

## **2025 Allied Health Workshop - Exploring the Spectrum of Gluten-Related Disorders - Dr Isabel Skypala PhD RD**

Gluten-related disorders can be divided up into three types; celiac disease (CD), non-celiac gluten sensitivity (NCGS), wheat allergy (WA) and wheat intolerance (WI). CD affects 1% of the UK population and can present at any age. CD is a genetically determined condition; first degree relatives have a 10% higher risk of developing the condition than the general population. Approximately 0.4% of children in the USA are allergic to wheat, but the condition is rare in adults as most children experience by adolescence. Adults are more likely to suffer from wheat-dependant, exercise-induced anaphylaxis (WDEIA); the sufferer only experiences symptoms to the food if it is consumed in close proximity to taking exercise. The overall prevalence of NCGS is unknown, but data suggests this is not an uncommon disorder. Wheat is often reported to provoke gastro-intestinal symptoms in those with irritable bowel syndrome (IBS); one study found that 14.3% of subjects associated wheat with abdominal symptoms and another, 30%.

CD and WA are both mediated by the immune system; CD is an autoimmune disorder, involving T-cell activation when gluten is consumed, resulting in villous atrophy and varying degrees of damage to the gut. Specific serologic autoantibodies, serum anti-tissue transglutaminase and anti-endomysial antibodies, will be present in CD, whereas the response in WA involves the development of IgE antibodies specific to wheat. These antibodies bind to the surface of mast cells and on exposure to wheat, they cross-link with the gluten peptides, leading to the destruction of the mast cells and release of histamine and other inflammatory mediators. Other types of gluten reactions involved in NCGS do not involve the immune system but the pathogenesis of the condition is unclear. Gluten proteins, along with the gliadins in wheat are major storage proteins known as prolamins; their resistance to heat and digestion makes them the primary proteins involved in WA and CD. Alpha, gamma and omega-5 gliadin all have a role to play in WA, although it is omega-5 gliadin which may be the most important provoking wheat allergen responsible for both WA in children and in WDEIA in adults.

CD is a multi-system disorder which presents with failure to thrive, diarrhoea, vomiting, abdominal distention, constipation, muscle wasting and irritability in infants. Symptoms in older children and adults vary; less than half will have symptoms of diarrhoea, and a significant proportion are of normal or even over-weight at diagnosis. Poor growth, anaemia, recurrent mouth ulcers and IBS-type symptoms are also reported. Diagnosis involves measuring serum anti-tissue transglutaminase and anti-endomysial antibodies. A biopsy of the small intestinal biopsy is considered the 'gold standard'. All tests require the patient to be consuming sufficient wheat for serology and biopsy results to be meaningful. The diagnosis of WA involves history, skin prick and specific IgE testing, followed by oral food challenge. Presenting symptoms can include erythema, pruritis, urticarial rash, laryngeal oedema, angio-oedema, and anaphylaxis. Skin prick and specific IgE tests for wheat often have poor predictive values, especially if the patient is also grass allergic, although the measurement of specific IgE antibodies to omega-5 gliadin is a useful predictor of wheat allergy in children and WDEIA in adults. For NCGS and other wheat-dependant hypersensitivity conditions, there are no markers which can be measured as yet. Thus the best test is an exclusion of wheat from the diet for a period of 6-8 weeks. If symptoms have improved then wheat should be re-introduced to ascertain the validity of the result.