

Delayed introduction to gluten appears not to prevent celiac disease in at-risk infants

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How can parents with the autoimmune disorder celiac disease prevent or delay the condition's development in their children? The results of an international study led by investigators associated with the Center for Celiac Research and Treatment at MassGeneral Hospital for Children (MGHfC) challenge some of the current thinking on possible measures to take. The report in the Oct. 2 *New England Journal of Medicine* finds that loss of tolerance to gluten – a protein composite found in wheat, rye and barley – is a dynamic process and that neither breastfeeding or delaying the introduction of gluten-containing foods provides significant protection against the disorder.

"One of our most important findings was that the timing of gluten introduction – whether early or late in the first year of life – made no difference to the subsequent development of [celiac disease](#)," says Carlo Catassi, MD, co-director of the Center for Celiac Research and Treatment and principal investigator of the study. "While earlier studies led to the hypothesis that there was a time window, between 4 and 7 months of age, during which gluten could safely be introduced to at-risk [children](#), our results indicate we can tell mother not to worry so much about when they introduce gluten into their children's diet."

Alessio Fasano, MD, PhD, director of the Center for Celiac Research and Treatment and a co-author of the *NEJM* report adds, "Of the several factors we studied, it's very clear that genetic background is by far the most important in determining which [infants](#) will develop this autoimmune condition. We were particularly surprised that

breastfeeding at any age provided no protective effect."

Between 2003 and 2008 the investigation – the Italian Baby Study on Weaning and CD Risk – enrolled more than 700 infants considered to be at risk because of the presence of celiac disease in a first-degree relative – a parent or sibling. Participants at 20 centers in Italy were randomly assigned to two groups, the first of which was introduced to gluten-containing foods at 6 months of age and the second, at 12 months. The children's mothers provided information on their child's diet – including amount of gluten ingested – intestinal infections, breastfeeding and other factors thought to have an effect on celiac risk. Participants were followed for at least five years, during which they were periodically tested for the presence of immune system factors indicating gluten-associated autoimmune reactions. If signs of autoimmunity were detected, intestinal biopsies were conducted to determine whether or not celiac disease had developed.

While a greater percentage of infants who had been introduced to gluten at 6 months had evidence of possible celiac disease at the two-year follow up, there was little difference between the two groups by five years. Overall, 64 children in the early-introduction group developed celiac disease, while 53 in the late-introduction group did so, a difference not considered to be statistically significant. The only factor that the study found to increase risk was inheriting versions of the immune system's HLA molecules, which flag antigens for immune system attack, that are known to be associated with celiac disease and other autoimmune disorders.

Catassi notes that a simple blood test of HLA genotype could quickly determine which infants are at high risk of celiac disease, possibly a first step toward primary prevention efforts. In addition, delaying the development of celiac disease by later introduction to gluten could prove to be beneficial by reducing the impact of the condition on developing

organs, such as the brain. The fact that 80 percent of the children who did develop celiac disease did so within the first three years of life, he adds, points to the importance of screening children when they reach school age.

Fasano notes that the results of this investigation will "pave the way for breakthrough studies that will capitalize on these findings and lead to preventive interventions." There have been many developments in the treatment and study of celiac disease since this study began more than 10 years ago, he adds, particularly the increased recognition of the importance of the gut microbiome – the microbial population of the gastrointestinal system – in the development of autoimmune and other disorders.

After completing a small 2011 pilot study finding that increases in particular bacterial species preceding the development of celiac disease and type 1 diabetes in infants, Fasano and Catassi have embarked on a larger study that will enroll approximately 500 infants with the goal of learning more about how a wide variety of factors contribute the development of celiac disease. More information on the study is available at <http://www.cdgemm.org>.

Provided by Massachusetts General Hospital

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