A New Diagnostic Paradigm for Celiac Disease

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Since the middle of the 20th century and into the 21st century, the incidence of celiac disease has been rising significantly throughout the Western world. Here is what you need to know about this autoimmune condition.

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Celiac disease (CD) is an autoimmune disease in which a reaction to gluten consumption damages the small intestine. With a steadily increasing global prevalence of close to 1%[1], public awareness of CD and gluten-related disorders has grown considerably over the last few decades.

CD is more common in children with the following risk factors:[2]

- A family member with celiac disease or dermatitis herpetiformis
- Type 1 diabetes
- Down syndrome or Turner syndrome
- Autoimmune thyroid disease

Celiac disease can be challenging to diagnose as patients may present with gastrointestinal and/or extraintestinal symptoms, and many are apparently asymptomatic.[3] Furthermore, there is a poor correlation between gastrointestinal damage and symptoms.

Timely diagnosis of celiac disease and optimization of nutrition is particularly important in childhood to prevent irreversible complications such as short stature and osteoporosis. All individuals with untreated CD are at risk for long-term complications, whether or not they present with symptoms.

COMMON SIGNS/SYMPTOMS OF PEDIATRIC CD INCLUDE:[2]

- Chronic or intermittent diarrhea
- Chronic constipation not responding to usual treatment
- Chronic abdominal pain
- Abdominal distension
- Recurrent nausea or vomiting
- Weight loss or failure to thrive
- Stunted growth or short stature
- Delayed puberty
- Iron-deficiency anemia
- Irritability and behavioral issues
- Headaches
- Arthritis/arthralgia
- Dental enamel defects
- Recurrent aphthous stomatitis
- Elevated aminotransaminases

With the growing prevalence of CD and the heterogenous, often non-specific nature of symptoms, many patients remain untested and diagnosis may be delayed by several years. Currently, it is estimated that 43% of the celiac disease population remains undiagnosed.[4]

Like many autoimmune diseases, the exact

trigger of CD is unknown; however, the genetic risk factors (HLA-DQ2/DQ8) are well defined.[1,2] Additional environmental factors including infant-feeding practices, gastrointestinal infections, and the intestinal microbiome may all play a role.

Whatever the cause, when the body's immune system mounts an attack against the "invasion" of gluten, the reaction damages the villi: slight hair-like projections that line the small intestine. This damage prevents the villi from performing the function of absorbing vitamins, minerals, and other nutrients, which means the celiac patient cannot get enough nutritional value from the food they're eating.[5] This can be especially disruptive to normal growth and development in children.

Left unchecked, chronic intestinal inflammation and malabsorption from CD can cause a host of complications, including:[6]

- Malnutrition
- Bone fractures
- Infertility and miscarriage (in adults)
- Lactose intolerance[7]
- Cancer, especially intestinal lymphoma and small bowel cancers
- Cardiac disease (myocarditis, cardiomyopathy)
- Neuropsychiatric disease

All of these comorbidities represent an enormous human toll, as well as an expensive strain on the healthcare system.

Updated testing recommendations

Historically, the cornerstone of CD diagnosis has been a duodenal biopsy with histological analysis.[1] Now serological tests are available, each with a role to play: tissue transglutaminase-IgA (tTG IgA), total IgA, endomysial IgA (anti-EMA), and IgG-based tests.[1]

Given the time-consuming, expensive, and invasive nature of duodenal histology, there has been increased focus on finding the most efficient algorithm and omitting duodenal histology in patients who fulfill other CD diagnostic criteria.[1]

Recently, both the American Gastroenterological Association (AGA) and the European Society of Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) released updated guidelines for diagnosing CD.[1,2] Both reports were based on available published evidence and emphasize that the diagnosis should be made by a specialist (eg, gastroenterologist).

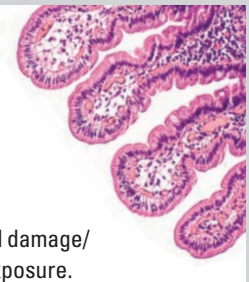
The pediatric testing algorithm[2]

For pediatricians managing patients with symptoms of celiac disease or an affected first degree relative, the recommended diagnostic approach is to begin with an initial test for total serum IgA in addition to a test for

THE DIAGNOSIS OF CD IS VARIABLY DEFINED BY THREE MAIN COMPONENTS:[2]

1. Celiac antibodies in serum
2. Duodenal histology
3. The presence of HLA-DQ2/DQ8

MANAGEMENT AND FOLLOW-UP



After diagnosis of CD, there are a number of important factors to keep in mind:[1]

- At present, the only way to mitigate celiac disease is a gluten-free diet (GFD), so implementing the GFD is essential. However, prior to CD diagnosis, reduction or avoidance of gluten is not recommended, as it may reduce the sensitivity of both serology and biopsy testing.
- The implementation of a GFD is the only way to heal intestinal mucosa in CD patients. This means not only avoiding wheat, but also rye and barley.
- Negative serology in a patient does not guarantee that intestinal mucosa has healed; however, persistently positive serology is a strong indicator of ongoing intestinal damage/gluten exposure.
- Providers should consider follow-up serology 6 and 12 months after diagnosis, then yearly thereafter.
- Factors that have been shown to increase adherence to a GFD include a team-based approach between pediatric gastroenterologist, pediatrician, family, and dietician, and open-access or online services with SMS options.
- For pediatric patients, a satisfactory increase in height and weight is an essential marker of the success of a GFD.

serum antitissue transglutaminase IgA antibodies (tTG IgA) while the child continues to consume a gluten-containing diet. This is the most clinically and cost-effective screening method. All patients with elevated serum tTG IgA should be referred to a pediatric gastroenterologist for additional testing to confirm the diagnosis of CD (Figure A).

A gluten-containing diet should be continued until the diagnosis is confirmed, as diagnostic testing is less reliable on a gluten-free diet. The degree of tTG IgA elevation is somewhat proportionate to the likelihood of CD such that those with very high tTG IgA levels (>10 times the upper normal limit) may not require a duodenal biopsy for their gastroenterologist to confirm the diagnosis if the more specific anti-endomysial IgA (EMA IgA) test is also positive (see Figure A).

In these cases, the guidelines give the option to omit duodenal histology.[1,2] Proceeding with a no-biopsy approach should be decided on a case-by-case basis with informed discussion among the caregivers, pediatric gastroenterologist, pediatrician, and child. In practice, this strategy may reduce the need for gastroscopy with biopsy by 30-50%.[1]

Pediatric patients under the age of 2-3 years may have a less robust presence of IgA rendering tTG IgA testing less efficient. In these cases, pediatricians may choose to test for IgG deamidated gliadin antibodies (anti-DGP IgG) in addition to the recommended tTG IgA (see Figure A). Performing both tTG IgA and DGP IgG may increase diagnostic sensitivity as some patients with CD have DGP IgG antibodies but not tTG IgA antibodies.

Other relevant, specific markers for CD are anti-endomysial antibodies (anti-EMA). Testing for anti-EMA is labor-intensive and expensive, and should be used as a confirmatory test, particularly if the non-biopsy algorithm proposed in the most recent 2020 clinical practice update is being considered (see Figure A). ■

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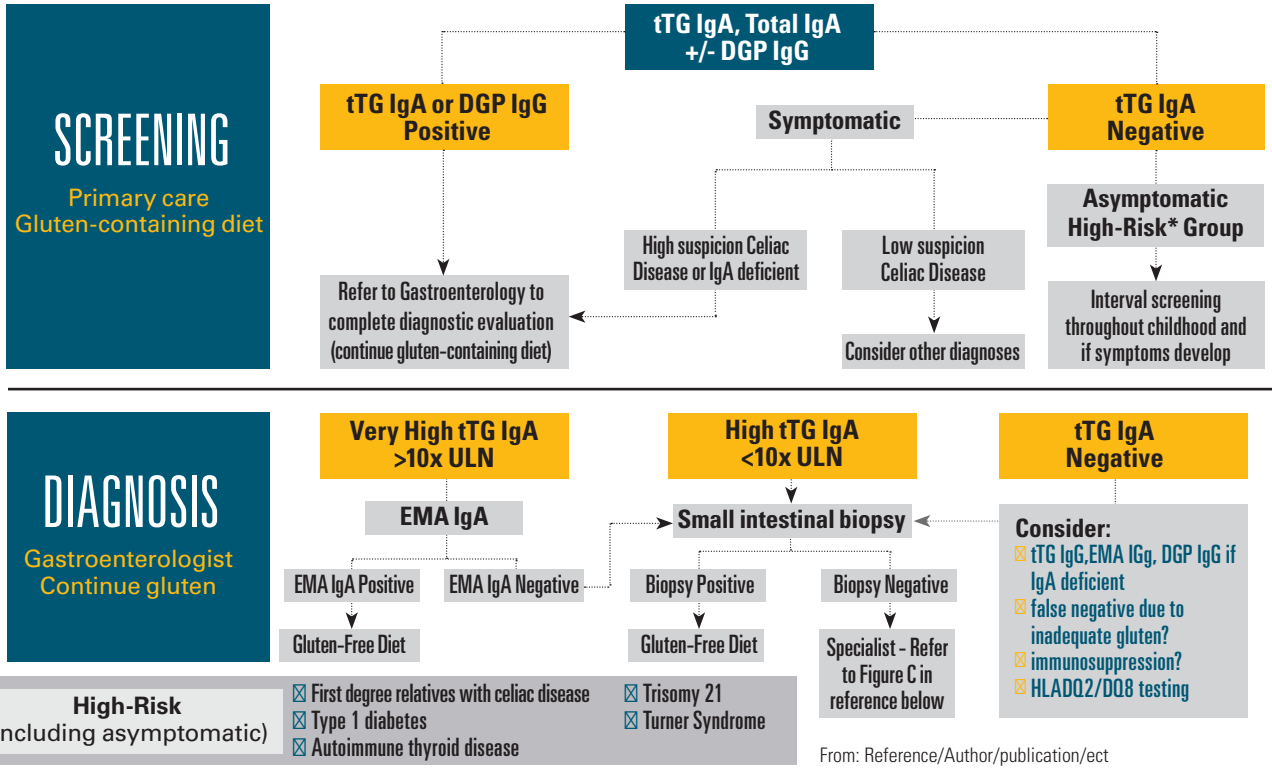
For references, go to **ContemporaryPediatrics.com/new-paradigm-celiac-disease**

FIGURE A[2]:

SYMPTOMATIC (INTESTINAL OR EXTRAINTESTINAL MANIFESTATIONS) **OR HIGH-RISK*** (REGARDLESS OF SYMPROMS)



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