Risk of Celiac Disease According to HLA Haplotype and Country REPLY

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Risk of Celiac Disease According to HLA Haplotype and Country

TO THE EDITOR: The Environmental Determinants of Diabetes in the Young (TEDDY) study by Liu et al. (July 3 issue)[1] explored the genetic and environmental contributions to the development of celiac disease autoimmunity. However, the authors did not address gut colonization as a cornerstone environmental factor.

Important components of initial gut colonization in infants are the method of delivery and diet. Normal colonization occurs when full-term neonates are born by vaginal delivery and are exclusively breast-fed during the first 6 months of life.

In contrast, infants who are born by cesarean section or bottle-fed have inadequate initial colonization and mucosal immune dysfunction, leading to an increased risk of allergic and autoimmune diseases.[2]

There is strong evidence that disruption of the normal colonization process with aberrant probiotic flora can lead to alterations in the symbiotic relationship that is necessary for immune homeostasis and may be involved in the development of autoimmunity (e.g., in celiac disease and type 1 diabetes).[3,4]

We think that the method of delivery, as well as the method of feeding, should be considered as relevant variables and important environmental risk factors.

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No potential conflict of interest relevant to this letter was reported.

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TO THE EDITOR: Liu and colleagues conclude that environmental risk factors, which in their study correlated with Swedish residence, influence the development of celiac disease. One striking result that was not commented on was the role of female sex as a strong risk factor.

The literature is inconsistent regarding whether celiac disease is more common in women. Three screening studies from the United States showed that it is equally prevalent among men and women.[1-3] However, a Swedish study showed that the prevalence of celiac disease among girls was approximately double that among boys[4]; this finding was similar to the finding by Liu and colleagues. Since it appears that environmental risk factors may differentially affect the two sexes, it would be of particular interest to know whether the effect of sex on the risk of celiac disease varied among the countries in this study.

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No potential conflict of interest relevant to this letter was reported.

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THE AUTHORS REPLY: In the TEDDY study, we found that HLA genotype, family history, and sex were all important factors for the development of celiac disease. The discovery of differences in the incidence of celiac disease among participating countries does indeed suggest that there are environmental determinants of celiac disease, and this effect is probably multifactorial.

To specifically address two of these factors mentioned by Rahmoune and coworkers, our study showed neither an effect of the form of delivery (cesarean section or vaginal delivery) nor an effect of exclusive breast-feeding for the first 6 months of life on the risk of the development of celiac disease. We have examined the effect of these two additional factors in our analysis (in case there was still a biologic effect), and it did not change the outcomes of our study. The analysis of how genes and environmental factors interact would be quite complex and is beyond the scope of our article.

In addition, Lebwohl and Green raise the issue of a potential difference among countries with respect to the role of female sex in the risk of celiac disease. In our study, the female predominance among children with a diagnosis of celiac disease was seen across all countries, not just in Sweden.

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The Child or Adolescent with Elevated Blood Pressure

TO THE EDITOR: In the Clinical Practice article on pediatric hypertension (June 12 issue),[1] the discussion of evaluation did not emphasize the importance of a detailed sleep history, with attention to sleep duration and sleep-disordered breathing, in all hypertension evaluations. The fourth report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents[2] recommends taking a history to rule out sleep-disordered breathing as part of the evaluation of hypertension.

Sleep-disordered breathing in children is associated with higher baseline blood pressure. Continuous positive airway pressure (CPAP) therapy for sleep apnea in adults improves blood-pressure levels. Treatment of sleep-disordered breathing in children has been shown to improve diastolic blood pressure.[3] Short sleep duration also has been associated with higher blood pressure in normal-weight adolescents[4] and in children being evaluated for hypertension.[5] Actual sleep duration in children often falls short of that recommended.

Although more research is needed to make firm treatment recommendations in children, cumulative evidence suggests that children with hypertension should be counseled on adequate sleep duration and that sleep-disordered breathing, if identified, should be considered for treatment.

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No potential conflict of interest relevant to this letter was reported.

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