CELIAC DISEASE AND DENTAL ENAMEL DEFECTS

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Chapter 1

Celiac Disease and Dental Enamel Defects

Introduction:

Celiac Disease is a serious genetic autoimmune disorder where the ingestion of gluten leads to damage in the small intestine. It is estimated to affect 1 in 100 people worldwide. Two and one-half million Americans are undiagnosed and are at risk for long-term health complications. (Celiac Disease Foundation, 2017) Celiac Disease is not age dependent, the disease can affect both adults and children. You do not “catch” Celiac Disease and the potential to develop Celiac Disease begins at birth. To develop Celiac Disease there are three things that are required, a genetic disposition, an external trigger, and gluten in your diet. (Celiac Support Association, 2016)

Statement of the Problem:

It has been reported since the early 1990’s that there appears to be an association between Celiac Disease and dental enamel defects as well as recurrent aphthous stomatitis. The prevalence of Celiac Disease related enamel defects varies in several studies and different European countries from 38% to 96%. This prevalence should be an early identification marker of silent cases of Celiac Disease. (Majorana, 2010)

Significance of the Study:

The significance of Celiac Disease and the dental professional is that Celiac Disease can cause dental enamel defects of permanent teeth. Tooth defects that result from Celiac Disease may resemble those caused by too much fluoride or a maternal or early childhood illness. (The National Institute of Diabetes and Digestive and Kidney Diseases, 2014) “Dentists mostly say it’s from fluoride, that the mother took tetracycline,
or that there was an illness early on,” said Peter H.R. Green, M.D., director of the Celiac Disease Center at Columbia University. “Celiac Disease isn’t on the radar screen of dentists in this country. Dentists should be made aware of these manifestations to help them identify people and get them to see their doctors so they can exclude Celiac Disease.” Dental enamel defects might be the only presenting manifestations of Celiac Disease. Tooth defects resulting from Celiac Disease are permanent and do not improve after adopting a gluten-free diet. (The National Institute of Diabetes and Digestive and Kidney Diseases, 2014)

**The Purpose of the Study:**

This research is important for all healthcare professionals as well as professionals in the dental field to help identify people who may have Celiac Disease and refer them to a gastroenterologist for a proper diagnosis. While dental enamel defects are the most prominent oral condition of Celiac Disease, dentists and physicians should examine a patient’s mouth for other signs or symptoms such as cancer, sores or ulcers inside the mouth, a red smooth shiny tongue and chronic dry mouth. In more serious cases the patient with Celiac Disease can presents with squamous cell carcinoma of the pharynx and mouth. Studies have demonstrated that Celiac Disease is highly associated with dental enamel defects in childhood, most likely due to the onset of Celiac Disease during enamel formation. (The National Institute of Diabetes and Digestive and Kidney Diseases, 2014)
Definition of Terms:

Amelogenesis – formation of dental enamel on teeth and begins when the crown is forming during the bell stage of tooth development. (Merriam-Webster, 2017)

Anemia - a condition in which the blood is deficient in red blood cells, in hemoglobin, or in total volume. (Merriam-Webster, 2017)

Aqueous - of, relating to, or resembling water (Merriam-Webster, 2017)

Autoimmune disease – is a condition arising from an abnormal immune response to a normal body part. (Merriam-Webster, 2017)

Celiac disease – a serious genetic autoimmune disease where the ingestion of gluten leads damage in the small intestines. (Merriam-Webster, 2017)

Biopsy – the removal and examination of tissue, cells, or fluids from the living body. (Merriam-Webster, 2017)

Chameleon - one that is subject to quick or frequent change especially in appearance. (Merriam-Webster, 2017)

Cheilosis - an abnormal condition of the lips characterized by scaling of the surface and by the formation of fissures in the corners of the mouth. (Merriam-Webster, 2017)

Dental caries – breakdown of teeth die to activities of bacteria. (Merriam-Webster, 2017)

Dental enamel – the hard-white substance on the outer layer covering the crown of the tooth. (Merriam-Webster, 2017)

Dental fluorosis – change of the appearance of dental enamel caused by excessive fluoride during the formation of the teeth. (Merriam-Webster, 2017)

DMFT index – Decay, Missing, Filled Teeth index measures the prevalence of dental caries. (Merriam-Webster, 2017)

Dermatitis Herpetiformis - chronic dermatitis characterized by eruption of itching papules, vesicles, and lesions resembling hives typically in clusters. (Merriam-Webster, 2017)

Duodenal – the first part of the small intestine extending from the pylorus to the jejunum. (Merriam-Webster, 2017)

Fluoride - a chemical that is sometimes added to drinking water and toothpaste to help keep teeth healthy. (Merriam-Webster, 2017)
Gastroenterologist – a physician with dedicated training and unique experience in the management of diseases if the gastrointestinal tract and liver. (Merriam-Webster, 2017)

Enzymes - any of numerous complex proteins that are produced by living cells and catalyze specific biochemical reactions at body temperatures. (Merriam-Webster, 2017)

Genetic disposition – an increased likelihood of developing a particular disease based on a person’s genetic makeup. (Merriam-Webster, 2017)

Gliadins – one obtained by alcoholic extraction of gluten from wheat and rye. (Merriam-Webster, 2017)

Gluten – a tenacious elastic protein substance especially of wheat flour that gives cohesiveness to dough. (Merriam-Webster, 2017)

Glutenins – found especially in wheat and obtained by extracting gluten with dilute alkali. (Merriam-Webster, 2017)

Human Leukocyte Antigen - any of various proteins that are encoded by genes of the major histocompatibility complex in humans and are found on the surface of many cell types (as white blood cells). (Merriam-Webster, 2017)

HLA typing – Human leukocyte antigen aiding in the diagnoses of Celiac Disease. (Merriam-Webster, 2017)

Hypocalcemia – low levels of calcium in the blood serum. (Merriam-Webster, 2017)

Hypoplasia - a condition of arrested development in which an organ or part remains below the normal size or in an immature state. (Merriam-Webster, 2017)

Intolerance - exceptional sensitivity (as to a drug); specifically: inability to properly metabolize or absorb a substance. (Merriam-Webster, 2017)

Jejunum - the section of the small intestine that comprises the first two fifths beyond the duodenum. (Merriam-Webster, 2017)

Lymphocytes - any of the white blood cells of the immune system that play a role in recognizing and destroying foreign cells, particles, or substances that have invaded the body. (Merriam-Webster, 2017)

Malabsorption – involves problems absorbing certain sugars, fats, proteins, or vitamins. (Merriam-Webster, 2017)

Manifestation - a perceptible, outward, or visible expression (as of a disease or abnormal condition. (Merriam-Webster, 2017)
Oral Lichen Planus - a skin disease characterized by an eruption of wide flat papules covered by a horny glazed film, marked by intense itching, and often accompanied by lesions on the oral mucosa. (Merriam-Webster, 2017)

Porphyria - any of several usually hereditary abnormalities of porphyrin metabolism characterized by excretion of excess porphyrins in the urine and by extreme sensitivity to light. (Merriam-Webster, 2017)

Prophylaxis – action taken to prevent disease. (Merriam-Webster, 2017)

Proline - an amino acid C5H9NO2 that can be synthesized by animals from glutamate. (Merriam-Webster, 2017)

Protein – any of various naturally occurring extremely complex substances that consist of amino-acid residues joined by peptide bonds, contain the elements carbon, hydrogen, nitrogen, oxygen, usually sulfur, and occasionally other elements (as phosphorus or iron), and include many essential biological compounds (as enzymes, hormones, or antibodies). (Merriam-Webster, 2017)

Recurrent aphthous stomatitis – condition where round or ovoid painful ulcers recur on the oral mucosa. (Merriam-Webster, 2017)

Serum antibody – the part of blood that is like water and that contains substances (called antibodies) that fight disease. (Merriam-Webster, 2017)

Squamous cell carcinoma – common form of skin cancer that develops in the squamous cells. (Merriam-Webster, 2017)

Tetracycline – broad spectrum antibiotic that can cause discoloration of the teeth during formation. (Merriam-Webster, 2017)

Villi - one of the minute finger-shaped processes of the mucous membrane of the small intestine that serve in the absorption of nutriment. (Merriam-Webster, 2017)

Limitations of the Study: The studies were limited to children that were diagnosed with Celiac Disease after the formation of their permanent dentition.

Delimitations of the Study: The studies were limited to six years.

Children that were clinically proven to have no history of Celiac Disease, family or otherwise, no history of dental trauma, no chemotherapeutic
agents used and no use of tetracycline antibiotics.
Chapter 2 –

Review of the Related Literature:

Chapter Introduction:

Celiac Disease is a permanent intolerance to gluten. It was once believed that Celiac Disease was a rare malabsorptive disorder of infancy and childhood, but is now considered to be a common, chronic, multi symptom disorder that can present at any age when gluten is present in the diet. Celiac Disease has been called a “Clinical Chameleon” (Rashid, 2011) Traditionally, it presents with diarrhea and failure to thrive within the first couple of years. Failure to thrive in a child is defined as “lack of expected normal physical growth”. Inadequate nutrition is the key reason for failure to thrive. (Barker, 2008)

Characteristic symptoms are abdominal pain, weight loss, and diarrhea. However, many people present with non-gastrointestinal symptoms including anemia, extreme weakness, short stature, osteoporosis, menstrual irregularities and infertility. Further symptoms in children include delayed growth and puberty, vomiting and dental enamel defects. Dermatitis herpetiformis is “Celiac Disease of the skin.” It presents with a chronic, severely itchy, blisting rash that is poorly responsive to established therapies. The diagnosis of dermatitis herpetiformis can be confirmed with a skin biopsy. (Rashid, 2011)

Celiac Disease is classified as an autoimmune disease. Autoimmune disorders occur when the immune system attacks the body’s own tissues and organs. Individuals diagnosed with Celiac Disease must live a strict lifestyle following a gluten-free diet, to prevent inflammation resulting from the immune systems over activity that can cause a
wide variety of sign and symptoms involving many parts of the body. (NIH U.S. National Library of Medicine, 2017)

Gluten is the main protein complex in wheat, barley, and rye. Gluten proteins play a key role in determining the unique baking quality of wheat by conferring water absorption capacity, cohesivity, viscosity and elasticity on dough. Gluten proteins can be divided into two main fractions per their solubility in aqueous alcohols. A mixture of alcohol-insoluble proteins is called glutenins and alcohol-soluble proteins are called gliadins. Celiac Disease is associated with an inappropriate immune response to a segment of the gluten protein called gliadin. Gliadins are a group of proline and glutamine-rich proteins resistant to digestion in the gastrointestinal tract. (Weiser, 2007) Gliadin, the alcohol-soluble protein fraction of wheat, contains the toxic factor for Celiac patients. Celiac toxicity of gliadin is not destroyed by digestion with gastropancreatic enzymes. Invitro testing established the toxicity of a –type gliadins and invitro testing of gliadins peptides revealed that domain I of a-type gliadins is involved in activating Celiac Disease. (Relation between Gliadin Structure and Coeliac Toxity, 1996)

The diagnosis of Celiac Disease follows well standardized practices and is clearly defined. There are occurrences where the disease cannot be recognized as the process has not yet reached the point of being detected either by serum antibody testing or by pathology. Individuals believed to be affected by a gluten-related disorders should be advised to seek medical guidance and be screened for Celiac Disease. In most cases having a duodenal biopsy is recommended for an accurate diagnosis of Celiac Disease. (Guandalini MD, 2015)
The risk of developing Celiac Disease is increased by certain variants of the HLA-DQA1 and HLA-DQB1 genes. These genes provide instructions for making proteins that play a critical role in the immune system. These genes called the human leukocyte antigen (HLA) complex. The HLA complex helps the immune system distinguish the body’s own proteins from proteins made by foreign invaders such as viruses and bacteria. (NIH U.S. National Library of Medicine, 2017)

Celiac Disease is one of the most common chronic gastrointestinal disorders in the world. Population based serologic studies have estimated that 1% of North Americans may have the disorder, and approximately 90% of the cases go undiagnosed. (Rashid, 2011) Celiac Disease tends to run in families. Because Celiac Disease is hereditary, parents, siblings, or children of people with Celiac Disease have between a 4 and 15 percent chance of developing the disorder. Celiac Disease can develop at any age after an individual starts eating food containing gluten. Other high-risk groups at risk for Celiac Disease can include patients with other auto-immune disorders such as Down’s Syndrome, Type I Diabetes Mellitus and Thyroiditis. (Rashid, 2011)

The classic symptoms of Celiac Disease results from inflammation affecting the gastrointestinal tract. The inflammation damages the villi, which are small, finger-like projections that line the small intestines and provide a prominently increased area to absorb nutrients. With Celiac Disease, the villi become shortened and eventually flatten out. The atrophy of the villi can cause the malabsorption of numerous micro and macro-nutrients including but not limited to calcium, iron, fat soluble vitamins and folate. (Rashid, 2011)
The damage to the intestines can cause diarrhea and poor absorption of nutrients which can lead to weight loss. Not all individuals with Celiac Disease present with gastrointestinal symptoms. Neurological problems including possible migraines can also be a symptom of Celiac Disease. Celiac Disease can cause inflammation affecting other organs and systems of the body including oral and dental manifestation including defects in the enamel of developing teeth. On average, a diagnosis of Celiac Disease is not made until 6 to 10 years after symptom begin. (NIH U.S. National Library of Medicine, 2017)

Oral and dental manifestations of Celiac Disease can appear as enamel defects, delays in tooth eruption, recurrent aphthous ulcers, oral lichen planus, cheilosis, and atrophic glossitis. The cause of dental enamel defects with Celiac Disease is still unknown, but immune-mediated damage is believed to be the primary factor. Studies have suggested that hypocalcemia, due to malabsorption during the period of undetected disease, might provoke the enamel defects on developing teeth. (Majorana, 2010) Hypocalcemia is commonly due to inadequate levels of parathyroid hormone or vitamin D. (Fong, 2012) Some theories have been hypothesized that the stimulation of naïve lymphocytes by gluten in the oral cavity can also be suspected. (Rashid, 2011)

Celiac Disease can develop at any age when solid foods are introduced into the diet, however, if it appears in children while the permanent dentition is developing usually before the age of 7 years old, abnormalities in the dental enamel structure can occur. Enamel defects can include pitting, grooving of the enamel and even complete loss of enamel. The crowns of the permanent teeth develop between the early months of life and the 7th year. The development of deciduous teeth occurs primarily in utero. The
involvement of deciduous teeth in some cases supports the hypothesis that immunologic and genetic factors are more important in the etiology of the defects versus nutritional deficiencies. (Rashid, 2011) These defects are more commonly seen in the permanent teeth and tend to appear symmetrically and chronologically in all four quadrants with more defects in the maxillary and mandibular incisors and molars. Hypomineralization and hypoplasia of the enamel can also occur. A band of hypoplastic enamel, often with intact cusps is a common occurrence. (Rashid, 2011) According to the study *Essentiality of Early Diagnosis of Molar Incisor Hypomineralization in Children and Review of its Clinical Presentation, Etiology and Management*, these alternations can be found in two different stages: Enamel matrix formation and enamel mineralization. If an unbalance occurs during the enamel matrix formation, the enamel defect is call hypoplasia. If it occurs during enamel mineralization, it is called hypomineralization. (Garg, 2012)

It is important to remember that a child or adult with Celiac Disease may have no symptoms other than oral dental abnormalities. Children with Celiac Disease whose teeth were examined under an electron microscope were found to have significantly different appearance in the dental enamel than children without Celiac Disease. (The National Institute of Diabetes and Digestive and Kidney Diseases, 2014)

**Review of Literature:**

The focus of the research was to evaluate the oral manifestations of Celiac Disease and the occurrence of dental enamel defects in children. In a Letter to the Editor in the International Journal of Colorectal Disease published May 2016, author Raffaella Mormile writes “Although CD patients may suffer primarily from gastrointestinal symptoms, any organ system may be involved CD including permanent teeth.” He goes
on to say that “It has been reported that developmental defects of the dental enamel are more frequently detected in patients with Celiac Disease in comparison to healthy people.” It has been determined that dental enamel defects correlate with the period of interruption of amelogenesis. (Mormile, 2016)

**Study One**

In a recent study by Kitazono de Carvalho, et al it was acknowledged that the American Academy of Pediatric Gastroenterology, Hepatology, and Nutrition has reported there is a high prevalence of dental enamel defects in patients with Celiac Disease, and they also acknowledge that there have been only a few studies that considered the correlation of Celiac Disease and dental enamel defects in children. (Kitazono de Carvalho, 2015)

The study was published in “Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology” where researchers studied 52 children with Celiac Disease and 52 controls were examined for dental enamel defects, recurrent aphthous stomatitis, dental caries and saliva. The focus of this study was to evaluate the chemical alterations in dental enamel in a sample of Brazilian children. The oral manifestations of dental enamel defects, recurrent aphthous stomatitis, dental caries and saliva parameters were evaluated. The findings were then compared to a control group of children that were not diagnosed with Celiac Disease.
Methodology:

The sample group consisted of 52 children aging in range from 2 – 15 years old who were clinically diagnosed with Celiac Disease. The control group consisted of 52 children in the same age group and gender matching who had a negative diagnosis and a negative family history of Celiac Disease. They also had no gastrointestinal signs and symptoms of the disease. Some exclusion criteria for this study was a history of traumatic injury to the primary dentition, a history of dental fluorosis or any other systemic condition. Other exclusions included porphyria, chronic renal failure, congenital hemolytic anemia, premature birth, and any use of medications that could cause changes in the enamel such as tetracycline.

The children received a prophylaxis and exam by a single pediatric dentist. He recorded both unspecific and systemic dental enamel defects. Systemic dental enamel defects involved the same teeth in both the left and right hemi-arch. If the teeth had two-thirds or more of the coronal surface restored they would be excluded from the study.

The pediatric dentist then recorded the presence of aphthous stomatitis lesions that were present during the exam. A self-reported assessment of recurrent aphthous stomatitis was also recorded. A dental caries assessment was also performed using a mirror, direct lighting and a ball-ended probe using the DMFT index.

Saliva samples were also collected from the participants of the study in the morning. They were instructed not to use mouthwash for at least 12 hours prior to the sample collection. They were also advised not to perform any oral hygiene one hour prior to the salivary sample being taken. The participants were also not allowed to eat, drink or smoke within one hour of collection.
Another part of the study was to evaluate exfoliated maxillary and mandibular primary molars. These teeth came from children with and without Celiac Disease. A quantitative analysis was performed on the dental enamel to detect the concentrations of oxygen, calcium and phosphorous.

Summary of Findings:

The results of the study were: Among the children with Celiac Disease, there was a higher prevalence of dental enamel defects along with recurrent aphthous stomatitis. There was also a lower incidence of dental caries and a reduction in the salivary flow. The teeth that were evaluated found that there was a lower calcium to phosphate ratio but no difference in the carbonate to phosphate ratio. It was determined that Celiac Disease was a protective factor for dental caries. (Kitazono de Carvalho, 2015)

The study concluded that children with Celiac Disease presented with more recurrent aphthous stomatitis, dental enamel defects, reduction of salivary flow, and chemical alterations in the enamel. (Kitazono de Carvalho, 2015)

Study Two:

In a study published in the “International Journal of Paediatric Dentistry” 250 children were enrolled in a case-control study. 125 children including 79 females and 46 males who were diagnosed with Celiac Disease and 125 healthy children matched to cases for age, sex, race and area of residence were studied over an 18-month period.

Methodology/Process:

The age of diagnosis of Celiac Disease and the beginning of the gluten-free diet were recorded. Dental and medical histories for each child was collected. Children that had a history of infectious disease, dental trauma, treated with immunosuppressant drugs
or chemotherapy or other medications with a known effect on the dental enamel were withdrawn from the study. (Majorana, 2010)

The children all received a prophylaxis and dental examination by the same pediatric dental examiner. All dental enamel defects were noted and photographed. The dental enamel defects were graded 0 to IV according to the Aine’s classification. The subjects also had HLA class II typing using polymerase chain reaction-based DNA typing.

**Summary of Findings:**

The results of the study determined that 46.4% of the children diagnosed with Celiac Disease presented with dental enamel defects compared to 5.6% of the control group. The presence of HLA DR 52-53 and DQ7 antigens significantly increased the risk of dental enamel defects in children diagnosed with Celiac Disease. The study concluded that the results confirmed a possible correlation between HLA antigens and dental enamel defects. (Majorana, 2010)

**Study Three:**

Additionally, another study found that “Celiac Disease has adverse effects on oral health in terms of enamel defects, recurrent aphthous stomatitis and caries scores.” Of the 25 children in the Celiac Disease group 48% presented with enamel defects compared to 16% of healthy children. Recurrent aphthous stomatitis was found in 44% of the celiac group as compared to 0% in the control group. (Cantekin, 2015)
Study Four:

In a similar study published in the *International Journal of Paediatric Dentistry*, researchers investigated whether Dutch children with proven Celiac Disease showed specific dental enamel defects and to access whether children with the same gastrointestinal complaints but without a diagnosis of Celiac Disease, lack dental enamel defects.

Methodology/Process:

243 children who were clinically suspected of having Celiac Disease underwent a biopsy of the jejunal intestinal mucosa and 126 children were confirmed with Celiac Disease. All the families were approached regarding the study but ultimately only 54 Celiac patients and 31 for the control group were willing to participate. The participants along with their parents answered questionnaires and 4 more children were eliminated from the study.

Summary of Findings:

81 children were then examined, 53 had a clinical diagnosis of Celiac Disease and 28 children who were clinically diagnosed with Celiac Disease were in the control group. The children were classified according to the systematic and chronological enamel defects according to the AINE Dental Enamel classifications and the results were consistent with other studies and showed 55% of Celiac patients had dental enamel defects as compared to 18% of the control group. (Claar D. Wierink, 2007)
Summary:

The research validates that dental enamel defects are a manifestation of Celiac Disease. Evidence supports that it is very important for dental professionals to consider Celiac Disease as a diagnosis when a patient presents with dental enamel defects and be prepared to refer the patient to a Gastroenterologist. Dental professionals should question patients and their parents regarding other clinical symptoms that could present with Celiac Disease such as recurrent aphthous stomatitis, poor growth, weight loss, abdominal pain, diarrhea and extreme fatigue if a patient presents with dental enamel defects. (Rashid, 2011)
Chapter 5:

Discussions/Conclusion:

The American Dental Association and the American Academy of Pediatric Dentistry recommend that the first dental visit should occur within the first six months after the baby’s first tooth appears, but no later than one year of age. (American Dental Association, 2017) Dental professionals should have an understanding that enamel defects are common manifestations of Celiac Disease. With an increased awareness of the signs and symptoms of Celiac Disease and being thoroughly educated to ask the appropriate questions, the dental professional can confidently make a referral for the patient to their medical doctor in a timely manner to prevent further complications of Celiac Disease.

Future Studies:

The evidence is clear that Celiac Disease can cause dental enamel defects but what the exact mechanism is that causes the defects still needs further research. These studies may be hard to do because Celiac Disease can go undiagnosed for several years while the tooth formation is going on. To do more research on the cause and effect, children at a very young age would need to be diagnosed with Celiac Disease to prevent the disease from causing the defects in the enamel.
Works Cited


Majorana, A. e. (2010, March 1). *Implications of gluten exposure period, CD clinical forms, and HLA typing in the association between celiac disease and dental*


