LETTERS TO THE EDITOR

Death from malignant disease after surgery for duodenal ulcer

EDITOR,—We note with interest that Macintyre and O'Brien found no significant increase in the incidence of colorectal cancer in patients who had undergone gastric surgery for peptic ulcer disease (*Gut* 1994; **35:** 451–4). While they correctly state that their findings do not support Caygill's hypothesis[1] (that is, the production of carcinogens by the post-surgery stomach acting at distant sites), it is important to recognise that in this study, as in several other reported series, most patients had undergone distal gastric resection (Billroth II 59·9%; Billroth I 1·1%) rather than truncal vagotomy and drainage (29·1%). These operations have differing effects on plasma concentrations of the antral hormone gastrin, and this may be important in determining the cancer risk.

Gastrin is trophic for colorectal mucosa and there is considerable evidence to suggest that the hormone may have a role in the development and progression of large bowel cancer. Gastrin receptors have been demonstrated on colorectal tumours[2] and gastrin stimulates the proliferation of normal and malignant colonic epithelial cells in vitro.[3] Furthermore, in experimental models of colorectal carcinogenesis, exogenously administered pentagastrin and surgical procedures that result in endogenous hypergastrinaemia enhance tumour yield.[4 5] The effect of truncal vagotomy in humans is to increase basal gastrin concentrations by up to fourfold, whereas distal gastric resection results in either no change or a decrease in circulating gastrin.[7 8] We would therefore be interested to know if Macintyre and O'Brien performed separate analyses of the operation groups and, if so, what were their findings?

Clearly the association between gastric surgery for peptic ulcer disease and colorectal cancer remains controversial. It is interesting to note, however, that two studies that have dealt exclusively with patients after vagotomy have reported an increased cancer incidence.[9 10] The number of patients who have had a vagotomy in published series ranges from 39[11] to 737[9] compared with many thousands of patients studied after gastric resection. It may well be that studies with greater numbers of patients and longer follow up will clarify the issue. Until such information is available, however, conclusions regarding the longterm implications of vagotomy in terms of colorectal cancer risk must remain uncertain.

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Reply

EDITOR,—We are grateful to Mr Duncan and his colleagues who raise an important issue in suggesting that vagotomy may predispose to subsequent colorectal cancer, because of the associated hypergastrinaemia, whereas gastric resection will not.

The evidence that hypergastrinaemia may predispose to colorectal cancer is, as they point out, controversial. Both of the clinical human studies that they cite came from the one centre and one of these studies was significant only at the 5% value.[1 2] The evidence from animal models is also conflicting with at least one study[3] showing no increase in chemically induced colorectal tumours after either vagotomy and pyloroplasty or polyagastrectomy. A more recent study has also failed to show any significant increase of colorectal cancer after vagotomy in rats.[4] A study reported from your correspondent's own laboratories has also shown a significantly lower tumour incidence in rats where significant hypergastrinaemia was induced by omeprazole.[5] The evidence suggests that while pharmacological concentrations from exogenous pentagastrin may predispose to colorectal cancer physiological concentrations of gastrin in animal models do not.

While we did not undertake a separate analysis on the operation groups to compare observed versus expected colorectal cancers from these subgroups, it seems unlikely that such as analysis would show any difference. There have now been 41 deaths from colorectal cancer in the patients undergoing gastric resection compared with only six after vagotomy. Even allowing for the fact that the person years at risk is greater in the first group a difference seems unlikely although we accept that it would be appropriate to perform such an analysis.

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Association between coeliac disease and autoimmune thyroid disease

EDITOR,—Collin *et al* report that, on the basis of a retrospective review of case notes, 5·4% of their patients with coeliac disease had autoimmune thyroid disease, and that this was not significantly greater than the prevalence of thyroid disease in a control group (Gut 1994; **35:** 1215–8). This does not agree with our findings.[1] In a prospective study of 107 patients with coeliac disease, all of whom were screened for thyroid disease and thyroid autoantibodies, we found that 14% (95% confidence intervals, 7 to 21%) had autoimmune thyroid disease (10·3% hypothyroidism, 3·7% hyperthyroidism). Although we did not have a control group, the numbers of coeliac patients with both hypothyroidism and hyperthyroidism were significantly greater than the numbers expected based on prevalence figures for thyroid disease in the United Kingdom.[1 2]

There may be several reasons for the difference in our results. Perhaps the most important is that prevalence figures based on retrospective review of case notes may be inaccurate. The symptoms and signs of thyroid disease are often mild and non-specific and, therefore, thyroid disease may be missed unless it is specifically screened for. The prevalence of thyroid disease – and other conditions with non-specific features – is therefore, probably underestimated in retrospective studies. In addition, the fact that the symptoms of thyroid disease may mimic those of coeliac disease[1] may lead to bias in its detection in retrospective case control studies. For instance, symptoms of fatigue, weight loss or diarrhoea in patients with coeliac disease may be attributed to the coeliac disease, while in control patients without coeliac disease, they may trigger a hunt for other causes such as thyroid disease. The definition of thyroid disease may also have differed between the two studies. We included all patients who had a past history of confirmed autoimmune thyroid disease even if they had been adequately treated and were euthyroid at the time of screening.

In conclusion, we feel that the true prevalence of autoimmune thyroid disease in patients with coeliac disease is higher than quoted in most previous reports. It is clinically important to recognise thyroid disease in patients with coeliac disease and so we recommend routinely checking thyroid function in all newly diagnosed coeliac patients.

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Reply

EDITOR,—Eighteen coeliac patients and nine control patients in our study suffered from autoimmune thyroid diseases. We included all patients who had a past history of autoimmune thyroid disease. It is possible that the increased frequency among coeliac patients is real, even though the difference was not statistically significant. The findings of Counsell *et al* suggest that the association between these diseases is more than coincidental. Supporting this, in another study that we conducted, four (4·8%) of 83 patients with autoimmune thyroid disease had silent coeliac disease, when they were screened by the IgA reticulin and gliadin antibody tests.[1]

It is correct that we did not search for autoimmune thyroid diseases vigorously among either coeliac patients or control patients. Some cases may have remained undiagnosed in both groups. We consider that prospective controlled studies would be essential to confirm the association between these diseases.

We agree with Counsell *et al* that thyroid function should be examined in all coeliac patients. Nowadays we also screen all patients with autoimmune thyroid diseases by reticulin and gliadin antibody tests.

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1 Collin P, Salmi J Hällström O, Reunala T, Pasternack A. Autoimmune thyroid disorders and coeliac disease. *Eur J Endocrinol* 1994; **130:** 137–40.

BOOK REVIEW

Constipation. Edited by M A Kamm, J E Lennard-Jones. (Pp 402; illustrated; £75.00.) Petersfield: Wrightson Biomedical Publishing, 1994.

What is a long time coming, solid, and makes a big splash? One answer is this book. Aside from a 1972 work by Sir Francis Avery Jones and Edmund Godding, *The Management of Constipation*, this is the first serious treatise on the subject since 1909 when Sir Arthur Hurst published his classic volume *Constipation and Allied Intestinal Disorders.*

It is a rich fruit-cake of a book with a world class team of contributors who cover nearly every aspect – from the role of sexual abuse to the role of the surgeon. In between, the physiologists, radiologists, and clinical investigators describe a range of techniques for unravelling bowel problems, which would have amazed and delighted Sir Arthur. He would have been pleased too by the emphasis on thorough and sensitive history taking. As someone who published on neuropsychiatric topics he would have been fascinated by the key role of biofeedback in treatment – a topic that is well covered.

The book is up to date with many 1993 references and some unpublished data (perhaps a bit too much). Most of the 45 contributors are concise and thorough, the editors themselves setting a fine example. There is occasional overlap, as in the two laxative chapters but, mostly, the editing is seamless. One visionary, Devroede, is given his head but then, he is irrepressible – and full of unexpected gems. Like how to diagnose hysteria: move your chair away, the patient will come closer; move it nearer, they will back away!

This book is not just about constipation. There are good reviews of colonic and anorectal physiology, of innervation and of neurotransmitters (at least 20 of which could be relevant to bowel dysfunction). Oddly, there is no detailed discussion of the act of defecation nor of the nature of stools, let alone of the psychology or sociology of defecation. These matters are, surely, crucial to understanding many cases of difficulty with defecation and I hope they will be tackled in the second edition. No doubt there had to be a section on Hirschsprung's disease, if only to bring genes into the book, but Chagas too?

But these are minor quibbles. It is a fine book that will become a classic. The price of £75 is not unreasonable and it should be in every self respecting gastroenterology department's library. There is much in it too for paediatricians and geriatricians. I for one shall refer to it often.

K W HEATON

NOTES

American Board of Internal Medicine

Information on the 1995 certification and qualifying examinations in gastroenterology can be obtained from the Registration Section, American Board of Internal Medicine, 3624 Market Street, Philadelphia, Pennsylvania 19104, USA. Tel: 1 800 441 2246 or 1 215 243 1500; fax: 1 215 382 5515.

Upper gastrointestinal tract

A meeting on Diagnostic and Management Decisions in the Upper Gastrointestinal Tract will be held at Fairmont Resort, Leura, NSW, Australia on 28–29 April 1995. Further information from Gastroenterological Society of Australia, 145 Macquarie Street, Sydney, NSW 2000, Australia. Tel: 61-2-256 5454 or 61-2-256 5417; fax: 61-2-241 4586.

Antineutrophil cytoplasm antibodies

The Sixth International ANCA Workshop will be held from 28 June to 1 July 1995 in Paris. Further information from the Secretariat: ANCA Workshop, c/o Ph Lesavre, Département de Néphrologie, Hôpital Necker, 161 Rue de Sèvres, 75743 Paris Cédex 15, France. Fax: 33 1 45 66 51 33.

Conference on gastroenterology

The Third International Conference of Gastroenterology will be held in Hong Kong and Shanghai on 10–17 November 1995. Further information from Conference Secretariat, c/o Orient Network (HK) Ltd, Room 1611-13, World Finance Centre, North Tower, Harbour City, Kowloon, Hong Kong. Tel: 852 736 7837; fax: 852 376 0329.