Rethinking Strategies to Screen for Celiac Disease

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KEY WORDS
celiac disease, screening, children

ABBREVIATIONS
CD—celiac disease
IgA—immunoglobulin A
NCGS—nonceliac gluten sensitivity
tTG—transglutaminase

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www.pediatrics.org/cgi/doi/10.1542/peds.2013-3631

doi:10.1542/peds.2013-3631

Accepted for publication Nov 7, 2013

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: The author has indicated she has no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The author has indicated she has no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found on page 211, and online at www.pediatrics.org/cgi/doi/10.1542/peds.2012-3765.

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Celiac disease (CD) is likely an ancient disease. It is thought that CD became a health problem as people moved from a hunter-gatherer economy to farming-based economy some time during the Neolithic period and geographically in the Fertile Crescent. Indeed, the earliest description of CD is attributed to Aretaeus the Cappadocian. Cappaddocia is adjacent to the Fertile Crescent.[1] Recent studies on the introduction of farming, however, demonstrate a complex coexistence of hunter-gatherers and farmers over 2 millennia, and this new observation may affect how we understand the history of CD.[2,3]

CD is not a benign disease; it can be associated with malnutrition, malabsorption, osteoporosis, liver disease, skin disease, mental health issues, and other health problems. In addition, and of particular concern, undiagnosed CD is associated with a fourfold increased risk of death.[4] CD is not a rare disease; prevalence ranges from 0.3% to 3%.[5]

These observations make it imperative that a diagnosis of CD be definitively made, that consideration be given to screening tools and the populations to whom they should be applied, and that parameters are carefully defined to correctly interpret the results of the screen. Currently there are at least 3 guidelines, 2 written for children and 1 for adults, on how to evaluate for and treat CD.[5–7] These guidelines recommend screening based on family history, health status, and symptoms and rely on the immunoglobulin A (IgA) antibody for transglutaminase (tTG). For IgA-deficient people, the immunoglobulin G tTG is often used. All of the guidelines focus on symptoms as the factor used to initiate screening for CD, unless a first-degree relative has CD or the patient suffers with one of the diseases closely associated with CD, such as type 1 diabetes or Down syndrome, among others.

The large and carefully designed study by Rosen et al in this issue[8] calls into question the validity of using symptoms to identify children for screening. The authors invited 10 041 children and their parents to participate in a population-based CD screening of 12-year-olds. Children known to have CD were excluded. Before learning their CD marker results, children completed a questionnaire on symptoms in their classrooms, supervised by a teacher or nurse. Parents reported on the child's CD-associated conditions. Serology was then obtained. Children underwent a small-bowel biopsy if their tTG-IgA or tTG-immunoglobulin levels were elevated. Surprisingly, the authors found there was no correlation between the presence of symptoms and the diagnosis of CD; symptoms did not discriminate unrecognized CD children from their non-CD peers. In addition, there was no difference in CD prevalence between those with and without CD-associated conditions. These results call into question the recommendations of the guidelines. Importantly, they raise concern for the guideline that recommends a gluten-free diet be initiated without a biopsy when "signs or symptoms suggestive of CD and high anti-TG2 titers with levels >10 times ULN" are present.

Knowing how important it is to diagnose CD for longevity and health, the Rosen et al article adds a layer of complexity to identifying children at risk for CD; the authors show that neither symptoms nor CD-associated conditions are reliable markers for CD. These observations raise many questions. For example, if symptoms cannot be used to identify candidates for screening, what can be used? With the relatively high prevalence, should all children be screened? If so, at what age? Are repeat screenings necessary because CD can present at any age, and if so, at what intervals? Is it ever justifiable to place a child with gastrointestinal symptoms on a gluten-free diet without clearly making a diagnosis of CD? This last question is important because some advocate the use of a "trial of a gluten-free diet" for children with functional gastrointestinal symptoms.

Although not addressed in this study, the lack of correlation of symptoms with the diagnosis of CD raises questions about the diagnosis of nonceliac gluten "sensitivity" (NCGS). The diagnosis of this entity rests solely on symptoms and the response to a trial of a gluten-free diet. With Rosen's observations, can we rely on symptoms to make a diagnosis? Can there be another way to diagnose NCGS? Or is NCGS related to other factors[9] and the response to the withdrawal of gluten simply a highly effective placebo?[10] Before initiating a gluten-free diet in these children, CD must be excluded.

This carefully designed and executed study raises important questions, suggests recommendations for screening of CD be revisited, and further suggests that care be taken in prescribing a gluten-free diet when a diagnosis of CD has not been made.

REFERENCES

1. Losowsky MS. A history of coeliac disease. *Dig Dis*. 2008;26(2):112–120
2. Bollongino R, Nehlich O, Richards MP, et al. 2000 years of parallel societies in Stone Age Central Europe. *Science*. 2013;342 (6157):479–481
3. Brandt G, Haak W, Adler CJ, et al; Genographic Consortium. Ancient DNA reveals key stages in the formation of central European mitochondrial genetic diversity. *Science*. 2013;342(6155):257–261
4. Rubio-Tapia A, Kyle RA, Kaplan EL, et al. Increased prevalence and mortality in undiagnosed celiac disease. *Gastroenterology*. 2009;137(1):88–93
5. Hill ID, Dirks MH, Liptak GS, et al; North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. Guideline for the diagnosis and treatment of celiac disease in children: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J Pediatr Gastroenterol Nutr*. 2005;40(1): 1–19
6. Rubio-Tapia A, Hill ID, Kelly CP, Calderwood AH, Murray JA; American College of Gastroenterology. ACG clinical guidelines: diagnosis and management of celiac disease. *Am J Gastroenterol*. 2013;108(5):656–676, quiz 677
7. Husby S, Koletzko S, Korponay-Szabó IR, et al; ESPGHAN Working Group on Coeliac Disease Diagnosis; ESPGHAN Gastroenterology Committee; European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines for the diagnosis of coeliac disease. *J Pediatr Gastroenterol Nutr*. 2012;54 (1):136–160
8. Rosén A, Sandström O, Carlsson A, et al. Usefulness of symptoms to screen for celiac disease. *Pediatrics*. 2014;133(2):211–218
9. Biesiekierski JR, Peters SL, Newnham ED, Rosella O, Muir JG, Gibson PR. No effects of gluten in patients with self-reported nonceliac gluten sensitivity after dietary reduction of fermentable, poorly absorbed, short-chain carbohydrates. *Gastroenterology*. 2013;145(2):320–328, e1–e3
10. Kaptchuk TJ, Friedlander E, Kelley JM, et al. Placebos without deception: a randomized controlled trial in irritable bowel syndrome. *PLoS ONE*. 2010;5(12):e15591

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Pediatrics originally published online January 13, 2014;

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Pediatrics originally published online January 13, 2014;