Coeliac disease is on the rise

Robert P Anderson

An estimated four out of five Australians with coeliac disease are undiagnosed — we need greater awareness and increased testing

According to criteria published in 1990, which remain the most widely accepted, the diagnosis of coeliac disease is based on typical histological features of the small intestine of an individual on a gluten-containing diet: villous atrophy, crypt hyperplasia and intra-epithelial lymphocytosis.[1] Serological tests for coeliac disease, such as for endomysial IgA or transglutaminase IgA, are predictive, but alone are not sufficient for diagnosis. The diagnosis of coeliac disease is confirmed by clinical, serological or histological improvement on a gluten-free diet.[1]

To become a member of a state coeliac society in Australia, a person requires a doctor's letter indicating a medical need for a gluten-free diet. As a result, over 80% of members have biopsy confirmation of coeliac disease; this is also the case in the United Kingdom. Over the past 10 years, there has been a steady compound annual growth of a little less than 10% in new memberships for coeliac societies in the UK and Australia (Norma McGough, Head of Diet and Health, Coeliac UK; Graham Price, President, Coeliac Society of New South Wales; and Jane Davies, Executive Officer, Coeliac Society of Victoria, personal communication). Both countries have now developed active education programs for doctors in family medicine. It appears that these programs have been successful in increasing serological testing and reducing the "backlog" of symptomatic patients with coeliac disease who were previously unrecognised.[2] Today, coeliac disease is very much a diagnosis made in adulthood; children under the age of 10 years make up only 11% of new members joining coeliac societies in the UK and Australia, while the median age of new members is 40 years.

However, best estimates, based on there being about 1% prevalence of coeliac disease in Western populations, suggest that no more than one in five Australians with coeliac disease are now diagnosed.[3,4] Finland, where about 0.5% of the total population have now been formally diagnosed with coeliac disease,[5] is accepted as having the most coeliac-aware health system. Australia still has a long way to go to achieve the level of awareness present in Finland, where gluten-free Big Macs have been available for more than 20 years and restaurant menus routinely indicate whether food is gluten free.

Although awareness of coeliac disease has generally been low in the United States, a recent report by Mayo Clinic suggested that in Olmsted County, the home of Mayo Clinic, as many as 0.35% of the local community have been formally diagnosed with coeliac disease, suggesting a 35% ascertainment rate.[6] It was also reported that no additional mortality was observed in the residual group of individuals with unrecognised coeliac disease in Olmsted County, suggesting that aware physicians and prompt, appropriate diagnosis of symptomatic coeliac disease are effective in minimising serious complications.[7] Conversely, very low clinical awareness of coeliac disease, observed by researchers of historical cohorts in Germany and the US, is associated with substantially increased mortality, usually caused by malignancies and infection.[8,9] Experience in Finland also supports the principle that high levels of clinical awareness and diagnosis minimise morbidity and mortality among individuals with unrecognised coeliac disease.[10]

Three reports, including one published in July 2010, suggest that, because of the rise in the disease's prevalence, progress in clearing the backlog of undiagnosed coeliac disease may be slower than we thought.[5,8,9] In Finland, the prevalence of coeliac disease doubled from 1% to 2% between 1979 and 2000, while diagnosed coeliac disease increased from 0.03% to 0.52% of the population.[5] In the US, Mayo Clinic researchers showed that the seroprevalence of coeliac disease rose almost five times, from 0.2% to 1%, between 1950 and 2000.[8] Now researchers have shown that, in a cohort of mostly adult volunteers in Maryland, US, who were enrolled in 1974 and followed up in 1989, the seroprevalence of coeliac disease more than doubled from 0.2% to 0.5% in 15 years.[10] Those who showed seroconversion between 1974 and 1989 were all adults, indicating that coeliac disease does not necessarily begin in childhood. Data from Finland also show that the prevalence of coeliac disease in older people is double that in children.[11-13]

Although confirmation of coeliac disease by biopsy is ideal, these new epidemiological insights are reshaping our understanding of coeliac disease and should better inform clinical practice. No longer can we assume that a single serological test for coeliac disease is adequate to exclude coeliac disease for life. The only test that seems capable of excluding coeliac disease for life is HLA-DQ genetic testing.[14,15] Absence of genes encoding the susceptibility antigens HLA-DQ2 or HLA-DQ8 effectively excludes coeliac disease; however, over a third of European populations possess these genes, while only 1% to 2% of the population has coeliac disease.[16] Increased testing for coeliac disease using transglutaminase IgA and the new generation "deamidated gliadin peptide" IgA and IgG, and more systematic collection of small bowel biopsy samples by endoscopists, will steadily define those patients with coeliac disease who have a clear medical need for a strict gluten-free diet.[17,18] The popularity of the "fad" gluten-free diet might be peaking,[19] but the medical need for gluten-free diets continues to rise.

Competing interests

I am a consultant for Inova Diagnostics (USA), Prometheus Laboratories (USA), and Given Imaging (USA). I hold patents that pertain to the diagnosis, treatment and prevention of coeliac disease, and am the founding director of and a substantial shareholder in Nexpep (Australia). Nexpep is a holding company with shares in ImmusanT (USA), which is developing tests and treatments for coeliac disease. I am a founding shareholder of ImmusanT. My employer, Walter and Eliza Hall Institute of Medical Research (WEHI), has received research funds from Nexpep and Inova Diagnostics. WEHI is a Nexpep shareholder. I am a paid speaker and have developed lecture programs on coeliac disease for AstraZeneca Australia.

Author details

Robert P Anderson, MB ChB, PhD, FRACP, Gastroenterologist,[1,2] Laboratory Head,[3] and Chief Scientist[4]
1 The Alfred Hospital, Melbourne, VIC.
2 The Royal Melbourne Hospital, Melbourne, VIC.

3 Immunology Division, Walter and Eliza Hall Institute of Medical Research, Melbourne, VIC.
4 ImmusanT, Cambridge, Mass, USA.
Correspondence: banderson@wehi.edu.au

References

1 Revised criteria for diagnosis of coeliac disease. Report of Working Group of European Society of Paediatric Gastroenterology and Nutrition. *Arch Dis Child* 1990; 65: 909-911.
2 Anderson RP. Coeliac disease: current approach and future prospects. *Intern Med J* 2008; 38: 790-799.
3 Chin MW, Mallon DF, Cullen DJ, et al. Screening for coeliac disease using anti-tissue transglutaminase antibody assays, and prevalence of the disease in an Australian community. *Med J Aust* 2009; 190: 429-432.
4 Hovell CJ, Collett JA, Vautier G, et al. High prevalence of coeliac disease in a population-based study from Western Australia: a case for screening? *Med J Aust* 2001; 175: 247-250.
5 Lohi S, Mustalahti K, Kaukinen K, et al. Increasing prevalence of coeliac disease over time. *Aliment Pharmacol Ther* 2007; 26: 1217-1225.
6 Godfrey JD, Brantner TL, Brinjikji W, et al. Morbidity and mortality among older individuals with undiagnosed celiac disease. *Gastroenterology* 2010; 139: 763-769.
7 Lohi S, Mäki M, Rissanen H, et al. Prognosis of unrecognized coeliac disease as regards mortality: a population-based cohort study. *Ann Med* 2009; 41: 508-515.
8 Metzger MH, Heier M, Mäki M, et al. Mortality excess in individuals with elevated IgA anti-transglutaminase antibodies: the KORA/MONICA Augsburg cohort study 1989–1998. *Eur J Epidemiol* 2006; 21: 359-365.
9 Catassi C, Kryszak D, Bhatti B, et al. Natural history of celiac disease autoimmunity in a USA cohort followed since 1974. *Ann Med* 2010; 42: 530-538.
10 Rubio-Tapia A, Kyle RA, Kaplan EL, et al. Increased prevalence and mortality in undiagnosed celiac disease. *Gastroenterology* 2009; 137: 88-93.
11 Vilppula A, Collin P, Mäki M, et al. Undetected coeliac disease in the elderly: a biopsy-proven population-based study. *Dig Liver Dis* 2008; 40: 809-813.
12 Vilppula A, Kaukinen K, Luostarinen L, et al. Increasing prevalence and high incidence of celiac disease in elderly people: a population-based study. *BMC Gastroenterol* 2009; 9: 49.
13 Mäki M, Mustalahti K, Kokkonen J, et al. Prevalence of celiac disease among children in Finland. *N Engl J Med* 2003; 348: 2517-2524.
14 Karell K, Louka AS, Moodie SJ, et al. HLA types in celiac disease patients not carrying the DQA1*05-DQB1*02 (DQ2) heterodimer: results from the European Genetics Cluster on Celiac Disease. *Hum Immunol* 2003; 64: 469-477.
15 Hadithi M, von Blomberg BM, Crusius JB, et al. Accuracy of serologic tests and HLA-DQ typing for diagnosing celiac disease. *Ann Intern Med* 2007; 147: 294-302.
16 Klitz W, Maiers M, Spellman S, et al. New HLA haplotype frequency reference standards: high-resolution and large sample typing of HLA DR-DQ haplotypes in a sample of European Americans. *Tissue Antigens* 2003; 62: 296-307.
17 Kaukinen K, Collin P, Laurila K, et al. Resurrection of gliadin antibodies in coeliac disease. Deamidated gliadin peptide antibody test provides additional diagnostic benefit. *Scand J Gastroenterol* 2007; 42: 1428-1433.
18 Gonzalez S, Gupta A, Cheng J, et al. Prospective study of the role of duodenal bulb biopsies in the diagnosis of celiac disease. *Gastrointest Endosc* 2010; 72: 758-765.
19 Datamonitor Research Store. The future of gluten-free: consumer insight and product opportunities. http://www.datamonitor.com/store/Product/the_future_of_gluten_free_consumer_insight_and_product_opportunities?productid=BFCM0387 (accessed Jan 2011). ❑