

CONCLUSIONS. In a nonselected population of mothers, consumption of probiotics decreased the cumulative incidence of AD but had no effect on asthma, allergic rhinoconjunctivitis, or atopic sensitization.

REVIEWER COMMENTS. This study found that probiotic bacteria given to the mother during pregnancy and early lactation might prevent AD in the child. Previous randomized controlled trials that used various probiotics have involved administration directly to all or the majority of children. The results of this study are exciting in that treatment of the mother over a limited period of time seemed to make a difference in the cumulative incidence of AD and severity of atopic dermatitis in affected children.

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Synbiotics Prevent Asthma-Like Symptoms in Infants With Atopic Dermatitis

van der Aa LB, van Aalderen WM, Heymans HS, et al; Synbad Study Group. *Allergy*. 2011;66(2):170-177

PURPOSE OF THE STUDY. Infants with atopic dermatitis (AD) are at high risk of developing asthma. These researchers sought to examine the effect of early intervention with synbiotics, a combination of probiotics and prebiotics, on the prevalence of asthma-like symptoms in infants with AD.

STUDY POPULATION. Ninety term infants less than 7 months of age with AD were recruited from 2005 to 2007 in the Netherlands. Inclusion criteria included an AD score (Severity Scoring of Atopic Dermatitis [SCORAD]) of >15, exclusive formula feeding at the time of enrollment, no other major medical problems, and no use of probiotics or immunomodulatory medications during the 4 weeks before enrollment.

METHODS. In a double-blind, placebo-controlled multicenter trial, infants were randomly assigned to receive an extensively hydrolyzed formula with *Bifidobacterium breve* M-16V and a galacto-oligosaccharide/fructo-oligosaccharide mixture or the same formula without the synbiotics during a 12-week period. After 1 year, the prevalence of respiratory symptoms and asthma medication use was evaluated by using a validated questionnaire, and the total serum immunoglobulin E (IgE) level and level of specific IgE against aeroallergens were determined.

RESULTS. Seventy-five children completed the 1-year follow-up evaluation. The prevalence of "frequent wheezing" and "wheezing and/or noisy breathing apart from colds" was significantly lower in the synbiotic than

in the placebo groups (13.9% vs 34.2% [absolute risk reduction (ARR): -20.3%] and 2.8% vs 30.8% [ARR: -28.0%], respectively). Significantly fewer children in the synbiotic than in the placebo group had started to use asthma medication after baseline (5.6% vs 25.6% [ARR: -20.1%]). There were no differences in total IgE levels between groups. However, no children in the synbiotic group and 5 children (15.2%) in the placebo group developed an elevated IgE level against cat (ARR: -15.2%).

CONCLUSIONS. This study found a significant benefit in the prevention of asthma-like symptoms in infants with AD followed for 1-year after a 12-week trial of a synbiotic mixture.

REVIEWER COMMENTS. Results of this prospective study support the concept that a specific probiotic and prebiotic mixture might be effective in reducing the prevalence of asthma-like symptoms in the near term. Variable results have been noted in other studies that used only probiotics. Larger clinical studies and a longer longitudinal follow-up period to determine whether this mixture might ultimately prevent the development of asthma are needed.

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Reduced Occurrence of Early Atopic Dermatitis Because of Immunoactive Prebiotics Among Low-Atopy-Risk Infants

Grüber C, van Stuijvenberg M, Mosca F, et al; MIPS 1 Working Group. *J Allergy Clin Immunol*. 2010;126(4):791-797

PURPOSE OF THE STUDY. To determine whether the supplementation of prebiotics and immunoactive oligosaccharides can prevent the development of atopic dermatitis in infants.

STUDY POPULATION. Term weaned infants younger than 8 weeks without a family history of atopy in a parent or sibling were recruited from several northern European study centers.

METHODS. This was a double-blind, placebo-controlled, randomized, prospective study. Infants were randomly assigned to the prebiotics group (PG), control group (CG), or exclusively breastfed group (BG). Infants in the PG received a nonhydrolyzed cow's milk-based formula with a specific mixture of short- and long-chain oligosaccharides (ratio 9:1, 85% of mixture) and pectin-derived acidic oligosaccharides (15% of mixture). The PG and CG received a starter formula for the first 6 months of life, and then a follow-on formula was

offered. Parents were contacted every 2 weeks until the infants turned 1 year old, and clinical visits were conducted at 2, 4, 6, and 12 months of life.

RESULTS. Of 1187 infants screened, 1130 infants (95%) were recruited. The cumulative incidence of atopic dermatitis in the PG (5.7% [SE: 1.2%]) was significantly less than that in the CG (9.7% [SE: 1.5%]; $P = .04$) and similar to the lower range in the BG (7.3% [SE: 1.6%]). Median time to the development of atopic dermatitis was similar in the PG (15.1 weeks [range: 5.1–49 weeks]) and the CG (16.8 weeks [range: 4.4–50.3 weeks]) but longer in the BG (22.5 weeks [range: 4.4–50.3 weeks]). In a Cox regression model, the rate of atopic dermatitis was 44% lower in the PG versus CG ($P = .04$). The disease-free survival period was greater in the PG versus that in the CG ($P = .0377$). The number needed to treat with prebiotic supplementation to prevent 1 case of atopic dermatitis was 25 infants. Atopic dermatitis in the PG at the age of 12 months tended to be less severe than in the CG (median SCORAD score: 8 vs 12; $P = .08$). T-helper 2–specific thymus and activation-regulated chemokine levels, total immunoglobulin E levels, and percentage sensitized to hen's egg or cow's milk were not significantly different in all 3 groups.

CONCLUSIONS. Prebiotic supplementation in low-risk infants reduced the risk of atopic dermatitis by 44% in the first year of life and might be an effective preventive measure in formula-fed infants. Severity of atopic dermatitis was not significantly affected.

REVIEWER COMMENTS. These results might have far-reaching public health implications, because the study focused on preventing food allergy in infants who might not otherwise be identified by personal or family history of atopy. Prebiotics are generally considered safe and might be an alternative to hydrolysate formula or probiotics, which have shown variable results in infants at low risk. It is interesting to note that prebiotics might be less effective once disease has started and does not seem to have an effect on sensitization or other allergic diseases. The next step would be to investigate whether the benefit is transient or persistent and what mechanism might be responsible for the observed effects.

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Efficacy of Probiotic *Lactobacillus GG* on Allergic Sensitization and Asthma in Infants at Risk

Rose MA, Stieglitz F, Köksal A, Schubert R, Schulze J, Zielen S. *Clin Exp Allergy*. 2010;40(9):1398–1405

PURPOSE OF THE STUDY. Previous studies have yielded conflicting data regarding the effects of probiotics on the prevention and treatment of allergic diseases. This prospective study examined the impact of dietary supplementation with *Lactobacillus rhamnosus* strain GG (ATCC 53103) on allergic sensitization, asthma, and atopic eczema.

STUDY POPULATION. Children ($N = 131$) between the ages of 6 and 24 months with a history of at least 2 physician-diagnosed episodes of wheezing within the previous year and a first-degree relative with atopic disease were recruited from a clinic of the Children's Hospital at Goethe University (Frankfurt, Germany) and were randomly assigned to double-blind supplementation with *L rhamnosus* or placebo twice daily for 6 months.

METHODS. Clinical monitoring was performed before intervention and at 3, 6, 9, and 12 months. Outcome measures included the Severity Scoring of Atopic Dermatitis (SCORAD) index, asthma symptom scores defined by cough, wheeze, and need for intervention, and allergic sensitization. Serum samples were taken at 0, 6, and 12 months. Serum levels of egg, milk protein, lactalbumin, cat, horse, dust mite, birch, timothy, and *Alternaria*-specific immunoglobulin E were used as markers of allergic sensitization. Serum eosinophils, eosinophil cationic protein, and transforming growth factor β were also measured.

RESULTS. There were no significant differences in SCORAD indices or asthma-related events between the intervention and placebo groups. In a subgroup of patients with previous aeroallergen sensitization, asthma symptom scores were significantly lower in the placebo group. In a subgroup of patients with previous food-allergen sensitization, patients who received probiotics had fewer rescue-free days and required more inhaled β agonists. Cumulative levels of aeroallergen-specific immunoglobulin E were lower in patients assigned to probiotic supplementation. In the subgroup sensitized to aeroallergens, median eosinophil cationic protein values were lower in the probiotic group. Transforming growth factor β was significantly reduced in the probiotic group.

CONCLUSIONS. In young children with a history of recurrent wheeze and a family history of atopic disease, oral supplementation with *L rhamnosus* had mild negative effects on clinical respiratory status in children with antecedent allergic sensitization. Probiotic supplementation had no beneficial effects on atopic eczema. Probiotic supplementation was associated with mild changes in laboratory assessments of allergic sensitization.

REVIEWER COMMENTS. In the current study, probiotic supplementation did not alleviate clinical symptoms of asthma or atopic eczema. In contrast, probiotic supplementation was associated with increased respiratory symptoms in patients with food and aeroallergen sensitivity. Potential

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