LETTERS TO THE EDITOR

Utility of surveillance colonoscopy in ulcerative colitis

EDITOR,—We have read with great interest the article by Lynch *et al* (*Gut* 1993; 34: 1075–80) examining the utility of colonoscopic surveillance in ulcerative colitis. We cannot agree, however, that their findings negate the value of regular surveillance in patients with ulcerative colitis.

In their study, only one patient whose cancer was detected as a direct result of cancer surveillance was found to have a favourable Duke's stage A cancer. In contrast, the patient who defaulted and developed carcinoma three years after the last surveillance colonoscopy died of metastatic disease. Similarly, most cancer patients who did not receive surveillance were found to have advanced disease. Instead of showing the futility of surveillance colonoscopy, we believe these results suggest a trend toward its benefit, although the number of patients may have been too small to derive a meaningful conclusion.

Several explanations may be provided for their difficulty in showing the benefit of colonoscopic surveillance. For example, there was only one patient who developed cancer among patients under regular cancer surveillance. It is obviously very difficult to draw a firm conclusion on the utility of a surveillance programme based on such a small number. One explanation for the small number of carcinoma detected in their programme is that the study period may not have been sufficiently long. This is reminiscent of a similar difficulty we and others have encountered previously that could be overcome only after an extended study duration.¹ In addition, the comparatively short mean disease duration of 14.1 years suggests that these patients were at comparatively low risk for developing cancer.² This aspect of the study may have been further compounded by the fact that 26% of patients in the surveillance programme had defaulted and 10% had had colectomy for failed medical treatment, leaving a smaller number of patients available for analysis. Taken together, their difficulty in detecting the benefit of surveillance may have been the result of the comparatively small sample size and short duration of study, rather than a true 'failure' of colonoscopic surveillance.

We agree that the current surveillance technique may benefit from reassessment. Their recommendation, however, of screening colonoscopy at eight years followed by an expectant management may not be the optimal solution. The clinical course of the patient who developed metastatic disease after initial negative surveillance colonoscopies emphasises some of the problems with this approach. Others^{1,3} have also shown a similar problem with an expectant management after a negative 'screening' colonoscopy. Instead of abandoning it altogether, a method of improving the diagnostic yield of colonoscopic surveillance may be what is necessary.

This may include adjustments of sampling interval and timing of colonoscopy to better utilise the rectosigmoid predominance of ulcerative colitis-related neoplasia⁴ and the duration dependent exponential increase in cancer risk.² Other proposals have included analysis of various molecular markers of neoplasia in patients at increased risk. With the better understanding of the natural biology of colorectal cancer complicating ulcerative colitis, it is hoped that these modifications would further enhance our ability to predict patients at increased risk and thereby effectively reduce the mortality related to colorectal cancer in ulcerative colitis.

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Reply

EDITOR,—We are grateful to Drs Kim and Choi for drawing attention to our paper.

They point out that the patient whose cancer was detected as a result of direct cancer surveillance had a favourable Duke's stage A. We accept that some patients undergoing surveillance do benefit, our concern is that the discovery of one early cancer for 476 colonoscopies is not the best use of resources. Furthermore, the fact that more cancers occurred in patients who defaulted or were not recruited for surveillance is mirrored in other studies and draws attention to the fact that surveillance is also ineffective because in practice protocols fail to survey those subjects who are at risk. These findings are confirmed by Dr Choi's own recent paper in *Gastroenterology*.¹ Had all 2050 of their patients been colonoscoped on a two yearly basis as they recommend the pick up rate of early cancer per colonoscopy over 12 years' surveillance would have been 1:512 (assuming that those not surveyed would have behaved in the same way as those who were under surveillance).

The problem that arises from more avid surveillance and closer follow up is that even more colonoscopies have to be performed for a diminishing return of cancers. The fact is that the incidence of cancer in ulcerative colitis is such that regular annual and biannual colonoscopic surveillance will never produce better results than those already published and it is therefore difficult to justify this form of surveillance on a cost/benefit basis.

Drs Kim and Choi criticise the size of our study. It is in fact the third largest in the world medical literature.

We accept that the length of history in the patients we surveyed was only 14.1 years, however, any surveillance programme that recruits at eight years from onset is bound to

have figures skewed towards the lower end, particularly as some patients default or are operated on over the years. The mean disease duration to diagnosis of carcinoma in the nine patients who did develop cancer was 18.2 years (7–26) so the period of surveillance is not greatly different taking into account those who dropped out of the study.

We agree with the comments on potential new methods of screening.

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Duodenal ulcer pain – the role of acid and inflammation

EDITOR,—We read with interest the leading article by McColl and Fullarton (*Gut* 1993; 34: 1300–2). The authors argued that duodenal ulcer pain cannot be entirely due to the effect of duodenal acid on the ulcer crater and cited evidence for a weak correlation between the presence of active duodenal ulceration and epigastric pain. They suggested that duodenal ulcer pain is not directly related to the ulcer but perhaps to a combination of acid hypersecretion and mucosal inflammation, in the stomach as well as in the duodenum.

We agree that duodenal ulcer pain cannot be totally explained by the effect of acid on the ulcer crater. In our own studies on direct acidification of the duodenal ulcer crater in symptomatic duodenal ulcer subjects, ulcer pain was reproduced in only one third of cases.¹ We feel, however, that available data are still compatible with duodenal ulcer pain arising only from the duodenum. It is true that among patients with painful duodenal ulcer, correlation between ulcer pain and active ulceration is imperfect. In some,^{2–4} although not all⁵ of these studies, however, it is not stated whether residual erosive duodenitis was present in patients who were said to have healed ulcer. Erosive duodenitis may have the same significance as active duodenal ulcer in this respect in that there is a mucosal breach. In our own studies, we did not encounter subjects who remained actively symptomatic after total re-epithelialisation of their ulcer crater. Among treated asymptomatic subjects, however, whose last episode of pain occurred more than 24 hours previously, four of 14 with active ulcers developed pain compared with none of 20 whose ulcers have totally re-epithelialised ($p < 0.05$).⁶ This would seem to suggest that the presence of a mucosal breach in the duodenum may be important in the development of duodenal ulcer pain. The common finding of painless duodenal ulcer does not support the hypothesis that duodenal ulcer pain arises from inflamed antral mucosa as subjects with painless ulcer would be expected to have gastric mucosal inflammation also.

McColl and Fullarton did not consider the possibility that spasm or dysmotility may contribute to duodenal ulcer pain. Texter found that anti-cholinergics lead to cessation of gastroduodenal motility and abolishment of acid induced duodenal ulcer pain in 25 of 26 cases.⁷ Although other workers did not

find such a good correlation between motility and ulcer pain^{8,9} and although in our own studies the use of an anti-spasmodic did not affect the development of acid induced duodenal ulcer pain,⁶ we feel that duodenal wall tension or dysmotility deserve further study as a possible cause of duodenal ulcer pain and a possible explanation for the imperfect correlation between the pH around the ulcer crater and development of ulcer pain in patients with symptomatic duodenal ulcer.

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Reply

EDITOR,—We would like to thank Professor Kang for his constructive comments on our article. He suggests that the pain commonly experienced by patients with healed duodenal ulcers may be explained by erosive duodenitis producing small breaches in the mucosa. It does seem possible that such breaches may occur in severely inflamed duodenal mucosa and that they would be too small to be seen during endoscopic examination. Indeed, small and scattered breaches in the mucosa could also be missed with microscopic examination of endoscopic biopsy specimens because of the very small area of mucosa examined in this way. These small breaches would permit acidic gastric juice to penetrate the underlying inflamed mucosa and thus possibly lead to the pain. Such a process could occur both in severely inflamed gastric, as well as duodenal, mucosa and hence our suggestion that pain could result from the interaction of inflammation and acid at either site.

Microscopic breaches in the mucosa would be more likely in severely inflamed mucosa and thus the occurrence of pain may relate to the severity of mucosal inflammation as well as the degree of hyperacidity.

We agree also that spasm or dysmotility may play a part in duodenal ulcer pain. Such disturbed motility probably arises from neuronal stimuli triggered by the interaction of acid with the inflamed mucosa and would thus be a secondary, rather than primary, event. We agree, however, that the pain could originate from either events at the mucosal

level or from disturbed muscle function secondary to these mucosal events.

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Malabsorption and motor dysfunction in patients with small bowel amyloidosis

EDITOR,—It was with great interest that we read the article by Tada *et al* (*Gut* 1993; 34: 1412-7). The authors confirm our findings that it is not only familial forms of amyloidosis that cause intestinal motor dysfunction. In their fairly large series of patients they showed that amyloidosis causes either myopathy or neuropathy and that chemical types of amyloid, AL and AH, and AA respectively may determine which of the two factors will predominate the pathological findings and thus have repercussions on the clinical signs.

Recently we reported two cases of a non-familial form of amyloidosis with malabsorption and motor dysfunction.¹ The patient diagnosed as having Waldenström disease and AL amyloidosis was investigated for chronic, watery diarrhoea while the other patient diagnosed with Bechterew's disease and AA amyloidosis suffered from untreatable ferriprive anaemia but also with difficulties of swallowing, bouts of diarrhoea, and episodes of abdominal cramps. Malabsorption tests, among others the bile acid breath tests suggested malabsorption caused by motor dysfunction or bacterial overgrowth, or both. Amyloid deposits in the small intestine were shown in the submucosal blood vessels in case one (endoscopic biopsy specimens) and in the muscularis mucosae, the myenteric plexus, and submucosal blood vessels in case two (necropsy material).

Unlike Tada *et al* we cannot, however, confirm the difference in prognosis in the advantage of the AA amyloidosis. All their AL (n=2) and AH (n=1) cases died during follow up, while 62% of the AA cases (n=8/13) survived. The follow up of our first case (four years) was long but uneventful.

In the second case the clinical situation remained fairly stable for five years. Thereafter ischaemia induced necrosis of the terminal ileum was responsible for faecal peritonitis and death of the patient.

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Reply

EDITOR,—We are grateful to Drs Ectors, Geboes, and Rutgeerts for their comments on our paper. In patients with every type of amyloidosis, the prognosis seems to depend

on the extent and degree of amyloid deposits. Pathological examination of the necropsy specimens in our AL and AH cases showed extensive infiltration and replacement of the muscularis propria by amyloid deposits throughout the gastrointestinal tract. Therefore, we thought that they did not respond to any treatment and had a poor prognosis. Varying degrees of amyloid deposits in the gut, however, have been found among the patients with amyloidosis.¹ In the patients with AL or AH, as shown in a case of Fraser *et al*² some treatments may be effective and improve the life span until the amyloid deposits become extensive. As in the AA case of Ectors *et al*,³ submucosal vascular deposits, which were commonly and noticeably found in our AA cases, may produce life threatening symptoms. In amyloidosis patients with clinical manifestations of intestinal pseudo-obstruction, however, life threatening organopathy seems to be more common in AL amyloidosis than in AA amyloidosis.

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Iron deficiency anaemia

EDITOR,—I enjoyed the excellent leading article by Drs Sayer and Long (*Gut* 1993; 34: 1297-9), but differ from them when they state 'hiatus hernia alone seems unlikely to cause iron deficiency anaemia'. I showed that anaemia was 18 times more common in patients with hiatus hernias large enough to be seen on a plain chest x ray, than in age and sex matched controls.¹ Subsequently, Dr J A Higgins and I prospectively evaluated 109 patients with large hernias, having at least one third of the stomach above the diaphragm.² Endoscopy in these patients showed a correlation between anaemia and the presence of superficial linear erosions of the gastric mucosal folds where the body of the stomach was constricted by the diaphragm. We suggested that these lesions resulted from local trauma. Anaemia did not correlate with oesophagitis or peptic ulcers. We confirmed earlier findings by Holt *et al* that repair of the hernia prevented recurrence of anaemia.³

Having observed many subsequent cases in which no other cause for anaemia was found, my colleagues at this institution have generally accepted that large hernias can cause iron deficiency anaemia secondary to the erosions we described.

In my experience, this is a common cause of chronic blood loss anaemia in older patients.

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