

Celiac Disease:

THE MASKED ENEMY

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Research Question: What is Celiac Disease (CD)? How can more people become aware of the seriousness of this autoimmune disease? What are all of the underlying factors of this disease and how does it affect one's life emotionally, physically, and mentally?

Main argument: Help the reader understand more about what Celiac Disease is, explain what is occurring within the body, and inform the community on the impact CD has on an individual.

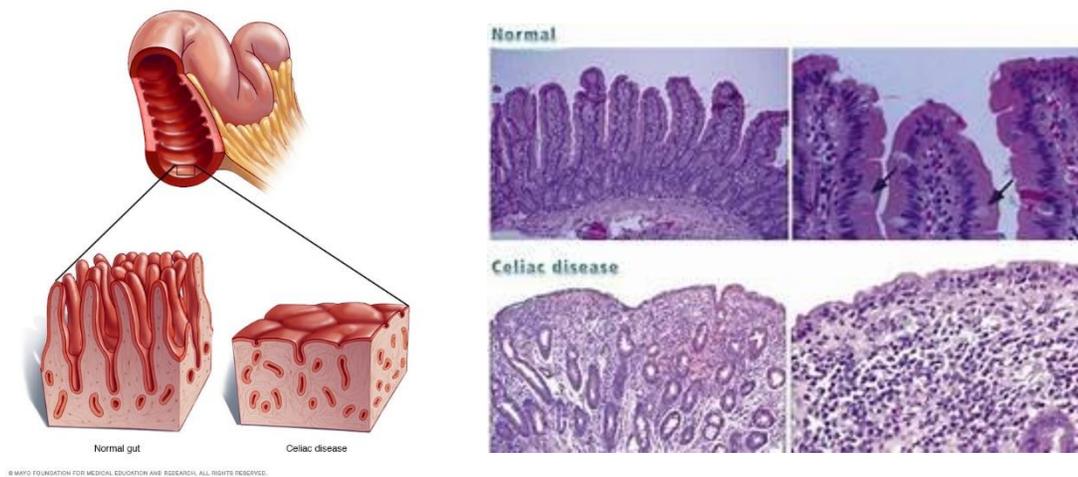
Personal aspect

When you say you have a gluten allergy, other people either do not understand gluten or think that it only applies to bread and pasta. For Celiac Disease (CD) patients it is more complicated than that and can create a much larger impact on the affected individual. My personal encounter with CD, an autoimmune disease, has been unbelievable and life changing. After I was diagnosed with a concussion in spring 2018, I had been experiencing constant migraine headaches, which acted as a stressor on my body. The symptoms of CD became more apparent and my body was under constant stress between the daily headaches and other neurological and physical symptoms. I developed more of a mental fog, digestive issues, significant weight loss, malnutrition, constant abdominal pain, lack of energy, and the list could go on. Since my concussion, the main concern of myself, my family, and my doctors was the headaches, the severity of them, and how I could lower the degree of them. I had multiple tests done to scan my brain and determine the possibilities of different autoimmune disorders. I continued to have diarrhea and continued to lose weight, which resulted in more bloodwork being done. The results were very direct in showing I had CD after having the Celiac Panel test because the range for the antibody, Tissue Transglutaminase IgA, is usually 1-3 but my number

was approximately 120, which is abnormally high. In order for this test to be valid, one must be eating gluten or have gluten in his or her diet, which at the time, I did.

Because my blood test results came back positive, I had to follow up with a colonoscopy and endoscopy of my small intestine to evaluate the damage done, as well as check for Crohn's Disease. The results of the endoscopy confirmed CD because of the rippling of the intestinal wall and somewhat flattened villi, which can be seen in Figure 1. The treatment plan from the doctors involves maintaining a strict gluten-free diet and following up in a year to have the same testing done.

Figure 1. Normal versus Celiac (damaged) villi in small intestine in a diagram and at a cellular level.¹



Since CD is known to be inherited and more likely to occur in individuals with family members who have it, it was not a huge surprise to my family because my paternal grandmother also has this disease and was diagnosed ten years ago. She has been a huge support system for me through this whole process and understands the complete mental toll that comes along with CD. One of the symptoms is depression, which I can fully understand why. This is because once you are diagnosed, you can no longer eat all the foods you love. Your entire world is flipped upside down because your favorite restaurant does not have a separate fryer for their fries, therefore you cannot eat them, and you must resort to the safe options of salad, grilled chicken, or vegetables. It makes you feel secluded and unsatisfied all the time when you eat because your body is craving something that it can no longer eat. It is mentally draining when you must explicitly explain why you cannot eat the salad after croutons were put on it or that you need your chicken or steak cooked without seasoning, preferably on a piece of foil to avoid cross-contamination.

For the past four months, I have been eating gluten free and it has drastically helped with the weight loss, malnutrition, energy level, mental fog, abdominal pains, and bowel issues. I have come to notice if I eat or drink something containing a small amount of gluten, my headache levels will increase and linger for about a month. Each day is a constant battle and stressor with having to depend on other people to prepare food that you put into your body, and therefore not fully knowing whether you will get sick or not. This specifically happens when you go out to eat or eat in the cafeteria because you put complete trust in someone who may not care to understand the seriousness of your disease. Throughout this paper, it will be further explained as to what Celiac Disease is, what gluten is and where it is found, the difference between Celiac Disease,

Non-Celiac gluten sensitivity, and wheat allergies, cross contamination, symptoms, diagnosis, treatment, and mental health related to CD.

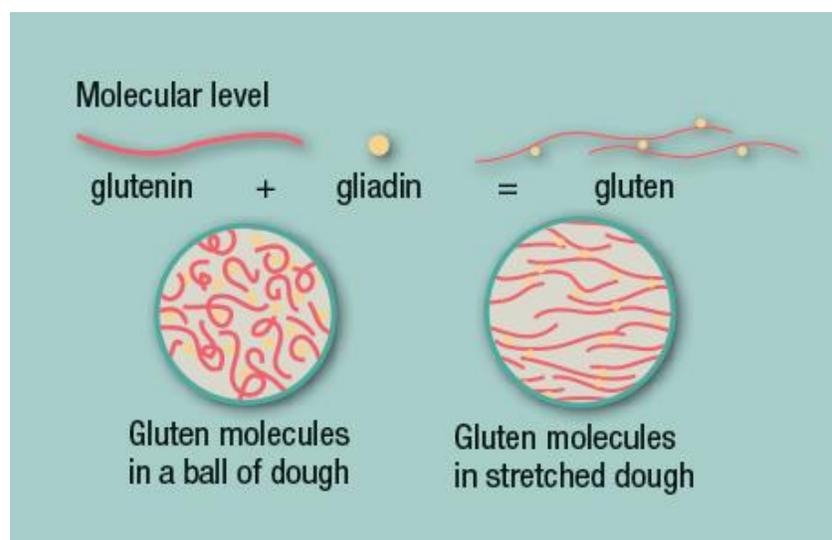
What is Celiac Disease?

Celiac Disease (CD) is an autoimmune digestive disorder which can also be known as nontropical sprue or celiac sprue.^{1,2} By definition, an autoimmune disease results when the immune system mistakenly attacks the body's own tissues. Specifically, CD is a digestive disease that interferes with the absorption of the nutritional contents of food and causes atrophy (death) of the villi in the small intestine.^{3,4} This specific disease is inherited and creates an intolerance with the protein gluten.^{2,5} The main autoimmune component is transglutaminase 2.⁶ CD is different than a common food allergy because it does not involve IgE antibody, like a normal allergy response, but instead the body responds negatively to gluten which involves the IgA antibody.³ Wheat, barley, rye, and malt all contain the protein constituent, gluten, which causes inflammation in the small intestine. About 1 in 100 people worldwide are affected by CD and approximately 2.5 million Americans remain undiagnosed.¹ In most societies worldwide, it is an overall prevalence of around 1% of the population, which ranges from young children to elderly adults.^{6,7,8} Since CD is hereditary, there is a 1 in 10 risk of developing CD if you have a first-degree relative with it.¹

What is gluten and where is it found?

In general, gluten is a protein group including prolamins (gliadin) and glutelins.⁹ Figure 2 displays a visualization, at the molecular level, of the combination of gliadin and glutelin to create gluten. It shows how gluten may be crammed together in a ball of dough or stretched out if the dough is being stretched. Gluten is used in food as a glue or structure holder. Gluten is usually hidden in many places in food without the public even knowing. The protein is found not only in the three main items wheat, barley, and rye, but also their derivatives. Wheat derivatives can be found under the names of wheatberries, durum, emmer, semolina, spelt, farina, farro, graham, KAMUT, and einkorn wheat. Then, there is the cross between wheat and rye which is triticale, and the consumer also needs to watch the label for malt, brewer's yeast or wheat flour, and wheat starch. Foods that usually contain gluten are pasta, bread, baked goods, cereals and granola, some breakfast foods, sauces, gravies, dressings, snack foods, candy, soups, packaged meat or meat substitutes, and some alcohol. Gluten can also be found in some make-up products, medications, vitamins and supplements, and playdough.¹

Figure 2. Gluten visualized at a molecular level.⁹



Celiac Disease, Non-Celiac Gluten Sensitivity, or Wheat Allergy

Celiac Disease (CD), Non-Celiac Gluten Sensitivity (NCGS), and wheat allergies are conditions which require avoiding certain components of a diet. CD and wheat allergy can be defined clearly, but NCGS is not as easily defined. The difference between the three is the CD is an autoimmune disease, wheat allergy is an immune response (not autoimmune), and NCGS is unknown. CD and NCGS share symptoms such as gastrointestinal symptoms and discomfort in bones or joints, headaches, or fatigue. A wheat allergy can include allergic reactions such as anaphylaxis, itching, or hives. To treat CD and NCGS, the individual must remove gluten from his or her diet, whereas a wheat allergy requires the removal of wheat from one's diet. CD is a genetic autoimmune disease that is caused by ingesting gluten. NCGS is not very defined because it has no positive diagnostic tests to determine whether it is an autoimmune disease or an allergy causing an immunoglobulin E (IgE) response. Wheat allergy is an immune reaction where B-cells send out IgE antibodies to attack the wheat ingested. The body's response is cued by the natural chemical messengers, and they cause the allergic reaction.^{10,11}

Cross-contamination

Cross-contamination is a major aspect when an individual with CD is cooking food or going out to eat. Since gluten can be problematic in microscopic quantities for individuals with CD, it is important to eliminate traces of gluten to avoid exposure. Cross-contamination occurs when foods are prepared on common surfaces or with the same utensils as gluten containing foods. If these items are not cleaned properly, it can easily be cross contaminated. Sometimes cookware such as wooden utensils, cutting boards, nonstick pans, cast iron skillets, sink sponges,

food storage containers, cake pans, and muffin tins, may need additional cleaning or should not be used while cooking gluten free foods. In some cases, the gluten may be absorbed into the material or get stuck in crevices. Other household appliances that could cause cross-contamination are a toaster, microwave, air fryer, or waffle iron. In commercial kitchens, cross-contamination can occur with using the same surfaces or colanders, frying oil, or from gluten-containing flours being airborne and settling upon the gluten-free utensils or food. Grocery stores may be a location of cross-contamination as well because of the foods sold in the store's deli in which surfaces and utensils may be switched between gluten-free and gluten-containing foods.¹¹

Symptoms

According to Allegheny Health Network (AHN), when someone with CD ingests gluten, the natural defense system of the body called the immune system, attacks the cells lining the small intestine.¹¹ Some symptoms for a person with CD that are a result from gluten consumption are diarrhea, decreased appetite, malnutrition, vitamin deficiencies, abdominal pains, migraines, skin rashes, defects in tooth enamel, anemia, osteoporosis, mental fog, and depression. The symptoms one experiences vary between three categories: gastrointestinal issues, neurological issues, or no symptoms at all. One third of affected individuals will experience the gastrointestinal discomfort along with other symptoms relating to the gastrointestinal system. The second third will experience the mental effects such as foginess, confusion or forgetfulness, depression, or anxiety.¹³ The final third has CD genetically within them but will not experience any symptoms and will not be aware they have the disease until it

flares up due to stressors on the body. These symptoms could result in either gastrointestinal, neurological, or both.²

Furthermore, the defects in tooth enamel are similar to too much fluoride or maternal or early childhood illness but are not directly related to the malnutrition the disease may cause. This can be a discoloration in the tooth, poor enamel formation, banding in the teeth, or translucent appearance of the teeth. Unlike many of the other symptoms that may be resolved with a gluten free diet, the tooth defects do not resolve.¹⁴ Symptoms such as malnutrition, decreased appetite, vitamin deficiencies, anemia, and osteoporosis are caused from the internal reaction with the gluten and damage of the villi in the small intestine. When the villi are damaged it is more difficult for the body to absorb the nutritional aspects of the food that the body needs. These symptoms may be resolved with a gluten free diet. The mental fog, migraines, depression, and anxiety can be connected to the malabsorption of nutrients, as well as the stress of eating anything that does not fall within the gluten free diet. Furthermore, vitamin deficiencies in B1, B6, B12, E, and Niacin will all cause a type of neuropathy.¹⁵ Along with some of these deficiencies, ataxia, confusion, impaired short-term memory, and other sensory changes may also result. While on a gluten free diet, neurological disabilities such as amnesia, acalculia, confusion, and personality changes may not resolve themselves just by the diet change or supplement addition, they may remain the same.^{15, 16}

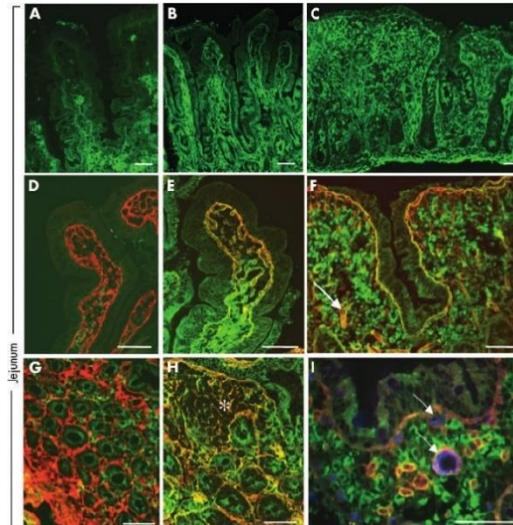
Diagnosis

In order to be diagnosed with CD, one must go through a physical exam and various tests including blood tests, stool tests, tests to check nutrient absorption, X-rays to monitor bowels,

and a biopsy of the small intestine. The blood tests check for any nutritional deficiencies and look for any signs of the body attacking cells in the small intestine by looking at tissue Transglutaminase (tTG)-IgA specifically. The blood test is the most cost-effective route because one blood sample with the “Celiac Panel” lab order from the doctor will present either a positive or negative result for CD. The patient must be on a gluten-containing diet for about a 2-4-week period before the testing is done in order to receive valid results and not false markers.⁷ The levels of transglutaminase are measured and usually should fall within a range of 1-3 to be normal or negative for CD, whereas a positive test results in values much higher. A positive test also should be followed up with the endoscopy of the small intestine with biopsies of the duodenum to evaluate the villous atrophy and damage.

Once the biopsy is taken, direct immunofluorescence (DIF) are used to identify immunoglobulins (IgA) in the biopsy. The IgA deposits show other antibodies against the tTG.⁶ Figure 3 is a visual of how DIF is used. It can be seen that in frames B, E, and H, CD is in its early stages whereas in C, F, and I there are flat lesions which show CD completely.¹⁷ Other tests are performed to check for nutrient absorption in the small intestine because once the cilia are damaged, it is difficult for one’s body to absorb and use all the nutrients being consumed. Annual endoscopy and bloodwork are performed once diagnosed to track the progression of the disease. Figure 1 shows the difference between the villi of a normal patient versus a CD diagnosed patient. The first picture shows a diagram of what the difference is between the villi whereas the second picture is at a cellular level. In both cases, it is found that the CD affected patients are smoother and do not have individual finger-like pieces. This is useful information because health care professionals can evaluate how the tTG levels decrease while on a gluten-free diet.

Figure 3. Example of DIF for IgA (green) and transglutaminase 2 (red) for normal and CD patient.¹⁷



Treatment

The treatment for CD is eating a strict gluten-free diet, as well as avoiding some dairy foods that are more difficult to digest. There is no cure for CD, but if one maintains a gluten-free diet, the symptoms will usually resolve and the individual will ultimately feel better. The symptoms will resolve due to the body no longer attacking itself when gluten is consumed creating the constant discomfort. According to doctors at Allegheny Health Network (AHN), it could take 3 months to 2 years for the intestine to heal from the damage caused by gluten and the body attacking itself and for the swelling to decrease and due to improved nutrition, the patient's symptoms may be resolved.¹² About 30% of diagnosed patients say the symptoms have not resolved by eating gluten-free, therefore other routes and diets are looked into.¹

A new study being looked into is CD therapy which includes reduced gluten exposure, decreased intestinal permeability, and decreased immune activation. The reduced gluten exposure is introducing genetically modified grains that eliminate the immunogenic gluten fragments from the plants or foods. Enzymatic degradation can be utilized by using proteases or

prolyl endopeptidases (PEPs) which break down the large immunogenic gliadin peptides into small harmless pieces. The struggle with this path is the acidity of the stomach, which would degrade the PEPs. The enzyme therapy is similar to how lactose intolerance is dealt with but is more complicated due to the gluten having to completely avoid interaction with the mucous, which would lead to inflammation.¹⁸ Another solution may be decreased intestinal permeability. Although more studies need done with this idea, it would be using zonulin, an endogenous peptide which is used in tight junction regulation. Larazotide or AT-1001 is being used to inhibit the action of zonulin. In continuation, another new study for treatment of CD is decreased immune activation. By inhibiting tissue transglutaminase (TTG), it prevents gliadin deamidation and blocks HLA DQ2 or DQ8 molecules from binding as well as the cytokines. The interest in nondietary treatments for CD is on a rise and medications are being discussed to help individuals cope with the effects of gluten.¹⁸

Mental Health Effects

Patients diagnosed with CD have a 10-22% increase in neurological disorders.¹⁵ The neurological and psychiatric symptoms can be misdiagnosed when CD is undiagnosed. In case studies provide by Celiac Disease Foundation, it can be seen and understood how a new chronic illness diagnosis may create some mental health issues. In the one case study, Daniel, a 14-year old boy who was diagnosed at age 8, did not want to obey the gluten-free diet because he wanted to “fit in” but he also experienced outbursts of anger and disappointment. In the other case study, Liz, a 12-years old girl who has Type 1 Diabetes and ADHD, was also diagnosed

with CD. Liz developed high anxiety, concentration difficulties, social withdrawal, hesitation to eat away from home, absences from school, and decline in academics. The case studies exhibit some reactions a diagnosed individual may have to the adjustment to a gluten free diet.¹ The mental health effects that occur with CD can come about due to discomfort, unknowingness, difficulties in eating, understanding the disease in full, and concentration.

Mental illnesses such as depression and anxiety have been found to have a relation to gut health. The Gut-Brain-Axis (GBA) includes the endocrine, neural, and immune pathways. When the microbiota of the gut, or all microorganisms in either the GI tract or skin, are affected, it correlates to the gut-brain axis.¹⁹ The IgA antibody provides immunity in the intestines as well as other mucosal membrane. In continuation, diet alterations can greatly affect the gut bacteria composition within a day. Intestinal permeability can be increased due to diet change, stress, antibiotics, or normal microbiome changes. This increased permeability effects the immune system and may cause inflammation in the bowels or other areas. Cytokines and neurotransmitters are released due to the stress caused on the system. The release of these influence brain function which may lead to depression, anxiety, or memory loss.^{19,20} Neurochemical or organizational changes may be a cause of depressive disorders. In depression and anxiety, it is found to have an increase of IL-6 and TNF-alpha, which is the elevated levels in the blood. These elevations will also increase the permeability of the blood-brain barrier.¹⁹

Conclusion:

In conclusion, my diagnosis of Celiac Disease this past summer has opened my eyes and given me a reason to further my research on the not commonly well-known autoimmune disease. The symptoms I was experiencing prior to being diagnosed seem to be justified and very

common for a CD patient. My life before CD compared to my life with CD has given me drive and reason to learn more, not only about CD, but gluten itself and how it interacts with the body causing the reactions. Overall, spreading knowledge about this topic in its entirety could potentially ease the minds of other CD patients, as well as educate people on the seriousness of this autoimmune disease.

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