

specific IgE level (sIgE), and eczema was assessed by Scoring Atopic Dermatitis (SCORAD) severity score.

**RESULTS.** The study was terminated when the interim analysis showed a protective effect of egg ingestion. Among infants completing the open egg challenge ( $N = 121$ ), 5 (8%) had an egg allergy in the egg group versus 23 (38%) in the placebo group (risk ratio 0.221 [95% CI 0.090–0.543],  $P = .0001$ ). In stratified analyses, egg ingestion was protective for egg-sensitized infants (sIgE  $\geq 0.35$  kUA/L,  $P = .001$ ) but not for nonsensitized infants (sIgE  $< 0.35$  kUA/L,  $P = .31$ ).

**CONCLUSIONS.** Daily consumption of a small amount of egg and aggressive eczema care starting at age 6 months prevents egg allergy in high-risk infants at age 12 months.

**REVIEWER COMMENTS.** This stepwise egg introduction to infants with eczema appeared to be safe; no severe, immediate allergic reactions were reported at home, although anaphylaxis occurred during some monitored egg challenges. The significantly higher baseline egg sensitization rate and SCORAD in the placebo group were important limitations that may have affected the rates of egg allergy in the 2 groups and biased the results. The median baseline SCORAD was in the moderate range for the placebo group and in the mild range for the egg group; eczema was well controlled with minimal topical steroid use, suggesting that few infants had severe or difficult-to-control eczema.

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### Timing of Allergenic Food Introduction to the Infant Diet and Risk of Allergic or Autoimmune Disease: A Systematic Review and Meta-analysis

Lerodiakokonou D, Garcia-Larsen V, Logan A, et al. *JAMA*. 2016;316(11):1181–1192

**PURPOSE OF THE STUDY.** To determine whether the timing of allergenic food introduction influences the risk of development of allergic or autoimmune disease.

**STUDY POPULATION.** Meta-analysis of studies evaluating the timing of allergenic food introduction in the first year of life and reported allergy, allergic sensitization, or autoimmune disease.

**METHODS.** A comprehensive literature search from January 1, 1946, to March 8, 2016, was performed. Participants were enrolled within 6 months of life, and outcomes were evaluated between 7 months and 6 years of age. Across the 146 studies evaluated, the age of allergenic food introduction and associated allergic or autoimmune outcomes were compared in 24 interventional/69 observational studies and in 6 interventional/48 observational studies, respectively. Bias and statistical heterogeneity were quantified by using validated methodology. A post hoc trial

sequential analysis quantified the statistical reliability of the moderate- to high-certainty findings with egg introduction and gluten introduction. The certainty of evidence score was determined by using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system.

**RESULTS.** The meta-analysis of 5 trials with 1915 participants found a decreased risk of developing an egg allergy with egg introduction at 4 to 6 months (RR 0.56; 95% CI, 0.36–0.87). Meta-analysis of 2 trials with 1550 participants found a lower risk of developing a peanut allergy when peanut was introduced at age 4 to 11 months (RR 0.29; 95% CI, 0.11–0.74). There was no association with the timing of introduction of other allergenic foods (milk, wheat, soy, tree nuts, and shellfish) and the risk of allergic sensitization or food allergy. There was conflicting evidence about the early introduction of fish and the associated risk of allergic sensitization. No association was found between the timing of gluten introduction and celiac disease, inflammatory bowel disease, or type I diabetes mellitus or between the timing of milk introduction and type 1 diabetes mellitus.

**CONCLUSIONS.** There is moderate-certainty evidence that the introduction of egg between 4–6 months of age and peanut between 4–11 months of age is associated with a reduced risk of egg and peanut allergy, respectively. There is low- to very-low-certainty evidence that fish introduction between 6–12 months of age is associated with decreased allergic sensitization or rhinitis. There is high-certainty evidence that the timing of gluten introduction has no association with celiac disease.

**REVIEWER COMMENTS.** This large-scale meta-analysis and systematic review concludes that the early ingestion of egg and peanut is associated with antigen-specific oral tolerance, a heartening finding with significant implications for families wondering about the right age to introduce these potentially allergenic foods. There was no consistent evidence, however, that the introduction of 1 food influences the development of a different food allergy. Reassuringly, there was no consistent evidence that the timing of food introduction impacts autoimmune diseases, including celiac disease, type I diabetes mellitus, or inflammatory bowel disease.

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### Parental Timing of Allergenic Food Introduction in Urban and Suburban Populations

Hartman H, Dodd C, Rao M, et al. *Ann Allergy Asthma Immunol*. 2016;117(1):56–60

**PURPOSE OF THE STUDY.** To investigate the differences in early food introduction in urban versus suburban populations.

**STUDY POPULATION.** The study included 200 caregiver questionnaires. The questionnaires were distributed among an urban Medicaid-based population affiliated with Cincinnati Children's Hospital Medical Center and a suburban private insurance-based population from Montgomery, Ohio (14 miles outside of Cincinnati, Ohio).

**METHODS.** A caregiver questionnaire was dispersed at 4-month-old to 3-year-old well-child checkups between January and March 2010. A total of 200 questionnaires were given out evenly among urban and suburban populations. Families were asked the age at which formula and solid foods were introduced and what food was introduced. The questionnaire also included questions relating to demographic characteristics, child's history of atopy, family history, practitioner recommendations on food introduction, and type of insurance. Data were analyzed by using the random forest method to determine which factors affecting the age of introduction were most significant.

**RESULTS.** Of the 200 questionnaires distributed, 185 were returned (99 from the suburban setting and 86 from the urban setting). The urban population included African Americans with public insurance primarily, whereas the suburban population was largely made up of white non-Hispanics with private health care insurance. In comparing the 2 groups, solids were introduced at similar ages. However, allergenic foods were introduced earlier in the urban population versus the suburban population. Specifically, whole cow's milk, peanut, fish, and egg were all introduced at a statistically significant earlier age in the urban population. The suburban population delayed the introduction of egg, fish, and peanut to 12 months or older on average. The recommended age of introduction by health care professionals was the most significant variable in the introduction of all foods.

**CONCLUSIONS.** Urban populations introduced allergenic foods earlier than suburban populations. Recommendations made by health care professionals were the most influential factors in food introduction.

**REVIEWER COMMENTS.** Recent guidelines regarding food introduction have dramatically changed our recommendations to families. As health care providers, we may forget the influence our advice has on many young lives and families. These results emphasize the significance and effectiveness of having clear and concise guidelines in practice. Additionally, this study highlights the gap and need for continued research into appropriate timing for the introduction of allergenic foods, so as to minimize disparities between different populations.

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## **Effects of Maternal Dietary Egg Intake During Early Lactation on Human Milk Ovalbumin Concentration: A Randomized Controlled Trial**

Metcalf JR, Marsh JA, D'Vaz N, et al. *Clin Exp Allergy*. 2016;46(12):1605-1613

**PURPOSE OF THE STUDY.** To investigate how maternal dietary egg ingestion during the early postnatal period influences egg protein levels (ovalbumin [OVA]) in breast milk.

**STUDY POPULATION.** Two thousand thirty-four pregnant women were initially screened for eligibility. One hundred and twenty breastfeeding mothers with a history of allergic disease (excluding egg allergy) whose infants were born at  $\geq 36$  weeks' gestation were randomized to modify their diet for egg consumption during their infants' first 6 weeks of life.

**METHODS.** This was a randomized controlled trial in which participants were allocated to 3 groups: high egg consumption ( $>4$  eggs a week), low egg consumption (1-3 eggs a week), or an egg-free group. Baseline data of family history of allergic disease, race, educational level, smoking during pregnancy, pets in the home, and egg intake were collected. Nonblinded participants recorded egg intake prospectively. OVA levels were measured in breast milk and collected at 2, 4, and 6 weeks of lactation. Infant blood samples measuring serum egg-specific IgE and IgG4 were collected at 6 and 16 weeks. All data were obtained prior to egg introduction to the infant.

**RESULTS.** One hundred and twenty women were randomized: 40 to high-egg, 44 to low-egg, and 36 to egg-free diets. No significant differences were found in baseline characteristics between the groups. One hundred and nine women completed the 6-week intervention. Compliance was 100% (36 of 36 women) in the high-egg group, 95% (40 of 42 women) in the low-egg group, and 23% (7 of 31 women) in the egg-free group. Women in the high-egg group had significantly higher breast milk OVA concentrations than women on an egg-free diet ( $P = .036$ ), but no detectable difference in OVA was seen between the low-egg and egg-free groups at 2, 4, or 6 weeks. One-third of the women did not have detectable breast milk OVA concentrations at any time during the study. Infant egg IgG4 levels were positively associated with average maternal egg ingestion. Each additional egg per week was associated with a 22% increase in infant IgG4 levels.

**CONCLUSIONS.** Increased maternal egg consumption is associated with more OVA in breast milk and increased serum IgG4 levels in infants, reflecting possible oral tolerance development in breastfed babies.

## Parental Timing of Allergenic Food Introduction in Urban and Suburban Populations

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