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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