Why is celiac disease so much more common in Sweden than in the US? A study compares differences in genes and environment, presenting this riddle as a model for other autoimmune disorders.

**Source:** Rheumatology Network


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**Why does Sweden have so much celiac disease?** For that matter, why does celiac disease develop in some children develop while most children with the same susceptibility genes and the same environment are unaffected? This study tried to gain some more insight into the **Swedish puzzle** by following 6,403 infants with four pairs of risk haplotypes in Sweden (where the risk is highest) and three other countries, including the US.

**As model for all autoimmune diseases, celiac disease** (one of the first autoimmune diseases to be recognized as such) is of interest by analogy to rheumatic disorders. Its genetic susceptibility and trigger proteins are well characterized. **DR3-DQ2 is the HLA haplotype with the highest risk** for celiac disease, and DR4-DQ8 also has an increased risk. Even so, most infants with those haplotypes do not get celiac disease.

Twenty-six percent of the children who were homozygous for DR3-DQ2 had celiac disease autoimmunity, defined by serum antibodies against tissue transglutaminase (tTG) by age 5 years. Eleven percent of those children had celiac disease itself, defined by biopsy or very high tTG levels by age 5 years.

This study, called **The Environmental Determinants of Diabetes in the Young (TEDDY)**, followed 8,677 children with high genetic risk for type 1 diabetes as a primary outcome. The development of celiac disease was a secondary outcome.

**The celiac disease risk for Swedish children was nearly double** that for children in the US. Sweden also had an epidemic of celiac disease between 1984 and 1996. The duration of breast-feeding is longest in the US, and shortest in Sweden, but Swedish infants are also given gluten-containing cereals at the earliest age. Rotavirus has been implicated.

“There seems to be an environmental factor that we still haven’t pinned down and that is lurking in Sweden,” comments Richard Lehman in the *British Medical Journal*. “Some kind of wholewheat cracker eaten with smoked fish, probably.”

**A perspective discusses the history of celiac disease** and its role in understanding autoimmune disease generally. Known for millennia, it was named and carefully described in 1888 by Samuel Gee, who asked “Why, out of a family of children all brought up in much the same way, should one alone suffer?”

In the early 19th century, following the medical-research fashion of the times, progress in bacteriology led to a **germ theory** for this and every disease. In 1944, Dutch pediatrician William Karel Dicke observed an association between **wheat proteins** and celiac disease, which was confirmed when the **death rate from celiac disease fell during the wartime famine** of 1944. In 1952, gluten and related proteins were identified as causes.

In the 1950s, researchers developed the idea (which was not well accepted at the time) that diseases such as multiple sclerosis, systemic lupus erythematosus, and rheumatoid arthritis, might be caused by **immunologic overreactions**.

Now familiar with the role of autoantibodies, lymphocyte function, and the human leukocyte antigens behind genetic predispositions, researchers are confident that they understand the broad outlines.
But the authors point out that we still don’t understand how heredity, environment and development interact to predict disease, and modern researchers are still using the methods of Gee and Dicke to figure out puzzles like celiac in Sweden.

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