

THESIS ABSTRACT:

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Gluten is a wheat kernel protein made of gliadins and glutenins. It can be found in all forms of **wheat, oats, rye, and barley.** Celiac disease (CD) is a permanent autoimmune reaction to the consumption of gluten. There may be signs for CD, but **many times it is asymptomatic.** CD patients suffer from **malabsorption issues, neurological problems, and a number of different diseases.** CD is most often found among patients with Type 1 diabetes (T1D), in that these conditions are both genetically predisposed, contain the same HLA genotypes, can be environmentally triggered, and impact the same areas of the body. Jejunal biopsies have tested positive for severe inflammation with the onset of both diseases. Eliminating gluten has been shown to reverse intestinal damage. Elimination diets also improve insulin secretion, increase glycemic control, and help sick patients to put weight back on for body mass index recovery. The two diseases are being diagnosed together during early life. Not getting this diagnosis early only worsens the conditions and brings a much younger mortality rate. This worldwide epidemic seems to have strong geographical factors. Accordingly, there is a need to find the cause.

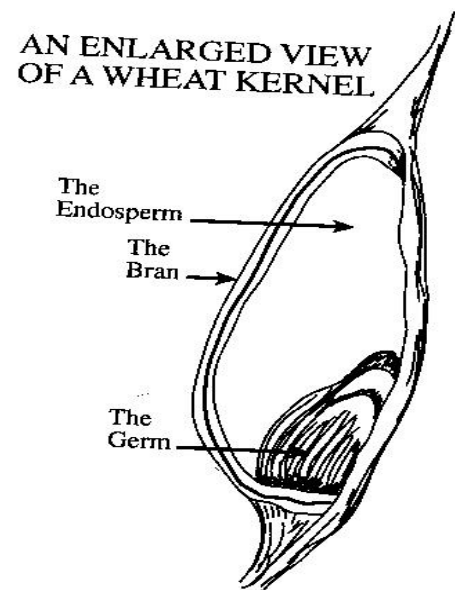
Together CD and T1D are rising epidemics, and it is possible that gluten is the predisposing factor for these two diseases.

INTRODUCTION:

Food allergens are proteins found in food, and once they are digested they travel through the bloodstream. The proteins travel to places in the body where allergy symptoms are known to occur: the lungs, skin, nose, throat, and our gastrointestinal tract. [1] The IgE antibodies will spot these proteins coming in, and as the body's defense it will release chemicals like histamines, thus allergy symptoms become present.[1] These days we have a much higher prevalence for food intolerance than for a mere food allergy alone. Food intolerances lead to autoimmune diseases such as CD and T1D.

COMPOSITION OF GLUTEN:

Gluten is a protein composed of gliadins and glutenins, which are found inside the endosperm of the wheat kernel. [2] After the starch gets washed away the gluten is left behind. This protein is best described as a sticky, gummy, elastic substance, which is useful for thickening food, and helping it to rise. It is found in all the different forms of wheat including spelt,



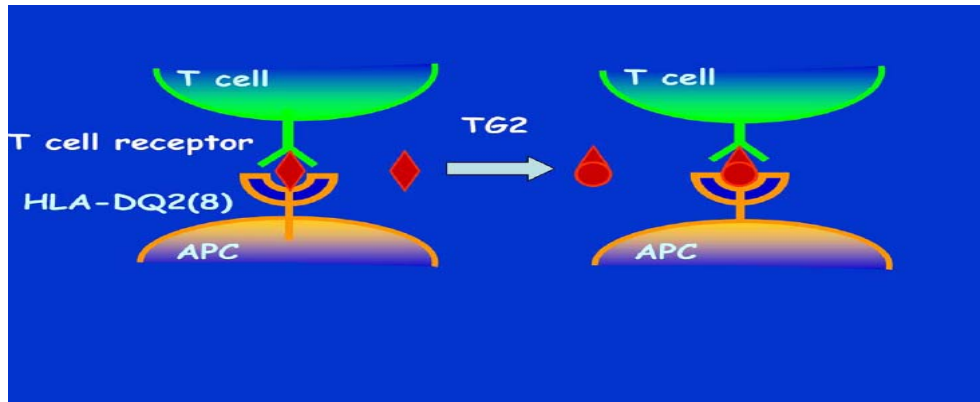
kamut, durum, semolina, oats, matza, etc. Gluten is also found in other grains such as: rye, tritical (a mixture of rye and wheat), and barley. [3, 4, and 5]

Gluten sensitivity manifests in people through two different forms: CD or a gluten intolerance. This is very different from the IgE antibody reacting to a food allergy. [5] **Gluten intolerance is a heightened immune reaction to the gluten protein,** which is linked to neurological problems like migraines, depression, anxiety, autism, MS, and ADHD. On the other hand, **CD is a permanent autoimmune reaction.** CD is known to cause damage to the villi of the small intestines and for causing classic gastrointestinal symptoms. Extreme damage to the villi of the small intestines and the inflammation cause a severe malabsorption problem. Nutrient malabsorption deficiencies include vitamins A, D, K, E, folic acid, B12, and iron. GI symptoms only account for ½ of CD patients. [7]. The autoimmune reaction causes a large number of other disorders such as osteopenic bone disease and osteoporosis, dental anomalies, reduced stature, infertility, lactose intolerance, ataxia, iron deficiency anemia, central and peripheral effects on the nervous system, and internal hemorrhaging. It is also linked to many autoimmune disorders, examples would include nephritis, acidosis, lupus, thyroid disease, myasthenia gravis, rheumatoid arthritis, Addison's disease, and a possible link to the epidemic of T1D. [2, 3, 4, 6, and 7]. CD is diagnosed either through intestinal

biopsies, serum antibody tests, or the disappearance of symptoms after gluten is removed from the patient's diet. [3]

Generally speaking, CD and certain gluten associated diseases (GAD's) are T-cell mediated diseases. [7] The most common genetic markers for the disease are human genotypes DQ2 and DQ8. Both the DQ2 and DQ8 are bound to the human leukocyte antigen (HLA), which is an antigen that prepares the cell's surface for essential elements in immune function and presents the protein to the body's T cells. HLA is also linked to other autoimmune disorders like T1D. [3, 6] It is known that the DQ2 gene is most common for the CD patient, and will typically be found in 90-95% of them. The DQ8 genotype is only present in 5-10% of the cases. [3, 8] Studies show that 20-50% of all humans carry this DQ2 gene and most likely many more that have not been discovered yet. [3]

Tissue transglutaminase (TG2) is an enterocyte enzyme that breaks down gluten, and also has a primary role in the development of disease. [3, 6] TG2 is the enzyme that helps to chemically bind the HLA to the DQ2 and DQ8 by changing gluten into negatively charged glutamic acid. [6] This leads to a greater gluten-binding affinity and more opportunities for T cell response against the gluten and associated CD. [6] The following receptor binding figure illustrates this relationship.



The same toll-like receptors (TLR) that are involved in our wound and tissue repair help to activate the TG2 in the small intestines. They alert the immune system to pathogens. [6] In a healthy individual with no signs of CD, the TG2 would remain inactive in the small intestines, and therefore inflammation would not develop. [6]

Diabetes is an inability for the body to properly use or secrete insulin from the pancreas. Insulin keeps serum glucose levels in control and also monitors glucose absorption into our cells. Insulin should be released from the pancreas when eating as blood glucose levels are increased. [4, 8] Blood sugar levels are maintained at normal levels because the insulin promotes storage of the excess glucose. Two characteristics of T1D are hyperglycemic (having excess amounts of blood sugar levels) and the occurrence of glycosuria, meaning that the kidneys are sending out extra glucose through the body's urine. [4]

Autoimmune diabetes is insulin dependent. The body's T cells attack

and kill its own insulin-producing islet of langerhans β cells. Sixty to eighty percent of the β cells are destroyed by the time symptoms occur. [4, 9]

Although this was diagnosed early in life, it is now also occurring in other age groups.

For example children with T1D have the highest amounts of autoantibodies in their systems. These help to easily identify a current disease. [9, 10] The three major autoantigens in T1D are those against tyrosine phosphatase (1A-2), glutamic acid decarboxylase (GAD-65), and insulin. [9]

A striking similarity in CD and T1D is that both disorders are strongly connected to HLA, especially with the genes DQ2 and DQ8, which are vulnerable to disease. [8, 9] Both CD and T1D have become epidemics, and both can be triggered by environmental factors. It is unclear whether or not food allergies can be the cause of T1D.

If the body identifies gluten as an allergen then an antibody to it might bind with the insulin receptors before the insulin ever gets a chance to slow down the insulin response. This speeds up the onset of T1D. [2] Antibodies affect a plethora of pancreatic β cells. Moreover, there are many other possible factors, both genetic and environment. The association between CD and T1D increases every day. The occurrence of CD and T1D happens in every 1 in 200 people treated for immune damage to the intestinal lining. [10] The latest studies for CD and T1D show a prevalence of 5.4 - 7.4% of

CD in patients with AIDDM. [3]

The purpose of this paper is to see if gluten is responsible for the etiology of T1D.

LITERATURE REVIEW:

The fact that CD has a higher occurrence rate with T1D patients has been known for quite some time. [11] There seems to be a direct relationship between the presence of gluten in the diet and the length of time of exposure. [11, 12] It is possible that if CD remains untreated, then the inflammation in the small intestines from the gluten, and internal virus infections, may cause AIDDM. [11]

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