LETTERS TO THE EDITOR

Ileal pouch-anal anastomosis for Crohn's disease

EDITOR,—In his leading article (*Gut* 1998;**43**:303–8), Mr Phillips makes a plea for realistic comparisons between outcomes for pouch surgery in Crohn's disease with other restorative procedures for this disease, rather than comparisons with restorative proctocolectomy for other diseases, specifically ulcerative colitis. We agree that like comparisons are important in scientific analysis, but point out that such comparisons are confounded by the difficulties of accurate histological diagnosis in inflammatory bowel disease. In particular we should like to highlight the diagnostic confusion and unreliability of a change in diagnosis from ulcerative colitis to Crohn's disease based on the histological examination of the defunctioned rectum in ulcerative colitis.[1] Nearly all of the inflammatory changes of Crohn's disease have been described in the defunctioned colorectum in ulcerative colitis.[2] Any change from a diagnosis of ulcerative colitis to Crohn's disease must be based on a re-examination of the colectomy specimen and placed in context with the clinical history. The misdiagnosis of diverted ulcerative colitis, as Crohn's disease, will only add further to the confusion surrounding the debate on the role of the pelvic ileal reservoir in Crohn's disease.

C M EDWARDS
Department of Gastroenterology, Gibson Laboratories, The Radcliffe Infirmary, Woodstock Road, Oxford OX2 6HE, UK

B F WARREN
Department of Cellular Pathology, The John Radcliffe Hospital, Headington, Oxford OX3 9DU, UK

N A SHEPHERD
Department of Histopathology, Gloucestershire Royal Hospital, Great Western Road, Gloucester GL1 3NN, UK

1 Deutsch AA, McLeod RS, Cullen J, *et al*. Results of the pelvic pouch procedure in patients with Crohn's disease. *Dis Colon Rectum* 1991;**23**:475–7.
2 Warren BF, Shepherd NA, Bartolo DCC, *et al*. Pathology of the defunctioned rectum in ulcerative colitis. *Gut* 1993;**34**:514–16.

A requiem for the cholecystokinin provocation test?

EDITOR,—We read with interest the study by Smythe *et al* (*Gut* 1998;**43**:571–4); however, we feel that on the basis of the data presented, the pronouncement of death for the test may perhaps be a little premature.

Firstly, despite the low sensitivity and specificity reported, the test still had positive and negative predictive values (66.7 and 57% respectively) which would be clinically useful in allowing patients to come to an informed decision regarding cholecystectomy.

Secondly, the authors conclude that there is no statistical difference between the positive and negative test groups in terms of their outcome after cholecystectomy. The relative benefit of the test expressed as the odds ratio is 2.7 with a 95% confidence interval from 0.7 (no benefit) to 10 (great benefit)—hence the authors cannot reach a conclusion with a study of this size regarding the usefulness of the test. We estimate that if the proportions of subjects in the various outcome groups remained the same, 148 subjects would be needed for the study to have 80% power with an odds ratio of 2.7. The ideal number of subjects for this study would depend on the size of difference in clinical outcome, which would be useful to detect. Obviously, if the true odds ratio is higher than 2.7 then fewer subjects would be required, but at a more realistic but still clinically useful odds ratio of less than 2.7 an even larger study would be necessary.

Thirdly, we obtained different figures for sensitivity, specificity and p value for the χ^2 test (with Yates' correction) of 75%, 47%, and p=0.26, respectively, with respect to symptomatic improvement after cholecystectomy—perhaps the authors' definition of these parameters was different to our own interpretation of their data.

Fourthly, the results of this study may not be applicable to a wider clinical setting. Cholecystectomy was performed on a highly selected group of subjects, after a variable time period and with the cholecystokinin provocation test result already known. It might have been more appropriate to offer all subjects cholecystectomy or to randomise them to management with or without knowledge of the test result.

S CAMPBELL
R A ELTON
P BRAMLEY
Stirling Royal Infirmary NHS Trust, Livilands, Stirling FK8 2AU, Scotland, UK

Reply

EDITOR,—We agree entirely with the concept that larger numbers in this study (as in any other) would yield narrower confidence intervals. In our study the cholecystokinin provocation test had low sensitivity and specificity (the use of Yates' correction is controversial) and we disagree that these positive and negative predictive values are clinically useful in counselling patients regarding outcome after cholecystectomy.

We also agree that a randomised blind study may be a more objective way of assessing the usefulness of this test; however, most patients in the study underwent cholecystectomy for symptoms and we have assessed symptomatic relief separately from cholecystokinin positivity. Indeed, most patients were given saline first (they were blinded to the infusion) and their symptoms recorded. We suggest that the comments raised by Campbell and colleagues do not detract from the fact that almost 50% of patients with acalculous biliary pain experience relief after cholecystectomy and the cholecystokinin provocation test is unable to predict those with good outcome.

A SMYTHE
A W MAJEED
Department of Surgical and Anaesthetic Sciences, K Floor, Royal Hallamshire Hospital, Sheffield S10 2JF, UK

Measles virus and Crohn's disease

EDITOR,—We read with interest the view of Professor ter Meulen (*Gut* 1998;**43**:733–4) regarding the possible association of measles virus and Crohn's disease. We are in complete agreement with the author that current data available in the literature, mostly derived from serological, epidemiological and case control studies, are controversial and need to be investigated further. Professor ter Meulen proposes that the definitive answer to the problem of the involvement of measles virus in inflammatory bowel disease (IBD) would come from amplification of measles virus genome from IBD tissues by polymerase chain reaction (PCR) and then characterisation of the amplified DNA fragment by nucleotide sequencing. We would like to draw attention to published studies from several groups including ourselves and the IBD study group, who formulated the original measles hypothesis, which have tackled this issue using PCR but have not been mentioned by Professor ter Meulen in his article. These papers report highly sensitive measles specific RT-PCR systems that have been used to examine both colonic biopsy specimens (from both newly diagnosed and treated patients with Crohn's disease) and resection specimens, and have targeted different regions of the measles virus gene using primers corresponding to the N, F and H gene regions.[1–5] All have produced negative results.

Professor ter Meulen also suggests that lack of detection of measles virus in diseased tissues may be a result of low copy number of viral genes in infected cells. The sensitivity limits of the detection systems established by the groups mentioned earlier varied considerably. One group reported amplification of the target sequence from a single copy of the measles virus genome.[5] We successfully amplified RNA templates extracted from virus particles corresponding to about 10^{-3} pfu (plaque forming units) and applied approaches which potentially improved the sensitivity of the detection system by examining the amplified DNA products by Southern blotting or digoxigenin antibody assay.[2] Others also used different approaches to improve the assay sensitivity including enriching the measles virus RNA templates by oligonucleotide capturing from IBD specimens.[3] In our laboratory we were able to amplify measles virus RNA from a nucleic acid mixture extracted from control tissues including material from SSPE brain, colonoscopic biopsy samples spiked with measles virus, and from virus infected tissue culture fluid.[2]

This evidence supports the view that measles virus does not persist in IBD tissues and therefore probably is not involved in the aetiology or pathogenesis of Crohn's disease. In addition we suggest that lack of detection of measles virus sequence is not due to low copy numbers of viral genes but perhaps their complete absence.

M A AFZAL
P D MINOR
Division of Virology, National Institute for Biological Standards and Control, South Mimms, Potters Bar, Hertfordshire EN6 3QG, UK

E ARMITAGE
S GHOSH
Gastrointestinal Unit, Department of Medicine, University of Edinburgh, Western General Hospital, Edinburgh, Scotland, UK