STUDY POPULATION. There were 158 term breastfed infants followed from birth, 113 of whom were born to allergic mothers. Allergic mothers selected for the study met criteria that included clinical manifestation of allergy for more than 24 months, positive allergy-test results, and response to allergy treatment.

METHODS. The infants were divided into groups of colonized infants of allergic mothers (56), control infants of allergic mothers (57), and control infants of healthy mothers (45). Infants of allergic mothers were randomly assigned to 1 of the first 2 groups. Incidence rates of bacterial pathogens in stool and levels of anti–*E coli* immunoglobulins and serum cytokines were determined, and secretory immunoglobulin A was monitored in stool filtrates and maternal milk. Clinical evaluation of infants aged 4 days, 3 and 6 months, and 1, 2, 3, and 5 years were carried out, and clinical symptoms of allergy were monitored. One milliliter of the probiotic *E coli* strain (0.8×10^9 lyophilized *E coli*, serotype O83:K24:H31) was administered orally to infants of allergic mothers within 48 hours after birth and subsequently 3 times per week over a period of 4 weeks. Control infants of allergic and healthy mothers were monitored in these intervals as well.

RESULTS. The *E coli* strain was not found in stool samples before its administration. At the 5-year conclusion of the study, allergy symptoms were found in 14 of 45 (31%) infants of control allergic mothers, 7 of 42 (16%) infants of healthy mothers, and 2 of 46 (4%) infants of allergic mothers who were colonized at birth with probiotic *E coli*. The incidence of allergy at 5 years was significantly lower in the colonized infants of allergic mothers compared with the infants of control allergic mothers ($P < .001$). The incidence reduction in the colonized group compared with that in the infants of healthy mothers was not significant. Allergic phenotype and higher interleukin 4 and 13 and lower interferon γ and transforming growth factor β levels dominated in the allergic group, but the values observed were not quantitatively different.

CONCLUSIONS. After birth, targeted colonization of the intestine by a probiotic *E coli* strain might be an effective means of allergy prevention for infants of allergic mothers.

REVIEWER COMMENTS. As allergic diseases continue to increase in prevalence around the world, primary prevention of allergic disease has been elusive. Although previous studies have found that probiotics might be an effective intervention for eczema, there is little evidence to show that probiotics are beneficial for preventing other allergic diseases. With a significant reduction in clinical signs of overall allergies in the group treated with probiotics, the results of this study raise an interesting therapeutic option, although when examining the types of allergies that these children had, the effect seems to have been primarily for skin-related allergic disease. Further studies will need to evaluate the true effectiveness of these probiotics in allergy prevention.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2011–2107WWW

Jacob D. Kattan, MD
Julie Wang, MD
New York, NY

Probiotics in Pregnant Women to Prevent Allergic Disease: A Randomized, Double-Blind Trial

Dotterud CK, Storrø O, Johnsen R, Oien T. *Br J Dermatol.* 2010;163(3):616–623

PURPOSE OF THE STUDY. To determine if probiotics given to pregnant and nursing women in a nonselected population could prevent allergic disease in the first 2 years of life.

STUDY POPULATION. There were 278 children (138 on probiotics, 140 on placebo) from a population of 415 women in Trondheim, Norway.

METHODS. This was a randomized, double-blind, placebo-controlled study. Women were given 250 mL of probiotic milk or placebo milk per day from 36 weeks' gestation to 3 months after delivery while breastfeeding. The probiotic milk contained *Lactobacillus rhamnosus*, *Lactobacillus acidophilus* La-5, and *Bifidobacterium animalis* subsp lactis Bb-12. At 2 years, all children were assessed for atopic dermatitis (AD), asthma, allergic rhinoconjunctivitis, and atopic sensitization (positive skin-prick-test result or elevated specific immunoglobulin E [IgE] level). The intention-to-treat analysis was enabled by multiple imputations, and the complete-case analysis included all subjects who completed end-point exams.

RESULTS. Using intention-to-treat analysis, the odds ratio (OR) for the cumulative incidence of AD was 0.51 for those in the probiotic group compared with those in the placebo group (95% confidence interval [CI]: 0.30–0.87]; $P = .013$). The effect was stronger for non–IgE-associated AD (OR: 0.43 [95% CI: 0.23–0.81]; $P = .009$). There was no effect on IgE-associated AD (OR: 0.90 [95% CI: 0.37–2.17]; $P = .812$). No significant effect was found for asthma, allergic rhinoconjunctivitis, or atopic sensitization. In complete-case analysis, there was a significant difference in the cumulative incidence of AD between the probiotic and placebo groups (log rank, $P = .022$), and the relative risk was 0.61 (95% CI: 0.41–0.91; $P = .013$; number needed to treat to benefit: 8). The hazard ratio was 0.58 (95% CI: 0.36–0.93) in the probiotic group compared with that in the placebo group ($P = .024$). There was a significantly ($P = .044$) reduced risk of having moderate AD compared with the placebo group.

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.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2011–2107XXX

Michael Pistiner, MD, MMSc
Boston, MA

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.

URL: www.pediatrics.org/cgi/doi/10.1542/peds.2011–2107YYY

Stuart L. Abramson, MD, PhD
Sugar Land, TX

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

Probiotics in Pregnant Women to Prevent Allergic Disease: A Randomized, Double-Blind Trial

Michael Pistiner

Pediatrics 2011;128;S137
DOI: 10.1542/peds.2011-2107XXX

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Probiotics in Pregnant Women to Prevent Allergic Disease: A Randomized, Double-Blind Trial

Michael Pistiner

Pediatrics 2011;128;S137
DOI: 10.1542/peds.2011-2107XXX