Reply

Sir,—The comments of Drs Colombel, Janin, and Torpier are of interest. We agree that the immune processes which may contribute to the mucosal lesion of coeliac disease may be multifactorial. The eosinophil is a major component of the inflammatory infiltrate in coeliac disease, although this is frequently not emphasised in descriptions of the lesion. We have recently produced additional evidence that eosinophils and polymorphs are present in increased numbers in the coeliac mucosa: using monoclonal antibodies to Fc receptors (for the gamma chain of IgG) types II and III, which are found on eosinophils and polymorphs, a marked increase in reactive cells was found. The evidence of Dr Colombel and colleagues that many of these eosinophils have degranulated and the associated finding of increased release of granule components points to mechanisms whereby eosinophils might mediate damage. The possibility that IgA, produced in large quantities in the damaged intestine, may be involved in eosinophil degranulation through interaction with IgA Fc receptors should also be considered.

The finding that many coeliac patients react rapidly to appropriate challenge (both symptomatically and histologically) is in keeping with more immediate mechanisms of damage also participating in the development of the lesion. Eosinophils are good candidates for such a mechanism.

CONLETH FEIGHERRY DONALD WEIR ALEX WHELAN St James's Hospital, PO Box 958 Dublin 8, Ireland

Omeprazole in H2 blocker non-responders

Sir,—The results of the study by Delchier et al.1 on the similar effectiveness of omeprazole 20 mg mane and ranitidine 150 mg twice daily in H2 receptor blocker non-responders are very interesting, but also the comments by Bate2 on this paper are important. We fully agree with Bate’s opinion that a six week treatment should be judged sufficient to define resistance to H2 blockers, because ulcer healing rates further increase by continuing therapy with these drugs to eight weeks. It must also be emphasised that the adoption of unstandardised definitions of ulcer refractoriness continues to generate confusion in this field and prevents a useful comparability of findings pertaining to different studies.

Even though Delchier and colleagues adopted patient selection criteria which may have greatly influenced their final results, it is worth pointing out that the reduced efficacy of omeprazole in their trial is a relevant factor in determining the lack of significant difference between this drug and ranitidine in healing resistant ulcers. As the authors discussed in their paper, the well known variability of individual response to single daily doses of omeprazole 20 mg1 may be the most reasonable explanation for the low efficacy of this dosage regimen in their study compared with the impressive one obtained in other trials, which tested single daily doses of omeprazole 40 mg.2 Some of our recent data seem to sustain their supposition. We used 24 hour continuous pH-metry3 to study two patients with endoscopically proven duodenal ulcers on the fifth day of treatment with omeprazole 20 mg mane. As reported in the Figure, the circadian profile of gastric acidity of both patients resulted poorly influenced by the drug. These findings show that the antisecretory effect of omeprazole 20 mg is very low in some subjects and the variability in acid suppression with this dosage can be even higher than previously reported.4 The reasons for this are at present unclear, but a derangement in the pharmacokinetic pathways of the drug might be involved.5 As regards patients’ compliance, we could check daily drug intake because they were hospitalised.

On the basis of our data, it seems advisable to take into consideration the authors’ suggestions that omeprazole 40 mg is probably the optimal dosage for treating H2 blocker non-responders and that 24 hour pH monitoring could be valid for verifying whether the clinically recommended dose of omeprazole 20 mg in duodenal ulcer disease1 is really appropriate in individual patients.

V SAVARINO G O MELA* A SUMBERAZ G CELLE ISM — Istituto di Gastroenterologia and Clinica Medica R Università di Genova, Italy


Reply

Sir,—I read with interest the comments by Bate and Savarino et al on our paper. They both pointed out that duodenal ulcers cannot be regarded as truly ‘resistant’ after only six weeks of treatment with an H2 blocker. I do not fully agree with their opinion. In 1990, a duodenal ulcer remaining unhealed after six weeks has to be considered as refractory. Indeed, the actual question is: What is the best strategy to accelerate ulcer healing? This is especially important in patients with persisting symptoms or/and at risk related to age, associated disease or anticoagulation. Our results and those of Tytgat et al clearly suggest that the adequate dosage of omeprazole is rather 40 mg than 20 mg. As recently outlined by Bardhan, another problem is to determine whether the adequate drug dosage be maintained in treatment once healing has been achieved in initially resistant patients. In this regard, results reported by Savarino et al suggest that 24 h-gastric pHmetry could be helpful to select patients requiring maintenance treatment with high doses of omeprazole.

Delchier Unité INSERM 99 et Service d’Hépatogastroentérologie Hôpital Mondon, 94010 CRETEIL, CEDEX, France


Epithelial dysplasia in Caroli’s disease

Sir,—We read with interest the report by Fozard et al of Caroli’s disease complicated by dysplasia of biliary epithelium in the absence of invasive carcinoma. We recently saw similar changes in a 60 year old man presenting with recurrent episodes of epigastric and right upper quadrant abdominal pain associated with jaundice, pruritus, and steatorrhoea. Ultrasound, CT and ERCP showed numerous calculi within a grossly dilated left intrahepatic ductal system but no proximal stricture or obstruction, changes consistent with Caroli’s disease. A formal left hepatic lobectomy was performed. In the resected liver, parenchyma was largely replaced by dilated bile ducts containing
In the discussion the author refers to our article ‘IgA class antibody against human jejunum in sera of children with dermatitis herpetiformis’ (J Invest Dermatol 1986; 87: 703-6), as follows: ‘...type of reticulin antibodies reacting with human liver and spleen has also been described previously and already Seath et al and Eerterm et al showed that such antibodies can react with human jejunum, a finding recently confirmed also by Karpáti et al. Here we described for the first time IgA type antibodies binding to human jejunum and that they may be related to reticulin antibodies. An IgG type reticulin antibody reacting with human small bowel was seen by Eerterm et al. ‘... the IgG type of reticulin antibodies were reported of low frequencies (16-46%) and low specificity (75-85%) in coeliac disease. In contrast, IgA class reticulin antibodies seem to be more sensitive and specific’. (From the introduction of Dr Hallström’s paper.)

Jejunal antibodies have distinctive characteristic signs compared with other IgA type reticulin antibodies: they bind to the small bowel, which is the damaged organ in gluten sensitive enteropathy and they bind at the site of gluten absorption which is the precursor of the disease. In addition, the binding site of IgA type jejunal antibodies corresponds to or is very similar to the extracellular IgA deposition detected in the diseased jejenum of patients with gluten sensitive enteropathy. Because of the damaged structure of coeliac jejunum, this similarity can be ascertained by investigating the diseased small bowel of patients with almost normal villous structure: (a) in jejunal biopsy samples taken several hours to one to two days after gluten challenge in coeliac patients who have recovered on gluten free diet; (b) we found IgA deposits in the small bowel of dermatitis herpetiformis patients with almost normal jejunal structure.

In the present work Dr Hallström found both the endomyxium, and IgA type reticulin antibodies to be very important in the diagnosis of gluten sensitive enteropathy, and by absorption studies the endomyxium antibody (sub-stratum oesophagous) was related to the human subtype of reticulin antibodies and was distinguished from that of rat subtype. We think that if anthimum antibodies are important in considering the pathogenesis of coeliac disease, they must be related to the IgA type antibodies reacting with human jejunum.

We conclude that one of the reticulin antibody categories mentioned does not correspond to the pathological concept of the IgA type jejunal antibodies supplied in our study.

Boehringer Ingelheim
Austria.

Figure: Severe dysplasia of epithelium in dilated bile duct.

Epithelial dysplasia is frequently seen adjacent to cholangiocarcinoma in the intra and extrahepatic bile ducts and carcinoma of the gall bladder which has a similar epithelial lining. Extensive severe epithelial dysplasia involving the gall bladder, cystic duct, and common bile duct, associated with adenocarcinoma of the common hepatic duct, was recently reported in a patient with primary sclerosing cholangitis and chronic ulcerative colitis, diseases which, like Caroli’s disease, are associated with an increased risk of cholangiocarcinoma. These findings, and that of epithelial dysplasia unassociated with carcinoma in Caroli’s disease, provide evidence of the premalignant nature of biliary epithelial dysplasia. Because such dysplasia is usually detected only in surgical specimens, we agree that early resection of localised forms of Caroli’s disease may be necessary to prevent late complication by cholangiocarcinoma.


IgA class reticulin antibodies of human subtype in gluten sensitive enteropathy

Sir,—We read with interest the paper of Dr Hallström in the September issue (Gut 1989; 30: 1225-32) entitled ‘Comparison of IgA-class reticulin and endomyxium antibodies in coeliac disease and dermatitis herpetiformis’.
Epithelial dysplasia in Caroli’s disease.

N I Walker and R W Strong

Gut 1990 31: 584-585
doi: 10.1136/gut.31.5.584-c

Updated information and services can be found at:
http://gut.bmj.com/content/31/5/584.4.citation

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/