

COELIAC DISEASE & GLUTEN SENSITIVITY

Going against the grain

Gluten, the protein that helps provide the 'glue' that binds certain foods also divides us into those who cannot eat it, those who can, and those who choose not to. Awareness and understanding of gluten-related disorders has improved over the past few decades as we began to understand the full spectrum of gluten-induced disease: from sensitivity, to allergy, to autoimmune response. In recognition of this renewed interest in the field, the past two issues of *Nature Reviews Gastroenterology & Hepatology* have featured specially commissioned articles from key opinion leaders, which have been brought together online in a special web [Focus](#).

Food is fundamental, it fuels us and provides nourishment, but what happens when components within our food can be a trigger of disease? Coeliac disease is a chronic, immune-based enteropathy for which that trigger is known—gluten. Moreover, the major susceptibility genes, HLA-DQ2 and HLA-DQ8, have been identified. In individuals with this condition, ingestion of gluten (found in wheat, barley and rye) triggers an autoimmune response. The resulting inflammation and damage to the small intestine leads to symptoms such as diarrhoea, abdominal pain, bloating and malabsorption.

The fact that both the environmental trigger and host genetics for susceptibility to coeliac disease is known does not mean we know everything about the condition. This scenario makes coeliac disease an interesting test case to examine additional disease modifiers and genetic overlap with other autoimmune conditions. In their Review, [Elena Verdu](#), [Heather Galipeau](#) and [Bana Jabri](#) explore how the gut microbiota might play a part in coeliac disease pathogenesis, whilst [Knut Lundin](#) and [Cisca Wijmenga](#) examine the interplay between coeliac disease and other autoimmune diseases, and how that might affect the rationale for disease screening.

Coeliac disease is not just about the small intestine, and several extraintestinal manifestations have been reported. [Alessio Fasano](#) and colleagues review these different manifestations that can affect the skin (dermatitis

herpetiformis), musculoskeletal system (osteoporosis) and, interestingly, brain (gluten ataxia) and behaviour (anxiety).

In a [unique article](#), experts from across the world provide insights into the practicalities of the gluten-free diet (GFD)—the only available treatment for patients with coeliac disease. Perspectives from both a gastroenterologist and registered dietitian are given in a bid to increase awareness of the challenges, management and follow-up necessary for patients with coeliac disease on a GFD. It sounds easy, but simply excluding gluten from your normal diet is more complex than anticipated: adherence, costs, cross-contamination, quality of life and effects on health are all complicating factors. Although rare, a small proportion of patients have persistent or recurring symptoms, with ongoing malabsorption and villous atrophy, despite a stringent GFD and, as explained by [Chris Mulder *et al.*](#), could have refractory coeliac disease.

Moving on to other gluten-related disorders, [Imran Aziz and co-workers](#) introduce noncoeliac gluten sensitivity (NCGS), a new clinical entity that has recently entered the medical vernacular. NCGS is not without controversy, as the full spectrum of the disease is debated—where the distinction between IBS ends and NCGS begins, and whether it is gluten or nongluten components of food that trigger symptoms—and a need for standardization in definitions and a positive diagnostic biomarker exists.

Finally, [Sabine Vriezinga *et al.*](#) describe the most common gluten-related conditions in childhood, including coeliac disease, wheat allergy and NCGS. Prevention of coeliac disease is hotly debated. In high-risk individuals (family history and genetic risk), the latest studies established that the timing of gluten introduction and breastfeeding do not influence disease development in childhood, in contrast with previous data that had indicated a 'window of opportunity' for prevention by introducing gluten at ~4–6 months of age. However, these findings might not be applicable to the general population or those at low risk.

The global gluten-free food industry is booming as individuals increasingly choose the GFD as part of a 'healthier' lifestyle, despite some processed gluten-free food being far from healthy (high in calories or fat, low in fibre and certain vitamins). For those individuals with coeliac disease, the GFD is not about a healthy diet, but a diet for health. By highlighting key issues in gluten-related disorders, we at *Nature Reviews Gastroenterology & Hepatology* hope that more attention can be focused in researching these conditions, to separate gluten fact from food fad.

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“...what happens when ... food can be a trigger of disease?”

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Competing interests
The author declares no competing interests.



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