REVIEWER COMMENTS. The landmark LEAP study turned our approach to the early introduction of highly allergenic foods 180° by showing that it decreased children's risk of developing PN allergy by ~80%. This extension study demonstrates that early peanut introduction also has no detrimental effects on growth or nutrition. How and to whom should early PN introduction be offered? Infants with severe atopic dermatitis and/or egg allergy should be tested before an observed, in-office challenge per the LEAP protocol is considered. Children without food allergy and with only mild-to-moderate atopic dermatitis are considered to be at low risk for the development of PN allergy. They may have peanut introduction as tolerated at ~6 months old only after at least 1 other solid is tolerated. Recipes for preparing PN to feed to appropriate infants are available (*J Allergy Clin Immunol*. 2017;139[1]:29–44).

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Introduction of Peanuts in Younger Siblings of Children With Peanut Allergy: A Prospective, Double-blinded Assessment of Risk, of Diagnostic Tests, and an Analysis of Patient Preferences

Bégin P, Graham F, Killer K, Paradis J, Paradis L, Des Roches A. *Allergy*. 2016;71(12):1762–1771

PURPOSE OF THE STUDY. The purpose of the Finding the Risk of Anaphylaxis and Testing Rational In youngEr Siblings (FRATRIES) study was to determine the risk of anaphylaxis, the predictive values of peanut allergy tests, and parents' preferences in the context of peanut introduction in the younger siblings of peanut-allergic children.

STUDY POPULATION. The study cohort included 154 peanut-naïve children (median age of 23 months) who each had an older sibling with a diagnosis of peanut allergy. Participants were recruited in Canada through advertising in allergy clinics and through local food allergy web-based communities. Reference cohorts included parents of (1) peanut-naïve children from nonallergy pediatric clinics and (2) peanut-allergic children.

METHODS. This was a prospective cohort study. Peanut-naïve younger siblings underwent double-blind skin prick testing (SPT) followed by parent-led peanut introduction. At least 2 g of peanut protein was ingested to consider the introduction complete. Subjects were observed in a clinic for 2 hours. A phone call 24 hours later inquired about delayed reactions. Parents were then advised to introduce peanut in the younger child's diet at least once a week. A phone follow-up occurred 1 year later. Questionnaires were dispensed prior to and up to a year after peanut introduction to investigate parental preferences with regard to peanut introduction in this subgroup.

RESULTS. Eight participants (5.2%) had an unequivocal IgE-mediated reaction upon peanut introduction, including 5 with anaphylaxis. Peanut-allergic participants were significantly older than the rest of the cohort (median age of 4.0 vs 1.9 years, $P = .04$). The negative predictive values of SPT with peanut extract, peanut butter, and peanut-specific IgE were 99%, 100%, and 100%, respectively. The absolute positive predictive values of peanut extract SPT, peanut butter SPT, and specific IgE were 88%, 72%, and 62%, respectively. Peanut introduction at home without supervision was associated with high levels of parental anxiety in parents with a previously peanut-allergic child (median of 8.4 on a 10-point Likert scale), compared with introduction under supervision without testing (median of 3.8, $P < .001$) and home introduction after negative testing (median of 4.3, $P < .001$). If a provider recommended home peanut introduction without prior testing, 82% of parents would keep avoiding the food.

CONCLUSIONS. Siblings of children with peanut allergy have an increased risk of anaphylaxis upon peanut introduction, with a potentially higher risk for older children who delayed introduction. Parents with a previously peanut-allergic child have significant anxiety regarding introducing peanut without prior skin testing or without supervision.

REVIEWER COMMENTS. This study supports previous studies showing that younger siblings of peanut-allergic children have a higher rate of peanut allergy. Recent NIAID guidelines for the prevention of peanut allergy recommend early introduction of peanut for high-risk children but do not make specific recommendations for siblings without other risk factors. In our practice, we do specifically recommend early and consistent peanut introduction in younger siblings of peanut-allergic patients, usually with prior testing. As highlighted in this study, parental anxiety regarding a possible reaction in the younger sibling, as well as the peanut-allergic child, is likely to impact home peanut introduction unless it is done with some level of medical supervision.

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The Association of the Delayed Introduction of Cow's Milk With IgE-Mediated Cow's Milk Allergies

Onizawa Y, Nogushi E, Masafumi O, et al. *J Allergy Clin Immunol Pract*. 2016;4(3):481–488

PURPOSE OF THE STUDY. To determine if the early introduction of cow's milk (CM) formula was either positively or negatively associated with the development of an IgE-mediated cow's milk allergy (IgE-CMA).

STUDY POPULATION. Patients were recruited at Ryugasaki Saiseikai Hospital in Japan. The study included 51 children with IgE-CMA (defined as having had immediate allergic reactions within 2 hours of ingestion, a CM IgE level ≥0.7 kU_A/L, and diagnosis by a board-certified allergy specialist) and 102 age- and sex-matched controls seen for the common cold or routine vaccination without having a CMA or other food allergy. An additional 32 unmatched patients with an IgE-mediated egg allergy (egg-IgE >0.7 kU_A/L and diagnosis by a specialist) and without a milk-related food allergy were also included. All patients were older than 1 year of age at the time of enrollment.

METHODS. This was a retrospective case-control study of pediatric patients recruited from November 2014 to February 2015. A standardized questionnaire was completed by the parents and included information regarding past histories of allergic diseases, family history of allergic diseases, time of introduction of nonregular (not used daily) CM formula, time of introduction of regular (used daily) CM formula, feeding patterns in the first month of life and reason for choosing those patterns, and timing of discontinuation of CM formula and reason for discontinuation. Feeding patterns in the first month of life were categorized as (1) exclusive breastfeeding with no formula; (2) almost exclusive breastfeeding with CM formula less than daily; (3) mixed, feeding predominantly with breast milk but with CM formula at least once a day; (4) mixed, feeding predominantly with CM formula; and (5) exclusive CM formula and no breast milk.

RESULTS. The rates of atopic dermatitis and bronchial asthma were significantly higher in the CMA group ($P < .001$ and $P = .12$, respectively). The CMA group also showed increased maternal age at delivery, paternal asthma, paternal rhinitis, maternal asthma, maternal food allergy, and decreased pet ownership ($P < .05$). Compared with the egg-allergic group, the CMA group showed significantly higher rhinitis and maternal asthma ($P < .05$). Exclusive breastfeeding was significantly higher in the CMA group, whereas early regular CM formula feeding (once daily within the first month of life) and early regular continuous CM formula feeding (once daily within the first month of life and continued until 6 months or until the onset of CMA) were significantly higher in the controls. In a multivariable logistic regression analysis that controlled for allergic symptoms, parental age at delivery, and family history of allergic diseases, the adjusted odds ratio of delayed (started 1 month after birth) or no cow's milk formula (less than once daily) was 23.74 (95% CI, 5.39–104.52) for the CMA group compared with the controls and 10.16 (95% CI, 2.48–41.64) compared with the egg-allergic group. The odds ratio of CMA versus control was even higher when looking at no early regular continuous CM formula feeding (92.76 [95% CI, 9.05–951.04]).

CONCLUSIONS. Early (starting in the first month of life) and regular (daily) exposure to CM is protective against the development of IgE-mediated CMA.

REVIEWER COMMENTS. This relatively small study supports the hypothesis that early ingestion of an allergen may be protective against the development of a food allergy. The general notion is supportive of a previous study on the early introduction of peanuts to prevent peanut allergy, although that trial introduced peanuts at 4 up to 11 months of age (Du Toit G et al, *N Engl J Med*. 2015;372[9]:803–813). There are limitations to this current study. The study was retrospective, and maternal recall can be inaccurate. The study does not delineate the time after initial exposure to regular ingestion of CM formula nor the amounts ingested. There may be an optimal time from initial exposure to regular introduction. A study by Katz Y et al (*J Allergy Clin Immunol*. 2010;126[1]:77–82) noted a window during which early regular consumption (in the first 14 days) was protective of IgE-CMA, but rates were also lower for any age other than introduction from 105–194 days. Randomized trials will be needed to better understand the role of very early introduction of CM, especially as this broaches the topic of exclusive breastfeeding.

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Two-step Egg Introduction for Prevention of Egg Allergy in High-risk Infants With Eczema (PETIT): A Randomized, Double-blind, Placebo-Controlled Trial

Natsume O, Kabashima S, Nakazato J, et al. *Lancet*. 2017; 389(10066):276–286

PURPOSE OF THE STUDY. The Prevention of Egg Allergy with Tiny Amount Intake is a double-blind, placebo-controlled trial that investigated the stepwise introduction of hen's egg and the optimal eczema treatment for preventing an egg allergy at the age of 1 year.

STUDY POPULATION. Healthy Japanese infants with eczema and without previous ingestion of or reactions to hen's egg ($N = 147$) were randomized (1:1, stratified by institution and sex) at the ages of 4–5 months to consume either egg or a placebo.

METHODS. Infants in the egg group consumed 50 mg of heated egg powder per day from ages 6–9 months and consumed 250 mg per day from ages 9–12 months. Infants in the placebo group consumed squash powder with matched color and volume. At the age of 12 months, the proportion of infants with an egg allergy in each group was confirmed by open food challenges to 7 g of egg powder. Sensitization to egg was measured by egg-

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