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) which stressed 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 folate acid is a common finding in newly diagnosed patients2; there are good theoretical reasons for hypothesising that coeliac disease could also be a maternal risk factor for birth defects.3 The seven coeliac women identified in the study of Martinelli et al had a further pregnancy and reached term. One of them had a boy with a major cardiac malformation; she was the only one on a gluten containing diet.

I examined sera from 40 mothers of children with non-syndromic spina bifida, 37 mothers of children with non-syndromic cleft lip with or without cleft palate, and 24 mothers of children with isolated cleft palate. I found that 1/40 and 1/37 women were positive for IgA class antiendomysium antibody (AEA). Jejunal biopsy of the mother of a child with cleft lip and palate showed normal villous height/crypt depth ratio and increased number of intraepithelial lymphocytes; jejunal biopsy of the mother of a child with spina bifida was normal. Both AEA positive women were two of the four smallest (<155 cm) among all investigated mothers (n=101). Coeliac patients have acquired the reputation of being 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 and the 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 report a rate of 1/70 among a general population of pregnant women which would be compatible with the number reported by Hozyasz. The increasing sensitivity of the screening tests now available for coeliac disease (antitissue transglutaminase and antigliadin antibodies) is likely to gradually change the estimate of the population prevalence of the disease, but also, repetition of screening over time increases considerably the rate of identification of previously negative cases.

I personally feel that we have little evidence that coeliac disease should be considered "...as a cause of birth defects associated with folate acid deficiency..." but I do agree that doctors and obstetricians should widely screen for coeliac disease as they do (often overdo) for many quite rare diseases.

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**References**

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 reconcilable if H. pylori eradication only benefits those with hidden peptic ulcer disease or those predisposed to subsequently developing 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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Letters, Book reviews, Notes
Conflict of interest: Professor Talley is a consultant for Astra Zeneca, Janssen, TAP, Pharmacis, Lederle, and GlaxoSmithKline.

Reply

Editor,—I am very confused by Professor Talley's comments regarding the symptomatic benefit from omeprazole in H. pylori positive versus negative subjects with functional dyspepsia. In his original paper,1 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 he refers 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 group 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 cases. I was disappointed to read Professor Talley's editorial on his original study is certainly not greater in H. pylori positive subjects.

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.2 3 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.4 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 1.2, 95% CI 0.98–1.6). Hence all of the studies and meta-analyses indicate that eradicating 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. As eradication treatment however has the advantage of producing this benefit by a one off course of treatment rather than requiring long term maintenance therapy.

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The future of ERCP training in the UK

Editor,—We read with great interest the leading article by Helier and Morris (Gut 2000;47:549–60) 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 Committee of Royal Colleges, produced endoscopy training guidelines.1 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 trainee 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 mailing (the response questionnaire), of whom 151 (84.8%) were performing ERCPs. Forty teaching hospitals (THs 75.5%) and 74 district general hospitals (DGHs 61.5%) offered ERCP procedures 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 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 44–311) 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

Figure 1 Relationship between number of procedures performed in centres per annum and average “hands on” endoscopic retrograde cholangiopancreatography (ERCP) experience of trainees. Results shown are mean (SEM).
the exception of three centres which train six or seven trainees and perform 600–2000 procedures per annum (summarised in fig 1): 32.5% of DGHs and 50% of THs had or planned to apply for JAG accreditation for ERCP training. At present, only 68 units were accredited for ERCP training. Despite this, 86.5% of DGHs and 90% of THs planned to continue with ERCP training.

Like the authors of this article and others preceding it, we believe that ERCP for every trainee is neither achievable nor desirable. We would urge that the revised JAG criteria should include guidelines to the number of procedures that may be trained in each centre according to the number of procedures performed. Otherwise the opportunity to train in smaller centres perhaps performs 200 procedures per annum but training a single trainee will be lost. Attention should also be paid to both the technical competence of the trainers and their ability to impart.

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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) recommendation 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 a smaller number 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 374 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 aspects. The first six of these seven units 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 trainers will have gone on such courses.

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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 “funnel 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 has been retired for the last two years.

The first 250 pages are devoted to the principles of evidence based surgery. Within these pages are a series of chapters which have little to do with any healthcare system outside the USA. For those of you who believe that the worst elements of American medicine usually do get across the Atlantic sooner or later, you might wish to dip into this section briefly, especially if you are in the brigade that is totally fed up with the Health Service and wonder just how it could get worse. This book is just the thing to convince yourself that fulfilment in the rest of your existence on this planet will not be in the field of clinical medicine.

To be honest, some chapters were so stupefyingly boring that I just could not finish them, notably “Administrative Data and Evidence-Based Surgery”, although “Leveraging Information Technology” ran it a close second! In the chapter on “Patient Reported Outcome Measures”, we were told that “because 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 a lot of 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 seven chapters are about 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 D, 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 pancreaticoduodenectomy. 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 can point out that 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. Although I don’t think that it is a good book, it is not a bad book and I did not enjoy reading it. I would not recommend that you read it or advise your library to purchase it.

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BOOK REVIEWS

D ALDERSON

An accessible practical text for doctors and senior health workers at first referral centres in developing countries is indeed a worth-while objective and this WHO sponsored guide largely succeeds. An impressive list of contributors combine to produce a 160 page manual to the most 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 solutions to feeding problems and nutrition is 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 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 to speak of the management of extraintestinal manifestations. Thirty two chapters deal with the surgical aspects of ulcerative colitis and Crohn’s. These chapters provide 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 understood 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 anticlotting 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.

A KNISELY


Hirschsprung’s disease, or congenital intestinal aganglionosis, was first described 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
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 recognized until 1948. It is now recognized 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 various 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 inoperative 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 hypoganglionosis and hyperganglionosis 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 colonic 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 feel 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 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 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, Leisterwegstr. 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/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

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: gi@targetconf.com