

LETTERS TO THE EDITOR

Cancer in an ileoanal reservoir

SIR,—Dr Appelman (*Gut* 1990; 31: 1161) has asked how we determined that the carcinoma within the rectal cuff surrounding an ileoanal reservoir that we described in our article¹ was a primary one and not a metastatic tumour. If one were only to assess the histology presented then the question would be extremely difficult to answer, as he has pointed out. In standard clinical practice, however, difficult diagnoses such as this are generally made by the clinician and pathologist in concert, considering both clinical and pathological features. Thus, if we do so in this case we believe we can defend the argument that we have put forward.

To establish a diagnosis of metastatic cancer we would have to accept that the original cancer which was resected in 1977 metastasised 10 years later in 1987. Moreover, the pattern of metastases would have been a selective trans-coelomic spread to predominate within the cuff of the new pouch with no evidence of other metastases to the true pelvis or to the remainder of the abdominal cavity. Although this is technically possible, the combination of events would be extraordinarily unlikely.

In favour of a new primary cancer the following evidence can be considered. The tumour predominated grossly within the cuff. Secondly, the original indication for the pouch procedure was for severe dysplasia in the remaining rectal stump.

Although it is not possible to clearly distinguish the two diagnoses on microscopy alone, the weight of evidence is sufficiently compelling in favour of a primary tumour developing in the mucosal fragments of the rectal cuff that we feel justified in the submission of the title of this article and its substance.

HARTLEY S STERN
Department of Surgery,
Mount Sinai Hospital,
Toronto, Ontario M5G 1X5,
Canada

1 Stern H, Walfisch S, Mullen B, McLeod R, Cohen Z. Cancer in an ileoanal reservoir: a new late complication? *Gut* 1990; 31: 473–5.

Interleukin 1 in ulcerative colitis

SIR,—We read with interest the recent article by Ligmusky *et al*¹ in which the authors reported a significantly higher interleukin 1 (IL 1) content and release from colonic mucosa of patients with untreated active inflammatory bowel disease, compared with that of control subjects.

We have recently conducted a similar study determining the IL 1 production from fresh and cultured biopsy specimens and its serum concentrations in 15 patients with active ulcerative colitis, 16 with ulcerative colitis in remission, and 13 normal control subjects. The disease activity was assessed clinically, sigmoidoscopically, and histologically, by using the criteria of Truelove and Richards.²

IL 1B was measured using ELISA (Cytrotron Biotechnology). Mucosal biopsy specimens, obtained at colonoscopy, were weighed (average weight 10 mg), washed vigorously in 1 ml of 9% sodium chloride solution, and then cultured for 24 hours in 10% fetal calf serum/RPMI.

IL 1B activity was determined in the 1 ml of washing solution and in the medium after the culture.

Only slight IL 1 activity was detected in three plasma samples, all from patients with active disease, confirming IL 1 production is only rarely found in plasma, even in active disease.³

Fresh and cultured colonic mucosa obtained from patients with ulcerative colitis in remission produced significantly higher values of IL 1 compared with control mucosa ($p < 0.01$). Furthermore, specimens from patients with active disease produced significantly more IL 1 than those from patients with disease in remission ($p < 0.01$).

In conclusion, our findings are very much in agreement with those of Ligmusky *et al*. We also found a significantly higher IL 1 production in active patients than in those with ulcerative colitis in remission. The determination of IL 1 production from fresh colonic mucosa in the washing solution seems to represent a reliable method.

P GIONCHETTI
M CAMPIERI
A BELLUZZI
P BONI*
C BRIGNOLA
H FERRETTI
P IANNONE
M MIGLIOLI
L BARBARA
Istituto di Clinica Medica e Gastroenterologia,
Laboratorio Centralizzato*;
Policlinico S. Orsola,
Università di Bologna,
Italy.

- 1 Ligmusky M, Simon PL, Karmeli F, Rachmilewitz D. Role of interleukin 1 in inflammatory bowel disease-enhanced production during active disease. *Gut* 1990; 31: 686–9.
- 2 Truelove SC, Richards WCD. Biopsy studies in ulcerative colitis. *BMJ* 1956; i: 1315–7.
- 3 Satsangi J, Wolstencroft RA, Cason J, Ainley CC, Dumonde DC, Thompson RPH. Interleukin 1 in Crohn's disease. *Clin Exp Immunol* 1987; 67: 594–605.

Non-steroidal anti-inflammatory drug induced enteropathy

SIR,—We read with interest the article by Bjarnason *et al* on treatment of non-steroidal anti-inflammatory drug (NSAID) induced enteropathy.¹ We wish to comment on some aspects of their study.

Although the authors set out to study the effect of sulphasalazine on the intestine in arthritic patients on NSAIDs, they have failed to design adequately the study to test their hypothesis. Such a drug study should have been done as a randomised double blind study. Particularly since the main outcome measure was estimation of faecal excretion of ¹¹¹indium labelled leucocytes. Inaccurate collection represents a potential major source of bias.

The evidence of small intestinal inflammation and subsequent improvement was provided by the above test. However, this test is unable to distinguish between leakage of leucocytes from large or small bowel.² There is increasing evidence that NSAIDs produce inflammation in large as well as small intestine.³

The authors' finding that patients on gold therapy did not show deterioration in leucocyte excretion is interesting. This seems to contradict current evidence which suggests that gold can be acutely toxic to buccal, gastric, and colonic mucosa.⁴ Do these findings in fact suggest that (as with NSAID treatment) initial mucous membrane damage heals in spite of continuing therapy with development of tolerance?

Further well designed studies should be done to confirm these important findings by Bjarnason *et al* before sulphasalazine can be considered as the preferred second line therapy in arthritic patients on indefinite NSAID therapy.

J D ARNOLD
W E WILKINS
Princess of Wales Hospital,
Coity Road,
Bridgend CF31 1RQ

- 1 Bjarnason I, Hopkinson N, Zanelli G, *et al*. Treatment of non-steroidal anti-inflammatory drug induced enteropathy. *Gut* 1990; 31: 777–80.
- 2 Saverymattu SH, Peters AM, Lavender PJ, Hodgson HJ, Chadwick VS. ¹¹¹Indium autologous leucocytes in inflammatory bowel disease. *Gut* 1983; 24: 293–9.
- 3 Carson J, Notis WM, Orris ES. Colonic ulceration and bleeding during diclofenac therapy. *N Engl J Med* 1990; 323: 135.
- 4 Flower RJ, Moncada S, Vane JR. Analgesic-anti pyretics and anti-inflammatory agents: drugs employed in the treatment of gout. In: Gilman AG, Goodman LS, Rall TW, Murrad F, eds. *The pharmacological basis of therapeutics*. New York: Macmillan, 1985; 704–707.

Reply

SIR,—It is not possible to construct a double blind trial without preliminary studies to show rates and magnitude of change.

Your correspondents fail to grasp the advantage of the ¹¹¹indium leucocyte technique. The four day faecal excretion of ¹¹¹indium is an objective and not a subjective measure of intestinal inflammation. Inaccurate faecal collections do not apply to our studies that are carried out in a purpose built metabolic research ward, where there is no access to an open lavatory. All that the patient passes is collected (or spilt and therefore recovered).

Saverymattu *et al*¹ are misquoted by your correspondents when they suggest that the ¹¹¹indium leucocyte technique cannot distinguish between small and large bowel inflammation. The article specifically comments on the accuracy of the technique for localising colonic disease but it may slightly underestimate the extent of small bowel disease.

While we agree that there is increasing evidence that non-steroidal anti-inflammatory drugs (NSAIDs) produce inflammation in the large bowel, the reference to this in a letter describing two patients on a number of drugs capable of damaging the large bowel is hardly appropriate and the association is refuted in a simultaneously published letter.² There are two recent comprehensive reviews on the effect of NSAIDs on the large bowel.^{3,4} We scanned all 60 patients in our study and found no evidence of colonic inflammation. Neither did De Vos *et al* during colonoscopy in more than 200 patients on NSAIDs.⁵

The mucocutaneous reactions to sodium aurothiomalate cited are very rare and tend to be idiosyncratic. No such patients were included.

We never suggested that sulphasalazine should be the preferred second line therapy in rheumatoid arthritis, nor would we contemplate its use in arthritic patients on indefinite NSAID therapy.⁶

There is no evidence whatsoever that the small intestinal mucosa develops tolerance to NSAIDs.

INGVAR BJARNASON
MICHAEL GUMPEL
Section of Gastroenterology and
Department of Rheumatology,
MRC Clinical Research Centre and
Northwick Park Hospital,
Harrow, Middx HA1 3UJ