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CELIAC DISEASE

Developed by Keiko Marshall, Emily Kacer, and Dr. Jenna Dowhaniuk for PedsCases.com.
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Introduction:

Keiko: Hi everyone! My name is Keiko Marshall.

Emily: And my name is Emily Kacer.

Keiko: We are both second year medical students studying at McMaster University. In this episode of PedsCases, we will be exploring the topic of celiac disease. We are happy to be joined by Dr. Jenna Dowhaniuk for this episode, and have greatly appreciated her support in the development of today's podcast.

Emily: Dr. Dowhaniuk is a Pediatric Gastroenterologist and Assistant Professor at McMaster University, who serves as the medical lead of the McMaster Children's Hospital pediatric celiac disease clinic. Welcome to PedsCases, Dr. Dowhaniuk!

Dr. Dowhaniuk: Thank you both so much for having me today.

Learning Objectives

Emily: The learning objectives for this podcast are as follows:

1. **Keiko:** Define celiac disease and its prevalence in Canada
2. **Emily:** Describe the clinical presentation of Celiac disease across childhood and identify common differential diagnoses
3. **Keiko:** Outline investigations required for the diagnosis of celiac disease
4. **Emily:** Discuss the management of celiac disease and review potential complications

Dr. Dowhaniuk: As we go through these objectives, we will work through a clinical case of child-onset celiac disease. Let's begin, Keiko!

Today's Case

Keiko: You are a third-year clinical clerk completing your family medicine rotation at a community clinic. You check the schedule and see that your next patient is Celia, a 3-year-old girl presenting with a 4 month history of diarrhea and abdominal bloating.

Emily: When you review her chart, you learn that Celia is a previously healthy toddler who does not take any regular medications and has no known allergies. Her past medical history includes one episode of acute otitis media but otherwise is unremarkable. Celia was born after an

uncomplicated pregnancy at 39 weeks of gestational age and to date, she has met all her developmental milestones.

Keiko: Your preceptor has made a note to closely monitor Celia's height and weight due to a recent slowing in growth on her growth curves. At her last appointment, Celia's weight deviated from her normal growth curve at the 30th percentile to the 5th percentile, where it remains today.

Dr. Dowhaniuk: As you begin to formulate your approach to this visit. What stands out to you?

Emily: Considering the recent changes in her growth curves, I'm concerned about a possible failure to thrive presentation.

Keiko: I also think that the chronic nature of these gastrointestinal symptoms is very worrisome.

Dr. Dowhaniuk: These are great thoughts about the case so far! For our listeners, what are some important questions you would include in your history? What differential diagnoses are you considering with Celia's clinical presentation?

Objective 1: Defining Celiac Disease in Pediatric Populations

Emily: Celiac disease is an autoimmune disease of the small intestine occurring in individuals who have a genetic predisposition and consume gluten (University of Chicago, 2023; Ediger & Hill, 2021).

Keiko: While I'm sure our listeners have likely heard the phrase "gluten-free", could you please explain what exactly gluten is Dr. Dowhaniuk?

Dr. Dowhaniuk: I'd be happy to! As a general overview, gluten is a protein that is found in grains such as wheat, barley, rye, and some less common grains (University of Chicago, 2023; Ediger & Hill, 2021). When gluten is consumed, it can be partially digested or broken down into various proteins, specifically gliadin (University of Chicago, 2023). In celiac disease, an inappropriate immune reaction is prompted by the presence of gliadin (Stahl & Liu, Epidemiology, pathogenesis, and clinical manifestations of celiac disease in children, 2024).

Emily: The associated inflammation leads to intestinal damage. Both the intestinal and extraintestinal manifestations of celiac disease can also be reversed upon removing gluten from the diet (University of Chicago, 2023). Over time, we expect a normalization of the small intestinal mucosa.

Keiko: Since first recognized in the 1900s by Dutch pediatrician Willem Dicke, celiac disease has been increasing in incidence (University of Chicago, 2023). Generally, we see more females than males with this diagnosis (Guandalini, 2023).

Emily: Celiac disease affects approximately 1% of Canadians (Butzner, 2020). Including me! I was diagnosed with this condition as a teenager, so today's episode topic is near and dear to my heart.

Dr. Dowhaniuk: Thank you for sharing, Emily. During my years of caring for patients, I have seen the challenges, as well as the huge successes, faced by those living with celiac disease.

Additionally, I want to highlight that the exact prevalence of celiac disease is difficult to capture because there are many undiagnosed cases (University of Chicago, 2023).

Keiko: As an autoimmune disease, celiac disease has a strong genetic component and is associated with two genotypes of the human leukocyte antigen: HLA-DQ2 and HLA-DQ8 (University of Chicago, 2023).

Emily: In those with celiac disease, approximately 90-95% have the DQ2 genotype while the remaining 5-10% have the DQ8 genotype (University of Chicago, 2023).

Dr. Dowhaniuk: If a patient doesn't have the genetic predisposition, they would not develop celiac disease. However, there are some challenges with the testing for these genes and therefore it is not a standard part of our work up for every person we're suspecting of celiac disease. Since nearly 40% of the population in Canada has these genetic markers, genetic testing does not help us find out who actually has the disease (Health Canada, 2018).

Keiko: To clarify, the genotype is required to develop celiac disease but just because a patient has the genotype they will not necessarily go on to have celiac disease?

Dr. Dowhaniuk: That's right! As we continue to learn more about the genetics of celiac disease, we recognize that there are high risk groups for celiac disease.

Emily: Individuals at increased risk include those who are first or second degree relatives of an individual with celiac disease (Stahl & Liu, Epidemiology, pathogenesis, and clinical manifestations of celiac disease in children, 2024). Additionally, celiac is found in higher rates for patients with other autoimmune disorders such as type 1 diabetes mellitus (University of Chicago, 2023).

Keiko: Finally, patients with certain genetic syndromes such as Trisomy 21 and immunodeficiencies like IgA deficiency also have higher prevalence of celiac disease (University of Chicago, 2023; Stahl & Liu, Epidemiology, pathogenesis, and clinical manifestations of celiac disease in children, 2024).

Dr. Dowhaniuk: Now that we know who is at higher risk of developing celiac disease, I think it's time to discuss the pathophysiology.

Emily: In our overview of celiac disease, we indicated that the development of this systemic autoimmune disorder requires both the genotypic susceptibility and trigger of gluten ingestion (University of Chicago, 2023; Ediger & Hill, 2021). Upon consumption, gluten is broken down into glutenins and gliadins. The enzyme tissue transglutaminase, or TTG, then acts on the gliadin peptide (University of Chicago, 2023; Guandalini, 2023).

Keiko: This deamidation occurs in the lamina propria of the small intestine (University of Chicago, 2023). This increases the peptide's negative charge, but they are not entirely digested or broken down. In celiac disease, these peptides bind to the HLA-DQ2 or DQ8 molecule on antigen presenting cells (Ediger & Hill, 2021).

Dr. Dowhaniuk: This binding initiates the inflammatory cascade with IL-15 and IFN gamma molecules. We also see the formation of antibodies and autoantibodies including those against TTG or anti-TTG, anti-gliadin, anti-DGP, and anti-endomysial antibody. There is both a T and B

cell response in celiac disease with the local cytokines playing a role in the mucosal damage and villous blunting.

Emily: This inflammatory process damages the intestine and alters the mucosal tight junctions to increase gut permeability. This is particularly concerning as the mucosa of the small intestine has a key role in digestion, nutrient and electrolyte absorption, and protection against antigens (University of Chicago, 2023; Guandalini, 2023).

Keiko: Beyond the small intestine, those with celiac disease also have manifestations in the skin, liver, joints, and other organs (University of Chicago, 2023). This leads us into our next topic, the clinical presentation of celiac disease.

Objective 2: Clinical Presentation of Celiac Disease Across Childhood

Dr. Dowhaniuk: Although we'll be discussing pediatric celiac disease, it is important to recognize that celiac disease may present at any age (Ediger & Hill, 2021). There is also a spectrum of manifestations from entirely asymptomatic to life-threatening malnutrition, especially in young pediatric patients (University of Chicago, 2023).

Emily: For instance, infants may present with major electrolyte disturbances, dehydration, lethargy, failure to thrive, and/or vitamin deficiencies (Ediger & Hill, 2021; Stahl & Liu, Epidemiology, pathogenesis, and clinical manifestations of celiac disease in children, 2024; Guandalini, 2023). This is a severe presentation of celiac disease that may present at less than age 2 with symptoms starting after gluten is introduced into the child's diet.

Young children can actually present at any age with symptoms of malabsorption including diarrhea, bloating, and poor weight gain. Looking back at my own journey with celiac disease, my symptom experience was fairly similar, but my malabsorption was much more mild than how we tend to picture the classic presentation of celiac disease.

Keiko: In pediatric patients, we may see diarrhea or paradoxically, constipation. Associated with the malabsorption, may also be a bloated or distended abdomen relative to thin extremities and a flat buttocks. Other classic symptoms include reduced appetite, vomiting, abdominal pain, and irritability (University of Chicago, 2023; Ediger & Hill, 2021; Stahl & Liu, Epidemiology, pathogenesis, and clinical manifestations of celiac disease in children, 2024; Guandalini, 2023).

Dr. Dowhaniuk: In contrast to the classic malabsorptive picture of celiac disease, we're now seeing increasing numbers of patients presenting with mild gastrointestinal and more substantial extraintestinal symptoms (University of Chicago, 2023; Stahl & Liu, Epidemiology, pathogenesis, and clinical manifestations of celiac disease in children, 2024). One of the specific extraintestinal manifestations of celiac disease is dermatitis herpetiformis which is a rash which erupts on the limb extensor surfaces, trunk, or scalp. This rash can appear as erythematous papules or vesicles which are incredibly itchy (University of Chicago, 2023; Ediger & Hill, 2021).

Emily: Our review of extraintestinal symptoms will be non-exhaustive but cover some of the more common presentations for our listeners' awareness. Childhood onset celiac disease can present with impacted growth and development including short stature, developmental delay, failure to thrive, behavioural difficulties or pubertal delay (University of Chicago, 2023; Ediger &

Hill, 2021; Stahl & Liu, Epidemiology, pathogenesis, and clinical manifestations of celiac disease in children, 2024).

Keiko: Nervous system manifestations of celiac disease are rare however may include depression, cerebellar ataxia, and headaches (University of Chicago, 2023; Ediger & Hill, 2021). More commonly children and parents may describe brain fog, irritability and fatigue. Additionally, iron deficiency anemia and vitamin D deficiency tend to be associated findings (University of Chicago, 2023; Guandalini, 2023).

Dr. Dowhaniuk: Within the musculoskeletal system, arthralgia, dental enamel defects, osteopenia, or osteomalacia may be present (University of Chicago, 2023; Stahl & Liu, Epidemiology, pathogenesis, and clinical manifestations of celiac disease in children, 2024). There are even some children who can have such profound Vitamin D deficiency and malabsorption that they can present with Rickets or recurrent fractures. Reproductive symptoms can include secondary amenorrhea due to poor weight gain and possible infertility in the future (University of Chicago, 2023; Ediger & Hill, 2021).

Emily: Within the gastrointestinal system, elevation of the liver enzymes AST and ALT, autoimmune hepatitis, and aphthous stomatitis are other possible manifestations (University of Chicago, 2023; Guandalini, 2023).

Keiko: Finally, it is important to remember that individuals with celiac disease may be entirely asymptomatic. Thus, certain patients may benefit from screening if they are at increased risk of developing celiac disease (Guandalini, 2023).

Differential Diagnoses of Pediatric Celiac Disease

Dr. Dowhaniuk: Considering the wide range of clinical presentations for celiac disease, let's review some important differential diagnoses. Within the gastrointestinal symptoms, we should also consider cystic fibrosis, inflammatory bowel disease, carbohydrate maldigestion such as lactose intolerance, irritable bowel syndromes, or even autoimmune enteropathy (Guandalini, 2023; Stahl & Liu, Diagnosis of celiac disease in children, 2024).

Emily: When developing a differential diagnosis for the atrophy of the small intestine, we also want to consider tropical sprue, Crohn's disease, and even infections such as Giardia (Stahl & Liu, Diagnosis of celiac disease in children, 2024).

Keiko: It is important to differentiate celiac disease from a wheat allergy. Relative to celiac disease, IgE-mediated wheat allergies are rare and would typically present with anaphylaxis. Conversely, when children with celiac disease accidentally eat gluten they can feel quite unwell with symptoms including vomiting, abdominal pain and diarrhea (Stahl & Liu, Diagnosis of celiac disease in children, 2024).

Dr. Dowhaniuk: Finally, non-celiac gluten sensitivity occurs when individuals experience symptoms associated that are gluten ingestion and that can include bloating, abdominal pain and diarrhea, however, they do not have celiac disease. After you have ruled out celiac disease, you could consider this diagnosis of exclusion as there is no diagnostic testing specific for non-celiac gluten sensitivity or NCGS. Of note, these patients improve once they are also on a gluten free diet.

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Emily: Management of non-celiac gluten sensitivity tends to be based on symptomatic control and is not as strict as the management required for celiac disease.

Keiko: That wraps up part 1 of our PedsCases podcast episode on Celiac Disease. Thank you so much for listening, and stay tuned for Part 2 where we discuss Investigations and Management of Celiac disease.

PedsCases: Celiac Disease (Part 2)

Emily: Welcome back to Part 2 of our PedsCases podcast on Celiac disease. In part 1, we went over the definition of celiac disease, clinical presentation, and differential diagnoses. In part 2, we will go over investigations and the management of celiac disease. Let's go!

Objective 3: Investigations for Celiac Disease

Keiko: Now that we've reviewed the differential diagnoses for celiac disease, I think that this is a great time to talk about screening and diagnostic tests. In practice, children that may have celiac disease will typically first present to their primary care physician. From here, screening tests will likely be ordered and if positive a referral to a celiac disease clinic, which would be run by a pediatric gastroenterologist, would be required for further testing and support from a multidisciplinary team.

Now let's discuss the Indications for Celiac Disease Screening Tests

Dr. Dowhaniuk: There are several indications for when a child should undergo screening tests for celiac disease. Patients that present with many of the symptoms suggestive of celiac disease will proceed with these screening tests (University of Chicago, 2023; Stahl & Liu, Diagnosis of celiac disease in children, 2024). Another group to test would be those that belong to high-risk groups even when they are asymptomatic.

Emily: As you'll recall, these groups include: 1st degree relatives of people with celiac disease, autoimmune thyroiditis, type 1 diabetes mellitus, Down syndrome, and selective IgA deficiency. Intervals for testing these groups tend to be variable but generally 1-3 years would be recommended, in between testing intervals, especially before the child reaches puberty.

Keiko: The North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) guidelines ultimately recommends screening for celiac in high-risk groups, arguing the importance of preventing long-term complications. So, for individuals that are eligible based on these criteria, screening tests should be performed at 3 years of age or older if they are asymptomatic or at any age if symptomatic (Hill, et al., 2016). After all this talk of who is indicated to get screening tests, what exactly are these tests?

Let's now discuss the Screening Tests for Celiac Disease

Dr. Dowhaniuk: The first test that is typically completed is a serologic test for IgA antibodies against tissue transglutaminase (tTG). This should be completed in conjunction with a total IgA measurement. This helps rule out IgA deficiency which would make your tTG-IgA test invalid (Stahl & Liu, Diagnosis of celiac disease in children, 2024).

Emily: All children with a positive tTG-IgA level should be referred to a pediatric gastroenterologist. Those with low positive levels may want to repeat it to determine that it was

a truly positive result. However, further testing is required for all children with a positive TTG and a pediatric gastroenterologist would discuss this further with the family. Children with a positive TTG would proceed to an upper endoscopy for confirmation of celiac disease if indicated.

Keiko: If a family wants to skip the biopsy, is that reasonable?

Dr. Dowhaniuk: For the majority of kids who are referred for possible celiac disease, unfortunately, no. Similar to Crohn's disease, the upper endoscopy is a critical step. This helps us to obtain the small intestine biopsy which we review under the microscope and confirm celiac disease. There is a smaller subset of kids who we may discuss what is known as the ESPGHAN guidelines, however in North America, we encourage all families to consider upper endoscopy.

Emily: What are the ESPGHAN guidelines?

Dr. Dowhaniuk: The ESPGHAN guidelines were published in Europe and are only applicable to kids who have symptoms (such as diarrhea) and have not been studied for children in other high-risk groups such as type 1 diabetes (Husby, et al., 2019). It is also for those with very high TTG results that have been repeated twice. In addition, these patients should also have tested positive for another autoantibody, called the anti-endomysial antibody (EMA) and possibly suggested to also have the HLA-DQ2 or DQ8 test done as well. If they meet clinical criteria for all of these, some pediatric GI may suggest the option of skipping the endoscopy with the family. However, it is not 100% specific and we do want to get the diagnosis right 100% of the time.

Keiko: How high would be very high for the TTG levels?

Dr. Dowhaniuk: We would only consider the TTG as being high enough for these guidelines when TTG greater than 10 times the upper reference value. So if the normal value is anything less 12, then we would consider ESPGHAN or very high to be >120 for these guidelines (Husby, et al., 2019).

Emily: What if the TTG value is 60 or 70, is that high enough?

Dr. Dowhaniuk: Unfortunately not. As with all families I see in clinic, an upper endoscopy is discussed as the most important next step to obtain the small intestine histology. The majority of patients who present to clinic do not, in fact, meet the ESPGHAN guideline. There are other diseases or differential diagnoses to consider for a positive TTG. This would be important for why we proceed with upper endoscopy and these would include peptic duodenitis, H. pylori, frequent NSAID use with duodenitis or gastroenteritis, or even Crohn's disease to name a few.

Emily: That sounds confusing. I can imagine it makes it hard for families to know if they meet these guidelines.

Dr. Dowhaniuk: It can be very confusing and one of the most common misconceptions is that any positive TTG blood test would indicate that a child has celiac disease but this is not true. Many kids can have a low positive blood test for TTG and this could still be a false positive. And it would be very unfortunate to start a family on a lifelong gluten free diet because they gave misinterpreted the blood test results. The important thing to remember for families and for primary care providers, is to refer all patients with a positive TTG to a pediatric

gastroenterologist. They can help put the puzzle pieces together and decide what tests are needed for confirmation for celiac disease.

Keiko: Okay that is very helpful. Are TTG and a baseline IgA level the only two tests needed for screening?

Dr. Dowhaniuk Yes they are. For most kids and adults that are wondering if they have celiac disease, these are the two tests needed (Stahl & Liu, Diagnosis of celiac disease in children, 2024; Guandalini, 2023). If the IgA test is normal and the TTG test is negative, this would rule out celiac disease. There are a few exceptions to keep in mind and this is where some other auto-antibodies might be tested.

Keiko: This would include children with Type 1 diabetes, where it is reasonable to also check anti-endomysial antibodies (EMA) if the TTG test is positive. For this particular group, the upper endoscopy is more likely to be abnormal when both tests are positive. Most patients however, do not need EMA testing.

Dr. Dowhaniuk: Other screening serologic tests include the deamidated gliadin peptide (DGP) as well as considering the HLA genetic testing. The deamidated gliadin peptide is an IgG test instead of the IgA test like the TTG.

Emily: Is it important to test the DGP blood test?

Keiko: No, it is not a helpful additional test for most children as it has a much lower specificity and sensitivity. Unfortunately, many local labs include it automatically when you request “celiac serology”. To help minimize ordering this less helpful test, order specifically the tests you need, which would be the TTG and the IgA.

Emily: Okay so when should we order a DGP IGG test?

Dr. Dowhaniuk: It can be helpful for those with a low IgA level which you often don’t know about until you first send off your first blood tests. We don’t know exactly how low the IgA level has to be for celiac tests to not be accurate. Some studies have suggested under 0.2. However, if there is a child with symptoms of celiac disease and a low IgA test, it is recommended to refer them to a pediatric gastroenterologist.

Emily: There is another group in which the DGP test can be useful and this is for children under the age of 2. In these children, some will have a positive DGP test but a negative TTG test and ultimately have celiac disease (Stahl & Liu, Diagnosis of celiac disease in children, 2024).

Keiko: Does that mean that children under the age of two also may not have reliable screening tests for celiac disease? Should we be sending these kids to a pediatric Gastroenterologist as well?

Dr. Dowhaniuk: That is correct. In children with symptoms concerning for celiac disease, don’t rely on the TTG blood test for those under the age of 2 (Stahl & Liu, Diagnosis of celiac disease in children, 2024). These kids could still have celiac disease despite the negative TTG test. The same is applicable for those with an IgA deficiency. These are the special groups where we may proceed with an upper endoscopy just based on symptoms. However, it is still a good idea to

send these tests even for kids under 2, as some do show a positive TTG test which helps make the plan more straightforward.

Keiko: And it is uncommon to need to order HLA testing. HLA testing is not regularly done for celiac disease screening, as it is of limited value. As you'll recall from our first episode, almost everyone with celiac disease will have either HLA-DQ2 or DQ8 genotypes but approximately 40% of the general population does as well!

Emily: This next point is incredibly high yield for learners. All of the celiac disease screening tests must be completed while the child is on a gluten-containing diet, as these tests will normalize if the child eats gluten free for some time (Stahl & Liu, Diagnosis of celiac disease in children, 2024; Guandalini, 2023; University of Chicago, 2023). This is very important to remember as some families will start a gluten free diet once they have one positive blood test and it will make the next phase of testing inaccurate including their upper endoscopy. All children should be told to remain on a gluten containing diet until they are seen by a pediatric gastroenterologist.

Keiko: Are there ever any situations where families are hesitant or uncomfortable with reintroducing gluten into the diet if they have started the gluten-free diet too soon? What steps are taken in those situations, Dr. Dowhaniuk?

Dr. Dowhaniuk: It's understandable that a family would be hesitant, and this situation definitely does arise. For these patients we explain that they need a gluten challenge before we proceed with any further tests. I also explain that we need to get the diagnosis right as this is something that they will live with for their entire lives and change what they would eat. It is so important for us to get this right for the child. A gluten challenge would consist of 3–6 grams of gluten per day for over 12 weeks which could be 2 slices of bread. I often suggest one meal be gluten based such as a sandwich for lunch or pasta for dinner. Then we would repeat the blood tests and proceed with an endoscopy.

We will now move on to the Diagnostic Tests for Celiac Disease

Emily: Throughout all this talk of screening tests, it may have seemed like all roads lead to endoscopy. Well, that's because performing a small intestine biopsy through endoscopy is the gold standard diagnostic test for celiac disease (Stahl & Liu, Diagnosis of celiac disease in children, 2024; Guandalini, 2023). The endoscopy is performed when a patient is on a gluten-containing diet, and multiple biopsies are taken from the duodenum as the disease can have patchy distribution.

Keiko: The biopsy will then be interpreted by a pathologist, looking for characteristic histologic changes, which include: inflammation of the mucosa (specifically intraepithelial lymphocytes) villous atrophy or blunting, and crypt hyperplasia (University of Chicago, 2023). These findings are described by the Marsh Classification scale, which runs from type 1 to type 4. Patients with a Marsh type 2 or higher are diagnosed with celiac disease (Stahl & Liu, Diagnosis of celiac disease in children, 2024).

Keiko: Once a diagnosis of celiac disease has been established, it's also important to do a few more tests to identify any comorbidities or complications. These tests may include a CBC, iron studies, vitamin D, liver enzymes including AST and ALT, TSH and free T4 (Guandalini, 2023).

With that, we will move on to our final objective, **Objective 4: Management of Celiac Disease**

Dr. Dowhaniuk: That was a great overview of the different steps taken to screen for and diagnose celiac disease. Let's now move onto how we manage children that have been newly diagnosed with celiac disease.

Emily: I'm excited to discuss an easy mnemonic to remember the 6 key elements of celiac disease management. The mnemonic is "CELIAC":

- Consultation with a skilled dietitian
- Education about the disease
- Lifelong adherence to a GF diet
- Identification and treatment of nutritional deficiencies
- Access to an advocacy or support group, and
- Continuous long-term follow-up by a multidisciplinary team (Guandalini, 2023)

Let's discuss the components of a Gluten-Free Diet

Keiko: As we previously defined gluten and the pathophysiology of celiac disease, it should come as no surprise that the core principle of celiac disease management is a lifelong gluten-free (GF) diet. As you may remember, gluten is found in grains such as wheat, barley and rye and it's also found in regularly packaged oats which may be manufactured in facilities with wheat. Therefore, these children need to completely remove wheat, rye, barley and regular oats from their diet. For many children and families, this can be a major lifestyle change due to how many common foods in Western diets contain gluten (Guandalini, 2023). This is where working with a registered dietitian with expertise in celiac disease, if possible, is incredibly important. These healthcare professionals can provide counseling and support adherence with GF diets.

Dr. Dowhaniuk: That's right, and many celiac disease clinics will include dietitians within the clinical team as they are so important to help facilitate patients getting connected and giving nutrition counseling. Many of the gastrointestinal symptoms associated with celiac disease should resolve within a couple of months and at times even weeks of initiating and adhering to a GF diet (Guandalini, 2023).

Emily: This was definitely my own experience with starting a gluten-free diet, it was such a drastic change and so quickly too! Children may also see improved height and weight, normalization of hematologic and biochemical parameters, and improvements in their psychosocial wellbeing on a GF diet (Guandalini, 2023).

Dr. Dowhaniuk: Given how important a GF diet is in symptom resolution, do you know what foods are typically recommended and avoided in GF diets?

Emily: There are many foods that are very safe to consume while on a GF diet, many of which I love to incorporate into my personal GF diet. Some safe foods include alternative starches like rice, corn, buckwheat, and potatoes (Stahl & Liu, Management of celiac disease in children, 2024). There are also many naturally gluten-free foods like fruits, vegetables, legumes, most dairy products, fish, tofu, and unprocessed meats (Canadian Pediatric Society, 2020).

Keiko: Many foods in a grocery store have gluten which include breads, pastas, pizza, desserts, and breaded meat (Canadian Pediatric Society, 2020). There are also many other

lesser-known gluten-containing foods, a few that I admittedly didn't know contained gluten until recently, including soy sauce, malt vinegar, Worcestershire sauce, fillers found in processed foods like hot dogs, certain chips, and many candies.

Dr. Dowhaniuk: Another hidden source of gluten for parents and children are non-food items that may be put into the mouth by young children, such as playdough. For young children, we would remind parents of this.

Emily: Wow! Having celiac disease myself, I have had to learn over time the ins and outs of a GF diet, but hearing all of these components listed out loud reminds me of how overwhelming it can feel to navigate a GF diet when someone is first starting out or even now, almost 10 years into my own diagnosis. Thankfully, Canadian label laws require that food packages indicate if wheat is present (Stahl & Liu, Management of celiac disease in children, 2024). Some foods are also certified to be gluten free by the Canadian Celiac Association or the CCA, and have the Gluten-Free Certification Program (GFCP) label on them (Celiac Canada, n.d.). These labels can help a lot when choosing foods, but it's still very important to read food labels carefully, especially with foods that are not regulated by Canadian label laws.

Keiko: For sure! Some products may have gluten-containing products added in (like stabilizers, emulsifiers), trace amounts of gluten present, or have had potential contamination during the manufacturing process. For example, oats are safe to eat if they have been labelled as gluten free by a reliable group such as the Gluten-Free certification program in Canada and have the CCA label.

Dr. Dowhaniuk: The gluten free diet also continues beyond selecting foods, and includes the preparation process as well as this is a period with many opportunities for contamination with gluten. To avoid cross-contamination at home and when dining out, methods can be employed such as: using a separate toaster for GF bread, using fat/oil that has never been used for gluten-containing foods when frying food (specifically asking about a dedicated gluten-free fryer at restaurants), cooking GF pasta in water that has never been used for gluten-containing foods, also to consider using warm soapy water to clean cookware once it has been touched by any gluten items (Canadian Pediatric Society, 2020).

Emily: With all of these rules, it's very easy to become anxious and fixated on the gluten content of foods. Despite the importance of education around a strict gluten free diet, it is also crucial to not promote hypervigilance in children and parents. Trace or accidental gluten exposure is inevitable at times, and hypervigilance has been described in some children which causes anxiety and can also lead to possible disordered eating in children (Stahl & Liu, Management of celiac disease in children, 2024).

Dr. Dowhaniuk: That is right Emily. Examples of this are children who become fearful of eating outside of their own house or are even worried to hug or embrace their parents if they know their parents have eaten gluten. It is important to balance this concern of hypervigilance and to monitor for anxiety or disordered eating for kids who have to follow restrictive diets like the gluten free diet.

Emily: And there will always be a time where a child accidentally eats gluten, so we have to normalize that part. Management of an accidental gluten exposure is purely supportive based on the children's symptoms and there are really no specific interventions within the post-exposure period. Some children may have diarrhea, abdominal pain or vomiting while others do

not experience many symptoms. The symptoms also can change as the children start following a gluten free diet for many years.

Now we'll discuss Other Dietary Modifications beyond a gluten free diet.

Keiko: Dr. Dowhaniuk, are there any other dietary considerations for children with celiac disease?

Dr. Dowhaniuk: Yes there are, although none are quite as important as the GF diet itself! Some people do find that avoiding dairy products, specifically lactose, can provide initial relief from some of the symptoms they have had such as diarrhea and bloating in the first couple months of being gluten free. Most kids do not need to do this, however some that have experienced a lot of diarrhea notice a real improvement once they are both lactose free and gluten free. The reason this happens is a child with celiac disease develops a secondary lactose intolerance due to a lactase deficiency, this is thought to accompany the flattened intestinal villi (Stahl & Liu, Management of celiac disease in children, 2024). For those that need this, lactose can be added back into the diet around 2-3 months into the GF diet (which is when we would assume that the mucosa has had some healing) and then usually continues to be tolerated (Stahl & Liu, Management of celiac disease in children, 2024).

Emily: Fiber is also an important consideration, as a GF diet is typically low in dietary fiber (Stahl & Liu, Management of celiac disease in children, 2024). Fiber can be added by increasing fruits and vegetables as well as nuts, seeds, beans and legumes. Children should also be counseled on age-appropriate calcium and vitamin D intake to reduce the risk of subsequent osteopenia and osteoporosis (Stahl & Liu, Management of celiac disease in children, 2024). Most children who have celiac disease are on a vitamin D supplement in Canada. The first ever gluten free food guide for children has now been published with the Canadian Celiac Association which highlights these key nutrients and even has food plan ideas for parents.

Keiko: Symptoms of celiac disease should eventually dissipate with adherence to a strict GF diet. One way we monitor for improvement is to repeat the initial screening test, the TTG, over time (Stahl & Liu, Management of celiac disease in children, 2024). Within about 24 months, the TTG should normalize and can then continue to be tested yearly to help ensure a gluten free diet is being followed. However, this test isn't perfect. The best way to review the gluten free diet adherence is to include a registered dietitian in the ongoing monitoring of a child with celiac disease. They can help identify if the diet may be high in ultra-processed foods, low in fiber, low in calcium or any other deficiencies.

Dr. Dowhaniuk: If the TTG remains high and doesn't normalize, or if it is surprisingly high one year, a registered dietitian can be helpful in detecting what the gluten exposure may be. This can be challenging. We have found gluten by investigating the brands of products such as finding gluten in the brands of deli meats, soup broth or cubes, as well as salad dressings.

Emily: Another worry is eating at restaurants due to a higher chance of misinformation between chefs and wait staff about what exactly gluten is, and how to be gluten-free, as well as the risks of cross contamination. People with celiac disease can still eat out but more work is needed before eating at a restaurant and this can include conversations with wait staff and potentially the chef to discuss the accommodations necessary.

Keiko: If hidden gluten is still a concern, a newer option to investigate for gluten in the diet, is testing for gluten immunogenic peptides (GIP) in urine or stool (Coto, Mendia, Sousa, Bai, & Cebolla, 2021). Most families do not need to do this as good education and monitoring is sufficient for teaching about the gluten free diet. However, for some children we may suggest this if they continue to experience symptoms or if they may be still ingesting gluten without their knowledge. In this case, these urine or stool tests would be positive, detecting gluten over a certain timeframe.

Now we can talk about the **Complications** of celiac disease.

Dr. Dowhaniuk: Unfortunately, there are many complications of celiac disease, several of which stem from either the difficulty adhering to the strict GF diet or delays in celiac disease diagnosis. There are many social complications that can arise from celiac disease. GF diets can lead to children feeling isolated or left out during social interactions if they aren't able to consume foods that other children are enjoying. The hypervigilance around gluten monitoring [discussed] earlier can also lead to anxiety in social situations where food is involved.

Keiko: Another social complication is that many of the symptoms associated with celiac disease can lead to poor academic performance due to a combination of feeling unwell and having to go to the washroom more frequently resulting in missed class time (Canadian Pediatric Society, 2020). There are also of course medical complications of untreated and treated celiac disease.

Emily: These complications include constipation due to the low-fiber levels of GF diets, iron-deficiency anemia, short stature and delayed puberty, osteopenia and osteoporosis, fertility problems, depression and anxiety, as well as malignancies (including lymphoma, although this is rare) (Georgara & Kannappa, 2018). Eating disorders like avoidant restrictive food intake disorder (ARFID) may also develop as a result of the hypervigilance around gluten-containing foods (Stahl & Liu, Management of celiac disease in children, 2024).

Dr. Dowhaniuk: It is reassuring that most kids that are diagnosed with celiac disease do very well. They follow a gluten free diet without many complications and have complete healing of their small intestine and reversal of previous symptoms. However, they require support given the restrictive nature of the diet and the social implications of having to eat differently than their peers.

I'd suggest we go back to our case and return to considering Celia.

Back to the Case:

Keiko: Now that we've learned about what celiac disease is, how it presents, relevant investigations, and an approach to management, let's revisit our patient, Celia.

Emily: As you'll recall, Celia presented with many symptoms that are in line with celiac disease, and appear to be otherwise unexplained, such as: prolonged diarrhea, abdominal bloating, and failure to thrive as evidenced by her deviating off her normal growth curve with a recent downward trend. When interviewing Celia and her parents, you learn that she has had to miss several days of daycare because of her abdominal pain and diarrhea. They are concerned that she has been more irritable lately and not acting like her normal energetic self. On examination, you note no guarding, rigidity, or organomegaly upon abdominal palpation. You note that her abdomen is very prominent relative to her small extremities and short stature.

Keiko: After you review Celia's presentation with your preceptor, your preceptor orders blood work including a tTG-IgA level and total IgA level. They also order a CBC, iron studies, vitamin D, AST, ALT, TSH and free T4 to rule out differential diagnoses and potential comorbidities of celiac disease.

Emily: Prior to her follow-up appointment in the family medicine clinic, Celia's blood work comes back with a normal total IgA level and a tTG-IgA value that was ≥3x the ULN, in this instance the TTG was 45 with the normal value of less than 12. She also was diagnosed with an iron deficiency anemia requiring iron supplementation. After communicating these findings and their implications to Celia and her family, Celia was referred to a Pediatric Celiac Disease Clinic to be seen by a pediatric gastroenterologist for further celiac disease testing.

Dr. Dowhaniuk: After referral to this specialized clinic, an informed discussion occurred with her gastroenterologist and it is mutually agreed upon that Celia will undergo a small intestine biopsy via endoscopy. Before her upper endoscopy, Celia and her family are told to maintain her on a gluten-containing diet and that her procedure would be used to obtain multiple intestinal biopsy samples. When Celia's samples are examined by a pathologist, they note the presence of the mucosa inflammation, crypt hyperplasia, and partial villous atrophy. A classification of Marsh Type 3c is provided, and Celia is officially diagnosed with celiac disease.

Keiko: After receiving this diagnosis, Celia and her family are provided with information on celiac disease and informed that she will need to adhere to a lifelong GF diet. They meet with a dietitian associated with the clinic, who gives counseling on which foods contain gluten, which foods do not, and how to approach interpreting food labels. They're also taught about how to avoid cross contamination during food preparation.

Emily: Celia and her family are connected with community resources and support groups for individuals living with celiac disease. They are also provided long-term follow-up by a multidisciplinary team at the Pediatric celiac disease clinic for ongoing support, monitoring, and counseling.

Dr. Dowhaniuk: I think it would be great to summarize today's podcast with some **Take Home Messages**

1. Celiac disease occurs in individuals who have a genetic predisposition and consume gluten. Upon ingestion of gluten-containing foods, there is an inappropriate immune reaction against gliadin that leads to autoantibody and cell-mediated intestinal damage.
2. The clinical presentation of celiac disease can vary widely from individuals being asymptomatic to having gastrointestinal symptoms (such as diarrhea and abdominal distension) to exhibiting very severe extraintestinal symptoms (including dermatitis herpetiformis), or life-threatening malnutrition which is rare but can been seen in young children.
3. Celiac disease screening is indicated for individuals that are either symptomatic, or a member of a high-risk group. The first-line screening test for celiac disease is a serologic tTG level alongside a total IgA level. Other serologic tests such as anti-EMA, DGP, or the genetic testing HLA-DQ2 and DQ8 are rarely helpful. When considering celiac disease in a child, it is important to remember that there are some special considerations for children under the age of two or if the IgA level has been found to be low. In these scenarios, referral to a pediatric gastroenterologist may be warranted for an endoscopy based on symptoms alone.

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4. **Emily:** The gold-standard for diagnosing celiac disease is an intestinal biopsy taken from multiple locations of the small intestine, which is then evaluated using the Marsh Classification System.
5. A gluten-free diet is the mainstay of treatment for celiac disease and should be accompanied by patient education and support from a multidisciplinary group including a registered dietitian and also connecting the patient with outside support groups.
6. Complications of untreated celiac disease include anxiety, academic impairment, malnutrition, constipation, anemia, FTT, and osteopenia. Meanwhile, treated celiac disease can manifest in complications including social isolation, eating disorders (such as ARFID), and refractory celiac disease.

Conclusions

Keiko: Thank you for listening to our podcast episode! We hope that this provided a comprehensive approach to celiac disease, so that you feel more comfortable identifying, investigating, and managing this condition in the future! We also want to say a special thank you to Dr. Dowhaniuk for providing mentorship and support throughout the development of this episode, and for taking the time to record with us today.

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