target biopsy specimens can be obtained from an abnormal area.

It is true that a small proportion of patients develop carcinoma in colitis without dysplasia elsewhere in the colon and that dysplasia, when present, is usually patchy. The paper by Rasonhoff *et al*, however, is quoted as evidence that dysplasia at a distance from the cancerous lesion occurs in only 50% of colectomy specimens. This paper was based on histological blocks from only 22 specimens with cancer in colitis, complete resections were performed in only 11 of the patients, and more than five blocks were available from only 13 of the specimens. Some dysplasia at a distance from the tumour was found in 73% of specimens and high grade dysplasia in 50%. The authors suggest that one reason why the incidence of dysplasia was less than in other reports may have been due to limited sampling. Careful examination of 62 colectomy specimens with cancer in colitis at St Mark's Hospital has shown dysplasia at a distance from the tumour in 87%.

Dr Gyde selected three clinical studies for comment and we appreciate her remarks about the importance of high levels of follow up and of clinical care in regard to our surveillance programme. It is a pity that she made no reference to two excellent Swedish series,^{4,5} one recently updated,⁶ in which there has been no cancer death and in which the three tumours treated surgically were at an early stage (Dukes's A).

Like Dr Gyde, we would welcome the development of a new marker of neoplastic potential in colitis. Apart possibly from analysis of aneuploidy, which is complex and expensive, no such marker has been identified. Despite its limitations, dysplasia is still the only thoroughly tested marker we have and it should not be rejected.

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- 1 Lennard-Jones JE. Cancer surveillance in ulcerative colitis. *Proceedings of the Royal College of Physicians Edinburgh* 1990; 20: 272-8.
- 2 Lashner BA, Kane SV, Hanauer SB. Colon cancer surveillance in chronic ulcerative colitis: historical cohort study. *Am J Gastroenterol* 1990; 85: 1083-7.
- 3 Butt JH, Konishi F, Morson BC, Lennard-Jones JE, Ritchie DM. Macroscopic lesions in dysplasia and carcinoma complicating ulcerative colitis. *Dig Dis Sci* 1983; 28: 18-26.
- 4 Rutegård J, Ahlgren L, Stenling R, Janunger KG. Ulcerative colitis: cancer surveillance in an unselected population. *Scand J Gastroenterol* 1988; 23: 139-45.
- 5 Broström O, Löfberg R, Öst Å, Reichard H. Cancer surveillance of patients with longstanding ulcerative colitis: a clinical, endoscopic, and histological study. *Gut* 1986; 27: 1408-13.
- 6 Löfberg R, Broström O, Karlén P, Tribukait B, Öst Å. Colonoscopic surveillance in long-standing total ulcerative colitis - a 15-year follow-up study. *Gastroenterology* 1990; 99: 1021-31.

Reply

SIR,—Professor Lennard-Jones makes several important points in his letter concerning screening for colorectal cancer. Firstly, whether 'screening' or 'surveillance' is the appropriate term, given that the population screened are not 'healthy' members of the population. Ulcerative colitis patients benefit from regular follow up or 'surveillance' directed towards the disease process itself. Gastroenterologists add to this general 'surveillance' a screening test for colorectal cancer (for which these patients are at high risk) in the form of colonoscopy and multiple biopsies to

detect 'dysplasia.' As far as colorectal cancer is concerned these patients are 'healthy' and the screening test is introduced (as with any other screening test for cancer elsewhere in the body) to detect either precancerous changes or cancer at an early stage. To call this screening procedure 'surveillance' confuses the issue, since it is no different from other 'screening' procedures for cancer.

The other major issue is whether a randomised controlled trial would be a practical proposition. Professor Lennard-Jones suggests that patients might not agree to participate in such a trial, and that a survey among patients at St Mark's Hospital showed that few would accept random allocation. This might or might not prove to be the case but would become apparent in any event in the pilot study. A trial might be a daunting prospect but given European collaboration, the necessary numbers could be recruited quickly. In my view there would be little value in following self selected groups since, whatever differences in survival between the two groups were found, it would not be clear whether the differences were due to selection biases between the two groups or whether the differences were due to 'screened' versus 'non-screened.' Random allocation is an essential prerequisite for meaningful results.

It could be argued that screening for cancer in ulcerative colitis patients is screening a small group relative to, for example, population screening for colorectal cancer. The costs and workload generated are therefore relatively small and a colonoscopy may be little more trouble than a flexible sigmoidoscopy. Also very few patients come to any harm from the procedure itself. The situation, however, is still unsatisfactory while screening remains of no proved benefit.

There must be many district general hospitals in the United Kingdom with limited facilities and many patients who would willingly forego the procedure if they knew it was not of proved benefit.

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Long-term maintenance therapy with sucralfate

SIR,—Professor Blum *et al* report the superiority of sucralfate over placebo in the prevention of gastric ulcer recurrence.¹ They speculate that continued treatment with sucralfate may have theoretical advantages over longterm maintenance therapy with antiseecretory drugs, but fail to discuss the potential risk of aluminium accumulation. Administration of sucralfate (1 g twice a day) will result in a daily intake of 414 mg aluminium. The aluminium moiety of sucralfate can dissociate at a low pH,² and short-term administration of 4 g daily can lead to appreciable increases in serum and urine aluminium concentrations.^{3,4} Longterm administration of sucralfate (1 g twice a day) did not result in statistically significant increases in plasma aluminium in either of two small maintenance studies⁵ but animal experiments indicate that bony accumulation of aluminium may occur in the absence of raised serum concentrations.⁶

Sucralfate may prove to be effective and safe for the prevention of gastric ulcer recurrence. However, further studies of aluminium accumulation from longterm use are likely to be needed before this drug can be widely

recommended as an alternative to antiseecretory agents.

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- 1 Blum AL, Bethge H, Bode JCH *et al*. Sucralfate in the treatment and prevention of gastric ulcer: multicentre double blind placebo controlled study. *Gut* 1990; 31: 825-30.
- 2 Nakazawa S, Nakashima R, Samloff M. Selective binding of sucralfate to gastric ulcer in man. *Dig Dis Sci* 1981; 26: 297-300.
- 3 Haram EM, Weberg R, Berstad A. Urinary excretion of aluminium after ingestion of sucralfate and an aluminium-containing antacid in man. *Scand J Gastroenterol* 1987; 22: 615-8.
- 4 Pai S, Melethil S, Cuddy P, Hall T. Elevation of serum aluminium in humans on a two-day sucralfate regimen. *J Clin Pharmacol* 1987; 27: 213-5.
- 5 Allain P, Maura Y, Krari N, Duchier J, Cournot A, Larcheveque J. Plasma and urine aluminium concentrations in healthy subjects after administration of sucralfate. *Br J Clin Pharmacol* 1990; 29: 391-5.
- 6 Kinoshita H, Kumaki K, Nakono H *et al*. Plasma aluminium levels of patients on long term sucralfate therapy. *Res Comm Chem Pathol Pharmacol* 1982; 35: 515-8.
- 7 Bolin TD, Davis AE, Duncombe VM, Billington B. The role of maintenance sucralfate in the prevention of duodenal ulcer recurrence. *Dig Dis Sci* 1986; 31 (suppl): 283S.
- 8 Burnatowska-Hledin MA, Mayor GH. The effects of sucralfate ingestion on serum and specific tissue aluminium concentrations in normal rats. *Clin Toxicol* 1984; 22: 87-93.

Reply

SIR,—MC Allison mentions in his letter experiments in rats which showed an increase of bone aluminium concentrations. This finding, however, could not be confirmed in patients receiving 4 g sucralfate daily for 8-10 weeks before total hip replacement. There was no increase of bone aluminium concentration compared with a control group.¹

Aluminium toxicity is mainly discussed in connection with uraemic patients and the application of high dose aluminium hydroxide as a phosphate binding agent. There is no evidence that longterm maintenance treatment with sucralfate in the recommended dosage in patients with normal kidney function will lead to unwanted side effects.

It should finally be mentioned that sucralfate is approved for the maintenance treatment of duodenal ulcer in several countries; recently it was approved for this indication also by the Federal Drug Administration in the USA.

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- 1 Bannwarth B, *et al*. Longterm sucralfate therapy. *J Rheumatol* 1986; 13: 1187.

BOOK REVIEWS

Liver transplantation. Edited by T E Starzl and Anthony J Demetris. (Pp 194; illustrated; £42.50.) London: Wolfe, 1990.

This monograph written by Starzl and Demetris is an up to date summary of liver