LETTERS TO THE EDITOR

Small bowel haemorrhage due to cytomegalovirus vasculitis

SIR,—We read with interest the report by Sackier *et al* (*Gut* 1991; 32: 1419–20) where the authors postulate a pathogenic role for cytomegalovirus in the small bowel of a patient on immunosuppressive therapy. Cytomegalovirus has been described associated with bleeding and ulceration of the upper and lower gastrointestinal tract in renal transplant recipients, although there has been no conclusive evidence that the virus is a pathogen in the gastrointestinal tract of these patients.^{1–3}

We have recently completed a prospective study of renal transplant recipients, obtaining endoscopic biopsies of the gastroduodenal mucosa for the study of cytomegalovirus. Immunohistochemical analysis of the specimens (mouse anti cytomegalovirus monoclonal antibody, Dako Ltd, High Wycombe, Bucks) revealed evidence of virus in 16 of 33 patients (48%). The virus was detected in the duodenum in 13 patients and in the gastric mucosa of six patients, three patients having both sites involved, and was found to involve surface epithelium and vascular endothelium. The presence of cytomegalovirus was significantly associated with histological duodenitis ($p=0.001$, Fisher's exact test) and was not associated with histological gastritis or with peptic ulceration. There was no significant relationship between cytomegalovirus infection and upper gastrointestinal symptoms. A prospective study by Alexander *et al* in liver transplant recipients reported a similar prevalence to our own and an association with duodenitis but not with dyspeptic symptoms.⁴

We feel that it is difficult to be certain that cytomegalovirus is a pathogen, and the histological changes witnessed by Sackier and other authors may merely be a casual association, reflecting the high prevalence of the virus in immunosuppressed patients.⁵ The vasculitis witnessed in their patient may have been because of the underlying disease process, as gastrointestinal involvement in Wegener's granulomatosis, while not common, certainly can occur.⁶

R P TEENAN
Department of Surgery,
Garnavel General Hospital,
Glasgow G12 0YN

W R MURRAY
Department of Surgery,
Glasgow Royal Infirmary,
Glasgow G4 0SE

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Reply

SIR,—It has been suggested by Teenan and Murray that the vasculitis witnessed in our patient may have been caused by the underlying disease process – that is, Wegener's granulomatosis, and that the presence of cytomegalovirus may have been a casual association, reflecting the high prevalence of the virus in immunosuppressed patients. The histological changes in the gut in our patient, however, were not compatible with Wegener's granulomatosis.

There have been numerous reports of cytomegalovirus causing bleeding and ulceration in the gastrointestinal tract.^{1–3} A recent report by Teixidor *et al*⁴ described 11 patients with AIDS and cytomegalovirus colitis and/or enteritis. Seven of the 11 patients had significant lower gastrointestinal tract bleeding, five of whom died as a result of it. Mucosal ulceration was present in the involved intestine and occasionally resulted in full thickness perforation of the bowel wall. The length of involved intestine is variable. Isolated cytomegalovirus colitis is more likely to involve the entire colon, whereas small bowel involvement tends to affect shorter segments. Occasional cases, however, have involved the entire gastrointestinal tract. Schwartz *et al*⁵ reported an infant with AIDS and cytomegalovirus infection which presented with massive life threatening lower intestinal haemorrhage. Arteriography was useful in localising a bleeding source before operation. The cytomegalovirus infection produced necrotising enterocolitis with deep ulcerations. Vasculitis was a prominent feature.

The mechanisms by which cytomegalovirus produces tissue damage are not known. Vasculitis has been reported in some cases and suggested as the basis for necrosis and ulceration.^{2,6–8} Muscle cell destruction has also been suggested as the basis for perforation.⁹

S B KELLY
J M SACKIER
D CLARKE
A J REES
C B WOOD

Departments of Surgery,
Renal Medicine and Pathology,
Royal Postgraduate Medical School,
Hammersmith Hospital,
London

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Adenocarcinoma and Barrett's oesophagus

SIR,—I read with much interest the article by Miros *et al* regarding the sequential dysplastic changes in Barrett's oesophagus (*Gut* 1991; 32: 1441–6). I found the article helped to improve the understanding of the pathogenesis of Barrett's adenocarcinoma. The authors, however, implied that if dysplasia is not detected in Barrett's mucosa those individuals should be 'endoscopically screened' less often. This latter point requires a word of caution and needs to be weighed against the potential risks of implementing such a policy.

First, the sampling error from a handful of mucosal biopsies, in a multifocal disease such as Barrett's mucosa, will be large and therefore more biopsies (six or more) and adjunctive use of brush cytology should be recommended.¹

Second, as stated in the article, the period of conversion from one type of metaplasia or dysplasia to a more premalignant variety is not yet fully established and therefore any time scale for subsequent re-endoscopy is at best empirical.

Third, individuals with Barrett's mucosa may also be more likely to develop carcinomas in immediately juxtaposed tissues – oesophageal squamous carcinoma² and possibly also gastric cardiac adenocarcinoma.³ Therefore, regardless of the presence or absence of dysplasia in the Barrett's mucosa, screening for premalignant lesions in these other areas should also be performed.

Fourth, by conventional screening techniques the three individuals found to have early adenocarcinoma in the present study either died postoperatively or were unsuitable for surgery. Therefore, the screening programme failed to make a desired impact on the incidence of oesophageal adenocarcinoma. This is partly because the markers of premalignant potential do not reflect any of the functional processes responsible for mitogenesis or oncogenesis.

It should perhaps, be emphasised therefore that the contemporary logic regarding who, how, and with what techniques to screen are highly unsatisfactory at present. In this regard we have shown that the expression of transforming growth factor alpha and epidermal growth factor receptors are significantly raised in dysplastic and malignant mucosa.⁴ In addition, we have also shown that flow cytometric analysis of the expression of transforming growth factor alpha and epidermal growth factor receptors can be a useful adjunct in the diagnosis and assessment of the prognosis of Barrett's mucosa.⁵

Finally, before clinicians exclude potentially well motivated patients from a screening programme perhaps we should first exclude those who have proven poor compliance at clinic visits and/or those who are more likely to develop complications from the endoscopy or subsequent surgery (those with respiratory diseases or ischaemic heart disease, etc).

J JANKOWSKI
Histopathology Unit,
Imperial Cancer Research Fund,
35–43 Lincoln's Inn Fields,
London WC2A 3PN

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Omeprazole versus ranitidine in the treatment of resistant duodenal ulcer

SIR,—Bardhan *et al* have clearly demonstrated the benefit of omeprazole in the therapy of refractory peptic ulcer (*Gut* 1991; 32: 435-8). It is well known that about 5-10% of peptic ulcers do not heal when treated with H₂ antagonists and are considered to be refractory. The optimal management of these patients is not yet established. Published data are contradictory about the efficacy of omeprazole therapy in patients with peptic ulcer that are resistant to the H₂ receptor antagonist treatment.^{1,2}

It is important, therefore, to take into consideration all experiences which could help us to find the best treatment. We have conducted a controlled randomised study to assess the efficacy of omeprazole 40 mg daily compared with ranitidine continued at the same dose in patients with duodenal ulcers that were refractory to the previous ranitidine treatment. Forty five outpatients were treated during this study. Patients with a duodenal ulcer of at least 5 mm diameter which did not heal after six weeks' treatment with 300 mg ranitidine were admitted to the trial. Endoscopy, performed at the beginning of the trial, showed active duodenal ulcer in all cases. Patients were randomly allocated to two groups – in 23 the ranitidine therapy was continued in the same dose (150 mg twice a day) and in 22 omeprazole 40 mg was given at bedtime. All patients received antacids for pain relief. No other anti-ulcer treatment was allowed.

The two groups were not significantly different as to age, duration of ulcer disease, smoking habits and alcohol consumption. Control endoscopy was carried out after 4 weeks' treatment. Omeprazole was significantly better than continued ranitidine therapy in healing rates of duodenal ulcers at the four week control endoscopy (healing rates: omeprazole group 19 (86%) patients; ranitidine 11 (50%) patients; χ^2 test: 7.81; $p < 0.01$). Omeprazole also gave better symptom relief than ranitidine. No side effects were reported and all patients completed the study.

Patients with unhealed ulcers received omeprazole (40 mg at bedtime) for a further four weeks. At the end of this period endoscopy was repeated and showed healed ulcer in all three patients from the omeprazole group and in nine of 12 patients from the ranitidine group.

Our results indicate that omeprazole is more effective in patients with duodenal ulcer that fail to heal with ranitidine treatment. Our findings agree with those of Bardhan *et al*, although in our study the previously unsuccessful H₂-receptor antagonist therapy was conducted with the same drug, and at the same dose in all cases and only patients with duodenal ulcer were included to the study.

Our results, obtained from strictly defined subset of patients with duodenal ulcer, confirm that omeprazole has a significant beneficial effect in the management of resistant duodenal ulcers.

Z TULASSAY
F SZALAY
M MACHARYA

Department of Internal Medicine,
Semmelweis University Medical School,
Budapest, Hungary

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BOOK REVIEWS

Diarrheal diseases. By Michael Field. (Pp 538; illustrated; US\$72.) New York: Elsevier, 1991.

This is just the sort of book that I wished that I had edited myself. To be truthful I nearly did except the idea of writing a book on 'Diarrhoea' was turned down by two publishers on the grounds that it was 'too specialised'. I am delighted that Michael Field has pulled it off and produced such a superb product. He has assembled approximately 30 experts in scientific and clinical aspects of diarrhoea from both sides of the Atlantic. The structure of the book is utterly logical moving from molecular mechanisms of diarrhoea through pathophysiology into two clinical sections describing the nature of clinically important diarrhoeal disease and their treatment. The book is a powerful data base for all those involved in laboratory and clinical research into diarrhoeal diseases. All chapters are extremely well referenced containing on average a hundred or more references. Most chapters are well illustrated although a few suffer from dense unrelenting text but the content is invariably of high quality.

I have few serious criticisms. Despite the impressive reference lists there are relatively few references beyond 1989, which is not uncommon for a book such as this but it is not beyond the wit of man to update the chapter during the final editing process. There is, however, one notable exception, namely the editor's own chapter on 'Intestinal ion transport mechanism' which is peppered with 1990 and 1991 references. Inevitably in a book of this nature there is overlap between chapters. The mechanisms of action of bacterial enterotoxins, for example, are covered in at least three chapters at slightly different levels of sophistication. Cross-referencing is by no means exhaustive and thus the reader needs to be willing to search the index and the chapters themselves to glean all there is on bacterial enterotoxins and their mode of action. When searching for deficiencies in the text one is always biased and notices omissions close to one's heart. The discussion of short bowel syndrome, perhaps more accurately called intestinal failure, is brief and limited to children. High output jejunostomy is an important clinical problem and more is known about the pathophysiology of the condition and its treatment than appears in this text. Similarly, the possible role of serotonin in

cholera toxin-induced intestinal secretion is mentioned in the basic science section of the book but serotonin antagonists for controlling intestinal secretion are not mentioned in the chapter on pharmacotherapy.

Despite these minor reservations this book should find a place on the shelves of all those interested in diarrhoeal diseases and is a must for biomedical libraries.

M J G FARTHING

Annual of gastrointestinal endoscopy. Edited by P B Cotton, G N J Tytgat, C B Williams. (Pp 175; illustrated; £60.) London: Current Science, 1991.

This publication is one of the Current Science series, which seeks to bring the reader up to date with a comprehensive review of the literature in a particular field for one year. In this issue the distinguished editors have involved established endoscopists from around the world to give a commentary on the literature in their particular field, and then at the end of each chapter a comprehensive list of references is given for 1990.

The book is well illustrated with colour endoscopic photographs, and is reader friendly. It is clear that the publishers have made a real effort to produce the annual as early in the year as possible, even though this has led to a number of typographical errors especially in the tables, but the standard of presentation is high. The 16 chapters deal with all aspects of endoscopy, and because the whole literature is reviewed the reader is brought up to date, with useful, practical comments from the authors. Some areas are developing faster than others so there are a variable number of references cited and commented upon in individual chapters. For example, endoscopy and upper gastrointestinal bleeding is in a large chapter, well reviewed, with a balanced opinion expressed on the new techniques in an exciting area. The use of monitoring in endoscopy inevitably has an American bias from its American author. The recommendations of the British Society of Gastroenterology, although well argued, are probably more practical for most endoscopists (*Gut* 1991; 32: 823).

Jerry Wayne concludes the book in typical punchy style, critically assessing some of the things that we do. There is an interesting chapter on developments in endoscopic instrumentation which are likely to be with us in the near future. This book can unreservedly be recommended for all active gastrointestinal endoscopy units. It is an excellent way of being kept abreast of changes in techniques and their application. This is an unusual case where an annual subscription is recommended!

D G COLIN-JONES

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