlled, double blind study to test the hypothesis that erythromycin improves gastric emptying and reduces the incidence of delayed gastric emptying after pancreatico-duodenectomy. The text clearly states that patients who received erythromycin had a shorter duration of nasogastric tube drainage and started foods earlier, and I suppose one could point out that according to that study, the author was not lying because on average, the group receiving erythromycin had their nasogastric tube removed after 5.5 days compared with 6.2 days in the controls and they were able to start solid feeding at 11.3 days versus 12.8 days. You will not be surprised to know that these differences were not statistically significant and it makes you wonder why people should write in this way.

So now you have a fair idea of exactly why I did not like this book. It would make a good bookshelf, do not waste time on it and in particular, do not be tempted to part with £100.00.

D ALDERSON

www.gutjnl.com

Letters, Book reviews, Notes

An accessible practical text for doctors and senior health workers at first referral centres in developing countries is indeed a worthwhile objective and this WHO sponsored guide largely succeeds. An impressive list of contributors combine to produce a 160 page manual to common paediatric presentations which maintains throughout that these children can be managed successfully with a combination of good clinical assessment, basic diagnostic facilities, and a core of essential drugs.

Designed to complement the Integrated Management of Childhood Illness guidelines, it has the feel of a classic textbook with many simple black and white drawings and tables which are also refreshingly new, given over as they are to demonstrations of practical clinical assessment and diagnostic procedures. There is even an appendix of toys for severely malnourished children. There is also an excellent chapter on supportive care, and there are to feeding problems and management in an important theme throughout. Monitoring of children's progress and an encouragement to audit outcomes are welcome as is the pragmatic approach to human immunodeficiency virus. By virtue of the fact that it is designed with brevity and clarity in mind, it is very didactic however. The reader is not invited to question why for instance “very severe pneumonia” is treated with chloramphenicol, “severe pneumonia” with penicillin, and “pneumonia (non-severe)” with septrin. More leeway is given in the advice to monitor local antibiotic sensitivity patterns in treating Shigella and Salmonella infections. Many may appreciate this approach but some will not.

The text of the management of the sick child in a developing country should perhaps be best reviewed by a doctor in a developing country. I agree, but in my own mitigation I might add that I have been lucky enough to have worked for several years in Bangladesh and I have sent this copy onto a good home—the hospital library of the paediatric hospital where I was based. This book deserves a wide distribution and a cover price of Sw Fr 10.50 will help.

INFLAMMATORY BOWEL DISEASE


An accessible practical text for doctors and senior health workers at first referral centres in developing countries is indeed a worthwhile objective and this WHO sponsored guide largely succeeds. An impressive list of contributors combine to produce a 160 page manual to common paediatric presentations which maintains throughout that these children can be managed successfully with a combination of good clinical assessment, basic diagnostic facilities, and a core of essential drugs.

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The format of the book is very convenient and helpful to every physician, especially gastroenterologists who treat IBD patients and are frequently confronted with a specific problem or question related to their management and treatment. The 138 chapters cover practically every issue related to the management of ulcerative colitis and Crohn's disease. Readers will find up to date application of diagnostic tools such as computed tomographic scanning and ultrasonography to the handling of IBD patients. A significant number of chapters are dedicated to the medical treatment not only of straightforward IBD but also its complications, such as pouchitis, severe perianal disease and Crohn's disease. There is even an appendix of toys for severely malnourished children. This book provides gastroenterologists with in depth information regarding surgical options, their advantages, and disadvantages. Even though the chapters that relate to surgical intervention of IBD have been written by experienced surgeons, they are easily understandable by medical people, who are usually those who refer patients for surgery. Reading these pertinent chapters will enable the medical man to better understand what is to be expected from the intervention, its details, and place in the therapeutic approach to the treatment of IBD.

The book contains all of the necessary and most current information about the novel medical treatment of IBD. A special chapter deals with anticytokine therapy and another with novel manipulation of the inflammatory mediator pathways.

Another feature that characterises this book is inclusion of a rather unusual number of chapters on the humanistic aspects of the management of chronic IBD and patient-physician interactions.

Most of the chapters include a short list of additional references and a brief comment by the editor calling attention to other views and highlighting other areas of potential interest. Because of the broad spectrum of the book and because the 138 chapters have been written by different authors, repetitiveness is unavoidable and many issues are dealt with more than once. In spite of this drawback, the book is an excellent source of information, practical as well as basic. It will be helpful for clinicians who handle IBD who are looking for a comprehensive resource, containing pertinent information on almost every problem that may arise in the management of patients with ulcerative colitis and Crohn's disease.

The authors ride their hobby horses now and again, and theirs are not mine (I have never understood why sections stained specifically for elastic tissue, or to point up type I collagen, or with the periodic acid-Schiff technique in the absence of preliminary diastase digestion are so often among those referred for consultative opinion). Nor do I have much use for aspiration cytology of solid masses, rather than cysts, liver lesions which the authors now give half a chapter. If you have a needle in the liver, I say take a true biopsy specimen for a more certain diagnosis.

But, quibbles aside, I know of no better English language liver biopsy handbook than this one. It should be part of the microscopeside library of any pathologist whose practice involves the liver. There it will help him or her not only to do good work, but to hold higher expectations because as consultant internists and surgeons familiarise themselves with this book, the standard of practice of liver histopathology that they demand, as better informed consumers, will necessarily rise.

LIVER BIOPSY


Hirschsprung's disease, or congenital intestinal aganglionosis, was first described by Jacques Hirschsprung, a Danish paediatrician who gave the first description of the condition in 1886. At first the massive dilatation of the colon was believed to be caused by an abnormality within the dilated colon itself and the condition was therefore called "congenital megacolon". Sir Frederick Treves (1898) performed the first curative operation. While operating on a six year old girl he noted that although there was massive dilatation of the proximal colon, the lower sigmoid colon and rectum were narrow. He performed an abdominoperineal resection of the distal colon and rectum with anastomosis of the proximal colon to the anal margin. The
patient was known to survive at least until 67 years of age.

The true cause of the disease, which is a congenital absence of ganglion cells in the wall of a variable segment of rectum and colon, was not recognised until 1948. It is now known that this abnormality involves the whole of the autonomic nerve supply to the affected bowel and that the RET proto-oncogene, which is expressed in vari- ous cell lines derived from the neural crest, is a major gene for the disease. This genetic abnormality has provided an explanation for the relationship of the disease to other genetic diseases such as multiple endocrine neoplasia and the Waardenburg syndrome. The successful surgical management of congenital aganglionosis now depends on an accurate resection of affected bowel which is aided by the use of histochemical methods for the investigative assessment of the myenteric plexus.

The many facets of this congenital abnormality, which has an incidence of approximately 1 in 5000 live births, have resulted in fascinating studies by physiologists, morphologists, and geneticists. These investigations have led to the recognition of a whole range of abnormalities in the innervation of the gut which include hyperganglionosis and hypoganglionosis as well as the classical aganglionosis.

The book reviewed here is the second edition of a text on Hirschsprung’s disease first published by Holtschneider in 1982. It starts with a brief historical overview, which includes a good description of Swenson’s original pull through operation for the condition in 1948, a procedure designed to conserve the anal sphincter mechanism. The editors have endeavoured to provide a wide range of current knowledge which they have presented in three main sections—physiology and pathophysiology (including molecular genetics); clinical aspects of the disease; and techniques and results of surgical treatment. Fifty experts in various fields have contributed to the very comprehensive text. The first section is particularly noteworthy for the reviews of the development and functional anatomy of the enteric nervous system written by JHC Meyers and MD Gershon, respectively. These are nicely presented with excellent overviews of the basic sciences which is essential knowledge for anyone involved in research of these congenital conditions. The next two chapters focus on molecular genetics and the section concludes with discussions of normal colon function and pathophysiology.

The second “clinical” section includes chapters on the typical presentation of a range of congenital diseases of the enteric nervous system as well as the radiological, functional, and histological methods of diagnosis. RA Brown and S Cywes have also provided a useful summary of the remarkable number of malformations which have been described in association with Hirschsprung’s disease. This section could perhaps have been enhanced by inclusion of colour illustrations which would have increased the value of the examples of histochemical techniques.

The third “surgical” section begins with a comprehensive description of the six most commonly used surgical techniques in Hirschsprung’s disease, and here the presentation could have been improved by a more consistent approach to the artwork. Further chapters discuss the reported complications of the various techniques and outline their management. I felt that a critical review of these operative techniques, perhaps with a meta-analysis of published data, would have been of interest and might have helped surgeons to decide whether there is a “best buy” among all of these procedures. Consistency in the reference lists, some of which are arranged alphabetically while others follow a strictly numerical system, would also have removed an irritation.

In summary, this book provides a wealth of data about Hirschsprung’s disease and related abnormalities. Although there are a few weaknesses in the editing of the text and artwork I have no hesitation in recommending it as a very useful reference book for surgeons and gastroenterologists, both in their research work and clinical practice.

E R HOWARD

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 Endoscopy 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) 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 127: Autoimmune Diseases in Pediatric Gastroenterology

This Falk Symposium will be held on 8–9 November 2001 in Basel, Switzerland. Further information: Falk Foundation e.V., Congress Division, Linenheimerstr. 5, PO Box 6529, D-79041 Freiburg, Germany. Tel: +49 761 15 14 0; fax: +49 761 15 14 359; email: symposia@falkfoundation.de

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/igso2001.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, Symposium 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

50th Anniversary of the First Right Hepatectomy: from Resection to Dona­tion

This event will be held on 14–15 December 2001 in Paris, France. Further information: Michèle Centonze Conseil, 6 bis rue des Cendriers, 7020 Paris, France. Tel: +33 1 44 62 68 80; fax: +33 1 43 49 68 58; email: mail@m-centonze-conseil.com; website: www.m-centonze-conseil.com

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

GI Malignancies Can be Prevented and Treated: from the Bench to the Bedside

This international meeting will be held on 15–20 January 2002 at the Dead Sea, Israel. Further information: Secretariat, GI Malignancies, PO Box 29041, Tel Aviv 61290, Israel. Tel: +972 3 5175150; fax: +972 3 5175155; email: gis@targetconf.com