

# The year after diagnosis

## Sue Shepherd\* reports on what changes in blood tests and biopsies tell us and don't tell us over the first twelve months of a gluten free diet.

The diagnosis of coeliac disease is based upon two features:

Characteristic changes evident in the lining of the small bowel as seen under the microscope on small bowel biopsies; AND improvement in symptoms and well being or on duodenal biopsy – after commencement of a gluten free diet.

There is a large amount of information on the biopsy and the use of serology (blood tests for antibodies that give clues to the possible presence of coeliac disease), but less information on how we should use tests to show improvement. For example, there is an expectation amongst medical and other health professionals - and amongst many sufferers of coeliac disease – that people who strictly adhere to their gluten free diet should return normal small bowel biopsies and normal blood tests. Do the biopsies always return to normal, how long does it take, and how does this complete healing relate to the level of strictness with the diet are questions without ready answers in Australia today. Can initial blood tests or severity of biopsy predict the speed of healing? Can blood tests be useful indicators of dietary compliance and small bowel healing?

With a research grant from the Australian and New Zealand Coeliac Research Fund (ANZCRF), I was able to address these issues as part of my studies towards a PhD. While the results are yet to be published, I have outlined some of the findings of these studies below to show the value of such research to how we interpret the tests performed.

### WHO PARTICIPATED?

Sixty people with newly diagnosed

coeliac disease were recruited for the study. Fifty three of these completed the study in which their progress was carefully monitored at 6 weeks and 3, 6 and 12 months after initiating a gluten free diet (taught to them all by me). Blood tests to look at levels of tissue transglutaminase (tTG) and endomysial antibodies (EMA) were taken on every occasion. How tightly they adhered to the gluten free diet was assessed by 7 day food diaries and a dietary intake interview at all these time points. Their adherence to the diet was classified as being 'always', 'mostly' or 'poorly' compliant.

Of course, all participants had a small bowel biopsy performed for the diagnosis. These were graded according to how severe the injury was – 16 had mild villous lesions (the villi, the finger-like processes on the bowel lining, were mildly or minimally shortened) and 37 had severe injury (villi were flattened or markedly shortened). All participants had a repeat biopsy approximately 12 months after starting the diet.

### DIET AND THE SMALL BOWEL

All 53 participants to a greater or lesser extent adhered to the gluten free diet. Two were considered poorly compliant, 17 mostly compliant, and 34 patients received a gold star (i.e., were always compliant). As might be expected, such dietary changes were associated with improvement in the appearances of the biopsies in nearly all and in the levels of antibodies found. But, who did best? those with mild injury, those with gold star dietary compliance?

Only about 50% of the participants had a normal small bowel biopsy (ie, they had healed) at the end of the study. As you might have anticipated, those with mild injury did heal more commonly (3 out of 4) than those with severe injury (1 out of 3). This suggests that the more severe villous lesions take longer to heal. Because nearly everybody complied well with the diet, we did not find differences in the rates of healing between those mostly compliant and those always compliant. However, neither of the two who were poorly compliant healed.

### WHAT ABOUT THE SEROLOGY?

The antibodies were negative in 2 out of 10 patients prior to diagnosis,

reminding us that the antibodies cannot completely exclude coeliac disease, just as they should not be used to diagnose the condition (that is the job of the small bowel biopsy). Most (but not all) of the negative tests were in those with mild intestinal injury. The really interesting results were in what happened to the levels of antibodies over 12 months.

The antibody levels fell over time in all participants, even in the two who were considered poorly compliant. Not all patients returned normal blood tests at 12 months, despite strict dietary compliance. Around half of the patients still had raised tTG and around 1 in 5 patients still had raised EMA. Furthermore, in the patients who had a normal biopsy at 12 months, tTG was still raised in 40% of patients. It was also raised in approximately half of patients who did not have normal biopsies.

### WHAT DOES ALL THIS MEAN?

We can expect improvement in the biopsy in the vast majority of people, but a normal biopsy is achieved by only around half after 12 months of diet. It is likely that many more will heal over the next 12 months. So the message is, have patience, as healing takes time even when you are strictly adherent to the gluten free diet!

Important insights have been gained on how to interpret the blood tests, tTG and EMA. First, restriction of gluten reduces their levels, but falling levels does not mean that adherence is strict. Second, the antibodies can disappear even if you have not healed. Third, and perhaps the most important, persistence of antibodies can occur even if the small bowel has completely healed. The bottom line then is that serological blood tests cannot be used to assess strictness of gluten free diet or healing of the small bowel. Unfortunately, the reality of this is that, if you want to know if you bowel has healed, a biopsy is the only way!

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