Current topics

Gluten intolerance, gluten enteropathy, and coeliac disease

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It is nearly a century since Gee first described the 'coeliac affection', and more than a generation since Dicke discovered the central role of gluten in its pathogenesis. In recent years it has been the sole subject of three international conferences, and the major topic discussed at the European Society for Paediatric Gastroenterology and Nutrition (ESPGAN) in at least two of their annual meetings.¹ Despite intensive study, understanding of coeliac disease is still far from complete, whether in children or adults. Although strict criteria for diagnosis have been recommended by ESPGAN,² the situation remains confused.

The criteria used currently for the diagnosis of coeliac disease are:

(1) Clinical symptoms accompanied by villous atrophy. (2) Clinical and histological recovery on gluten-free diet. (3) Histological relapse after gluten challenge.

For various reasons these criteria may be inadequate for some children whose symptoms improve on a gluten-free diet but whose disease is either transient or recurrent. The puzzled clinician then asks himself 'Is this coeliac disease?'—without the possibility of a satisfactory answer.

The diagnosis of 'transient' coeliac disease cannot be assigned with certainty to any patient unless he has been followed for a lifetime; while apparent spontaneous recovery after a prolonged course has been reported in some patients.³ Hard cases may make bad law, but perhaps it is time to ask whether the laws in this case should be abolished altogether, as being irrelevant to the real problem. Instead of trying to accommodate patients within a fixed diagnostic category, a problem-orientated approach may be more helpful. Thus, the important questions to be answered are: (1) Are the patient's symptoms

caused by gluten? (2) Does he or she have a jejunal mucosal lesion? And subsequently (3), is either (1) or (2), or both, (a) active? (b) in remission?

Clarity of thought would be aided by abandoning the nomenclature 'coeliac disease' altogether. Instead, we should move from the constraints of a 'disease' with strict criteria into a more flexible framework, where the emphasis is on the aetiological agent rather than on morbid anatomy. In untreated 'classical' coeliac disease, symptoms and enteropathy go together; but understanding of either is much more likely to occur when their varying relationships are worked out in a wider context. The clinical findings and the pathological lesion, which are not always correlated, should be separately defined (Table). Clinical symptoms, whether classical, transient, relapsing, recurrent, or atypical would be termed *gluten intolerance*. The confirmation of this diagnosis, like those of cows' milk protein intolerance and lactose intolerance, would depend on prompt remission of symptoms when the offending substance, in this case, gluten, is excluded from the diet.

The histological component of coeliac disease, a flat or hypotrophic jejunal mucosa, should be described as *gluten enteropathy*, which can only be diagnosed by a biopsy. This is analogous to lactase deficiency, a biochemical disorder which is not necessarily accompanied by clinical lactose

Table *Gluten intolerance and gluten enteropathy*

<i>Gluten intolerance</i> (clinical)	
Classical coeliac disease (untreated or in relapse)	
Transient coeliac disease	
Recurrent coeliac disease	
Atypical gastrointestinal symptoms responding to gluten exclusion	
Systemic symptoms responding to gluten exclusion	
<i>Gluten enteropathy</i> (histological)	
Coeliac disease	
Asymptomatic patients (undiagnosed or in clinical remission)	
Enteropathy of dermatitis herpetiformis	

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intolerance. Gluten is not the only aetiological agent producing villous 'atrophy', and similar appearances may be found in cows' milk and soya enteropathies, marasmus, and maternal deprivation, although the mucosal lesion is usually less severe in these conditions. A 'flat' jejunal mucosa is often found in asymptomatic patients who have stopped their diet,⁴ and was even discovered fortuitously in an adult who underwent ileal bypass for obesity: to call this coeliac disease is stretching the term beyond its credibility (A Ferguson, 1979, personal communication). Recovery of villous structure after gluten exclusion takes longer to occur than relief of symptoms, but should ideally be demonstrated if the diagnosis of gluten enteropathy is to be sustained. Finally, histological relapse on reintroduction of gluten, according to the ESPGAN recommendations, should confirm the diagnosis; but in practice paediatricians do not always proceed to this phase of investigation and content themselves and their patients with the often spectacular clinical and histological remission obtained when dietary treatment is introduced.

If the routine number of biopsies were to be reduced to two, a better case could be made for omitting the second of the present three: if clinical recovery occurs on a gluten-free diet, histological improvement would be expected. On the other hand, if the biopsy appearances remain abnormal despite clinical improvement, the inference is usually that the diet has not been strictly adhered to and the diagnosis is unlikely to be changed. (In

adults, histological remission is not as likely to occur as in children, and is not always regarded as an essential part of the diagnosis). In the Figure, a scheme of management with two biopsies is outlined. Those patients with significant symptoms on gluten will obviously wish to continue their gluten-free diet indefinitely. However, the postchallenge biopsy is important even for the remainder. It may demonstrate persistent enteropathy—that is *mucosal* as opposed to clinical intolerance to gluten, and in our present state of knowledge, would be an indication for long-term dietary exclusion of gluten. Whether this reduces the small but significant risk of lymphoma is not yet clear. It will improve growth and development in some patients and perhaps improve the general well-being of others with minor symptoms.

Recently, Fumigali and Challacombe⁵ described children with persistent gastrointestinal symptoms and weight loss, whose jejunal biopsies showed only minor changes which would not be accepted as coeliac disease by most pathologists, but who recovered on treatment with a gluten-free diet. They might be regarded as having gluten intolerance without gluten enteropathy (at least as currently defined), and the counterpart of asymptomatic patients with a flat mucosa.

Eventually, coeliac disease may be redefined in biochemical or immunological terms. Susceptibility to coeliac disease is closely, but not exclusively, associated with possession of HLA-DRW3 and B8 tissue antigens, but this genotype occurs in many

Figure A clinical approach to gluten intolerance.

unaffected persons. A characteristic gut hormone profile has been described.⁶ For the present, biopsy findings determine the investigative approach. The clinical disorder and its relationship to gluten (gluten intolerance) is of much more practical importance to the patient than the mucosal appearances. Medical scientists, interpreting the toxicity of gluten fractions according to their effects on the jejunal villi (gluten enteropathy) will no doubt some day clarify the pathological mechanisms. At least until then, and probably thereafter, the pragmatic introduction of a gluten-free diet is the correct treatment for intolerance and enteropathy alike.⁷

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