Publication of the Month

September 09/10: Cause, outbreak and course of celiac disease.

Tjon JM, van Bergen J, Koning F
Celiac disease: how complicated can it get?
Immunogenetics, DOI 10.1007/s00251-010-0465-9

Introduction:

Life used to be simple: CD was a rare disease, diagnosed in 1 in 1,000 individuals. Patients were HLA-DQ2+ of HLADQ8+ and could be treated effectively with a gluten-free diet. That was about it.
Now we know that CD affects ~1% of the population in Western Europe and the USA, most of which remain undiagnosed. Although good insight has been gained on the immunopathology of CD — inflammation in both lamina propria and epithelium — it remains unclear what triggers the development of CD and why not every patient is equally affected. In addition, with the recognition of refractory celiac disease (RCD) and RCD associated lymphoma that do not respond to a gluten-free diet, CD has become a far more complicated disease.

Summary:

Celiac disease (CD) affects 1% of the population in Western Europe and USA and is caused by gluten intolerance in the small intestine leading to tissue damages called villous atrophy and to elevated levels of intraepithelial lymphocytes (IELs). Most patients gain full recovery by a life-long gluten-free diet, but a small amount of patients (3% of CD patients) fail to recover and develop refractory celiac disease (RCD), a potential condition premalignant to Lymphoma.
Celiac disease development is strongly influenced by genetic predisposition. Individuals carrying genes for the human leukocyte antigen HLA-DQ2, especially HLA-DQ2.5, and HLA-DQ8 are much more susceptible for CD development, homozygous even more than heterozygous. HLA-DQ is a cell surface receptor found on antigen presenting cells. The antigen presenting cells bind gliadin peptides with their HLA-DQs, and present it to $CD4^+$ T cells. Normal gliadin in contrast to deamidated gliadin has a low affinity to HLA-DQ2 and HLA-DQ8 resulting in a low-level reactivity. But in case of an intestinal infection the pathogen-induced inflammation in combination with the low-level reactivity leads to tissue damage which is followed by the release and activation of gliadin-deamidating TG2. Deamidated gliadin is highly affine for HLA-DQ2 and –DQ8 which enhances immune response of $CD4^+$ T cells in the lamina propria ending in a higher amount of TG2 and also in a higher amount of interleukin 15 (IL-15). IL-15 upregulation during CD results in a chronic inflammation of the intestinal epithelium.
As displayed here, disease outbreak is the result of an unfortunate series of events, which, in isolation, would not lead to disease, but, combined, have a very detrimental outcome.

Comment:

This review summarises efficiently all aspects leading to celiac disease and possible gluten-free diet resistant outcomes, but also points out the ambiguity in disease outbreak and course. It mentions also the fact that celiac disease and possibly resulting severe complications were underestimated for a long time.