in an inversely proportional manner according to the severity of the disease'. In fact, the decrease in polyunsaturated fatty acids as the disease activity increases occurred for both series, although it was more noticeable for n6 polyunsaturated fatty acids. As a consequence our hypothesis was that in inflammatory bowel disease an increased polyunsaturated fatty acid biosynthesis coexists with an increased polyunsaturated fatty acid consumption, the second being associated with the disease activity. The increased polyunsaturated fatty acid biosynthesis would be more noticeable in the n3 series as these fatty acids have the highest affinity for desaturases. Hyperconsumption, although occurring in both polyunsaturated fatty acids series, is more evident in n6 products probably because of an increased arachidonate derived eicosanoid production. This hypothesis seems to be further supported by data from recent studies in patients with non-active inflammatory bowel disease.

Of course, it will be interesting to confirm these findings in different plasma lipid fractions, as well as in colonic mucosa. We are analysing these data, which hopefully will be reported soon. Nevertheless, as far as plasma long chain polyunsaturated fatty acids (mainly n3) are concerned, their concentration in total lipids mainly reflects that found in phospholipids, as most of them are bound to this fraction.²³

The dietary habits of the patients in our study were similar to that of healthy controls (standard Western diet). This type of diet contains negligible amounts of n3 polyunsaturated fatty acids (less than 1% of the total fat).⁴ In addition, most of the patients included were in hospital because of moderate to severe attacks of inflammatory bowel disease. Most of them were anorectic and tended to decrease their food intake rather than change to different types of food. No patient had been on artificial nutritional support before plasma sampling was performed.

Although a 14 hour overnight fast might theoretically be a source of error, it is generally assumed that this condition provides an easily reproducible state of metabolic equilibrium. In fact, approximately 15 hours after the last meal there is a progressive decrease in carbohydrate oxidation and a rise in fat oxidation. Increased lipolysis in adipose tissue and fatty acid mobilisation are seen whereas, in the liver, fatty acid synthesis is progressively replaced by fatty acid oxidation and ketone body production.³ Therefore, longer fasting would lead to misleading results.

We look forward to seeing the findings reported by Belluzzi *et al*⁸ published in full as it is difficult to draw real conclusions from an abstract. Data on the location and extent of the disease, bowel resections, nutritional state, and other factors liable to lead to fat malabsorption would be of utmost interest as in the patients described there is a decrease in essential precursors – that is, linoleic acid, which may account for the deficiency seen in long chain polyunsaturated fatty acids. In fact, similar data were also reported by Färkkilä *et al*⁷ in plasma lipids from a series including many Crohn's disease patients with bowel resection. So, the findings by Belluzzi *et al*, by contrast with our results, closely resemble the pattern of essential fatty acid deficiency.

Certainly, our results may be interpreted in different ways. On the one hand, as n3 polyunsaturated fatty acids are increased, it would not be necessary to supply them in increased dietary amounts. Conversely, a plasma long chain n3 polyunsaturated fatty acid increase might be seen as an unsuccessful

attempt to prevent an excessive production of arachidonate derived eicosanoids. In such cases the slight clinical response seen when fish oil is given, despite modifying eicosanoid production, could suggest that the amount of n3 polyunsaturated fatty acids given should be increased. All these data, however, provide an attractive insight into the pathogenesis of inflammatory bowel disease, in which the true role of fatty acid treatment also has to be investigated further.

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Open access gastroscopy

EDITOR, — Dr Bramble and colleagues describe a most efficient and well run open access endoscopy service (*Gut* 1993; 34: 422–7). Even they, however, only achieve a mean waiting time of 17 days for open access endoscopy. Most of us would fair far worse and therein lies one important problem of open access endoscopy. Do we deprive out symptomatic patients of effective ulcer healing treatment for 17 days so as to obtain a 'pure' endoscopic diagnosis but subject patients to 17 days of unnecessary symptoms and risk of complications, or do we treat patients in the knowledge that if an ulcer is present it may well have healed by the time the patient has an endoscopy, especially – as is increasingly so – the general practitioner has prescribed a proton pump inhibitor.

A short outpatient visit in a general clinic or a specialist dyspepsia clinic would seem a better solution. General practitioners can be encouraged to treat patients as they see fit and the patients seen on treatment. If still symptomatic and, if it is appropriate, they can have an endoscopy immediately. If asymptomatic they can be asked to complete their treatment and arrangements made for the patient to book themselves in for endoscopy by telephone if and when their symptoms next occur before starting treatment. Additional investigations can be arranged and the patient counselled as to the likely result of the endoscopy; normal endoscopy still being the single commonest finding. In our experience with this system¹ 35% of patients will be spared endoscopy.

We found 68% of patients that had an endoscopy preferred this system to open access endoscopy despite the need for two hospital visits and if those spared endoscopy are taken into account 81% preferred the clinic appointment first.

Pressure from general practitioners to set up open access endoscopy is considerable. We feel a clinic appointment first, however, is a more logical solution and the one favoured by the patient. The endoscopies saved may also make it more cost effective.

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Reply

EDITOR, — We are grateful for the opportunity to respond to the comments of Drs Trewby and Saunders. There is a basic misunderstanding in their letter. Our provision of an efficient open access gastroscopy service does not in any way deprive patients of effective treatment. We have not made any attempt to discourage general practitioners from treating patients with dyspepsia on clinical grounds. Our guidelines point out that it is appropriate to refer patients for investigation if it is felt that a diagnosis is important before treatment is given or if this has happened and there has been a failure to respond after a reasonable time. The general practitioners in our district have a range of options for patients with dyspepsia and almost one in three of dyspepsia referrals are still by standard letter to a targeted consultant. The type of service described by Drs Trewby and Saunders is still available in Middlesbrough alongside the open access system. (In the case of open access endoscopy, the general practitioner has a further choice of asking for 'report only' or giving the endoscopist discretion about treatment and further management. 'Report only' is specified on about 50% of open access endoscopy referral forms.) We are currently setting up a pilot scheme with a number of GP practices, which will allow them to gain direct access to our open access endoscopy computer scheduling system. This will mean that the general practitioner can give our system the details and obtain the booking and instruction sheet while the patient is still present. It is quite likely that this will bring the time from request to 'investigation' down to about 12 days.

There is no basis to an assumption that screening patients through a specialist hospital clinic will have much effect on the results of endoscopy. The proportion of different abnormalities found on our open access endoscopy lists is very similar to those lists generated from patients seen in clinic and to those published figures in other series. We are developing the software to permit us to send regular feedback to our general practitioners about their use of the open access endoscopy service. This will be similar to the information they receive regularly about their prescribing practice. It will be possible for them to see how they compare with their peers in terms of number of referrals, age, sex, and findings. General practitioners already deal with most cases of dyspepsia that they see.

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