



A CEREAL OFFENCE

PATHOLOGY IS VITAL AT EACH STEP TOWARDS A DIAGNOSIS OF COELIAC DISEASE,
AS MATT JOHNSON DISCOVERS.

We are a civilisation built on a tiny mutated protein. Nearly 7000 years ago a group of Middle Eastern nomads discovered a wild grass that, as a result of an unusual molecular arrangement, produced a grain so high in energy that it encouraged them to give up their wandering lifestyle and settle in one place.

Anthropologists will suggest everything that followed – buildings, cities, churches, writing, art – resulted from the discovery of wheat and the promise it fulfilled of a regular food supply.

It is ironic, then, that 1% of modern humans may now be sensitive to the very thing that inspired this great cultural expansion. For those suffering from coeliac disease, gluten – the glycoprotein present in wheat, and to a lesser extent rye, barley and oats – is a no-go zone that can cause highly unpleasant and life-changing symptoms.

Under a microscope, the apparently smooth lining of the small intestine is actually thousands of tiny finger-like projections, or villi, which protrude into the gastrointestinal space. The purpose of these villi is to increase the surface area of the bowel, increasing its ability to absorb nutrients and pass them into the bloodstream.

But expose these villi to gluten and, in up to 1% of the population, an inflammatory response will be provoked that can leave the villi sparse and stunted.

The subsequent reduction in available surface area can produce a bewildering range of symptoms felt across nearly

every system in the body. Abdominal pain, bloating, diarrhoea and weight loss are classic coeliac disease presentations.

In certain people, gluten causes the release of cytokines in the intestinal wall. Part of an immune response, the cytokines not only damage the tissue but they also activate other cells to produce antibodies to gluten and the bowel wall itself, further sensitising the intestine to subsequent exposures.

CHANGING PATTERNS

Coeliac disease was most commonly diagnosed in babies when they started on solid foods. But the pattern of the disease is now changing, with many sufferers presenting later in life with symptoms related to their inability to absorb vitamins, minerals and nutrients.

And these symptoms can be easily confused with other conditions such as irritable bowel syndrome, lupus, anaemia or just poor diet, leaving these ‘latent’ coeliacs to be treated for conditions they don’t have while their doctors work to slowly unravel the real cause of the problem.

Equally puzzling are the ‘silent’ coeliacs: sufferers who have virtually no symptoms.

But here is where pathology comes in.

With highly sensitive and specific blood tests, combined with laboratory analysis of biopsy tissue, a diagnosis of coeliac disease can be confirmed.

Years of medical training meant anatomical and cytopathologist Dr Peta

Fairweather knew all this in theory, but she has since experienced the lot of the ‘silent’ coeliac first hand after it became apparent the disease was in her family.

“I had the blood tests when it was found my sister had coeliac disease and it was suggested I should be tested,” says Dr Fairweather, from Sullivan Nicolaidis Pathology in Queensland.

The results came back strongly positive despite the lack of any obvious symptoms.

Dr Fairweather was tested because research has identified genes commonly associated with coeliac disease. The production of the HLA-DQ2 genotype is found in approximately 90% of coeliac disease cases, while the HLA-DQ8 genotype accounts for a further 5–10% of cases.

Unfortunately, the two genotypes are also common in nearly 30% of the normal population, so there is speculation another gene may be responsible for the 10% correlation of coeliac disease between first-degree relatives.

Blood assays – the first step in diagnosing coeliac disease – are simple, relatively inexpensive and extremely accurate. They usually include tests for endomysial antibodies, anti-tissue transglutaminase antibodies, and anti-gliadin antibodies. Anti-gliadin antibody is an antibody produced against gluten, while endomysial and anti-tissue transglutaminase antibodies are antibodies produced against the body’s own tissues as a result of the immune response to gluten.





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The endomysial and anti-tissue transglutaminase antibody tests are highly reliable, and an individual with abnormally elevated levels has a greater than 95% chance of having coeliac disease. Anti-gliadin antibodies are less reliable for

The Coeliac Society

Adult coeliacs and parents of coeliac children have formed coeliac societies in every state. These societies provide information on the disease, gluten-free diets, gluten-free ingredients and where to buy them, cooking and recipes, gluten-free medicines, overseas travel and education material.

The Coeliac Society of Australia
First Floor, 306 Victoria Avenue
Chatswood NSW 2067
(PO Box 703, Chatswood NSW 2057)
Ph: (02) 9411 4100
Web: www.coeliac.org.au
Email: info@coeliacsociety.com.au

diagnosis, but can be useful in monitoring the response to treatment.

Although the tests are highly accurate, a biopsy of the small bowel is needed to confirm the diagnosis. This involves a thin tube being passed down the mouth into the small intestine, where a sample of tissue is collected.

“Once the tissue is collected and processed,” Dr Fairweather explains, “it is carefully mounted, sectioned and stained so we see a cross-section of as many finger-like villous processes as possible.”

The sections are viewed by a pathologist through a microscope.

“The typical microscopic appearance of the small bowel of a coeliac patient is blunt or flat villi with too many inflammatory cells,” she says.

“In some cases the villi can appear normal, but there might be too many inflammatory cells present. If the pathologist is suspicious, a special test can be performed on the same piece of tissue to check for the number of T cells

“The tests are sensitive and specific, an effective and harmless treatment exists, and there’s an increased morbidity/mortality later in life if the disease is undiagnosed”
– Dr Glen Reeves

(the cells that cause damage in coeliac disease) in the bowel lining.”

In Dr Fairweather’s case, her positive blood tests did not correspond with her normal biopsy result.

“The tissue was normal, but my gastroenterologist wasn’t convinced and scheduled me for regular reviews,” she says.

Five years later her biopsy showed the changes typical of coeliac disease. Yet Dr Fairweather still had no overt symptoms.

PREVALENCE INCREASING

There is no cure for coeliac disease and the only treatment is to follow a gluten-free diet. Provided the diet is followed, the villi eventually recover and the symptoms will subside. But the life-long diet has long been considered to be complex, expensive and socially disruptive, which is why it must be preceded by histological proof from a biopsy. It is also why some have felt that ‘silent’ coeliacs – those with biopsy changes but no symptoms – could be spared the inconveniences of a gluten-free diet.

But that notion is changing as the prevalence of coeliac disease and the long-term effects are becoming more apparent.

Once thought to affect fewer than one in every 500 people with Northern European ancestry, there are now studies

COELIAC DISEASE FACTS

- The symptoms of coeliac disease vary widely: some people have few symptoms, but 43% complain of gastrointestinal symptoms, while 20% present primarily with 'tiredness'. Some of the more common symptoms include tiredness, intermittent diarrhoea, abdominal pain, flatulence, bloating, weight loss, fatigue, lethargy and anaemia.
- Children with coeliac disease may also have slow growth, irritability, a swollen abdomen and delayed development.
- A gluten-free diet should never be started before an endoscopy or blood tests, as it will interfere with establishing the correct diagnosis.
- Research has confirmed that while coeliac disease has a genetic component, it can also be triggered by various environmental factors, possibly explaining the late onset of the condition in 'latent' coeliacs.
- Australian doctors also routinely order tests to ensure the IgA deficiency common in patients with coeliac disease doesn't distort the results of the other tests. Blood tests to check for nutritional deficiencies may also be necessary, with iron, folate, vitamin B12, calcium and vitamin D levels the most commonly affected.

suggesting one in every 100 Australians has the condition.¹ This is more than 10 times the figure quoted a decade ago, and it's now estimated only 10–20% of coeliac sufferers are diagnosed, despite others showing symptoms or complications from the disease.

There has also been increased awareness about the disease's complications, with links to diabetes, liver disease, bowel cancer, epilepsy and infertility all being investigated.

TO SCREEN OR NOT TO SCREEN?

The increased prevalence and impact of the disease has led some to call for mass screening.

Dr Glenn Reeves, Senior Staff Specialist in the Department of Immunology and Immunopathology at John Hunter Hospital in NSW, strongly supports the proposal that children be routinely screened.

He argues that coeliac disease meets at least four of the five World Health Organization criteria for mass screening.

"The tests are sensitive and specific, an effective and harmless treatment exists, and there's an increased morbidity/mortality later in life if the disease is undiagnosed," he says.

However, critics of mass screening suggest that the social difficulties imposed by a gluten-free diet are too

serious to be inflicted on those with positive blood tests with normal biopsy results, especially while studies suggest blood tests alone are poor predictors of whether the disease will ultimately cause cell changes in the intestine.²

But other studies³ have disproved the notion that screen-detected, asymptomatic patients would be poorly compliant with a gluten-free diet, with Finnish research finding dietary compliance comparable with symptomatic coeliac patients.

The worldwide applicability of these results has been questioned, since coeliac disease in Finland is widely recognised and gluten-free foodstuffs are readily available.

However, Dr Fairweather has noticed an enormous change in Australia since she was diagnosed.

"There is definitely an increased awareness of gluten intolerance and coeliac disease amongst general practitioners and alternative therapists such as naturopaths," she says. "The restaurant industry is generally very educated now with even fast food restaurants carrying cards carefully detailing allergens in their products, and the range of prepared gluten-free products now available in supermarkets is amazing."

She adds that provided a person with coeliac disease uses principally fresh,

unprocessed food products, they can easily maintain a varied and balanced diet. Rice is naturally gluten free and gluten-free pasta and bread are widely available in health food stores and supermarkets.

While universal screening for coeliac disease may not be widely supported, studies^{4,5} show that an increased awareness of coeliac disease by GPs will capture patients who were not previously accurately diagnosed.

"The prevalence of coeliac disease among the general population is becoming more established," Dr Reeves says. "But the key is working with doctors to make them think about coeliac disease and to test for it even when there are other legitimate explanations for the symptoms their patients are presenting with.

"The tests are just too simple and too accurate, and the benefits too great for it to be ignored." 🔥

References

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GPs NOTE: This article is available for patients at <http://pathway.rcpa.edu.au>