Coeliac disease

Introduction

Coeliac disease is probably the most common auto-immune condition leading to dietary problems in the UK. It goes by a number of names, including the more descriptive gluten intolerance or gluten-sensitive enteropathy, and in America is it spelt at Celiac disease.

Epidemiology of the disease

Coeliac disease was regarded as quite rare in the west until the 1970s (Scanlon and Murray 2011), but is now considered common, particularly in the United Kingdom. It occurs in all ethnic groups, but its true rate is difficult to determine due to the wide range of manifestations and variations in the thoroughness of investigation of patients problems. It probably affects more than 1% of the population of the western world, in the United Kingdom one person is diagnosed for every one to three hundred population (Holmes 2009), but this is considered the "tip of the iceberg" (Scanlon and Murray 2011) as there is a great deal of variety in how it is experienced, and for every person diagnosed there are probably as many as between seven and ten people coping without a diagnosis. These people usually have mild symptoms, but may also be older (Holmes 2009, Scanlon and Murray 2011). Furthermore it may be even more common in Ireland and Scandinavia.

The increase in rates reported for the disease is only partly the result of improved diagnosis, and it does appear that there is a genuine increase in the prevalence of the disease; it has increased by about four fold between the 1950s and today (Scanlon and Murray 2011). The reasons for this are not clear, but there has certainly be changes in the genetics, processing and modifications of wheat and the age at which children are exposed to it. The increase could also be attributed the "hygiene hypothesis", which is the suggestion that children, in particular, are now growing up in such a clean environment that their immune system is not as efficiently regulated as it was in a simpler environment.

There is a genetic pre-disposition for the disease, so that a person who has a first degree relative (parent or sibling) with the disease has a 10-20% chance of having it themselves, and if one of a pair of monozygotic twins has the disorder, then there is a 75% chance that the other will also have it (Holmes 2010). Although this may be partly attributed to extra vigilance in diagnosing the condition, most of this correlation is due to the inheritance of human leukocyte antigens (HLA) DQ2 and DQ8. About 40% of the general population have these, but one or both are present in 90-97% of people with Coeliac disease. Conversely, the disease very rarely occurs in the 60% of the population that do not carry these antigens (Holmes 2010). Therefore it is widely assumed that coeliac disease will never occur without a genetic pre-disposition.

However, as described above, having a genetic disposition for the disease does not necessarily lead to the development of the disease, and environmental factors must probably always be present. These include early infection with enterpathic viruses. There has been a great deal of discussion of the role of breast feeding in protecting people from developing coeliac disease: it appears that very early or very late introduction of an infant to wheat are both associated with an increased chance of developing the disease. The optimum arrangement may be first offering the infant wheat between

4-6 months, whilst at the same time continuing with breast feeding (Scanlon and Murray 2011). How this helps is not certain, but it appears that breast milk moderates the immune system to make it tolerant to gluten, even in genetically susceptible individuals.

Pathology of coeliac disease

Coeliac disease occurs as a result of exposure to gliadens and glutenins, these are both components of gluten, which is the collective name for proteins that naturally occur in wheat. They are also present in barley and rye. However it is the gliadens that appear most troublesome. For people with coeliac disease these proteins are not fully broken down by the digestive enzymes and are able to cross the intestinal epithelium. The exact mechanism is not known, but is thought to include both crossing the cells themselves and faulty tight junction between cells (BMJ best practice 2012). The effect of the presence of these complete peptides within the mucosa has been reviewed by Scanlon and Murray (2011), and involves both the specific (acquired) and non-specific (innate) immune systems. The non specific response involves gliaden binding to the CXC3 chemokine receptor leading to the release of zonulin from the intestinal cells. Zonulin is a protein that regulates the permeability of the intestinal epithelium and brings about an increase in the permeability of the stomach and small intestine and an alteration in their electrical resistance. Gliadin also stimulates the specific immune system via the intestinal CD4 class of T helper (Th) cells. People with severe coeliac disease will react to the presence of all types of gliaden, but people who are less affected will only respond to the α subtype. The amino acids within the gliaden are deaminated to glutamic acid which has an increased affinity to HLA-DQ2 and possibly HLA-DQ8, leading to an increased chance of the gliaden being recognised as an antigen and therefore the target of an immune response. Plasma cells release immunoglobulin A and immunoglobulin G, but these may not be part of the disease process. However increased activity of the CD4 T helper cells, B cells, macrophages and dendritic cells all enhance the immune reaction leading to inflammation. This chronic inflammation leads to flattening and atrophy of the villi, resulting in a reduced surface area for the absorption of nutrients. At the same time new epithelial cells growing in the crypts are unable to migrate up the villi as they mature, so that the crypts display hyperplasia (an increase in the number of cells). This means that the nutrients in the lumen of the small intestine cannot be digested and absorbed efficiently, causing partly digested food to enter the large bowel. This leads to diarrhoea, bloating and other discomforts.

Effects on the individual

The problems people with coeliac disease experience vary greatly; some of these problems are caused by alteration to the functioning of the bowel, but people also report a wide range of extra gastrointestinal manifestations, many of which are inflammatory in origin. This variety can complicate and delay diagnosis, so that people can be diagnosed with disorders such as irritable bowel syndrome. There is also evidence, explored by Lionetti et al (2010), that coeliac disease often accompanies neurological problems, which can be quite severe. Some of these could be nutritional in origin, for instance caused by a lack of vitamin B12, but some may be inflammatory in origin.

The manifestations of coeliac disease are divided several subtypes, summarised in BMJ best practice (2012) and outlined below:

Classic coeliac disease

typically arises during infancy, between the ages of six to eighteen months, or shortly after the first exposure to gluten in their diet. These children display abdominal distension, muscle wasting, developmental delay, a decrease in weight or weight for height, and possibly malnutrition. Older children tend to display less dramatic symptoms, but may be of short stature and show signs of demineralisation in their dental enamel. Adults with the disease often display more obvious malabsrption, including weight loss, vitamin deficiency, anaemia and osteopenia from vitamin D and calcium deficiency.

Atypical coeliac disease

tend to be less severe, and can be mistaken for irritable bowel syndrome. These people can often present mainly with extra-gastrointestinal problems such as anaemia, infertility, osteoporosis and malaise (Ulasli et al 2010).

Latent or silent coeliac disease

have the HLA-DQ2 or DQ8 subtype, but do not display villous atrophy but may show some mild inflammatory symptoms. Authors vary in how much significance they attribute to these findings; some say that this is not a pathology and can be disregarded, whilst some state that this is a mild disease state and that patients enjoy better health if they embark on a gluten-free diet, such as improved appetite, reduced fatigue and enhanced mental health and behaviour (Scanlon 2011). Latent coeliac disease can also herald more serious disease.

Non-responsive coeliac disease and refractive coeliac disease

are two groups of patients that fail to respond to a strict gluten free diet, even after 6 months. They are thought to account for about 1% of all people with coeliac disease (BMJ best practice 2012).

Diagnosis and assessment

Coeliac disease in children has been traditionally associated with failure to thrive and malnutrition, usually in very young children. More recently, however, it is being diagnosed rather later (Scanlon 2011) in which cases they often do not present with gastro-intestinal problems so much as reduced stature and - for girls - delayed menarche.

When people present for the first time as adults, the peak age for doing so is in the fifth decade for women and the sixth decade for men (Scanlon and Murray 2011). Some of these people would have missed out on a diagnosis at a much younger age, but for most of them the disease has genuinely occurred for the first time later in life; presumably they had the genetic predisposition and now have been exposed to an environmental trigger. Just like children, adults are now less likely to present with diarrhoea than they were in the 1970s.

Anyone with chronic and unexplained malabsorption, diarrhoea, osteoporosis (Ulasli et al 2010), dyspepsia, and deficiency for vitamin D or iron should be investigated for Coeliac disease (Scanlon 2011). It is also found at an increased rate in people with other auto-immune disorders, particularly type 1 diabetes mellitus (Triolo et al 2011) and in a variety of neurological conditions (Lionette et al 2010) .

Several immunological and tissue diagnostic tests should be conducted, and the client should continue to take gluten throughout the diagnostic process, as coeliac disease will normalise in the

absence of gluten (BMJ best practice 2012). Definitive diagnostic requires a biopsy of the duodenum at endoscopy showing inflammatory changes, which resolve within two weeks of the onset of a gluten-free diet. Current guidelines recommend taking at least four, preferably six or more biopsies, as Coeliac disease can be patchy and there is a danger of false negatives (BMJ best practice 2012). There are also a number of visual changes, including a mosaic pattern to the mucosa; loss of duodenal folds; nodular pattern to the mucosa and visibility of the sub mucosal blood vessels, although none of these are unique to coeliac disease. The changes can vary from mild and superficial to a complete absence of villi. There are a number of schema that quantify the degree of damage, the Oberhuber classification being one of the most popular at the moment (BMJ best practice 2012), which records the presence and height of the villi, but their width is also important.

There are a number of tests for antibodies that can be used to confirm the diagnosis, and can also be used to screen in highly susceptible individuals, and these are reviewed by Scanlon and Murray (2011). Even highly specific tests such as that for tissue transglutaminase (TTG) can give both false positives and false negatives, and must be interpreted with caution, particularly in the presence of conflicting histological or clinical findings. Furthermore, TTG may not always indicate the extent or severity of the disease.

Management of Coeliac disease

The definitive treatment is the omission of wheat, rye and barley products from the diet, but unfortunately this is difficult to achieve in practice. The law allows food marked as gluten free to have up to 20mg\kg to allow for some cross contamination that often occurs as food are prepared, or from some gluten left behind when wheat products are processed to make them gluten free. Foods that one would normally expect to be gluten free can actually have even more gluten in them than this (Scanlon and Murray 2011), yet it has been found that an intake of 50mg a day can cause an adverse effect on susceptible mucosa (Scanlon and Murray 2011). Until recently a gluten free diet was not recommended for anyone without quite noticeable symptoms, however Scanlon and Murray (2011) reviews recent evidence that even people with silent Coeliac disease may benefit from a gluten free diet, for instance their bone density may improve.

Most people with well controlled coeliac disease can take oats, and these can be a useful source of nutrition for them. There is no scientific agreement about whether oats can be taken: they do not contain gluten and could provide a valuable source of complex carbohydrate, however in practice some people appear to be troubled even by oats. This may be because they are often prepared in the same premises and other cereals and so are at risk of contamination. It is also possible that some people with coeliac disease respond to avenin, which is a protein in oats that has a similar role to gluten in wheat. A study by Kilmartin et al (2003) failed to show any response to avenin in the nine patients he tested. However, a slightly larger Swedish study reporting in the same year (Hollén et al 2003) found that 34 children with coeliac disease had higher levels of antibodies to avenin than did controls. It seems likely that a tiny minority of people with coeliac disease are troubled by avenin, and that more are affected by cross contamination.

Black and Orfila (2012) report a pleasingly high concordance with the diet amongst adult patients in England with the disease, and their respondents reported good levels of health and well being. These patients were contacted through the coeliac UK charity, and it is likely that the support from this charity was key to their success. The nurse may well want to encourage patients to contact this

society (http://www.coeliac.org.uk), who provide a source of information and encouragement to anyone affected by the disease. This support takes the form on online and paper information, paper newsletters and local groups.

However, a gluten free diet should not be embarked upon lightly: it is a life-long requirement; restrictive and difficult to achieve (McCabe 2012). Gluten is found in many staple foods and following a gluten free diet involves lifestyle changes for all the family. Foods to be avoided include all baked cakes and biscuits containing wheat, rye and barley; pies and flans made with pastry; pasta; semolina; breaded products such as fish fingers; thickened gravies and sauces, flavourings containing wheat such as crisps; tea and coffees containing whiteners (that often come from a vending machine) and some sweets. Because the disease is so variable, patients may vary also in the amount of gluten they can tolerate. Even several of Black and Orfila's (2012) compliant patients reported taking gluten; sometimes these intakes were accidental, and sometimes deliberate, perhaps in a social situation. Many found that occasional intake caused little harm. Tolerance to small amounts of gluten would be very useful, particularly for children. For coeliac children it must feel as if every birthday is celebrated with pizza, sandwiches and cake. Slight flexibility is useful, but needs to be approached on an individual basis, as regularly causing an immune response can lead to discomfort and also to significant health problems, as this article has shown.

The gluten free diet thus excludes many foods that form a staple part of the British diet. The patients with coeliac disease studies by Black, J.L. and Orfila, C (2012) found breakfast was the most challenging time – toast and Weetabix is not for them! However, many were happy to eat breakfast cereals such as Rice Krispies or Cornflakes, which many children will also find acceptable. Some gluten free varieties are commercially available. These are expensive however and, as its name implies, gluten provides the mechanical structure of the food, thus gluten-free products are often crumbly and unappetising. Having excluded so many foods, the nurse will want to ensure the patient remains well nourished, and a dietician's help should be enlisted. There is a danger that they will not take enough fibre, and they should be encouraged to eat other starchy foods such as potato and rice. They should eat plenty of fruit and vegetable in any form; lentils; soya; meats and dairy products and freshly prepared tea; coffee; fruit juices and most squash drinks except barley water.

Many foods that should not contain gluten are now marked as "gluten free". This statement of the obvious could be seen as exploiting a vulnerable group, however they be useful as there is a high degree of cross contamination in products not marketed as gluten free. Gluten can be found in other products such as skin care products and cosmetics, however gluten cannot possibly be absorbed through the skin, so these products can be safely used (Holmes 2010). Drugs prescribed in the UK are gluten free, but other remedies may not be (Holmes 2010).

Many patients benefit from nutritional supplements, and providing supplements of iron, calcium and vitamin D should be considered. After about one year of the gluten-free diet they should be assessed for their bone density (BMJ best practice 2012).

Matters may become easier for the person with coeliac disease with the introduction of enzymes, taken with food, which will degrade proline-rich peptides that characterise gluten. Laboratory work on these suggests that they are effective, and early clinical results indicate that they can reduce inflammation caused by small amounts of accidentally ingested gluten (Scanlon and Murray 2011).

However, they are not currently expected to enable people with coeliac disease to resume taking gluten, but to make minor dietary lapses less serious.

Conclusion

Coeliac disease is a common inflammatory disorder that causes discomfort and some serious health problems. It appears to be under-diagnosed so that many people are coping with less severe, but never the less significant, symptoms. The control of coeliac disease depends totally on excluding gluten from the diet, which is a staple of British food, so people need careful counselling to ensure they remain healthy and well nourished, and are able to enjoy their meal times.

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