**Pathogenesis of Celiac Disease: An Autoimmune Disease of the Small Intestine**

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**Celiac disease (CD) affects millions of genetically susceptible people, but it is unclear as to what causes its onset. In hopes to find causes of CD pathogenesis, this study focused on intestinal microbiota and levels of anti-gliadin antibody IgG (AGA IgG) of genetically susceptible infants that are positive for the HLA-DQ2 and/or HLA-DQ8 genotype(s). Sellitto et al. tested the intestinal microbiota of at-risk and non-susceptible infants for levels phylum *Bacteroidetes* members. Additionally, two groups of at-risk infants were exposed to gluten in their diet at different times: 4-6 months and at 12 months. Within these two groups, levels of AGA IgG were measured. Evidence showed that lower levels of *Bacteroidetes* in the gut were associated with the infants that are genetically susceptible for CD and that infants who were exposed at a later age (12 months) showed delayed onset of CD.**

**Introduction**

Celiac Disease (CD) is an autoimmune, inflammatory disease in which the ingestion of gluten damages the small intestine of genetically inclined individuals. Gluten is the generic name for proteins that are found in wheat, barley, and rye. When individuals with CD ingest gluten it triggers an autoimmune response.

Current research shows that CD is directly related to the HLA-DQ2 and HLA-DQ8 genes found on chromosome 6p21; however, it is unclear as to what causes the onset of CD [2]. The onset of CD is most commonly seen in young adults and affects approximately 3 million (1%) Americans, yet 97% of those individuals go undiagnosed [1]. Due to these statistics, studying triggers of CD pathogenesis is imperative to understanding CD onset and could lead early diagnosis of affected individuals.

**Recent Progress**

Current knowledge of how CD affects individuals is abundant, but the causes of its onset lacks in understanding. Several studies have researched environmental factors that might contribute to CD pathogenesis, such as, early life exposure to gluten, and the quantity and quality of gluten ingested. However, results still left the pathogenesis of CD poorly understood.

More recently, scientists have also been analyzing intestinal microbiota and its role in CD onset. Sellitto et al. hypothesized that the intestinal microbiome, in its entirety, is what depicts the genetically predisposed individuals’ shift from gluten tolerance to CD autoimmunity [2]. In an effort to understand this shift, they studied infants who had parent(s) with diagnosed CD and that tested positive for the HLA-DQ2 and/or HLA-DQ8 genotype(s). Infants were chosen as the research participants in attempt to better characterize time and causes of CD pathogenesis. They analyzed changes in their intestinal microbiota for the first 24 months of life, the motifs of early versus late gluten ingestion on intestinal microbiota, and the shift from gluten tolerance to CD autoimmunity in infants.

A major finding of their study exhibited that at 12 months of age the intestinal microbiota of genetically susceptible infants illustrated a large absence in the phylum *Bacteroidetes*. In comparison, non-susceptible infants were found to have detectable ranges of *Bacteroidetes* in their intestinal microbiota by this age, which parallels the intestinal microbiota composition of mature adults. This indicates that infants susceptible to CD contain intestinal microbiota that fall short in the maturity stages of normal, non-compromised intestinal microbiota [2]. Members of the phylum *Bacteroidetes* were of interest in this study because recent findings illustrated that African children often have high levels of *Bacteroidetes* in their intestinal microbiota, which seems to provide greater protective abilities against gastrointestinal disorders. *Bacteroidetes* concentrations were also a prime focus in this study due to of their association with regulatory T-cells that produce anti-inflammatory cells [2].

In addition, Sellitto et al. determined that the infants with an early introduction (4-6 months of age) to gluten in their diet showed higher levels of anti-gliadin antibodies of the IgG class (AGA IgG) as compared to infants that had a delayed introduction (12 months of age) to gluten. These higher AGA IgG levels resulted in an increase of immune response and a higher occurrence of autoimmunity in the early exposure infants. By delaying the exposure to gluten by an additional 6 months lowered the levels of AGA IgG, thus slowing the transition from gluten tolerance to autoimmunity against gluten [2]. Anti-gliadin antibodies IgG were evaluated as a result of previous data that demonstrated a positive correlation between high levels of AGA IgG and increased intestinal permeability. This was a significant factor that was examined, considering that several gastro inflammatory diseases, including CD, are often characterized as having increased intestinal permeability.

**Discussion**

Although CD pathogenesis is still unclear, Sellitto et al. found evidence that will provide new directions for future researchers. They found that genetically susceptible infants showed untraceable levels of the phylum *Bacteroidetes* in their intestinal microbiota [2]. Defining *Bacteroidetes* levels in the gut was a compelling component in this study, as it offered evidence that the low levels of *Bacteroidetes* might be a cause of CD autoimmunity onset. Correspondingly, the study hinted at diet differences between two countries as possibly exhibiting a direct connection between large amounts of gluten intake and low *Bacteroidetes* levels in the gut [2]. This could indicate that CD pathogenesis could be directly related to the amount of gluten exposure of at-risk individuals. They also noted that higher amounts of *Bacteroidetes* in the gut provide protection against gastric inflammatory diseases due to their role in anti-inflammatory cell production [2]. This is essential knowledge for future researchers to take into consideration, as disruption of these cells could be a contributing source to the onset of gastric inflammatory diseases.

As previously mentioned, the relationship between AGA IgG levels and time of exposure was another sizable component in this study. This was a necessary analysis as it offered substantial indication that high levels AGA IgG are found in at-risk individuals that are exposed to gluten at earlier ages [2]. The conclusions made from the AGA IgG measurements have brought forward several ideas for future studies about CD pathogenesis. More specifically, this could indicate that avoiding gluten intake for longer periods (past 24 months of age) could reduce the chance of CD onset all together. Further studies could provide a significant answer to this question and possibly offer options of preventive medical practices. Such foreseen practices could include having the ability to delay CD pathogenesis by lagging the time of gluten exposure or allowing for early diagnosis of genetically predisposed individuals. However, further examination of AGA IgG levels in connection with CD pathogenesis is imperative for a better understanding.

**References**

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