

Why is the gluten free diet not helping me?

Following on from the article in the March 2010 edition titled “If it’s not coeliac disease, then why am I sick doctor”, Dr Jason Tye-Din* discusses the problem of persistent symptoms in coeliac disease.

INTRODUCTION

Some people with coeliac disease describe persistent symptoms despite a gluten free diet (GFD). Often called ‘non-responsive coeliac disease’, this is a common problem that can manifest as a lack of an initial beneficial response to the GFD or the recurrence of symptoms while following a GFD after having experienced an initial benefit. There are a variety of symptoms reported in non-responsive coeliac disease, but the most common include diarrhoea, abdominal pain and weight loss. While many symptoms, particularly gastrointestinal ones such as bloating, wind and abnormal bowel habit improve quite rapidly after instituting a GFD (often within days to weeks), some such as lethargy take longer to improve. In many cases it is simply a matter of time and maintaining a strict GFD before a benefit is experienced. This article will address issues to consider when this does not occur. As always, people should consult with their local doctor, specialist and dietitian to determine the best course of action for them.

IS COELIAC DISEASE THE RIGHT DIAGNOSIS?

A seemingly obvious but sometimes overlooked reason for a person failing to respond to a GFD is that their diagnosis of coeliac disease is wrong. Put simply, the benefits of a strict GFD

will only be realised in people with confirmed coeliac disease. If doubts remain about the diagnosis then it should be revisited and confirmed with the necessary investigations. My previous article (The Australian Coeliac, March 2010) discussed how a diagnosis of coeliac disease is best made, with some of the potential pitfalls of current diagnostic testing. The proper use and interpretation of blood tests and small bowel biopsy while a person is maintaining a gluten-containing diet, and the judicious use of gene (HLA) testing are all important. The coeliac gene test can be particularly informative in non-responsive coeliac disease as, compared to blood testing or biopsy, the results are not dependent on gluten consumption. If the coeliac associated genes HLA DQ2 or DQ8 are not present then coeliac disease can be confidently excluded and other conditions investigated.

Assuming the diagnosis of coeliac disease is correct, what next?

ASSESSING THE ADEQUACY OF THE GLUTEN FREE DIET

Persistent symptoms may be an indicator of active coeliac disease, where ongoing gluten ingestion continues to cause inflammation in the bowel and throughout the body. Active disease is remedied by adopting an appropriately strict GFD. To determine if coeliac disease is active additional information is required. Blood tests are used to assess coeliac serology (antibodies to transglutaminase and gliadin) as well as nutrient levels (such as iron, vitamins D, B12 and folate), while a gastroscopy is used to sample the small bowel lining.

Increased coeliac antibodies suggest ongoing inflammation caused by gluten. Coeliac antibody levels will eventually return to normal levels (i.e. become negative) in a person with coeliac disease maintaining a GFD. This can take up to a year and occasionally longer. During this time it is reassuring to observe antibody levels trending down towards normal. Reduced nutrient levels, such as iron deficiency, can also be an indicator of active coeliac disease. Antibody and



nutrient levels provide a rough guide as to how well coeliac disease is being treated, but can be inaccurate and sometimes misleading. Poorly treated coeliac disease can be associated with normal antibody and nutrient levels.

The best method to assess coeliac disease activity is to analyse tiny samples of the small bowel (biopsies) under the microscope. A simple day-case procedure called a gastroscopy, where a flexible instrument is inserted into the bowel while the patient is sedated, allows small bowel biopsies to be readily taken. Healthy lining, appearing as finger like projections called villi, suggest adequately treated coeliac disease, whereas flattened and inflamed lining (villous atrophy) indicates ongoing active coeliac disease. It used to be thought the small bowel heals back to normal within one year of commencing a GFD. While this may be true in most children, in adults this happens in less than half of cases. It can take two or more years for the small bowel to show evidence of complete healing on an adequately strict GFD¹. Adequacy of the GFD, age of coeliac disease diagnosis, severity of the initial bowel damage and genetic factors all influence how long the bowel takes to heal. It is common clinical practice to perform a gastroscopy some time after starting a GFD to confirm small bowel healing and adequate compliance to the diet. Doctors usually wait up to a year before repeating the gastroscopy,

but with the understanding that healing often takes longer periods of time, waiting 18 months to two years is becoming more commonly practised.

DIETARY GLUTEN IS THE MOST COMMON CAUSE OF PERSISTENT SYMPTOMS

Ongoing gluten intake, whether inadvertent or deliberate, is common and accounts for more than half of cases of persistently active coeliac disease². Accidental ingestion of gluten is common as it is ubiquitous in the Western diet. Deliberate consumption may occur when the coeliac sufferer thinks, “a little bit won’t hurt” and fails to appreciate what is a harmful amount of gluten. Unfortunately, as little as 50mg of gluten (1/100th of a slice of bread) over a period of time can cause damage. This inflammation is associated with several complications including osteoporosis and lymphoma. In practice, there is no way of determining a “safe” level of gluten. Notably, the absence of symptoms when ingesting gluten does not mean that the body is safely tolerating it; small bowel damage and inflammation can still occur without noticeable symptoms. The only solution is strict avoidance of all dietary gluten.

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Interestingly, people with coeliac disease often report becoming more sensitive to gluten exposure several months after commencing a strict GFD. This can lead to unexpected symptoms from small amounts of gluten that were previously “tolerated” before diagnosis. Consultation with an accredited

practising dietitian familiar with coeliac disease and the GFD can be extremely useful in highlighting potentially hidden sources of gluten and teaching important techniques to avoid gluten contamination. Even patients with a reasonably good understanding of the GFD can derive benefit. The consultation may uncover unsuspected hidden sources of gluten, reveal unsafe food preparation practices, issues with interpreting food labels and other problems commonly encountered by people grappling with the complexities of a GFD.

SOME COELIAC-RELATED DISORDERS CAN CAUSE PROBLEMS

A variety of medical problems can cause symptoms in people with coeliac disease already maintaining a GFD. Some of these are associated with coeliac disease (such as microscopic colitis, pancreatic insufficiency and refractory coeliac disease), and others appear to be unrelated (such as irritable bowel syndrome).

Microscopic colitis and pancreatic insufficiency are uncommon. Microscopic colitis is due to inflammation of the large bowel and causes watery diarrhoea. It is diagnosed by biopsies of the colon taken during a colonoscopy (examination of the large bowel) and is treated with a strict GFD and medications targeting the large bowel inflammation. Pancreatic insufficiency is due to a failure of the pancreas to produce adequate digestive enzymes leading to malabsorption of nutrients and fatty diarrhoea. It is tested by measuring the amount of fat in the faeces and readily treated by replacing pancreatic enzymes with each meal.

Refractory coeliac disease is, fortunately, quite rare. People with refractory coeliac disease usually have quite pronounced symptoms. It is a concerning condition as it is a potential precursor to small bowel lymphoma, a serious and lethal form of cancer. Refractory coeliac disease is associated with abnormal immune cells in the gut (“monoclonal T cells”) associated with small bowel inflammation despite a strict GFD. Special tests performed on small bowel biopsies can demonstrate the abnormal T cells, and tests such as CT scans are performed to screen for lymphoma. Treatment involves the use of immunosuppressant medication

or occasionally chemotherapeutic agents and regular surveillance for lymphoma. Specialist management is vital. As more is understood about why and how refractory coeliac disease occurs better therapies will become available.

IRRITABLE BOWEL SYNDROME AND NON-GLUTEN FOOD TRIGGERS ARE COMMON

A relatively common cause of gastrointestinal symptoms in coeliac disease is co-existent irritable bowel syndrome (IBS). While not dangerous in itself, it can contribute to symptoms such as bloating or abdominal pain in the absence of dietary gluten. Frequently, the symptoms of IBS are triggered by poorly absorbed fermentable sugars in the diet called FODMAPs (Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols). Major dietary FODMAPs include fructose, fructans (long molecules of fructose) and lactose (found in large amounts in some dairy products). A GFD invariably leads to a change in the types of food eaten, with greater intake of foods high in FODMAPs common. This can be one reason for the new onset of symptoms in a coeliac who initially responded very well to a GFD.

Bacterial overgrowth in the small bowel can occasionally trigger IBS symptoms. Antibiotics can be helpful. Investigation is with hydrogen breath testing, which can also be used to diagnose fructose malabsorption and lactose intolerance. Some people report benefit from excluding various food chemicals, additives and preservatives such as salicylates, but this requires a strict elimination diet. This is complex and should only be undertaken in consultation with a dietitian. More research is required to better understand the role of specific food chemicals in gastrointestinal symptoms and disease.

Other non-coeliac related causes of symptoms can co-exist with coeliac disease. These include problems like inflammatory bowel disease (such as Crohn’s disease), large bowel cancer (colorectal cancer) and infection. A specialist will consider all these possible diagnoses plus others when assessing anybody with coeliac disease who has persisting symptoms. Sometimes the clinical picture and type of symptom(s) provide clues as to the underlying cause. For instance, refractory coeliac disease may manifest as an unwell

patient with significant diarrhoea, weight loss and abdominal pain, while microscopic colitis typically causes watery diarrhoea with minimal other symptoms. Bleeding from the bowel is not usually due to coeliac disease but can be an important symptom of a serious underlying disorder such as colorectal cancer.

CONCLUSION

Symptoms caused by gluten in coeliac disease usually resolve over time with an adequate GFD. When they don't there are several possibilities. Raised coeliac antibodies and low nutrient levels can indicate active coeliac disease and an inadequate GFD, and this is best confirmed by small bowel biopsies documenting inflammation. Active coeliac disease is most commonly caused by ongoing

gluten ingestion, whether deliberate or inadvertent, and consultation with a specialist dietitian can be extremely rewarding. Co-existent IBS/FODMAP malabsorption is being increasingly recognised as a cause of symptoms independent of gluten intake. The involvement of a specialist is important to assess all possible causes, exclude serious underlying conditions, and institute the most appropriate treatment.

References

1. Rubio-Tapia, A., et al. Mucosal Recovery and Mortality in Adults With Celiac Disease After Treatment With a Gluten-Free Diet. *The American journal of gastroenterology* (2010).
2. Abdulkarim, A.S., Burgart, L.J., See, J. & Murray, J.A. Etiology of nonresponsive celiac disease: results of a systematic approach. *The American journal of gastroenterology* 97, 2016-2021 (2002).

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Table 1 – Potential causes for ongoing symptoms despite a gluten free diet

- > Wrong diagnosis (coeliac disease is not present)
- > Ongoing gluten ingestion (accidental or deliberate) – most common cause
- > Irritable bowel syndrome/FODMAPs and other food triggers
- > Microscopic colitis
- > Pancreatic insufficiency (uncommon)
- > Refractory coeliac disease (uncommon)
- > Other co-existing gastrointestinal disorders e.g. Inflammatory bowel disease, infection

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