We hope that the open access endoscopy service together with the feedback of information will enhance their skill at dealing with these problems. We have already shown that this takes a lot of the burden off the specialist clinics so there is more time to spend with patients with additional complications.

A reduction in gastroscopies is not necessarily a cost effective measure. We are looking at a wide range of outcome measures from the open access endoscopy service. The value of a negative endoscopy is rated highly by general practitioners and also by many patients. A wider view must be taken and factors such as the pressure on time in clinic, waiting times for clinic, numbers of visits to the general practitioner, and inappropriate treatments should all be considered. We already have some data suggesting that general practitioners do treat patients appropriately after open access endoscopy and we have identified appropriate changes in treatment.

Patients may have a natural tendency to prefer assessment in a hospital specialist clinic. This could apply to a variety of problems such as headaches or skin problems. The Darlington study on patient preference quoted in the letter was not a comparison with open access endoscopy. We understand that the patients were asked if they liked to be seen in a hospital clinic as well as having a gastroscopy. It does not follow that referral for secondary health care is a necessary or efficient use of resources.

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Antibodies to *Mycobacterium paratuberculosis*

EDITOR,—The recent paper by Stainsby *et al* concerning *Mycobacterium paratuberculosis* is a reminder of the generally held suspicion that Crohn's disease is caused by a transmissible agent (*Gut* 1993; 34: 371–4). No such transmissible agent, however, has been identified.¹ The agent, which results in inflammatory changes characteristic of Crohn's disease seems to be inadequately degraded by macrophages. This leads to an inflammatory change characterised by a granuloma. This suggests either an organism, which by its nature is resistant to macrophage action or alternatively that the macrophage population is somehow impaired and unable to cope with an otherwise innocent organism.² It is not unreasonable to look for the cause of this disease among those organisms that have cell walls resistant to macrophage activity and that are not readily grown on conventional bacterial growth media. An anaerobic fungi saprophytic in ruminant digesta has recently been discovered and distinct species have been described including *Neocallimastix frontalis*, *N. patriciarum*, *Sphaeromonas communis*, and other as yet unidentified strains.³ These organisms contain chitin in their walls, which make them less susceptible to macrophage digestion. Their widespread distribution in the ruminant make them a possible cause of Crohn's disease therefore we looked at seven patients with Crohn's disease and two with ulcerative colitis with active disease tested by histology and by anaerobic culture.

Freshly voided faeces (diluted 1 vol:1 vol diluent) were immediately transferred to anaerobic diluent (medium M2 of Hobson),⁴ modified rumen fluid, sugars, starch, and lactate. Anaerobic conditions were maintained using an atmosphere of 100% CO₂. It was calculated that the limit for detection of the cultural methods used was about 10 fungal propagules/ml. No growth of anaerobic fungi was seen after anaerobic culture at 37°C for seven days. Previously obtained biopsy tissues from these patients, mucosal or full thickness portions of inflamed bowel tissue were examined under light microscopy after staining for fungi with either periodic schiff (PAS) and the Grocott-Gomori methenamine silver stain for fungi. Careful examination of the cultures by light microscopy failed to show any organism resembling fungi. Similarly, careful examination of the tissues histologically using a series of sections failed to show any fungi.

From these results it seems that these anaerobic fungi are unlikely to participate in the cause of inflammatory bowel disease.

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Reply

EDITOR,—I found Dr Eastwood and colleagues' report of a negative search for anaerobic fungi in Crohn's disease of particular interest. The criteria justifying such a search, based on characteristics required of any putative agent responsible for the inflammation of Crohn's disease, are, perhaps, as valid for fungi as mycobacteria. Despite our mainly negative report, however, on the association between mycobacteria and Crohn's disease, quoted by Dr Eastwood, we feel that the evidence for a mycobacterial cause for Crohn's disease is stronger now than it has been before. In his recent review,¹ Dr Ciclitira also quoted our study as negative evidence of a role for mycobacteria in Crohn's disease and was critical of the more positive study of Elsaghier *et al*.² I believe, however, the two papers highlight the requirements of a successful study of humoral immunity directed at *Mycobacterium paratuberculosis*. In our report, in which we failed to show raised antibody titres to this organism in patients with Crohn's disease, we commented on the high degree of cross reactivity between *M paratuberculosis* and environmental species of mycobacteria, such as *M avium*, and the necessity to identify *M paratuberculosis* specific antigens to improve such studies. This has now been successfully

achieved by Elsaghier and colleagues, who found raised antibodies to at least one of three antigenic preparations, each with a high degree of specificity to *M paratuberculosis*, in 84% of patients with Crohn's disease, with 18% positive for all three. This study represents an important advance, showing that antibody levels to well characterised *M paratuberculosis* specific antigens are raised in Crohn's disease. The criticism of inadequate use of controls is currently being considered in a collaboration between our two groups using a different population of patients with Crohn's disease and an extended range of control populations.

In addition to these developments in immunological approaches for examining the role of mycobacteria in Crohn's disease, the other important advance has been the application of highly specific and sensitive techniques, such as the polymerase chain reaction, to the detection of *M paratuberculosis*. Culture of the organism from clinical samples has proved notoriously difficult. Amplification by polymerase chain reaction of DNA specific to *M paratuberculosis* has provided a rapid, highly specific, and far more sensitive alternative to culture or, indeed, previously used molecular biological techniques. In the study reported by Sanderson *et al*³ *M paratuberculosis* DNA was identified in gut wall tissues from 65% of Crohn's disease, 4.3% of ulcerative colitis, and 12.5% of control patients, providing further evidence of an association between *M paratuberculosis* and Crohn's disease.

In our own preliminary studies, we have used several pairs of primers for the detection by polymerase chain reaction of DNA from a wider range of mycobacterial species. In addition, we are using mesenteric lymph node tissues as an alternative to gut wall tissues which may have been exposed to environmental strains of mycobacteria. In the small number of samples so far analysed, we have successfully detected *M paratuberculosis* or *M avium* in a proportion of tissues from patients with Crohn's disease but not in tissues from controls (unpublished data).

While not providing conclusive evidence, these various findings suggest that *M paratuberculosis* is still the most promising candidate for a role in the pathogenesis of Crohn's disease: the application of these improved immunological and molecular biological approaches can only assist in determining the relevance of the clear association between *M paratuberculosis* and Crohn's disease.

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Extracorporeal shock wave lithotripsy and gall bladder stones

EDITOR,—We were interested in the paper by Elewaut *et al* on the results of extracorporeal shock wave lithotripsy of gall bladder stones (*Gut* 1993; 34: 274–8). Our figures exactly parallel theirs for we can get 98% clearance of solitary stones, less than 20 mm in diameter, in one year but not such good clearance in larger

stones or more than one stone. The paper fails to make any comment on symptom relief, however, and the surprising result of our lithotripsy trial¹ was that the symptoms were relieved, just as much as after cholecystectomy, within the first month of treatment, well before any stones had disappeared; and the pain relief for the whole year and the relief of many other symptoms did not depend on stone clearance: so we have to distinguish between success in terms of stone clearance and success in terms of symptom relief. Lithotripsy, for whatever reason seems a very cost effective way of doing the second, at least in the short term. We are at present following up our patients for longer periods to see if this symptom improvement is maintained.

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- 1 Nicholl JP, Brazier JE, Milner PC, Westlake L, Kohler B, Williams BT, *et al.* Randomised controlled trial of cost-effectiveness of lithotripsy and open cholecystectomy as treatments for gall bladder stones. *Lancet* 1992; **340**: 801–7.

Reply

EDITOR,—We fully agree with Johnson and Ross that during a lithotripsy trial most patients feel extremely comfortable. This is not because of the lithotripsy itself, however, but a result of the well known effect of bile acids on gall bladder contraction.¹ Although, the effect on gall bladder motility is still somewhat controversial,^{2,3} most authors agree that when ursodeoxycholic acid is given, gall bladder fasting volumes are larger^{4,5} and gall bladder emptying is reduced.^{3,5} The proposed mechanism is the decreased release of cholecystokinin through negative feedback control by an increased amount of intra-duodenal bile acid.⁴ The same effect was seen with chenodeoxycholic acid,³ and even with taurocholate a decreased cholecystokinin release and gall bladder contraction was seen.⁶ On the other hand, bile acid depletion by the concurrent administration of cholestyramine increased cholecystokinin release and gall bladder contraction.^{6,7}

This is the reason why, also in our experience, most patients with symptomatic gall stone disease remain free of symptoms when oral chemolytic treatment is started.

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Barrett's oesophagus and development of dysplasia and adenocarcinoma

EDITOR,—Iftikhar *et al* (*Gut* 1992; **33**: 1155–8) present results from a 15 year prospective study of endoscopic surveillance of 102 patients with columnar lined epithelium (for example, Barrett's oesophagus). The aim of the study was to identify any significant risk factors for the subsequent development of adenocarcinoma. Data are presented suggesting that the length of columnar lined oesophagus was considerably longer in patients with dysplasia. None of the patients with dysplasia had a columnar lined oesophagus of less than 8 cm. The authors conclude that the length of Barrett's oesophagus is a significant risk factor in the development of dysplasia and subsequent carcinoma and recommend intensive follow up of patients with Barrett's oesophagus greater than 8 cm in length.

The results and conclusions of the study are inappropriate given the exclusion of patients with less than 5 cm of circumferential Barrett's oesophagus. Adenocarcinoma has been reported in tongues or short segments of Barrett's oesophagus.¹ At least 32 per cent of a series of 28 resected specimens with adenocarcinomas centred in the oesophagus had a length of Barrett's less than 5 cm.² Additionally, adenocarcinomas occurring near the gastro-oesophageal junction may arise from small areas of specialised epithelium, which may be obliterated by the carcinoma or not discovered.

It would be inappropriate to ignore patients with the potential for dysplastic change when short segment Barrett's oesophagus is found at endoscopy. Systematic biopsies should be taken and subsequent follow up should not differ from those patients with longer segment Barrett's oesophagus unless appropriately conducted studies show a lesser risk of cancer.

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Reply

EDITOR,—Thank you for giving us the opportunity to reply to the comments by Drs Faris and Sampliner. They are concerned that we excluded patients with less than 5 cms of circumferential columnar lined oesophagus and point to a study of resection specimens, which suggests that a high proportion of

oesophageal adenocarcinoma arise in association with short segments of Barrett's oesophagus. We should like to make the following points.

Firstly, we adhered to the recognised criterion of at least 5 cms of columnar lined oesophagus as it is difficult to make a confident diagnosis of Barrett's oesophagus with shorter lengths especially in the presence of a hiatus hernia. Secondly, we do not argue that patients with short segment Barrett's oesophagus should not be kept under endoscopic surveillance; we have merely shown that those with long segment disease are at greater risk of dysplasia and warrant more intensive follow up. Thirdly, in the paper by Hamilton *et al*, the length of Barrett's oesophagus was measured on fixed resection specimens. This is extremely unreliable as it will certainly underestimate length as measured in vivo by the endoscopist.

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Screening and management of familial adenomatous polyposis

EDITOR,—Tait *et al* advocate annual colonoscopy as the ideal screening method for first degree relatives who carry the gene for familial adenomatous polyposis (FAP). (Correspondence on Letter to the Editor and reply *Gut* 1993; **34**: 576.) Bradburn and Rhodes on the other hand make the case for the selective use of colonoscopy, recommending it only for those at high risk for FAP but without obvious polyps (or microadenomas) by their late teens, and in those in whom prophylactic colectomy has been delayed. This selective approach is suggested to minimise the morbidity and mortality associated with colonoscopy.

We report on two cases of colonoscopic morbidity, which, though anecdotal, add 'meat to the bones' of the present discussion.

Case 1: A 12 year old son of a patient with FAP was found to have polyps at sigmoidoscopy. Histological examination showed these to be adenomas. At colonoscopy at 16 years, the bowel was perforated. A laparotomy was performed for peritonitis and a defunctioning colostomy was created; this was closed six months after laparotomy. He was referred to St Mark's Hospital after his father died from an upper gastrointestinal malignancy, but refused to attend for further hospital appointments or to have surgery, and is now under psychiatric counselling.

Case 2: A 15 year old son of a patient with FAP was confirmed to have FAP at sigmoidoscopy. Annual colonoscopies were then performed, and at the age of 19 years, 20 polyps (size 2 mm) were removed. After this procedure the patient became unwell. A laparotomy was performed and a pelvic abscess was drained. He was referred six months later to St Mark's Hospital for definitive surgery. At laparotomy a large mesenteric desmoid tumour (not apparent at the first operation) was found. Neither the colon nor the desmoid tumour was able to be removed.

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