

### Coeliac Disease – Local & Systemic Consequences



Coeliac disease is an inflammatory disorder with autoimmune features that is characterised by destruction of the intestinal epithelium and remodelling of the intestinal mucosa following the ingestion of dietary gluten. The human gut is home to trillions of commensal microorganisms, and we are just beginning to understand how these microorganisms interact with, and influence, the host immune system. This may also include the late onset development of Coeliac Disease, or gluten intolerance.

#### **Key Concepts**

- Coeliac disease (CD) is an autoimmune disorder triggered by ingestion of gluten, a major protein in wheat, or of related proteins in other grains.
- Research into the root causes indicates that the disorder develops when a person exposed to gluten also has a genetic susceptibility to CD and an unusually permeable intestinal wall.
- Surprisingly, essentially the same trio—an environmental trigger, a genetic susceptibility and a "leaky gut"—seems to underlie other autoimmune disorders as well. This finding raises the possibility that new treatments for CD may also ameliorate other conditions.
- CD is an immune mediated pathology that may be managed not simply through exclusion of the antigen gluten, but also through the improvement of digestion, reduction of gut permeability, support of <u>mucosal tolerance</u> and suitable SCFA supplementation.

#### A Clue to Delayed Onset CD

People with coeliac disease are born with a genetic susceptibility to it. So why do some individuals show no evidence of the disorder until late in life? In the past, I would have said that the disease process was probably occurring in early life, just too mildly to cause symptoms. But now it seems that a different answer, having to do with the bacteria that live in the digestive tract, may be more apt.

These microbes, collectively known as the microbiome, may differ from person to person and from one population to another, even varying in the same individual as life progresses. Apparently they can also influence which genes in



their hosts are active at any given time. Hence, a person whose immune system has managed to tolerate gluten for many years might suddenly lose tolerance if the microbiome changes in a way that causes formerly quiet susceptibility genes to become active.

# If this idea is correct, coeliac disease might one day be prevented or treated by ingestion of selected helpful microbes, or <u>probiotics</u>. [1]

CD and gluten intolerance represent distinct situations in which local tissue damage in the gut may manifest a wide range of illnesses elsewhere, supporting the notion that many illnesses have an origination in the <u>GI tract</u>.

## Why Is Gluten So Tough To Handle?

There are two unique features to gluten that may partly explain its ability to trigger an immune response.

- 1. They have a high content of proline in the gluten proteins, that are hard to break down using our natural proteases in the gut lumen. [2]
- 2. The gluten fragments are good substrates for the enzyme TransGlutamase (TG2) converting glutamine residues to glutamate. This increases the ability of the gluten peptides to bind to the genetically inherited molecules HLA-DQ2 or HLA-DQ8 [3]