**Coeliac disease: the great imitator**

"Know syphilis in all its manifestations and all other things clinical will be added unto you."1

**WHEN THE SUPREME CLINICIAN** William Osler wrote this, he was drawing attention to the ubiquity of syphilis and the remarkable range of its late-stage manifestations, today virtually unknown. However, I argue that its place has been taken by coeliac disease (CD), another great imitator. As a diagnostic challenge, CD is the "syphilis" of the 21st century.

Western civilisation owes much of its foundation to a strange molecular rearrangement of the chromosomes of wild grasses in the Middle East to produce a high-protein, high-yielding grain — wheat — with six sets of chromosomes. This enabled the nomads to settle down with some assurance of a regular food supply and time to think and develop skills such as writing. This progress, however, came at a price. Gliadin, the principal wheat protein, presented to sensitised T cells in conjunction with HLA-DQ2 or HLA-DQ8 antigen, leads to the production of cytokines. The cytokines cause tissue damage within the mucosa and activate plasma cells to the production of cytokines. The cytokines cause tissue conjunction with HLA-DQ2 or HLA-DQ8 antigen, leads to principal wheat protein, presented to sensitised T cells in conjunction with HLA-DQ2 or HLA-DQ8 antigen, leads to principal wheat protein, presented to sensitised T cells in conjunction with HLA-DQ2 or HLA-DQ8 antigen, leads to

It is becoming evident that a host of disorders in many systems are aetologically related to the presence of CD, often manifesting themselves in the context of an inapparent coeliac state (Box 1). For some, such as fatty liver "transaminitis" or hepatitis, the link is clear. Our research (as yet unpublished) shows that about 40% of both children and adults with this disorder (who typically have laboratory evidence of CD but few clinical signs) have liver abnormalities that resolve within a few months on an appropriate diet.

Dermatitis herpetiformis is another condition that is clearly linked to CD. Most, if not all, cases of this form of dermatitis are related to gluten intolerance, although the duodenal changes may only manifest themselves after prolonged high intake of gluten.34 With a gluten-free diet, the condition resolves and the intense itchiness subsides. Another association is with type 1 diabetes. The prevalence of CD in people with type 1 diabetes is about 3 to 8%,4 while the prevalence of type 1 diabetes in people with CD is about 5%.32 However, there are no data on whether patients with diabetes and CD experience improvement in their diabetes symptoms in response to a gluten-free diet. Another group of associations is exemplified by the anaemias — essentially a complication of malabsorption, particularly of iron and folate. These conditions respond fully to nutrient replacement. However, the largest, possibly most important and least understood group of diseases that appear to have links with CD are those with a statistical association, such as epilepsy,32 the neuropathies 32 and myelopathies,10 the ataxias,12 and male and female infertility.16,17 With these conditions, the story is only beginning to unfold, and responses to diet are less evident. Such associations are only likely to be detected, and their nature and course unravelled, if physicians have a much lower threshold for suspecting CD behind many different clinical syndromes (Box 2). By performing simple and relatively inexpensive laboratory tests — such as tests for transglutaminase antibody (sensitivity, 93%; specificity, 99%) and the endomysial antibody (sensitivity, 85%–98%; specificity, 97%–100%) — followed by endo-

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**ABSTRACT**

- Coeliac disease (CD) is caused by a complex immunological response provoked by grain protein in susceptible people.
- The majority of people with CD are symptom-free adults; the remainder are prone to a bewildering variety of signs and symptoms, ranging from infertility to type 1 diabetes.
- Many patients with undiagnosed CD spend years seeking help for complaints such as chronic tiredness or mild abdominal symptoms.
- In primary care, an appropriate target group to test for CD is people with anaemia (especially women), chronic tiredness, non-specific abdominal symptoms (including so-called "irritable bowel syndrome"), or a family history of CD.
- The response to an appropriate gluten-free diet is often life-transforming for symptomatic patients.
- Positive serological tests for CD require confirmation by duodenal biopsy and, if confirmed, referral to a dietician and a coeliac society, followed by a life-long gluten-free diet.

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17 May 2004 180 10 524-526

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and duodenal biopsy and referral to a coeliac society if CD is indicated. Given that GF diets are complex, lifelong, expensive and socially disruptive, they must always be preceded by histological proof from a biopsy. Nevertheless, the potential benefits for some patients may be enormous.

In the Australian context, an appropriate strategy is to request testing for endomysial and transglutaminase antibodies, ensuring that the laboratory tests for IgG antibodies in patients who have IgA deficiency, which is common in CD, are carried out.36 An appropriate group of patients to target would be those who have the type of symptoms described above in the UK study.36

In summary, there can be little doubt that the transglutaminase/endomysial antibody assay should be part and parcel of the diagnostic armamentarium of every physician, given that CD can manifest as a disturbance of function of virtually any body system. A priori, there must be many other associations yet to be discovered.

Competing interests

None identified.

References


(Received 17 Nov 2003, accepted 28 Feb 2004)