Reply

EDITOR,—We are glad that Dr Jolobe agreed with the importance of considering coeliac disease in patients with iron deficiency anaemia, even when symptomatology is atypical. The precaution of taking endoscopic biopsy specimens prevents oversight of the diagnosis. We also note his comment on the abnormal appearance of duodenal folds in coeliac disease. We indeed routinely comment on such abnormalities having previously published evidence¹ supporting the data of Brocchi *et al.*²

A S MCINTYRE
R G LONG
Wycombe General Hospital,
Queen Alexandra Road,
High Wycombe,
Buckinghamshire HP11 2TT

- 1 McIntyre AS, Ng DPK, Smith JA, Amoah J, Long RG. The endoscopic appearances of the duodenal folds are predictive of untreated adult coeliac disease. *Gastrointest Endosc* 1992; 38: 148–51.
- 2 Brocchi E, Corazza GR, Caletti G, Treggiari EA, Barbara L, Gasbarrini G. Endoscopic demonstration of loss of duodenal folds in the diagnosis of coeliac disease. *N Engl J Med* 1988; 319: 741–4.

The Nm23 gene and colorectal cancer

EDITOR,—In the leading article *Molecular biology of colorectal neoplasia* (*Gut* 1993; 34: 289–92), the authors quote a report suggesting that Nm23 allelic deletion may prove to be a useful prognostic indicator in colorectal cancer.¹ Cohn *et al* found that 73% of 11 large bowel cancer patients whose tumours had lost the Nm23 allele subsequently developed metastatic liver disease.

We also investigated allele loss at the Nm23 locus in 80 colorectal carcinomas using the same methodology, but could not detect allelic deletion in any of the 34 samples that were informative for this genetic marker (unpublished data). Myerhoff and Markowitz, using a ribonuclease protection assay, could not detect a single mutation in the Nm23 gene in 26 metastatic colon cancers, 17 non-metastatic colon cancers, or 43 matched normal controls. In addition, in this study, Nm23 gene expression was raised almost as often in metastatic as in non-metastatic cancers.² They conclude that metastasis suppression by the Nm23 gene is a tissue specific phenomenon that does not play an important part in colorectal carcinogenesis. This study in conjunction with our own findings fails to support a possible role for Nm23 inactivation as a predictor of distant metastasis in colorectal cancer.

S C WHITELAW
J M A NORTHOVER
Imperial Cancer Research Fund,
Colorectal Unit,
St Mark's Hospital,
London EC1V 2PS

- 1 Cohn KH, Wang F, DeSoto-LaPaix F, Solomon WB, Patterson LG, Arnold MR, *et al.* Association of nm23-H1 allelic deletion with distant metastases in colorectal cancer. *Lancet* 1991; 338: 722–4.

- 2 Myeroff LL, Markowitz SD. Increased nm23-H1 and nm23-H2 messenger RNA expression and absence of mutations in colon carcinomas of low and high metastatic potential. *J Natl Cancer Inst* 1993; 85: 147–52.

Reply

EDITOR,—We are grateful to Dr Whitelaw and Mr Northover for drawing our attention to recent work, some unpublished, which shows that the exact role of Nm23 in colorectal neoplasia is still unresolved. In their paper Myeroff and Markowitz report increased expression of the gene in 33 of 41 colonic tumours, an unexpected finding for what is purportedly a 'suppressor' gene.¹ While these results are not necessarily inconsistent with 'suppressor' function, p 53 for example is a tumour suppressor gene overexpressed by virtue of a point mutation that changes its biological activity, the finding in the same study that none of the cancers possessed mutations makes this improbable. Interestingly there has also been a paper published by Wang *et al* supporting the original association between Nm23 and colorectal metastasis described by Cohn *et al* and quoted in our review.² These workers using a combination of reverse transcriptase polymerase chain reaction, sequence analysis, and Southern blotting found either allele loss or deletions of the coding sequence in four of eight metastatic cancers. This was in contrast with 12 tumours that had not metastasised at the time of surgery and that possessed an intact, wild type Nm23 gene. Recently, like Whitelaw and Northover, we could not find evidence of Nm23 deletion using CA repeats in any of 20 informative cases (Cawkwell *et al*, unpublished data). The significance of changes to the Nm23 gene in large bowel cancer remains unresolved.

L CAWKWELL
Academic Unit of Pathological Sciences,
University of Leeds, Leeds LS2 9JT

P QUIRKE
N SCOTT
Department of Histopathology and Molecular Pathology,
United Leeds Teaching Hospitals NHS Trust,
Leeds LS1 3EX

- 1 Myeroff LL, Markowitz SD. Increased nm23-H1 and nm23-H2 messenger RNA expression and absence of mutations in colon carcinomas of low and high metastatic potential. *J Natl Cancer Inst* 1993; 85: 147–52.
- 2 Wang L, Patel U, Ghosh L, Chen H, Banerjee S. Mutation in the nm23 gene is associated with metastasis in colorectal cancer. *Cancer Res* 1993; 53: 717–20.

Platelet activating factor and Crohn's disease

EDITOR,—We read with interest the work of Ferraris *et al* (*Gut* 1993; 34: 665–8) reporting the contribution of intestinal epithelial cells to the enhanced generation of platelet activating factor (PAF) in ulcerative colitis. The authors emphasise that while PAF contributes to the pathogenesis of inflammatory damages in

ulcerative colitis, it has no implication in Crohn's disease.

We are very surprised by this conclusion. Ferraris *et al* can only assume that, in their *in vitro* model, intestinal epithelial cells or cells of the lamina propria of Crohn's disease patients cannot produce more PAF than those of healthy controls. These data do not argue against a role for PAF in Crohn's disease. For instance, other authors have reported increased contents of PAF in ileal and colonic mucosa of Crohn's disease patients compared with controls.^{1,2} Furthermore, other data have reported PAF in the stool of patients with Crohn's disease,³ and the decrease of faecal PAF contents after clinical remission.⁴ At this time, it is still unclear if PAF plays an important part, or is only a non-specific marker of inflammation, in Crohn's disease. The use of PAF receptor antagonists during inflammatory bowel disease may bring interesting data about the role of this mediator.

Y DENIZOT
Laboratoire d'Hématologie Expérimentale,
Faculté de Médecine, 2 rue Dr Marcland,
87025 Limoges, France

S CHAUSSADE
Service d'Hépatogastroentérologie,
Hôpital Cochin, 27 rue du Faubourg Saint-Jacques,
75014 Paris, France

- 1 Kald B, Olaison G, Sjö Dahl R, Tagesson C. Novel aspect of Crohn's disease: increased content of platelet-activating factor in ileal and colonic mucosa. *Digestion* 1990; 46: 199–204.
- 2 Sobhani I, Hochlaf S, Denizot Y, Vissuzaine C, Rene E, Benveniste J, *et al.* Raised concentrations of platelet activating factor in colonic mucosa of Crohn's disease patients. *Gut* 1992; 33: 1220–5.
- 3 Denizot Y, Chaussade S, Nathan N, Colombel JF, Bossant MJ, Cherouki N, *et al.* PAF-acether and acetylhydrolase in stool of patients with Crohn's disease. *Dig Dis Sci* 1992; 37: 432–7.
- 4 Chaussade S, Denizot Y, Colombel JF, Benveniste J, Couturier D. Paf-acether in stool as marker of intestinal inflammation. *Lancet* 1992; 339: 739.

Reply

EDITOR,—We are familiar with the work of Denizot *et al* on platelet activating factor (PAF) in Crohn's disease. We completely agree with them that the exact role of PAF in inflammatory bowel disease is still unclear and that the use of PAF receptor antagonists in clinical settings might help to clarify this issue. We expected that if PAF's contribution to the pathogenesis of Crohn's disease is significant, its generation by both epithelial and lamina propria mononuclear cells would be enhanced in a similar fashion as we have reported for ulcerative colitis. As this was not the case, we assumed and stated that PAF's implication in Crohn's disease is less pronounced than in ulcerative colitis. We were cautious not to state that PAF has no implication in the pathogenesis of Crohn's disease.

R ELIAKIM
D RACHMILEWITZ
Department of Medicine,
Hadassah University Hospital, Mount Scopus,
PO Box 24035,
Jerusalem 91240, Israel