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Time to Screen Children with Celiac Disease for Thyroid Disease?



The concept of augmented risk of autoimmune disorders in those with untreated celiac disease (CD) is not novel. Screening for CD is recommended for children with type 1 diabetes (T1D)¹ and autoimmune thyroid disease (ATD)² given the high risk for CD in these conditions. Thyroid autoimmunity as well as T1D autoimmunity are also common in children with untreated CD.³ However, whether such risks persist in individuals with treated CD and how to monitor patients who are more susceptible to additional autoimmune diseases warrant clarification.

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Age at diagnosis and presumed duration of gluten exposure are predictors of development of additional autoimmune disorders in young patients with CD,⁴ whereas in patients diagnosed with CD in adulthood, duration of exposure does not predict the development of additional autoimmune diseases.⁵ Treatment of CD with a gluten-free diet (GFD) may have a protective effect against development of additional autoimmune disorders—pooled risks of autoimmune disorders in a study of French adults and children with CD were significantly greater among those nonadherent to a GFD.⁶ This effect may be greater for certain conditions such as T1D,⁶ though less so or even absent for thyroid disease.^{7,8}

ATD	Autoimmune thyroid disease
CD	Celiac disease
GFD	Gluten-free diet
T1D	Type 1 diabetes

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Given that T1D, ATD, and CD share genetic features, overlap among these conditions is not surprising. Although the HLA DQ2 (DQA1*0501, *0505/DQB1*0201, *0202) and HLA DQ8 (DQA1*0301/DQB1*0302) heterodimers lead to CD risk, both DQ2 and DQ8 are associated with T1D and ATD,^{9,10} with DQA1*0501 demonstrating the clearest susceptibility overlap among CD, T1D, and ATD.¹¹ Despite an increasing understanding of the genetic basis of these conditions, there is a lack of data exploring the specific risks of subsequent development of ATD and T1D in individuals with treated CD, information required by clinicians managing patients with CD.

An earlier study described the presence of diabetes-related autoantibodies in a small group of children with treated CD, though true clinical T1D was not noted.¹² More recently, a population-based study of young Swedish patients diagnosed with CD by age 20 demonstrated that the risk of subsequently developing T1D was greater than among reference individuals.¹³ The authors also noted an augmented risk of diabetic ketoacidosis or coma before age 20 for those first diagnosed with CD.

Data regarding thyroid disorders and particularly ATD lack such sharp distinctions in risk between patients pre- and post-CD diagnosis. Thyroid disease was associated with CD regardless of the sequence of diagnosis in a Swedish cohort, with the highest risk estimates for thyroid disease after CD diagnosis seen in children.⁸ In this study, greater risks of hypothyroidism, hyperthyroidism, and thyroiditis were described among those with preceding CD than in reference individuals.⁸ ATD was noted in 18% of Italian children with CD on a GFD, significantly greater than in the 10% of control subjects ($P = .01$).¹⁴ Outcomes regarding the impact of a GFD in individuals with CD upon subsequent development of ATD remain unclear. A multicenter study of Italian adults with CD demonstrated that 16% of those with newly diagnosed CD showed evidence of euthyroid ATD—25% of whom eventually developed subclinical hypo- or hyperthyroidism, though were additionally noted to be noncompliant with the GFD.¹⁵ Of those in this study without evidence of thyroid disease at diagnosis with CD, 5% still developed subclinical or overt thyroid dysfunction.

Canova et al¹⁶ delve further into this issue in their study of T1D and ATD in regional Italian populations with CD. In this work, the authors have confirmed in an important population-based study what a number of smaller and single-center studies have demonstrated—that children with CD have a risk of thyroid disease (and particularly hypothyroidism), which is not likely to be meaningfully altered by GFD treatment. The same clarity was not attained concerning T1D, though. Risk estimates for a post-CD diagnosis of T1D did not reach statistical significance in this study when considering the entire population. However, children diagnosed with CD after age 6 years were at risk of developing T1D after diagnosis with CD (hazard ratio 5.00, 95% CI 1.01–24.78) once the first year of follow-up after CD diagnosis was excluded. Yet, few subjects demonstrated T1D following CD diagnosis, resulting in a wide CI, preventing further analyses, and arguably implying that risk for T1D is on a lower stratum than for thyroid disease in children with a prior diagnosis of CD. In a similar Swedish population-based study, Ludvigsson et al¹³ did not observe distinctions in T1D risk according to age at CD diagnosis but did report a more conclusively augmented

risk of T1D following CD diagnosis. The more decisive T1D risk estimates noted by Dr Ludvigsson were likely aided by greater statistical power (over 9000 Swedish patients with CD studied vs approximately 1200 cases with CD investigated by Canova) though also may be related to the generally greater incidence of T1D in Sweden when compared with Italy.¹⁷

The significance of this work by Canova et al¹⁶ is what it implies, in combination with other similar studies, for the care of young patients with the described conditions. In other words, do children with CD require screening for thyroid disease and/or T1D as routine aspects of health maintenance? Wessels et al¹⁸ recently published their study of 182 children with CD in The Netherlands and concluded after a 5-year follow-up period that empiric surveillance for thyroid disease was not warranted in their population. It is possible that longer follow-up periods are required to discern the development of true thyroid disease—while in Canova's study there was a 5-year difference in the median age of developing CD and thyroid disease, a broad range of ages to ATD diagnosis were noted. In fact, Elfström et al⁸ noted a median 9-year period from CD diagnosis until the first diagnosis of thyroid disease in his study of a large Swedish cohort. The same can be said for studies of T1D risk in those with CD, although symptoms of T1D are typically more discernible than of thyroid disease, making it difficult for T1D to present silently. In each of these large cohort studies, however, one must bear in mind that factors such as compliance with a GFD, and family history could not be accounted for, and that these as well as population-related distinctions may have influenced the outcomes observed.

The case for surveillance of children with CD for thyroid disease is strong; less so for T1D. Screening for thyroid disease is better understood than for T1D, and thyroid disease may be more easily missed than T1D outside of screening protocols. Further, alterations in quality of life and cardiac morphology have been noted in young adults with subclinical hyperthyroid disease,¹⁹ and adolescents with CD and Hashimoto thyroiditis with subclinical thyroid dysfunction have been found to be at greater risk of progressing to thyroid failure.²⁰ Conversely, despite considerable variability in the literature regarding frequency of T1D following CD diagnosis (for example, 7%²¹ vs 0.5%⁶), this condition is far less likely to go unrecognized, and evidence supporting whether to screen and how to screen for T1D among children with CD is lacking. Recommendations on surveillance for either of these conditions among those with CD are not clearly delineated in currently published pediatric or adult guidelines from North American^{22,23} or European societies.²⁴ At a minimum, retaining an index of suspicion for T1D among those with a history of CD is warranted, even when GFD adherence is nearly certain. Additional studies, including cost-benefit analyses of the implications of screening children with CD for additional autoimmune conditions, are warranted to further inform these practices. ■

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Gastrostomy Tube Complications



Those of us who manage medically complex children frequently encounter gastrostomies with their appliances and accessories. Some of us are responsible for creating the stoma and placing the initial tube. The actual placement technique recommended for a given patient is selected from among options, including open surgery (with or without

fundoplication), laparoscopy, or endoscopy. Multiple factors, including the indication for gastrostomy placement, comorbidities, and patient and provider preference ultimately dictate which procedure is performed. Patients and their caregivers become attuned to the presence and daily care of the stoma over time, and adapt to using and periodically replacing the tube.

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ED Emergency department
 GT Gastrostomy device

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