specialist alike to pursue a detailed history of the adverse event and to obtain diagnostic testing when indicated. This approach is now one of the recommended interventions issued by the American Academy of Allergy, Asthma, and Immunology as part of the "Choosing Wisely" campaign.

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Anne-Marie Irani, MD
Richmond, VA

Assessing the Diagnostic Properties of a Graded Oral Provocation Challenge for the Diagnosis of Immediate and Nonimmediate Reactions to Amoxicillin in Children

Mill C, Primeau MN, Medoff E, et al. *JAMA Pediatr*. 2016;170(6):e160033

PURPOSE OF THE STUDY. To assess the accuracy and the negative predictive value of the provocation challenge in a cohort of children referred to a single center with suspected amoxicillin allergy.

STUDY POPULATION. Children with suspected amoxicillin allergy who were referred to the Montreal Children's Hospital in Quebec, Canada, between March 1, 2012, and April 1, 2015, were recruited. Exclusion criteria were any reactions compatible with either Stevens-Johnson syndrome or toxic epidermal necrolysis.

METHODS. Children with a prior history of rash while receiving amoxicillin were administered oral drug challenges (10% of the therapeutic dose, then 90% of the dose 20 minutes later [ie, 50 mg/kg per dose to a maximum of 1.5g]). All children were observed for at least 1 hour after receiving their last dose. Only those with positive challenge results underwent skin testing (prick and intradermal) and were offered a subsequent graded provocation challenge to cefixime (3rd-generation cephalosporin). Univariate and multivariate logistic regressions were compared with determining factors associated with immediate (<1 hour) and nonimmediate reactions (>1 hour) to the provocation challenge.

RESULTS. Of 818 children assessed (median age of 1.7 years [interquartile range 1.0–3.9 years]; 441 [53.9%] male), 771 (94.1%) tolerated amoxicillin without any reaction, 17 (2.1%) developed immediate reactions (all were hives only; 5 reacted to initial 10%), and 31 (3.8%) developed nonimmediate reactions (maculopapular rashes and serum sickness–like reactions). For the 17 children who developed immediate reactions, skin tests were performed 2–3 months later with penicillin and the penicilloyl (major) determinant; the skin test was positive in only 1 patient (5.9%). All 17 tolerated cefixime. The graded amoxicillin challenge had a negative predictive value of 89.1% (95% CI, 77.1%–95.5%). A history of a reaction occurring within 5 minutes of exposure was associated with immediate reactions to amoxicillin. A rash that lasted longer than 7 days and parental history of drug allergy were associated with nonimmediate reactions to amoxicillin.

CONCLUSIONS. Graded provocation challenges provide an accurate and safe confirmatory test for skin-related reactions to amoxicillin. Further studies are required to assess factors associated with outcomes.

REVIEWER COMMENTS. Over half of the children enrolled in the study had their reaction to amoxicillin with their first exposure; such reactions are less likely to be immune mediated. Moreover, none had a history of anaphylaxis. Thus, these results may be applied to pediatric cases presenting with cutaneous, nonanaphylactic reactions.

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Jennifer S Kim, MD
Chicago, IL

FOOD ALLERGY

Impact of Peanut Consumption in the LEAP Study: Feasibility, Growth, and Nutrition

Feeney M, Du Toit G, Roberts G, et al. *J Allergy Clin Immunol*. 2016;138(4):1108–1118

PURPOSE OF THE STUDY. To evaluate the feasibility of peanut (PN) introduction in infancy and its effects on growth and nutrition.

STUDY POPULATION. This study was a planned secondary analysis from the LEAP trial (*N Engl J Med*. 2015;372:803–813), in which 4- to 11-month-old infants who tolerated PN were advised to eat 6 g of peanut protein per week to age 5 years. The control population included infants who did not tolerate PN during the LEAP trial.

METHODS. PN consumption was monitored by using a validated questionnaire. Anthropomorphic measurements were taken and 3-day food diaries completed for each study visit. Average daily caloric intake and that of macro- and micronutrients were calculated.

RESULTS. The median age at screening was 7.8 months. Median peanut consumption exceeded 6 g throughout the study. Peanut introduction in infancy did not shorten the duration of breastfeeding. There was no difference between groups in weight, height, BMI, tricep skinfold thickness, or other anthropomorphic measurements. Total caloric intake was the same between groups. The percent of energy from carbohydrates was higher in the avoidance group at all time points, whereas the percent of energy from fat was higher in the PN consumption group, especially in the upper quartiles of consumption. The percent of energy from protein was comparable between groups. Similarly, there were no differences in the intake of sodium, calcium, iron, zinc, or vitamin D.

CONCLUSIONS. Early dietary introduction of peanut in high-risk infants who tolerate it has no effect on the duration of breastfeeding, growth, or nutrition.

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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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Mitchell R. Lester, MD
Norwalk, CT

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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Jennifer A. Dantzer, MD
Robert A. Wood, MD
Baltimore, MD

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).

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Impact of Peanut Consumption in the LEAP Study: Feasibility, Growth, and Nutrition

Mitchell R. Lester

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Mitchell R. Lester

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