



Reducing Allergic Manifestations in Children with Cow's Milk Allergy: Current Research

Learning Objectives

At the conclusion of this activity, participants should be better able to:

- Identify the long-term risks associated with cow's milk allergy early in life
- Mediate allergic manifestations in infants by applying a probiotic nutritional strategy

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The National Institute of Allergy and Infectious Diseases (NIAID) currently recommends a hydrolyzed formula for infants who cannot be exclusively breast fed and are at risk for an allergic disease.¹ Dr. Canani's study, presented in this webcast, adds to the support for this recommendation. This very brief companion piece review will introduce 2 studies you may want to consider when developing your clinical protocols.

In the webcast, Dr. Canani presented data showing that extensively hydrolyzed casein formula (EHCF) supplemented with *Lactobacillus* GG reduced the incidence of atopic manifestations in children with cow's milk allergy (CMA).²

EHCF Complementary Studies

The German Infant Nutritional Intervention (GINI) study is one of the studies that supports the NIAID recommendation. This study is interesting because they now have 15 years of follow-up for participants enrolled in the original cohort.³ In addition, the infants enrolled in GINI were randomized to feeding with partial whey hydrolyzate formula (pHF-W), extensive whey hydrolyzate formula (eHF-W), extensive casein hydrolyzate formula (eHF-C), or a standard cow's milk formula (CMF). In GINI, the most consistent effects have been observed in infants fed pHF-W and—as in Dr. Canani's study—eHF-C. Unlike Dr. Canani's study, infants in GINI did not have demonstrated CMA, but rather were considered high risk for allergic disease based on a parent or sibling having a history of allergic disease.

Infants (N=2252) in GINI who could not be exclusively breast fed received supplemental formula for 4 months. Participants in the original GINI study were asked to report the incidence of asthma, allergic rhinitis, and eczema, and approximately 60% completed the survey. Adolescents who had been randomized to eHF-C formula had a lower occurrence of eczema from birth,^{4,5} and the prevalence between ages 11 and 15 years of age remained low (4.7%, compared to 10.6% in the CMF group). The prevalence of asthma and allergic rhinitis in 11–15 year olds was also significantly lower. This supports a long-term



Why Nutrition of the Preterm Matters

Long-Term Consequences of Adverse Early Nutrition and Growth

benefit to using EHCF, and taken with Dr. Canani's study, suggests that *Lactobacillus* GG may potentiate this effect.

EHCF Meta-Analysis Findings

A recent meta-analysis has concluded that any recommendation for the use of hydrolyzed formula for reducing the risk of allergic disease could not be supported.⁶ In this meta-analysis, the GINI study was criticized for problems with the intent-to-treat (ITT) and per-protocol (PP) analyses; the GINI study authors argue that the (PP) analysis is more appropriate because the (ITT) population includes many infants who never received treatment because they were breast fed. In addition, not all of the effects noted in the previous paragraph are observed in both the ITT and PP populations.

The promising research in this field is not complete, and additional studies are needed to validate both the use of extensively hydrolyzed formulas and probiotics⁷ in the prevention and treatment of cow's milk allergy.

Suggested Readings and Resources

1. Boyce JA, Assa'a A, Burks AW, et al. Guidelines for the diagnosis and management of food allergy in the United States: summary of the NIAID-Sponsored Expert Panel Report. *Nutrition*. 2011;27(2):253-267.
2. Berni Canani R, Di Costanzo M, Bedogni G, et al. Extensively hydrolyzed casein formula containing *Lactobacillus rhamnosus* GG reduces the occurrence of other allergic manifestations in children with cow's milk allergy: 3-year randomized controlled trial. *J Allergy Clin Immunol*. 2016; In press.
3. von Berg A, Filipiak-Pittroff B, Schulz H, et al. Allergic manifestation 15 years after early intervention with hydrolyzed formulas – the GINI Study. *Allergy*. 2016;71(2):210-219.
4. von Berg A, Filipiak-Pittroff B, Kramer U, et al. Allergies in high-risk schoolchildren after early intervention with cow's milk protein hydrolysates: 10-year results from the German Infant Nutritional Intervention (GINI) study. *J Allergy Clin Immunol*. 2013;131(6):1565-1573.
5. von Berg A, Koletzko S, Grubl A, et al. The effect of hydrolyzed cow's milk formula for allergy prevention in the first year of life: the German Infant Nutritional Intervention Study, a randomized double-blind trial. *J Allergy Clin Immunol*. 2003;111(3):533-540.
6. Boyle RJ, Ierodiakonou D, Khan T, et al. Hydrolysed formula and risk of allergic or autoimmune disease: systematic review and meta-analysis. *BMJ*. 2016;352:i974.
7. Osborn DA, Sinn JK. Probiotics in infants for prevention of allergic disease and food hypersensitivity. *Cochrane Database Syst Rev*. 2007(4):Cd006475.