The role of biopsies in childhood celiac disease - do we need less or more?

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The role of an intestinal biopsy in the diagnosis and management of celiac disease (CD) in children continues to evolve. Originally 3 biopsies were required to confirm the diagnosis; the first on presentation to demonstrate characteristic changes, the second after a year on the gluten free diet (GFD) to demonstrate mucosal healing and a third after a gluten challenge to show recurrence of damage. (1) With the introduction of reliable serological testing for CD, recommendations changed to require only a single biopsy on presentation that demonstrated the typical histology. Provided there was complete symptom resolution on a GFD the diagnosis of CD was considered confirmed, and normalization of the antibody tests added further support for the diagnosis. (2) Most recently the European Society for Pediatric Gastroenterology, Hepatology and Nutrition published recommendations suggesting that in some cases a biopsy may not be necessary. Children with typical symptoms of CD, who have a tissue transglutaminase antibody level greater than 10 times the upper limit of normal together with a positive endomysium antibody and are HLA-DQ2 and or HLA-DQ8 heterodimer positive, can be presumed to have CD and started on a GFD without a biopsy. The diagnosis is then considered confirmed if there is subsequent complete symptom resolution with normalization of antibody levels. (3) The presumption is that absence of symptoms and normalization of CD associated antibody tests equals mucosal healing in children. This differs from the experience of our adult gastroenterology colleagues. Over 50% of adults with CD have persistent villous atrophy (VA) on repeat biopsies despite being on a GFD for 2 or more years. (4) Furthermore there is no correlation between the histological findings and the presence or absence of symptoms, or elevations in CD antibody levels. (4,5) The importance of this observation is that long term adverse health consequences associated with CD appears related to persistence of VA. (5,6)
raises several questions. Are children really different from adults and if so why? Are absence of symptoms and normal CD antibody levels reliable indicators of mucosal healing in children? Are we as pediatricians missing persistent VA in children and potentially exposing them to long term complications?

The article by Leonard and colleagues in this issue of JPGN is both timely and thought provoking. (7) In reviewing 103 children with biopsy proven CD who had undergone a repeat biopsy at least 1 year after starting a GFD they found that 19% (1 in 5 children) had persistent VA. Furthermore, neither the presence nor absence of symptoms could reliably predict mucosal healing, or the lack thereof, nor were CD serological tests of benefit for this purpose. While there is one report suggesting a combination of serological tests can be used to predict mucosal recovery (8) others have found the serological tests are less reliable for monitoring response to treatment as compared to initial diagnosis. (9) Persistence of VA in children on a GFD has been described by others but not as frequently as that reported by Leonard et al. (9,10) However, given that relatively few children with CD now undergo repeat biopsies after starting a GFD, it is possible that the number with persistent VA is much higher than we currently believe.

Perhaps it is time for us to rethink our approach to children with CD. Is a non-biopsy diagnosis of CD a good idea or should all children have a diagnostic biopsy, not only to confirm the diagnosis, but establish a baseline for future evaluation? Should all children undergo repeat biopsies after starting a GFD and if so after what period of time? What is the true prevalence of persistent VA in children and what are the likely causative factors? What are the long term implications of failure to achieve complete mucosal healing? Until we have a reliable non-invasive means of determining mucosal healing in children with CD it seems the biopsy will remain important both for initial diagnosis and subsequent monitoring.
References.


