including skin-prick testing (SPT) to food allergens; total and specific serum immunoglobulin E (IgE) levels; serum IgA, IgG₄, and IgG₄ antibodies to ovalbumin and β-lactoglobulin; total IgA levels; and saliva IgA levels. At study completion, children were categorized as being egg or milk tolerant if the food was reintroduced into the diet after passage of a challenge in the clinic or at home.

RESULTS. Of the 89 participating children, 60 were prescribed elimination diets that were based on SPT results, as follows: 24 egg, 11 milk, and 25 both. At study completion (4.5 years of age), 37 of 49 previously egg-allergic and 11 of 36 previously milk-allergic children were considered to be tolerant. Children who were egg or milk tolerant at 4.5 years of age had significantly higher levels of ovalbumin- or β-lactoglobulin-specific IgG₄ at enrollment, respectively. Tolerant children also had higher food-specific IgG₄/IgE ratios at 4.5 years. The highest IgG₄/IgE ratios were found in children who had circulating milk- and/or egg-specific IgE antibodies but negative SPT results at enrollment. There was no significant difference between total or food-specific IgE levels at enrollment between the tolerant and non-tolerant groups; however, children in the tolerant group had significantly lower food-specific IgE antibodies at 4.5 years, compared with those in the nontolerant group. There were no significant differences in total IgA, saliva IgA, or food-specific IgA levels between groups at enrollment or at 4.5 years.

CONCLUSIONS. High food-specific IgG₄ antibodies at <2 years of age and high IgG₄/IgE ratios were related to oral tolerance to milk and egg at 4.5 years of age.

REVIEWER COMMENTS. This study demonstrates that early immunologic markers may be indicators of oral tolerance acquisition among a subset of children with eczema and milk and/or egg allergy. These data may be useful in conjunction with other measures such as serum-specific IgE levels, history of past reactions, and SPT to predict future oral tolerance acquisition. One weakness of the study was the fact that participants did not undergo a diagnostic food challenge to confirm clinical reactivity at enrollment, and recommendations for food elimination were made on the basis of SPT results. It is likely that elimination diets were prescribed for some participants who were actually clinically tolerant at enrollment despite having a positive SPT result. Future studies to determine the utility of immunologic markers should confirm clinical reactivity by performing a diagnostic food challenge or confirming a convincing history of past reactions.

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The Use of Serum-Specific IgE Measurements for the Diagnosis of Peanut, Tree Nut, and Seed Allergy

PURPOSE OF THE STUDY. The authors of this study sought to determine the usefulness of peanut-, tree nut-, and seed-specific immunoglobulin E (IgE) measurements for the diagnosis of symptomatic allergies and to learn more about the relationships among these foods.

STUDY POPULATION. Children and adults (N = 324) referred to a private allergy practice and to an academic center allergy clinic for evaluation of suspected IgE-mediated peanut, tree nut, or seed (sesame seed, mustard seed, poppy seed, rapeseed, and cottonseed) hypersensitivity were enrolled in the study. Patients ranged in age from 2.4 months to 40.2 years (median: 6.1 years). The male/female ratio was 198:126. Atopic dermatitis occurred at some point in life in 57% and asthma in 58%. Many had or “outgrew” other food allergies.

METHODS. Patients answered a questionnaire about their perceived food allergies. Allergen-specific diagnoses were based on questionnaire, medical history, and, when relevant, skin-prick test results and serum-specific IgE levels. Sera were analyzed for specific IgE to peanuts, tree nuts, and seeds by ImmunoCAP (Phadia AB, Uppsala, Sweden).

RESULTS. Seventy-two percent of the patients had convincing histories of peanut allergy. Of these, 86% had sensitization to ≥1 tree nut, with 34% having clinical allergy. The majority of study patients had never ingested tree nuts, which made it difficult to determine the true prevalence of these nut allergies. Tree nut clinical allergy occurred with a frequency ranging from 16.4% for walnut to 1.5% for Brazil nut. Seventeen percent of the patients reported reactions to sesame seed. The ranges of increased serum-specific IgE levels for each food varied widely among patients with positive histories. The relationship between diagnoses and allergen-specific IgE levels was estimated through logistic regression, with curves illustrating the likelihood of receiving a positive clinical diagnosis in relation to the specific IgE concentration. Positive predictive values (95%) were established for peanut and walnut (13 and 18.5 kUA/L, respectively) but with sensitivities of just 60% and 17%, respectively. High correlations were found between IgE results for walnut and pecan and between those for cashew and pistachio.

CONCLUSIONS. Quantification of food-specific IgE is a valuable tool that can aid in the diagnosis of symptomatic food allergy and might decrease the need for double-blind, placebo-controlled, food challenges.
In Vitro and In Vivo Cross-reactivity Studies of Legume Allergy in a Mediterranean Population

PURPOSE OF THE STUDY. Legume allergy, mainly to lentils and chickpeas, is the fifth most common cause of food allergy in Spanish children. Serological cross-reactivity among legumes is frequent, but its clinical relevance is controversial. The aim of this study was to investigate the cross-reactivity among lentils, chickpeas, peas, white beans, and peanuts and its clinical relevance in pediatric patients.

STUDY POPULATION. Fifty-four children with clinical allergy to legumes were included.

METHODS. Cross-reactivity was evaluated with enzyme-linked immunosorbent assay inhibition experiments and oral food challenges to legumes. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis immunoblots were conducted with raw and boiled legume extracts.

RESULTS. Enzyme-linked immunosorbent assay inhibition experiments demonstrated >80% inhibition with lentil, chickpea, and pea extracts. Immunoblots performed with raw legume extracts (lentil, chickpea, and pea) and individual sera revealed that >50% of the sera identified an allergen of ~50 kDa in all 3 legume extracts. In all 3 boiled extracts, an intense band at ~50 kDa was visualized by using a serum pool. The oral legume challenges demonstrated that 37 children (69%) were allergic to ≥2 legumes (median: 3 legumes). The most frequent associations were allergy to lentils and chickpeas (57%), allergy to lentils and peas (54%), and allergy to lentils, chickpeas, and peas (43%).

CONCLUSIONS. In vitro inhibition experiments demonstrated a high degree of cross-reactivity among lentils, chickpeas, and peas. Food challenges confirmed that clinical allergy to all 3 legumes is frequent in this cohort of Spanish children.

REVIEWER COMMENTS. Although legumes are not major allergens in the United States and some European countries, they are a common cause of food allergies in Mediterranean countries. The authors demonstrated that, in their group of Spanish children, there was a high degree of in vitro and in vivo cross-reactivity among legumes, which is in contrast to North American children, in whom clinical reactivity to >1 legume is considered to be infrequent (eg, children with peanut allergy typically tolerate most legumes). These contrasting results highlight the fact that genetic and dietary influences (among other factors) can have significant influences on food allergy. Additional studies are needed to elucidate the contribution of dietary habits and genetics to food allergy.

Epidemiology of Atopy Patch Tests With Food and Inhalant Allergens in an Unselected Population of Children

PURPOSE OF THE STUDY. The atopy patch test (APT) has been used as a diagnostic tool for patients with suspected food or inhalant allergy. The authors of this study assessed the prevalence of positive APT results with food or inhalant allergens in an unselected population of schoolchildren. The authors also evaluated the link between positive APT reactions and skin-prick tests (SPTs) for food and inhalant allergens, circulating eosinophils, and histamine skin reactivity.

STUDY POPULATION. The study included an unselected population of 380 children 9 or 13 years of age living in Rome, Italy.

METHODS. APTs were carried out with food (native or standardized) and inhalant allergens. All children also underwent SPTs with 5 common inhalant and 4 food allergens.

RESULTS. The prevalence of positive APT reactions for foods in unselected children ranged between 4% and 11% for hen’s egg, tomato, and wheat flour and was similar for the 2 age groups studied. The prevalence of
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