with the other studies. Also, of note, this study used heated whole egg powder, whereas most of the studies used pasteurized raw egg powder. Additional studies are needed with a true-to-life approach in which egg would be prepared by various means of cooking.


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The Health and Economic Outcomes of Early Egg Introduction Strategies

PURPOSE OF THE STUDY: Researchers in this study modeled rates of egg allergy development and costs associated with early egg introduction (EEI) without screening compared with skin prick test (SPT) or serum-specific immunoglobulin E (sIgE) screening and delayed egg introduction.

STUDY POPULATION: The computer simulation modeled high-risk infants with early-onset eczema in the United States, Canada, and Europe.

METHODS: The Markov modeling was based on published data including risks and benefits of EEI with cooked egg, eczema prevalence, 24% positive egg SPT results in infants with eczema, 6.6% annual egg tolerance development, and 5% annual inadvertent reactions to egg over a 20-year time frame. Infant cohorts were as follows: (1) EEI without screening, (2) SPT for egg sensitization in consultation with a board-certified allergist, (3) egg sIgE testing by a primary care provider, and (4) delayed egg introduction (>12 months of age) without screening. Costs considered included SPT, sIgE, allergy consultation, epinephrine autoinjectors, additional visits, and job-related opportunity costs.

RESULTS: Egg allergy occurred in 2.5% of infants with EEI without screening versus 9.5%, 12%, and 21.4% with SPT screening, delayed introduction, and sIgE screening, respectively. Base model per patient incremental costs were $68 665 US dollars for SPT by an allergist and $16 722 for sIgE by a primary care provider. Quality of life was similar across groups. Cooked EEI without screening remained the preferred strategy across multiple sensitivity analyses, including higher rates of allergy on first egg-exposure, lower rates of subsequent accidental egg reactions in children with egg allergy, lower rates of natural egg tolerance, higher rates of anaphylaxis fatality, exclusion of discount rates, and across both shorter and longer time horizons. A supplemental analysis of raw pasteurized EEI demonstrated that although this strategy was inferior to cooked EEI, raw pasteurized EEI was still preferred to screening testing (and also to delayed cooked egg introduction provided no more than 15.6% of infants reacted to initial raw pasteurized egg exposure).

CONCLUSIONS: EEI without screening for high-risk infants resulted in the lowest percentage of infants developing egg allergy and the lowest cost. EEI after SPT screening and challenge for all positive SPT results resulted in fewer children with egg allergy and lower cost than delayed introduction.

REVIEWER COMMENTS: These simulations suggest that EEI without screening for egg sensitization is the preferred strategy for infants with no previous reactions to egg. SPT followed by a challenge if the SPT result is positive is associated with less egg allergy than delayed introduction, suggesting a role for limited SPT screening to facilitate early introduction in infants with eczema whose families are reluctant to introduce egg without screening. Although the modeling required making assumptions, extensive sensitivity analyses were performed and demonstrated robustness of EEI as the preferred strategy.


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Relevance of Low Specific IgE Levels to Egg, Milk and Peanut in Infancy

PURPOSE OF THE STUDY: To evaluate the clinical importance of low specific immunoglobulin E (IgE) to hen’s egg, cow’s milk, and peanut at 6 months in relation to doctor’s diagnosis of allergy-related disease at 5 years of age.

STUDY POPULATION: Families in Sweden were recruited between 2004 and 2011 (ALADDIN prospective birth cohort). This study included 372 children, all of whom contributed a blood sample at 6 months and at 1, 2, and/or 5 years of age. Fifty percent were girls, 17% were born via cesarean delivery, and 26% were breastfed exclusively for 6 months. At 6 months, 11% had a doctor’s diagnosis of asthma, 12% had a diagnosis of eczema, 3% had a diagnosis of allergic rhinoconjunctivitis, and 8% had a diagnosis of food allergy.

METHODS: Questionnaires regarding lifestyle, background, diet, and health were completed at enrollment, 2 and 6 months, and 1, 2, and 5 years of age. Serum IgE to specific foods and aeroallergens was measured in children at 6 months and 1, 2, and 5 years. For the statistical analysis, 3 categories were designated: nonsensitized (<0.1 kU/L), low sensitized (0.1–0.34 kU/L), and sensitized (≥0.35 kU/L); proportion with allergy-related disease was assessed.

RESULTS: For egg and milk, having specific IgE in the interval of 0.1 to 0.34 kU/L at 6 months was significantly associated with being sensitized (≥0.35 kU/L) to that specific allergen at 1 year (P = .01 and <.01, respectively) and to...
aeroallergens at 5 years ($P = <.01$ and $.01$), compared with nonsensitized children. Being sensitized ($\geq 0.35$ kU/L) to egg or milk at 6 months was significantly associated with sensitization to the food at 1 and 2 years of age and to any food allergen, but it was not associated with aeroallergen sensitization at 5 years as compared with those with low sensitization ($P = .69$). Approximately 50% of children with low sensitization to milk or egg at 6 months had IgE that declined to nonsensitized levels at 2 years of age. For peanut, low sensitization at 6 months was only significantly associated with being sensitized to aeroallergens at 5 years of age ($P = .04$). Low-level sensitization to egg was associated with higher rates of eczema ($P < .01$).

CONCLUSIONS: Specific IgE to milk, egg, and peanut in the range of 0.1 to 0.34 kU/L at 6 months appeared to decrease over time. However, low-level sensitization at 6 months appeared to increase the likelihood of sensitization to aeroallergens at 5 years. Compared with those who were nonsensitized at 6 months, children with low sensitization to milk or egg had higher rates of sensitization to that allergen at 1 year of age. Having low sensitization to egg at 6 months was associated with the development of eczema.

REVIEWER COMMENTS: Researchers in this study evaluated whether specific IgE at 6 months was associated with further IgE sensitization and allergy-related diagnosis. The strengths of the study include that it was population based and managed children over the course of 5 years. The study does not provide any data about the development of clinical food allergy. This study suggests that children with low sensitization at 6 months can be counseled that $\sim 50\%$ had undetectable IgE to the relevant allergen at 2 years, but the low sensitization could suggest a higher risk of future aeroallergen sensitization as well as potentially eczema for those with egg-specific IgE.

**Patterns of Tree Nut Sensitization and Allergy in the First 6 Years of Life in a Population-Based Cohort**


**PURPOSE OF THE STUDY:** To determine the prevalence of tree nut allergy at age 6 years and investigate the relationship between egg and peanut allergy at age 1 year and tree nut allergy at age 6 years to guide testing and introduction advice.

**STUDY POPULATION:** This study included infants recruited between 11 and 15 months for the longitudinal HealthNuts study in Melbourne, Australia.

**METHODS:** At entry, all subjects underwent skin prick testing (SPT) to egg, peanut, and sesame. At age 1 year, egg and peanut allergy were determined by oral food challenge. SPT to tree nuts (almond, cashew, hazelnut) was performed, and parental history of symptoms with tree nut ingestion was obtained. Those with negative SPT results were advised to introduce tree nuts at home; avoidance was recommended for those with positive SPT results. At age 6 years, a questionnaire was administered, SPT was performed, and tree nut allergy was assessed by food challenge.

**RESULTS:** Five thousand two hundred seventy-six children participated in the HealthNuts study at age 1. One thousand one hundred fourteen (21%) underwent additional evaluation, including SPT for tree nuts. At age 1 year, 6 parents (0.1%) reported a history consistent with tree nut allergy. Among those with challenge-confirmed egg or peanut allergy at age 1 year, 41% were already sensitized to 1 or more tree nuts, with an even higher rate in those with both allergies. At age 6, the prevalence of tree nut allergy was 3.3%, with cashew being the most common trigger, followed by hazelnut and almond. Forty-three percent of those with any tree nut allergy had peanut allergy. Of those with peanut allergy, 45% reacted to 1 or more tree nuts, most commonly cashew. In examining predictors of tree nut allergy, 14% of those with egg allergy at age 1 year, 27% of those with peanut allergy at age 1, and 37% of those with both egg and peanut allergy at age 1 had tree nut allergy at age 6 years.

**CONCLUSIONS:** There is a low parent-reported rate of tree nut allergy at age 1 year, likely due to low tree nut consumption in the first year of life. However, 33% of those with peanut allergy and 41% of those with peanut or egg allergy are already sensitized to 1 or more tree nuts at age 1, with a higher rate in those with allergy to both foods. More than one-third of those with tree nut sensitization at age 1 are allergic to 1 or more tree nuts at age 6. Almost half of those with both peanut and egg allergy at age 1 have tree nut allergy at age 6. The prevalence of tree nut allergy at age 6 (3.3%) is similar to that of peanut allergy (2.8%), with cashew being the most common tree nut allergen.

**REVIEWER COMMENTS:** This study reports a high rate of tree nut sensitization and potential for allergy in those with egg and/or peanut allergy at age 1 and highlights the need to investigate the best approach to tree nut evaluation in those with known food allergy as well as strategies to prevent tree nut allergy in this at-risk population.
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Suzanne Kochis and Jennifer Dantzer
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