Immunopathogenesis of coeliac disease

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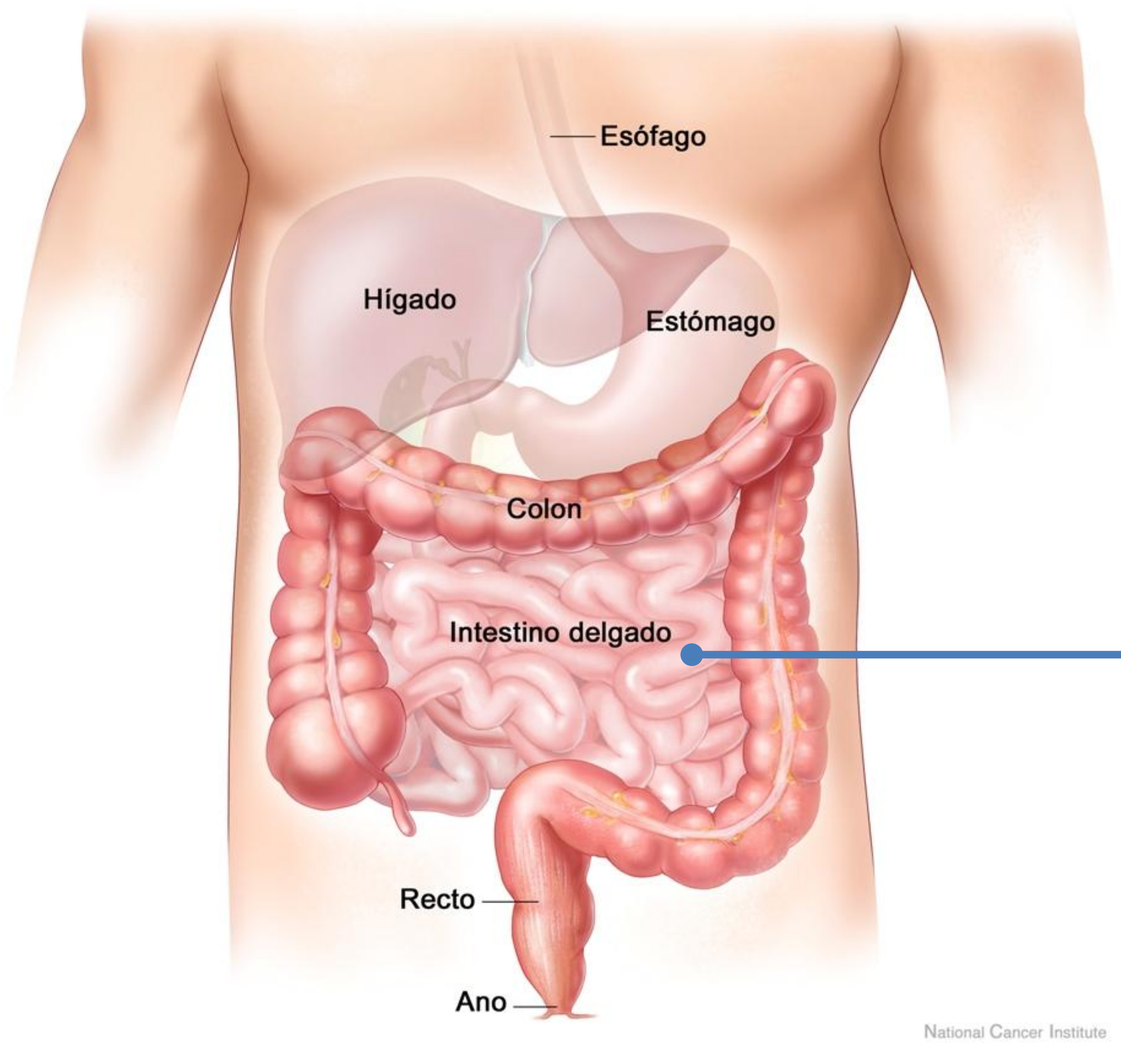
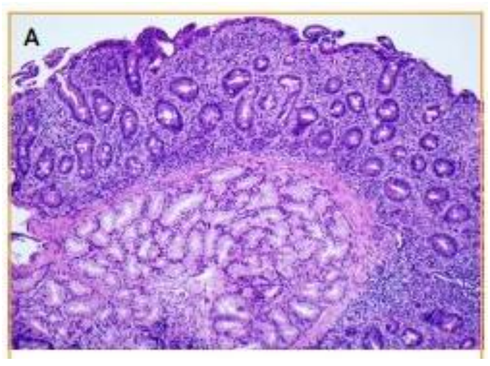


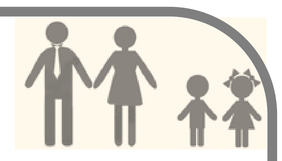
Coeliac disease is a intolerance to the gluten found in wheat, barley and rye. The intestinal mucosa becomes damaged by an autoimmune response that is initiated by peptide fragment from the gluten component α-gliadin, leading to severe malabsorption.
Developing the disease is related to the presence of alleles that encode for HLA-DQ2 or HLA-DQ8 proteins.

Villous atrophy

There is a complete loss of villi and hypertrophy of the mucosa that results in a flat mucosa.



Prevalence

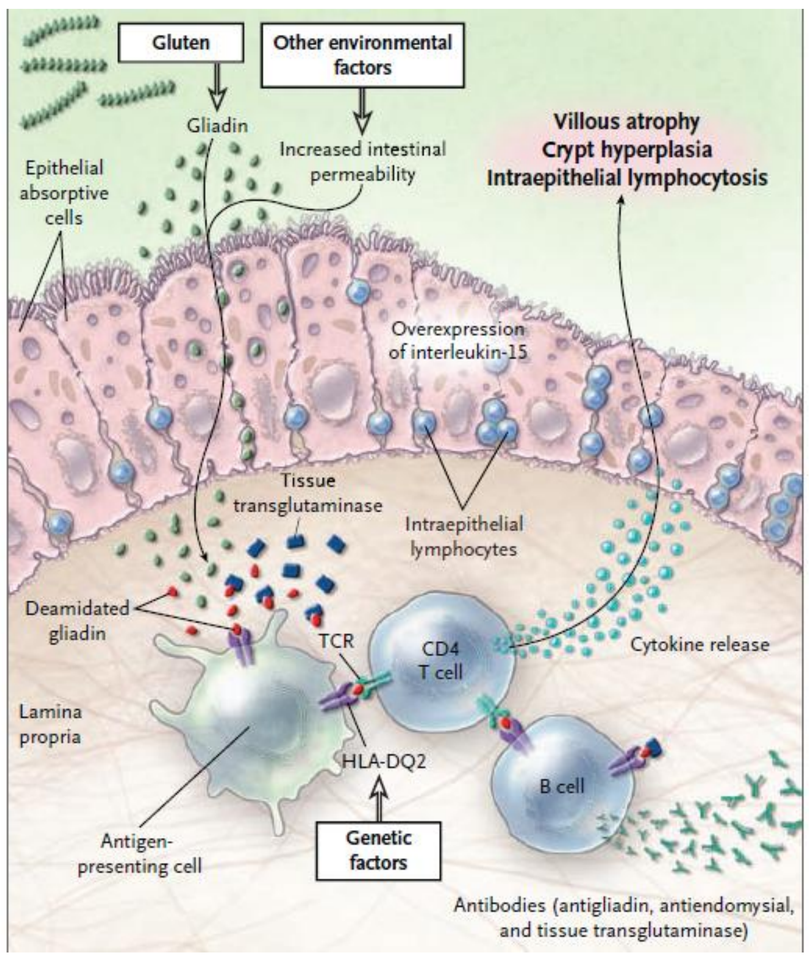


- It is the commonest chronic disease.
- It occurs in adults and children at rates approaching 1% of the population.
- It affects developed and underdeveloped countries.
- Its epidemiology is like an iceberg→ most affected people with coeliac disease remains undiagnosed.

Immunological process

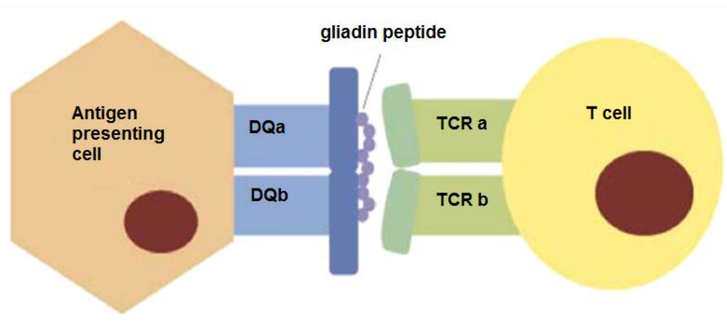
The immune response includes an innate component responsible for epithelial injury, and other adaptive components mediated by CD4 + T cells specific of the lamina propria that cause a mucosa remodeling.

Gluten is digested by enzymes into peptides. In the epithelium, gliadin damages epithelial cells, resulting in increased expression of interleukin-15, which in turn activates intraepithelial lymphocytes. These lymphocytes become cytotoxic and kill enterocytes. During infections or as result of permeability changes, gliadin enters the lamina propria, where it is deamidated by tissue transglutaminase, allowing presentation by HLA-DQ on the surface of antigen-presenting cells. Gliadin is presented to gliadin-reactive CD4+ T cells through a T-cell receptor, resulting in the production of cytokines that cause tissue damage.



Genetic factor

When the gliadin is deamidated by transglutaminase enzym, it exposes negatively charged amino acids and this epitope has a high affinity for the HLA-DQ molecule.
There is a strong genetic component to CD: almost all patients carry the HLA-DQ2 allele and rarely DQ8.



Autoimmunity

Gluten → Toxic peptides → Immune response → Auto-antibodies

Coeliac disease is an autoimmune process triggered by an external factor such as gluten in genetically predisposed people .
The only way to prevent it is to eliminate gluten from the diet.

Peter H.R. Green, M.D., and Christophe Cellier, M.D., Ph.D: *Celiac Disease (*2007). The new England journal of medicine. N Engl J Med;357:1731-43.
Walbutga Dieterich, Tobias Ehnis, Michael Bauer, Peter Donner, Umberto Volta, Ernst Otto Riecken & Detlef Schuppan. *Identification of tissue transglutaminase as the autoantigen of celiac disease*(1997). Nature Medicine. Volume 3,Number 7.
Shan L, Molberg O, Parrot I, Hausch F, File F, Gray GM et al. *Structural basis for gluten intolerance in celiac sprue(2002). Science. vol 297.*