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