

Researchers in this study investigated whether egg component-resolved diagnostic (CRD) technology could predict baked egg tolerance and development of tolerance to egg. Ovalbumin (Gal d 2) is the most abundant protein in egg white and is heat labile. Ovomuroid (Gal d 1) makes up a smaller percentage of protein in egg white but may be more significant because it is resistant to heating. The role of sensitization to Gal d 3 and egg yolk allergen Gal d 5 has not been well characterized.

**STUDY POPULATION:** A subset of 451 subjects from the HealthNuts cohort were selected for this study. HealthNuts is a large population-based sample of 5276 Australian children recruited at age 1 year. Peanut and egg allergy were determined by oral food challenge.

**METHODS:** A total of 297 children with egg allergy had positive egg challenge results and were egg sensitized by a skin prick test (SPT) wheal >2 mm. This group was compared with 154 egg-tolerant children who passed egg challenge (57 had negative SPT results and 97 showed sensitization with an SPT wheal <2 mm). All children with egg allergy at 12 months of age were invited to participate in an additional baked egg oral food challenge. At 2 and 4 years of age, children with egg allergy had repeat egg challenge, SPTs, and specific immunoglobulin E (sIgE) tests (including CRD test for egg, which included Gal d 1, 2, 3, and 5 using ImmunoCAP). The association between egg allergen component sIgE and the risk of raw, baked, and persistent egg allergy was studied by generating the receiver operating characteristic (ROC) curve on the basis of sensitivities and specificities for a range of cutoff values for sIgE measurements. The area under the curve (AUC) along with 95% confidence intervals (CIs) were calculated.

**RESULTS:** To determine egg allergy at 1 year of age, Gal d 1 sIgE and Gal d 2 sIgE provided ROC curves with AUC values of 0.83 (95% CI: 0.81–0.87) and 0.63 (95% CI: 0.60–0.67), respectively, whereas the AUC of egg white sIgE was 0.89 (95% CI: 0.85–0.92). To determine baked egg allergy at 1 year of age, sIgE to Gal d 1 and Gal d 2 provided ROC curves with AUC values of 0.65 (95% CI: 0.61–0.70) and 0.77 (95% CI: 0.73–0.81), respectively, whereas egg white sIgE generated an ROC curve with an AUC of 0.80 (95% CI: 0.76–0.84). Gal d 1 sensitization increased risk of persistent egg allergy by 2.5-fold. The presence of sIgE to all 4 egg allergens increased the risk of persistent egg allergy fourfold (95% CI: 1.25–14.07).

**CONCLUSIONS:** Egg CRD testing offers no advantage over egg white sIgE for evaluating raw egg allergy and baked egg allergy at 1 year of age. Sensitization to multiple egg allergens Gal d 1, 2, 3, and 5 increases risk of persistent raw egg allergy.

**REVIEWER COMMENTS:** Baked egg challenges are frequently conducted when evaluating infants and young toddlers

with egg allergy. Unfortunately, egg CRD testing does not appear to be any more helpful than egg white sIgE when selecting appropriate children for baked egg food challenges. There does not appear to be a role for routinely obtaining egg CRD testing when evaluating children with histories of adverse egg reactions.

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## Differences in Egg and Milk Food Challenge Outcomes Based on Tolerance to the Baked Form

Capcuilli P, Cianferoni A, Fiedler J, et al. *Ann Allergy Asthma Immunol.* 2018;121(5):580–587

**PURPOSE OF THE STUDY:** To determine if a history of tolerance versus avoidance of baked egg or cow's milk influenced the outcomes of an oral food challenge to egg or whole cow's milk.

**STUDY POPULATION:** The study included 569 pediatric patients who underwent egg or cow's milk oral challenges at the Children's Hospital of Philadelphia from 2012 to 2015.

**METHODS:** This was a retrospective chart review of pediatric patients who underwent whole egg and cow's milk oral food challenges.

**RESULTS:** More patients passed the whole egg food challenge if they previously tolerated baked egg (75%) versus avoidance (58%,  $P = .01$ ) or never ingested (45%,  $P < .0001$ ). Among the positive reactions, those patients who tolerated baked egg reacted at higher doses (3.0 g) and required epinephrine less often (10%) than those patients with egg avoidance (0.69 g,  $P = .03$ ; 22%,  $P = .02$ ) or who never ingested (0.88 g,  $P = .01$ ; 32%,  $P = .0001$ ). No difference was found among patients with cow's milk allergy. Those who never ingested egg or cow's milk had the poorest oral food challenge outcomes and the highest rates of atopic dermatitis (66% for patients with egg allergy and 86% for patients with milk allergy).

**CONCLUSIONS:** This study shows that children who were known to be able to tolerate baked egg had higher food challenge pass rates (tolerance). Additionally, in those patients who did react, they were able to tolerate higher doses and had less-severe reactions if they previously tolerated baked egg. This association was not observed with patients with cow's milk allergy.

**REVIEWER COMMENTS:** Known tolerance of baked egg may be a helpful marker for identifying children who will have more favorable food challenge outcomes. Although the effects of including baked egg in the diet on altering the natural history of egg allergy remains inconclusive,

the results of this study support that tolerance of baked egg may help to promote tolerance of concentrated egg. Patients should be evaluated by an allergist early to possibly allow for introduction of baked egg into the diet. If baked egg tolerance has been established, the pediatrician can encourage parents to continue it in the diet. Further studies are needed to determine if the same benefit may be seen with cow's milk and identify markers for favorable food challenge outcome.

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### Oral Food Challenge Failures Among Foods Restricted Because of Atopic Dermatitis

Eapen AA, Kloepfer KM, Leickly FE, Slaven JE, Vitalpur G. *Ann Allergy Asthma Immunol.* 2019;122(2):193-197

**PURPOSE OF THE STUDY:** To evaluate the frequency of office-based oral food challenge (OFC) failures to previously tolerated foods eliminated from diets to treat atopic dermatitis (AD) based on positive skin prick test (SPT) results and/or specific immunoglobulin E (sIgE) testing.

**STUDY POPULATION:** A total of 442 patients were included who had undergone OFCs to peanut, wheat, soy, milk, and egg (the top 5 allergens in the United States) at the allergy clinics of Riley Hospital for Children at Indiana University Health from 2008 to 2014.

**METHODS:** By retrospective chart review, subjects were classified into 3 groups according to the reason for food avoidance, as follows: food allergy (defined as typical signs of an allergic reaction within 2 hours of ingestion, with supporting SPT or sIgE results), sensitization without introduction (food item never introduced because of positive SPT and/or sIgE results found during evaluation for AD or other food allergies), and avoidance based on positive SPT and/or sIgE test results found during AD workup (all had previously tolerated the food without reaction within 2 hours). OFCs were offered if the subject had sIgE levels predicting passing the OFC on the basis of 95% positive predictive values and no reaction to the food in the last 12 months. Plain and extensively heated milk OFCs were grouped together, as were those for egg. Extensively heated food challenges were offered regardless of sIgE levels. Total IgE levels were not reported.

**RESULTS:** Indications for OFCs were a history of food allergy (320 of 442, 72.4%) and sensitization (77 of 442, 17.4%) and AD (45 of 442, 10.2%). There were no significant differences among these 3 groups at OFC in age, sex, race, asthma, allergic rhinitis, or percentage of positive SPT results to the food. The overall OFC failure rate was 20.1%, including 21.9% of the food allergy group, 16.9%

of the sensitization group, and 13.3% of the AD group, which was not statistically significant comparing groups ( $P = .30$ ). There was no significant difference with regard to OFC pass and fail rates among the 5 foods challenged or the length of time of food avoidance (range: 3-120 months,  $P = .97$ ). Wheat was significantly more likely to be avoided because of AD ( $P < .001$ ), and milk was likely to be avoided because of food allergy ( $P = .002$ ).

**CONCLUSIONS:** In this study, 13.3% of children with AD who had removed a previously tolerated food from their diet because of a positive SPT and/or sIgE test result failed an OFC to that food in as quickly as after 3 months of avoidance. This demonstrates the potentially rapid loss of tolerance that can occur with food elimination for AD therapy and bolsters evidence that SPT and/or sIgE test results in patients with AD who do not have a history of immediate reaction to the foods tested are often clinically irrelevant.

**REVIEWER COMMENTS:** Data on the role of food triggers in AD have been conflicting, but overall there is lack of high-quality evidence. Aggressive skin care regimens should be pursued over elimination diets, which carry the risk of loss of tolerance to a food previously consumed without immediate reaction.

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### Long-term Follow-up After Baked Milk Introduction

Dunlop JH, Keet CA, Mudd K, Wood RA. *J Allergy Clin Immunol Pract.* 2018;6(5):1699-1704

**PURPOSE OF THE STUDY:** Introduction of baked milk (BM) to children with milk allergy is associated with accelerated resolution of milk allergy. This study was designed to characterize the clinical experience of one center with the introduction of BM and other forms of milk after challenge, including the relations of prechallenge and in-challenge characteristics with future successful milk introduction, as well as safety.

**STUDY POPULATION:** The population included 206 children with milk allergy who had undergone a BM challenge in this center from 2009 to 2014 and who had at least 24 months of follow-up.

**METHODS:** Methods included retrospective chart review or telephone follow-up. Protocol includes an advancement in dose as tolerated over time if the starting dose is  $<2$  g of BM. After consuming 2 g of BM 3 to 5 times per week for 2 to 3 months, patients are permitted to advance their milk ingestion to less-heated forms of milk (such as pancakes and waffles), then oven-baked cheese, then uncooked dairy products, as tolerated.

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Jennifer Pier and Theresa Bingemann

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