Clinical and pathological spectrum of coeliac disease

Editor,—In their article, Ferguson et al propose new terminologies— that is, active, silent, latent, and potential to accommodate evolving concepts for gluten sensitivity ('coeliac disease') (Gut 1993; 34: 150-1). There are, however, a number of problems in their thesis that requires examination.

The first difficulty lies in their method of defining terms. 'Silent' appears in the title but only once textually (line 6), while 'latent' and 'potential' become blurred by combined use, like 'potential latent', which then later equates with 'low grade coeliac'. A latent coeliac patient is identified as someone who (a) has a normal mucosa while eating a normal diet but who (b) either found a flat mucosa responsive to gluten withdrawal. In the final paragraph, it is suggested replacing 'latent' and 'low grade coeliac' by a more generally applicable expression—'potential'.

A second difficulty arises from the 'two stage model' of coeliac disease based on experiments in which either anaphylactic, or graft v host, reactions caused further, albeit modest, changes in mucosal architecture in gluten fed mice. This leads to the proposal that environmental (second) factors are vital in driving a mild intestinal lesion to the more severe, flat lesion typical of classic coeliac disease. As Weinstein showed first and many others since, complete flattening simply requires (a) a sufficient intake of gluten on (b) an appropriate genetic background. The candidate 'second' factors proposed by the authors lack conviction: for example, what is the evidence that either intraluminal digestion of gluten, or nutrient deficiency, or episodes of increased permeability cause mucosal flattening?

Usually it would seem unnecessary to propose an 'adjuvant effect of intestinal infection' as another factor in mucosal flattening. This is not so in the tropics where prolonged exposure to repeated microbial infections/toxin production fails to drive the mucosa to flatness in tropical sprue; indeed, in those subjects who mount host mediated mucosal responses to such a heavy intestinal microbial load, the lesion may be exceptionally mild, less than 5% (Indian or Caribbean patients developing a really flat mucosa).

As concepts ever change and widen, new terminologies will be required, but we must keep them simple. There seem to be reasonable grounds for getting away from earlier definitions of 'coeliac disease' as a malabsorption syndrome with a flat mucosa responsive to gluten withdrawal: such a definition is now redundant as it only encompasses about 30% of all sensitised subjects. Thus 'coeliac disease' needs to be replaced by a more generally inclusive and flexible term such as 'gluten sensitivity', defined as a state of T cell sensitisation to gluten in a genetically predisposed subject (the occurrence of gluten sensitivity in patients with severe immunodeficiency excludes a primary role for antibody). Underlying that state of gluten sensitivity seem to be certain arbitrary mucosal gradings—namely, (a) infiltrative, (b) inflammatory-hyperplastic, (c) flat-destructive, and (d) irrevocable hypoplastic/atrophic.

Thus, a sensitised patient will either be (a) asymptomatic ('latent') irrespective of degree of mucosal damage, or (b) symptomatic (have gluten driven malabsorption (coeliac disease), skin blisters, or clinical features of malignancy) irrespective of degree of proximal mucosal damage. Note, however, that most gluten sensitised subjects are 'latent' or asymptomatic, even though many have a typical 'flat' proximal mucosal lesion. The difficulty lies in identifying subjects with minimal (infiltrative or inflammatory-hyperplastic) lesions that are a result of gluten sensitivity rather than to other known causes like giardiasis, cryptosporidiosis, tropical enteric disease, etc. Eventually, it is hoped that identification of all gluten sensitised subjects will be based on tests other than mucosal sampling and mucosal imagery. In the meanwhile, many physicians and pathologists need to acquaint themselves with these new concepts and vistas, which now typify the widening clinical and pathological spectrum of gluten sensitivity. Gluten sensitivity, in contrast with conventional beliefs, is extremely common, but because of its latency is often missed, or even never thought of.

M N MARSH
Hope Hospital, Eccles Old Road, Salford M6 8HD


C J MULDER
Department of Hepa-gastroenterology, Rijnstate Hospital, Arnhem

Letter to the Editor, Ferguson et al have reviewed some of the new concepts concerning the clinical and pathological spectrum of coeliac disease. Unfortunately, the views expressed in their leading article may bring confusion rather than clarity.

We agree with Ferguson et al that the pathological spectrum of coeliac disease as generally accepted in the past, needed to be revised. We think, however, that this has already been done by Marsh in his excellent review. Based on his own experiments, Marsh has shown that the small intestinal pathology of coeliac disease occurs in a continuum: from a mucosa with (nearly) a normal architecture (preinfiltrative lesion), to increased lymphocytic infiltrate (infiltrative lesion), and finally to the classic 'flat mucosa' (hypertrophic lesion). Marsh has shown that coeliac patients may develop any of these types of mucosal lesions and yet be asymptomatic. Whether it is the degree and the extent of the lesion, or alternatively the influence of environmental factors (infection, pregnancy, extra gluten intake) determine the clinical presentation of the disease, deserves further investigation.

We agree with Ferguson et al that a gluten free diet should be advised to more patients with coeliac disease or gluten enteropathy. We disagree, however, with their suggested two stage model of coeliac disease. This classification is a simplification of a proteiform condition. Recognising all (sub) clinical forms of coeliac disease is a diagnostic utopia for clinicians and is, to some extent, a reflection of the uncommon diagnosis of this disease in the USA and in some European countries, for example in the Netherlands. The use of different terms such as active, silent, latent, potential, high density intraepithelial lymphocyte enteropathy, the coeliac like intestinal antibody pattern, is potential coeliac disease, all refer to an asymptomatic state with different degree of mucosal change. The term latent coeliac disease should only be used in those states in which a (sub) normal histological examination of small intestinal biopsy specimen is found in patients consuming gluten before developing typical small intestinal lesions characteristic of coeliac disease.

The importance, however, of the recognition of these atypical forms of presentation and asymptomatic cases, is that these patients may be at risk of developing malignancies and that the adherence to a gluten free diet may be protective.

Immunogenetic studies in families of coeliac patients will help to define the subjects at risk. Until otherwise proved, a gluten free diet should be advised to all patients with the corresponding immunogenic markers and histological abnormalities. When the diagnosis is uncertain, a gluten challenge under appropriate surveillance followed by the study of the intestinal morphology is often helpful to clarify the situation. Revised criteria for the diagnosis of the spectrum of coeliac disease should be formulated by working parties, as was done before.

M L MEARIN
Department of Paediatrics, Academic University Hospital, Liden

A S PENA
Department of Gastroenterology, Free University, Amsterdam, The Netherlands

It was Watson's crypts, of spectrum mends the density of which (length, surface epithelium itself histological entirely normal villus and crypt architecture. A normal mucosa, are in biopsy diagnostic symptoms and diet, of coeliac disease. There might be a gluten-free diet with gluten sensitive antibodies, serum anti-endomyosal antibody or intestinal IgA anti-gluten and other antibodies. Our clinical, colleagues, and the patients understand and use it more conveniently to use the term 'potential coeliac' 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.

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

Editor,—It was interesting 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 layer, and the protective effects of prostaglandins in recent years, the phenomenon of the 'gastric mucosal barrier' is still incompletely understood; of relevance, however, 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. In patients with duodenal ulcer rates of positivity for H pylori vary from 70% to 100%; and chronic gastritis, from 13–92%, depending on the amount of atrophy and activity in the biopsy specimen. 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 report about gastric surfactant and the possible interaction between it and H pylori makes this oversight in patient selection even more problematic. 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

Gastric mucosal phospholipids and gastroduodenal diseases

Editor,—We were grateful for Dr Shorvon's comments on our paper. The aim of our study was to compare the severity 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% 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.

G. DESCOIT
Clinique des Maladies de l'Appareil Digestif,
Hopital Claude Huriez,
5 place de Verdun,
59045 Lille Cedex, France