

- 6 Walker-Smith JA, Guandalini S, Schmitz J, Schmerling DH, Visakorpi JK. Revised criteria for the diagnosis of coeliac disease. Report of the working group of the European Society for Paediatric Gastroenterology and Nutrition. *Arch Dis Child* 1990; 65: 909–11.

Reply

EDITOR,—It was during the 1970s that Wright and Watson highlighted the significance of crypt hyperplasia in the mucosal pathology of coeliac disease, not only in a severely damaged flat mucosa but also in less severe lesions. Large crypts, with abnormally high cell count per crypt, increased crypt cell mitotic rate, and crypt cell production rate have been found in coeliac disease by many workers using a variety of techniques. Mulder *et al* misquote Marsh's suggested terminology for the severe end of the spectrum of the pathology of coeliac disease – his 'hyperplastic' grade equates to Wright and Watson's crypt hyperplasia with short or virtually normal sized villi. Marsh recommends the term 'flat' for the avillus lesion, which (except in the unusual circumstances of a true mucosal atrophy) also has crypt hyperplasia.

There is also wide, general agreement, for at least a decade and using a variety of methods of quantitative histological tests, that when the surface epithelium itself is used as the reference (length, cell number or tissue volume) the density of lymphocyte infiltrate is high, not only in coeliac disease with crypt hyperplasia but in some treated coeliac patients with entirely normal villus and crypt architecture. Marsh has shown this by using computerised image analysis of tissue volumes in his *in vivo* gluten challenge work, and in dermatitis herpetiformis patients. We are not persuaded that 'infiltrative' is the best way to describe this specific pathological entity. In various diseases there may be abnormal infiltration of the mucosa by lymphocytes, plasma cells, eosinophils, mast cells, macrophages, tumour cells or parasites, and the microenvironment that is infiltrated maybe intraepithelial, the villus lamina propria, or pericryptal regions.

Much more important than semantics is the plea to pathologists that they should formally quantify the intraepithelial lymphocyte density in some way, when on subjective assessment it seems probable that this feature of intestinal pathology is abnormal. A high count or density of intraepithelial lymphocytes, and increased mitotic activity of intraepithelial lymphocytes, can, of course, occur in conditions other than coeliac disease, for example, in travellers' diarrhoea and giardiasis.

Patients with classic, unarguable, gluten sensitive biopsy pathology of coeliac disease are often comparatively asymptomatic. Paediatricians in Europe use the terms 'active' and 'silent' in relation to the presence or absence of symptoms and signs of malabsorption and we find this a clinically useful way of subdividing patients who, of course, all fulfil current diagnostic criteria for coeliac disease.

On the other hand, 'latent' coeliac disease as defined 20 years ago referred to patients with normal jejunal biopsy histology while receiving a normal diet, but who have a gluten sensitive enteropathy at some other time. Despite much research effort, no one has yet found a way to measure antigen specific T cell sensitisation in the gut mucosa, though cytokine production by antigen challenged biopsy specimens in organ cultures holds potential. When *in vivo* challenge tests are done, the evolution of enteropathy, or of changes in the rectal mucosa, are good evidence that gluten intolerance

exists, but do not show the precise mechanism. There is still much work to be done before we can confidently assign the diagnosis of latent gluten sensitivity to any patient with a histologically normal jejunal biopsy specimen, whether on the basis of genetic makeup, intestinal IgM anti-gliadin antibodies or gamma/delta intraepithelial lymphocyte counts.

In our early enthusiasm for the use of such immunological tests to identify patients at the mild end of the pathological spectrum of coeliac disease, we carelessly used the term 'latent coeliacs' in our day to day discussion of the clinical progress and research results for such patients. In fact we should have classified them as 'might be latent coeliac disease, we will know in 3–6 months time after the effects of gluten free diet or gluten challenge or gluten loading or all three have been monitored by biopsy'. In other words they were potentially latent coeliacs, which is still rather a mouthful. There are many symptomatic patients with normal mucosal architecture but a high count of total or gamma/delta intraepithelial lymphocytes, intestinal IgM anti-gliadin and other antibodies, serum anti-endomysial antibody or clinical wheat sensitivity. We, our clinical colleagues, and the patients understand and find it more convenient simply to use the term 'potential coeliacs' until we have unequivocally shown by dietary manipulations whether they are or are not gluten sensitive. If they are not, then other avenues of investigation and treatment must be pursued.

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Perioperative endoscopy of the whole small bowel in Crohn's disease

EDITOR,—Lescut, *et al* (*Gut* 1993; 34: 647–9) are to be congratulated on their very interesting findings on the widespread nature of small bowel Crohn's disease when assessed by perioperative endoscopy.

As a radiologist, what saddens me is the repetition of the pattern of discrediting radiology by comparing it with endoscopic techniques without rigorous methodology. The barium meal has almost been discounted on remarkably little sound trial evidence. This study seems to be subjecting small bowel barium radiology to the same fate. At no point in the study are we told of the level of experience of the radiologist who performed the small bowel studies, whether these studies were 'double read', what type of investigation was performed (single contrast follow through, or single or double contrast small bowel enema), how lesions were scored, the interval of the studies before surgery, whether the studies were all performed in the same institution, whether a careful search for aphthoid lesions was made, etc.

While I realise that comparison with radiology was not the main thrust of the paper, it was nevertheless made. If radiological data are going to be included then the same careful scientific method should be applied to these as any other data recorded. If this is not done it will soon become dogma that radiology misses '54 per cent' of lesions without proper scientific validation.

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Reply

EDITOR,—We are grateful to Dr Shorvon for his comments on our paper. The aim of our study was to assess silent lesions of Crohn's disease in patients being operated on and to compare those endoscopic findings with the ones provided by radiology before operation. We have insisted that almost all the important lesions of the small bowel were identified by single contrast follow through before perioperative enteroscopy. This technique could only recognise milder lesions, which did not appreciably influence treatment of patients. Single contrast follow through investigations were performed in the same institution, by senior radiologists, and double read. The interval between x ray and surgery was variable but never more than three months.

We would be sorry if the main conclusion of our study was that 54 per cent of lesions of small bowel would be missed by radiology. We think that a good radiological examination of small bowel remains a simple and efficient tool for identifying the clinically significant lesions of Crohn's disease.

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Gastric mucosal phospholipids and gastroduodenal diseases

EDITOR,—I was interested to read the study of Professor Budillon's group on changes in gastric mucosal phospholipids in various gastroduodenal diseases (*Gut* 1993; 34: 456–60). Despite progress in the understanding of mucosal blood flow, the mucous bicarbonate blanket, and the protective effects of prostaglandins in recent years, the phenomenal ability of the 'gastric mucosal barrier' is still incompletely understood; of relevance, however, is that phospholipids probably play a part because of their hydrophobicity. Progress has also been made on the other side of the peptic ulcer equation, with non-steroidal anti-inflammatory agents and *Helicobacter pylori* (*H. pylori*) both clearly implicated in the causation of both ulcers and various forms of gastritis.¹ In patients with duodenal ulcers rates of positivity for *H. pylori* vary from 70 to 100%; and in chronic gastritis, from 13–92% depending on the amount of atrophy and activity in the biopsy specimen.^{3,4} It is on these grounds that I question the findings of their study, as we are told that all 28 of their apparently unselected patient group are *H. pylori* negative, 12 with duodenal ulcer disease and eight with chronic atrophic gastritis (activity of inflammation not given). This makes them an unusual subgroup of both peptic ulcer disease and gastritis and the findings cannot therefore be generalised without further study.

Another recent report² about gastric surfactant and the possible interaction between it and *H. pylori* makes this oversight in patient selection even more problematic. If, as Professor Hills proposes, surface active phospholipids play a key part in gastric cytoprotection, and if *H. pylori*'s pathogenicity is related to ingesting surfactant and thus exposing the gastric mucosa to acid attack, the findings of Professor Budillon's group are distanced even further from any relevance to most patients with peptic ulcer disease. It would be therefore very interesting to see if the phospholipid composition of gastric biopsy specimens in patients