described the long-term protective effects of early microbial exposures. Specifying the length of breastfeeding and duration of different food exposures varying across studies may help future researchers with further in-depth analyses. The consistency of the findings across different studies and countries provides evidence that early microbial exposures may play a role in the development of allergic diseases. However, further research is needed to elucidate the specific mechanisms involved and to identify the optimal strategies for intervention.

CONCLUSION. The findings from this systematic review indicate that early microbial exposures may play a role in the prevention of allergic diseases. Further research is needed to identify the specific mechanisms involved and to develop effective strategies for intervention.

REVIEWER COMMENTS. These findings further support the role of environmental factors in the development of allergic disease. Limitations of this study, however, include self-report of allergic disease without clinical verification. The majority of the participants currently reside in a metropolitan area, and it is unknown what proportion of foreign-born families moved from a developing country (compared with an industrialized country) to the United States. Country of origin was not ascertained, although race/ethnicity data were collected as a proxy. Other potential confounding factors not evaluated include diet, allergenic exposures, use of antibiotics, use of antibacterial cleaning products, and history of helminthic infections.

Primary Prevention of Food Allergy in Children and Adults: Systematic Review

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Prenatal Food Allergen Exposures and Odds of Childhood Peanut, Tree Nut, or Sesame Seed Sensitization

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Prenatal Food Allergen Exposures and Odds of Childhood Peanut, Tree Nut, or Sesame Seed Sensitization


Purposes of the study. The goal of this study was to examine whether prenatal exposure to peanut or sesame seed oil as a vehicle for progesterone injection increases the child’s odds of peanut (PN), tree nut (TN), or sesame seed (SS) allergy. The study population. A total of 1272 food-allergic children were evaluated at Boston Children’s Hospital. Control subjects were children allergic to foods including dairy or eggs but not PN, TNs, or SS. Case subjects included those allergic to PN, TNs, and/or SS.

Methods. Parents completed a questionnaire addressing demographic characteristics, family history, child’s history of allergies, use of assisted reproduction, and prenatal exposure to food allergens. The child’s skin prick and specific immunoglobulin E test results were reviewed. Two samples of progesterone suspended in SS oil were assayed for SS protein content during the study.

Results. A total of 1272 questionnaires were analyzed. There were no statistical differences between case subjects and control subjects in demographic characteristics, parental atopy, or birth history. History of parental infertility, in vitro fertilization treatment, progesterone support, and
treatment with intramuscular progesterone during pregnancy were not associated with significant differences in the frequency of childhood PN/TN/SS sensitization versus sensitization to other foods. Maternal ingestion of eggs, dairy, or seafood did not increase the odds of PN/TN/SS sensitization in the child; however, ingestion of TN and SS during the first trimester of pregnancy was associated with increased odds of PN/TN/SS sensitization. Maternal PN ingestion during pregnancy was associated with increased odds of PN/TN/SS sensitization in the child.

CONCLUSIONS. There was no increase in the prevalence of PN/TN/SS sensitization in children born to parents with a history of infertility or conception with medical assistance with or without progesterone. Maternal ingestion of TN/SS during pregnancy was associated with increased odds of PN/TN/SS sensitization in the child.

REVIEWER COMMENTS. The effect of prenatal exposure and possible alterations to the prenatal milieu, such as substances used in fertility treatments, are important questions in addressing the possible causes of the increasing prevalence of food allergy. Limitations of this study include its retrospective nature, possible dietary recall bias, and limited information on the composition of the oil for the progesterone treatments.


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Role of Maternal Elimination Diets and Human Milk IgA in the Development of Cow’s Milk Allergy in the Infants

PURPOSE OF THE STUDY. The goal of this study was to evaluate the association of maternal cow’s milk (CM) avoidance during breastfeeding with specific IgA levels in human milk and the development of CM allergy in infants.

STUDY POPULATION. This prospective birth cohort study evaluated 145 mother–infant pairs who were recruited at birth and followed up prospectively at 0 to 2 weeks and at 1, 3, 6, 12, and 18 months to determine development of food allergy in the infants. Infants were all term and classified into 2 groups: high risk because of sibling(s) with food allergy and low risk, defined as having only nonatopic first-degree relatives.

METHODS. Human milk and/or serum samples were obtained from 286 visits with an average of 2 visits per each mother–infant pair. Maternal and infant diets were obtained by using dietary records. Thirty-seven mothers implemented a strict maternal CM avoidance diet within the first 3 months’ postpartum, 49 mothers started a CM elimination diet between 3 and 7 months of breastfeeding, and 56 mothers continued CM in their diet without restrictions. Seventy-five infants in this cohort developed challenge-proven CM allergy. Maternal serum samples and breast milk samples were assayed for casein and β-lactoglobulin (BLG)-specific IgA and IgG by using an enzyme-linked immunosorbent assay. Infants’ sera were evaluated for casein and BLG-specific IgA, IgG, and IgE. The impact of human milk on β-lactoglobulin uptake was assessed in transcytosis assays by using Caco-2 intestinal epithelial cell lines.

RESULTS. Breast milk samples (n = 23) from mothers avoiding CM had lower casein- and BLG-specific IgA levels than milk from mothers (n = 56) with no CM restriction (P = .019 and P = .047, respectively). Their infants had lower serum casein- and BLG-specific IgG1 (P = .025 and P < .001) and BLG-specific IgG4 (P = .037) levels, and their casein- and BLG-specific IgA levels were less often detectable than those with no CM elimination diet (P = .003 and P = .007). Lower CM-specific IgG4 and IgA levels, in turn, were associated with infant CM allergy. In the in vitro model for evaluating the transcytosis of BLG through enterocytes, high levels of BLG-specific IgA (the no CM restriction group) in breast milk impaired movement of BLG across the “gut mucosa.”

CONCLUSIONS. Maternal avoidance of CM was associated with lower levels of mucosal-specific IgA levels and the development of CM allergy in infants.

REVIEWER COMMENTS. This article refutes the practice of food avoidance during breastfeeding. Maternal elimination diets resulted in lower levels of breast milk–specific IgA, which was associated with the development of CM allergy in infants. The study found that human milk IgA may play a role in preventing excessive food antigen uptake in the gut lumen and thereby possibly prevent the development of CM allergy. The participants chosen for this study, however, had a significant atopic family history, which could mean application to the general population may not be as straightforward. Further research with elimination diets and other allergenic foods in a less atopic study population is necessary to confirm the relationship between dietary restriction, breastfeeding, and the development of pediatric food allergy.

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Increased Food Diversity in the First Year of Life Is Inversely Associated With Allergic Diseases

PURPOSE OF THE STUDY. The investigators sought to test the relationship between food diversity in the first year of life and outcome of allergic diseases.
## Prenatal Food Allergen Exposures and Odds of Childhood Peanut, Tree Nut, or Sesame Seed Sensitization

Jessica Stern and Theresa Bingemann

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