STUDY POPULATION. There were a total of 856 children included in this study with data available on allergic diseases up to 6 years of age. They were part of a prospective birth cohort called Protection Against Allergy Study in Rural Environments/EFRIAM in which pregnant women were recruited during the third trimester of pregnancy in 2002–2005 in rural Austria, Finland, France, Germany, and Switzerland.

METHODS. Data were collected by using questionnaires identifying a physician’s diagnosis of asthma or food allergy, as well as history of symptoms of allergic rhinitis. Immunoglobulin (IgE) antibodies to common allergens were measured at 4.5 and 6 years of age. Diet records were kept and food diversity scores assigned based on the number of different foods in the child’s diet and by what age the foods were introduced.

RESULTS. There was an inverse dose–response effect between food diversity and asthma even after adjusting for confounders (odds ratio [OR]: 0.74 [95% confidence interval (CI): 0.61–0.89]). There was a 26% reduction in asthma for every additional item of food added in the first year of life. An increased association was found between children with a low food diversity score and development of food allergies by 6 years of age (OR: 0.70 [95% CI: 0.57–0.86]) compared with children with a more diverse diet after adjusting for confounding variables. This variable, however, was no longer statistically significant after excluding children with food allergy within the first year of life. Those with low food diversity were also found to have increased sensitization to food allergens at 4.5 or 6 years of age (OR: 0.72 [95% CI: 0.57–0.90]). No significant association was found between food diversity and allergic rhinitis or sensitization to inhalant allergens. Children with a low food diversity score also had significantly increased levels of Cε germine transcript, a marker of antibody isotope switching to IgE (geometric mean ratio: 1.81 [95% CI: 1.21–2.70]) and lower levels of Foxp3, a marker for regulatory T cells that helps limit inflammation (geometric mean ratio: 0.7 [95% CI: 0.51–0.96]). Higher levels of Cε found among children with lower food diversity suggest that increasing food diversity may play a role in inhibiting isotype switching to IgE.

CONCLUSIONS. Introducing an increasing diversity of foods within the first year of life may have a protective effect on development of asthma, food allergy, and food sensitization in children up to 6 years of age. Higher levels of Cε found among children with lower food diversity suggest that increasing food diversity may play a role in inhibiting isotype switching to IgE.

REVIEWER COMMENTS. This study is the first linking increased food diversity in the first year of life with a decrease in allergic diseases. The investigators were careful to limit reverse causality by using multiple models for statistical analysis. The findings of this study are encouraging because the role of nutrition in the development of allergic diseases is still a topic of debate.

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Introduction of Complementary Foods and the Relationship to Food Allergy

PURPOSE OF THE STUDY. The study analyzed the significance of complementary feeding and breastfeeding in association with allergy development.

STUDY POPULATION. This study was a nested case-control trial of 41 infants with food allergy diagnosed by age 2 years and 82 matched controls within a cohort study involving 1140 infants. The infants’ food allergies were confirmed by using double-blind, placebo-controlled food challenges, the gold standard for diagnosing food allergies.

METHODS. Infants with food allergies were recruited from the PIFA (Prevalence of Infant Food Allergy) study in the United Kingdom. Parents kept prospective daily food diaries and were also asked to complete a telephone questionnaire when their infant was 12 and 24 months old. The questionnaire was designed to identify infants with potential food allergies. Infants with potential food allergies based on food diary and telephone questionnaire data underwent skin prick tests and serum-specific IgE tests to common food allergens. Infants provisionally diagnosed as food allergic based on results of their skin prick test or serum-specific IgE tests then underwent double-blind, placebo-controlled food challenges.

RESULTS. Most (95%) mothers initiated breastfeeding. Exclusive breastfeeding occurred for a median of 8 weeks, total breastfeeding occurred for a median of 20 weeks (0–64 weeks), and there was no significant difference between infants who developed food allergy compared with control subjects. However, infants who developed food allergy had a shorter duration of concurrent breastfeeding when cow’s milk was introduced compared with control subjects (5.5 vs 9 weeks; \(P = .47\)). The mean age of introduction of solids was \(\sim20\) weeks. Significantly more food-allergic infants were introduced to complementary foods (not necessarily common allergens) at \(<17\) weeks of age than control subjects (35% vs 14%; \(P = .011\)). Infants with food allergy were introduced to cow’s milk and peanut significantly earlier compared with the control infants.

CONCLUSIONS. The infants who were diagnosed with food allergy by age 2 years were less frequently breastfed when
cow’s milk protein was first introduced into their diet and were also introduced to solids earlier than the control infants.

**REVIEWER COMMENTS.** The authors conclude that early introduction of solids was associated with the development of food allergy, which supports the current recommendations by the American Academy of Pediatrics to breastfeed exclusively and to delay introduction of solids until 4 to 6 months of age. Data are accumulating to suggest that breastfeeding seems protective against food allergies and that there is a critical window in which solid foods, including highly allergenic foods such as cow’s milk, eggs, and peanut, should be introduced in infancy. Breastfeeding should also continue concurrently for 2 to 3 months while cow’s milk and solids are introduced into the diet because it is thought to play a role in the development of oral tolerance.

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Probiotic Administration in Early Life, Atopy, and Asthma: A Meta-Analysis of Clinical Trials  

**PURPOSE OF THE STUDY.** Some studies suggest that early probiotic administration reduces the risk of allergies and asthma in childhood. This study evaluates the effects of probiotic supplementation on asthma and atopic sensitization.

**STUDY POPULATION.** The study included 4031 subjects in 20 cohorts primarily in Europe, Asia, and Australia. Probiotics were administered prenatally to pregnant mothers (2 studies), prenatally and postnatally (10 studies), or only postnatally directly to the child (9 studies).

**METHODS.** This meta-analysis included 25 double-blind, randomized, placebo-controlled trials published between 2001 and 2012. Meta-regression was performed to evaluate the effect of potential factors on probiotic efficacy. The pooled risk estimates were calculated by using random effect models. Atopic sensitization was measured by a positive skin prick test or elevated serum-specific IgE level to any food or inhalant allergen. Asthma was diagnosed directly by a physician or indirectly by parental report of a physician diagnosis.

**RESULTS.** Total IgE and atopic sensitization was significantly reduced in subjects who received probiotics. This reduction was more pronounced with longer follow-up for total IgE levels (correlation coefficient: -1.95 [95% confidence interval: -3.69 to -0.21]; *P* = .028). The effect on atopic sensitization was only significant when probiotics were administered both prenatally and postnatally (relative risk: 0.08 [95% confidence interval: 0.78 to 0.99]; *P* = .035) but not when only administered postnatally (*P* = .825). However, probiotics did not significantly reduce the prevalence of asthma or wheeze. *Lactobacillus* was found to be associated with increased atopic sensitization.

**CONCLUSIONS.** Early probiotic administration reduces the risk of atopic sensitization, but it does not reduce the risk of developing asthma. There was no significant association in subgroup analysis according to age group or treatment length.

**REVIEWER COMMENTS.** Results on atopy and asthma in association with probiotic administration have been conflicting. This study showed that probiotic administration was significant in reducing atopic sensitization but not disease. Similar to the hygiene hypothesis, in which a relative lack of microbial exposure during infancy and early childhood could result in an imbalance with a shift of Th1/Th2 cytokine balance toward a more allergic Th2 response, probiotics may promote a healthy gut microbiome, shifting this balance to a nonallergic Th1 response. Future trials are still needed to achieve more consistency among studies.

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No Effect of Probiotics on Respiratory Allergies: A Seven-Year Follow-up of a Randomized Controlled Trial in Infancy  

**PURPOSE OF THE STUDY.** The goal of this study was to determine if supplementation with the probiotic *Lactobacillus reuteri* during the perinatal period and infancy, which had reduced the incidence of allergic sensitization and allergic eczema at age 2 years, reduces the incidence of asthma and allergic rhinoconjunctivitis in school-aged children.

**STUDY POPULATION.** The study population included 184 of 232 Swedish children who had participated in a double-blind, placebo-controlled, randomized controlled trial (RCT) of probiotic supplementation perinatally and during infancy. To be eligible for the RCT, children had to have a family history of allergic disease.

**METHODS.** Families were contacted when the children were 7 years old, and the follow-up visit included administration of questionnaires, physical examination, spirometry, measurement of fractional exhaled nitric oxide, and assessment of eczema. Skin prick testing and IgE testing were also performed by using a panel of common food and environmental allergens. The outcome of allergic disease was defined as symptomatic asthma, allergic rhinoconjunctivitis,
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