COELIAC DISEASE — A CASE STUDY

By Pamela Mason, PhD, MRPharmS

With the advent of more sensitive testing, it is estimated that the prevalence of coeliac disease has risen to as many as one in 300. Pharmacists need to have an appreciation of the difficulties faced by patients with coeliac disease and be able to offer good practical advice

Alison is a 32-year old woman who has a history of bowel frequency with occasional bouts of constipation going back over 15 years. About 12 months ago, she was diagnosed by her doctor as having irritable bowel syndrome (IBS) for which she has occasionally tried mebeverine tablets with little beneficial effect. Today she comes to the pharmacy and asks for a medicine for diarrhoea. On questioning, Alison says she had a meal in an Italian restaurant yesterday evening after which she began to suffer what she felt to be the worst bout of diarrhoea and abdominal pains she had experienced for several years. She then admits that her bowels do seem to have been more troublesome than normal recently, and she is beginning to feel very miserable.

HOW WOULD YOU ADVISE ALISON?

The history here is not straightforward. Although the symptoms Alison describes could be indicative of IBS, other possibilities should be considered. Alison should therefore be referred to her general practitioner.

About a week later Alison returns to your pharmacy with a prescription for erythromycin for her four-year-old son. At the same time she tells you that her GP has referred her to a gastroenterologist for tests for coeliac disease.

WHAT IS COELIAC DISEASE?

Coeliac disease is a condition where there is a permanent intolerance to gluten. This results in stunting and disorganisation of the intestinal villi, with lymphocytic infiltration of the epithelial surface and malabsorption of nutrients.

WHAT IS GLUTEN?

Gluten has been defined as the viscoelastic mass which remains when a wheat flour dough is washed exhaustively in tap water.[1] The term has now been extended to include all those proteins which are harmful to individuals with gluten sensitivity, ie, the storage proteins of wheat, rye, barley and, possibly, oats (the role of oats in this regard is now much in doubt). Within wheat gluten, it is the gliadin (a simple protein seperable from wheat gluten) fraction that is known to trigger disease in susceptible individuals.

HOW DOES GLUTEN EXERT ITS HARMFUL EFFECTS?

Several hypotheses have been developed as to the aetiology of coeliac disease. Initially, it was thought that incomplete brush border hydrolysis of gluten occurred as a result of a deficiency of mucosal peptidase or carbohydrase, leading to the formation of toxic products. However, inability to show low activity of such enzymes following treatment with a gluten-free diet rendered this idea untenable. There is now growing acceptance that the immune system is involved. Ingestion of gluten activates T-cells in the small intestine, which results in release of inflammatory mediators. This causes damage to the absorptive surface of the small bowel and malabsorption of nutrients.

Alison asks you what the tests for coeliac disease will involve and having read something about the condition, she wonders whether she should try a gluten-free diet straight away.

HOW DO YOU RESPOND? HOW IS COELIAC DISEASE DIAGNOSED?

Biopsy of the small intestine is the gold standard for diagnosis of coeliac disease. There must be defined histological abnormalities (eg, villous atrophy) of the small intestinal mucosa in a patient eating a gluten-containing diet, which — and this is vital — revert to normal when gluten is removed from the diet. Conditions other than coeliac disease may also cause destruction of the villi; these include cows' milk protein intolerance, soya protein intolerance, gastroenteritis in children, infections (eg, giardia and HIV), Zollinger-Ellison syndrome (a syndrome caused by non beta-cell tumour of pancreatic islets) and tropical sprue (inflammation of the mucous membrane of the alimentary tract characterised by diarrhoea and stomatitis). This means that the appearance of biopsy specimens is non-specific, and definitive diagnosis requires repeat biopsy to demonstrate histological improvement on a gluten-free diet. Thus, if Alison embarks on a gluten-free diet before the biopsy, she will risk either misdiagnosis or having to go through a much lengthier diagnostic process. Indeed, if there is any doubt whether the patient has coeliac disease, he or she should be rechallenged with gluten. A return of the mucosal abnormalities will then confirm the diagnosis.

Some patients have milder lesions, and in some cases microvillous architecture is normal. However, the epithelium may contain an increased number of lymphocytes, and the diagnosis may therefore rely on a raised intra-epithelial lymphocyte count, which must, of course, be shown to be gluten-dependent.

The growing recognition that coeliac disease involves the immune system has led to the identification of a variety of antibodies to both dietary and endogenous antigens in patients with untreated coeliac disease. These include both IgA and IgG antigliadin antibodies and also IgA anti-endomysium (connective tissue surrounding intestinal smooth muscle) antibodies. This in turn has led to the development of a variety of serological tests.

However, although these tests can be useful for population screening, they currently lack sufficient sensitivity and specificity for diagnosis. Patients with conditions other than coeliac disease, such as Crohn's disease, also have raised serum anti-gliadin antibodies, although measurement of anti-endomysium antibodies is more specific. Within the endomysial tissue, it is now recognised that the target antigen is the enzyme known as tissue transglutaminase (tTG), and this has allowed the development of a cheap and simple enzyme-linked immunosorbant assay (ELISA) for IgA-tTG,[2] which could prove invaluable for screening in GP surgeries.

Dr Pamela Mason is a pharmacist and freelance pharmaceutical journalist, with a special interest in nutrition. She is based in Sydenham, South London

A few weeks later you see Alison in the queue at the local post office and she tells you that she has been diagnosed with coeliac disease. Clearly upset by this, she is also angry that she has suffered bowel problems for so long without receiving a proper diagnosis.

WHY DO YOU THINK THIS COULD HAVE HAPPENED?

Coeliac disease may well be considerably underdiagnosed. Traditionally, the prevalence of coeliac disease in the UK was believed to be about one in 1,500. However, the advent of sensitive serological tests has encouraged more research into the condition, suggesting that the true prevalence may be higher and that about one in 300 of the general population may be gluten-sensitive. Moreover, 30 years ago, coeliac disease was almost exclusively a paediatric condition, and failure to have caught up with the fact that it is now more prevalent in adults than children may mean that a diagnosis is missed.

The presentation of the disease is highly variable and the classic symptoms of diarrhoea, weight loss and general malaise do not always occur. Some patients may be constipated and a few may be obese, while others, like Alison, may present with irritable-bowel like symptoms. Others may not present with gastrointestinal symptoms, but with depression, infertility, or fatigue and breathlessness, which in the case of coeliac disease are usually due to the anaemia resulting from poor absorption of iron and folic acid. The difficulty is, of course, that many illnesses can start in this way.

In addition, the clinical features of coeliac disease may sometimes be overshadowed by the more dramatic manifestations of diseases that are associated with it, thus delaying diagnosis. Conditions linked with coeliac disease include dermatitis herpetiformis, epilepsy, type 1 diabetes mellitus and Down's syndrome. The possibility that there might be a connection between coeliac disease and autism and multiple sclerosis has also attracted interest, but evidence for these associations is not conclusive.

Diagnosis may also be delayed because of clinically silent lesions. It is now thought that the clinically obvious forms of coeliac disease may actually form the tip of the iceberg, underneath which there is a large base of silent gluten sensitivity. In these cases there are no signs and symptoms although there is histological evidence of enteropathy. In addition, there is a group of patients who have positive serological tests for gluten sensitivity, but in whom a small bowel biopsy appears normal. The term "latent coeliac disease" is applied to these individuals meaning that they do not currently have symptoms while consuming a normal gluten-containing diet, but they will develop gluten-sensitive enteropathy in later life.

WHAT IS THE TREATMENT FOR COELIAC DISEASE? HOW SOON CAN ALISON EXPECT TO FEEL BETTER?

Dietary avoidance of gluten is central to the management of coeliac disease and most patients notice a significant improvement in their symptoms within a few days. Mucosal improvement takes longer and full recovery of the normal appearance of the villi may take up two to three months.

Wheat, rye, barley and triticale (a hybrid of wheat and rye) are the main sources of gluten, and foodstuffs made from these cereals, including bread, biscuits, cakes and pastry should be excluded. In the UK, as in many other countries, wheat forms an important part of the diet, and cutting out bread and cereals may encourage the consumption of excessive fat. A large number of processed, gluten-free foods such as bread, pasta, cakes and biscuits are available commercially, some of which are available on prescription for those with a definite diagnosis. Some of these products are made from naturally gluten-free foods such as soya, rice and maize; others are based on wheat starch rendered gluten-free. The latter are prepared by washing flour so that the water-insoluble gluten is removed leaving the starch behind.

CAN ALISON EAT OATS?

Traditionally, oats were excluded from the diet of patients with coeliac disease, but this practice is now questioned. Oats contain less gluten than other cereals and a Finnish study showed no adverse nutritional or mucosal effects from a daily intake of 50g of oats.[3] Preliminary studies also suggest that oats are safe for children, although further confirmation is necessary.[4] Nevertheless, patients should take care to buy oats from a dedicated oats miller, as contamination with wheat during harvesting, storage and milling may occur.[1]

A few weeks later Alison comes to the pharmacy for her repeat prescription for gluten-free flour. She tells you she has been doing fine until about 10 days ago when the diarrhoea returned on an almost daily basis. Clearly miserable, she says she cannot understand it because she has been sticking to her diet closely.

WHAT COULD BE THE CAUSE OF ALISON'S DIARRHOEA?

Many manufactured foods contain gluten because cereal proteins are often used as fillers or binders, and these are a frequent cause of dietary problems. Other substances that may contain gluten include malt, malt extract, malt flavouring, beer and lager (malting enzymes do not fully break down barley gluten so gliadin-like substances may remain). In addition, malt extract is frequently used as a flavouring agent in foods such as breakfast cereals, which may be consumed by patients with coeliac disease as a convenient snack instead of bread.[1] The use of breakfast cereals should therefore be considered in any individual not responding to an apparently gluten-free diet. Patients should be wary of all processed foods unless specifically advised they are gluten-free. Coeliac UK (formerly the Coeliac Society) works with food manufacturers to produce a regularly updated list of gluten-free foods.

The advent of new technology has also increased the hazards for people with coeliac disease. For example, some manufacturers have attempted to use gluten as a coating to make apples shine, and there have been moves to replace the traditional wax coating on Edam cheese with a gluten coating.[1] There is also a biodegradable cling film based on gluten. Tablets may occasionally contain gluten. Communion wafers are another potential risk, although gluten-free wafers are available.

WHY IS DIETARY COMPLIANCE SO IMPORTANT?

Compliance with the gluten-free diet is important not only because it prevents relapse, but also because it helps to reduce the risk of more sinister complications, in particular small bowel lymphoma, to which patients with coeliac disease are at increased risk. Poor compliance may also increase the risk of osteoporosis due to reduced absorption of calcium, failure to achieve peak bone mass and increased loss of bone in later life.

It has sometimes been thought that people can grow out of coeliac disease. This idea emerged when it was noted that not all coeliac patients relapsed when gluten was added to their diets. However, with tighter diagnostic criteria it became apparent that coeliac disease which had apparently disappeared did show histological relapse when gluten was added to the diet. Today this would be known as silent coeliac disease because there are no signs and symptoms. The gluten-free diet should be followed strictly and for life and pharmacists have a vital role in encouraging compliance.

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