Children with seafood allergy have a higher incidence of other atopic diseases compared with peanut-allergic children. Children with fish allergy may be able to tolerate canned fish, but tolerance must be proven first.

REVIEWER COMMENTS. This study offers important advice for the clinical management of seafood allergy. This study also offers additional evidence that children with fish allergy may also be allergic to shellfish. Shortcomings of this study include a lack of standardized skin test panels to evaluate cross-reactivity and other allergic sensitivities that may be related.


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Ovomucoid (Gal d 1) Specific IgE Detected by Microarray System Predict Tolerability to Boiled Hen’s Egg and an Increased Risk to Progress to Multiple Environmental Allergen Sensitisation

PURPOSE OF THE STUDY. To evaluate the usefulness of the molecular diagnostic approach in children with suspected hen’s egg (HE) allergy, the response to skin prick test by using the white boiled HE, and specific immunoglobulin E (IgE) to HE allergens (Gal d 1, Gal d 2, Gal d 3, and Gal d 5).

STUDY POPULATION. The study included 68 children, ranging from 1 to 11 years of age, enrolled at the Centre for Molecular Allergology in Rome, Italy. All patients were referred for suspected HE allergy.

METHODS. Double blind, placebo-controlled HE challenges were performed by using boiled eggs, and if these were tolerated, challenges were performed with raw eggs. Subjects were placed in 3 groups: group A (allergic) subjects were clinically reactive to boiled egg and were considered likely to be reactive to raw egg; group PT (partially tolerant) reacted to raw egg but tolerated boiled egg; and group ST (sensitized but tolerant) subjects were sensitized with HE and were referred for suspected HE allergy.

RESULTS. Subjects were assigned as follows: group A, 19 subjects (28%); PT, 14 (20.5%); and ST, 35 (51.4%). Most (44 of 47, 94%) Gal d 1 negative patients tolerated boiled egg. Conversely, 20 of 21 Gal d 1 positive patients (95%) reacted to raw egg.

CONCLUSIONS. Gal d 1 negative children (specific IgE = 0 kU/L) showed a high frequency of tolerance to boiled egg (94%), whereas Gal d 1 positive children (>0 kU/L) showed a high frequency of raw HE allergy (95%). Therefore, Gal d 1 IgE results seem to be a useful tool to predict oral tolerance to boiled eggs.

REVIEWER COMMENTS. In recent years, there has been great interest in the measurement of the response to individual allergens, rather than whole extracts, in the management of allergic diseases. This study identifies 1 such allergen, Gal d 1, as a very useful marker for identifying whether a patient may tolerate boiled egg. It should be pointed out that although Gal d 1 performance was a helpful tool, it was <90% sensitive in identifying subjects allergic to boiled egg. A negative Gal d 1 would likely not be a definitive test obviating the need for physician-supervised oral food challenge in a patient with suspected HE allergy. The test used, which is not yet Food and Drug Administration cleared, measures many different allergens, and so one must be careful to avoid diagnosing an allergy based on a sensitization that most often may not be clinically relevant.


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Significance of Ovomucoid- and Ovalbumin-Specific IgE/IgG4 Ratios in Egg Allergy

PURPOSE OF THE STUDY. To determine the functional significance of immunoglobulin (Ig)G4 antibodies to ovalbumin (OVA) and ovomucoid (OVM) in egg-allergic children.

STUDY POPULATION. Data from 117 egg-allergic children from a study of tolerance to baked egg were investigated.

METHODS. Tolerance to baked egg was defined by oral food challenge (OFC) and was the reference parameter. Serum antibody measurements for egg white, OVM, and OVA IgE and IgG4 were performed with the UniCAP system (Phadia US, Portage, MI). Serum mediator release assays were performed on 10 baked-egg reactive children and 9 baked-egg tolerant children by using rat basophil leukemia cells transfected with human Fce receptor I. These were sensitized with human sera and then stimulated with various concentrations of egg white, OVM, and OVA followed by measurement of N-Hexosaminidase in the supernatant as a marker of mediator release.

RESULTS. OVA- and OVM-specific IgE/IgG4 ratios were significantly higher in baked-egg-reactive subjects than in those who were tolerant (P = .001 and P = .003,
Dietary Baked Milk Accelerates the Resolution of Cow’s Milk Allergy in Children

PURPOSE OF THE STUDY. To evaluate outcomes of children with cow’s milk allergy that incorporate extensively heated (baked) milk products into the diet.

STUDY POPULATION. Eighty-nine subjects aged 0.5 to 21 years were recruited from a large academic pediatric allergy clinic. Subjects were diagnosed with milk allergy based on a positive skin prick test (SPT) or detectable serum milk-specific immunoglobulin (Ig) E and history of allergic reaction to milk. Subjects were also included if milk-specific IgE or SPT responses were >95% of predicted value for clinical reactivity.

METHODS. Subjects underwent an initial baked milk oral challenge with a muffin containing 1.3 g of milk protein baked at 350°F for 30 minutes. Subjects who were reactive to baked milk (n = 23) were instructed to completely avoid all forms of milk and were offered a repeat challenge ≥6 months from the initial challenge. Patients who were tolerant to baked milk (n = 65) were instructed to incorporate baked milk products daily into their diets. After ≥6 months, these patients were offered challenges to baked cheese products (cheese pizza with 4.6 g of milk baked at 425°F for >13 minutes). After 6 months of tolerating baked cheese, subjects were offered challenges to unheated milk. A historical comparison group of subjects who fulfilled the inclusion criteria but were not initially ingesting baked milk was included.

RESULTS. Challenges were conducted over a median of 37 months (range: 8–75 months). In the group of 65 subjects initially tolerant to baked milk, 39 (60%) now tolerated unheated milk. Over the same time period, 2 (9%) of the 23 subjects who were originally reactive to baked milk tolerated unheated milk. Subjects who were initially tolerant to baked milk were 28 times more likely to become unheated milk tolerant compared with baked milk–reactive subjects (P < .001). Subjects who introduced dietary baked milk were 16 times more likely than comparison group subjects to become unheated milk tolerant (P < .001). Median casein IgG4 levels in baked milk–tolerant group increased significantly (P < .001), but median milk IgE values did not change significantly.

CONCLUSIONS. Tolerance of baked milk suggests a transient IgE-mediated cow’s milk allergy. The addition of baked milk to the diet in children tolerating such foods appears to accelerate the development of unheated milk tolerance compared with strict avoidance.

Oral Desensitization as a Useful Treatment in 2-Year-old Children With Cow’s Milk Allergy

PURPOSE OF THE STUDY. To assess the safety and efficacy of an oral desensitization protocol in 2-year-old children with allergy to cow’s milk protein (CMP) as a therapeutic alternative to elimination diet.

STUDY POPULATION. Sixty patients aged 24 to 36 months with immunoglobulin (Ig) E-mediated allergy to CMP enrolled in this multicenter study. Inclusion criteria

respectively). Adding OVA- and OVM-specific IgG4 to a model with IgE alone resulted in better prediction of baked-egg tolerance. In addition, children with severe reactions during OFC who required epinephrine had higher IgE/IgG4 ratio to OVM and/or OVA. Baked-egg reactive children also had higher mediator release, and those with higher natural log transformed IgE/IgG4 ratio to OVA were more likely to have nonzero mediator release.

CONCLUSIONS. The balance between IgE and IgG4 to OVA and OVM has functional implications in baked-egg reactivity/tolerance. High IgE/IgG4 ratios to OVA and OVM are associated with baked-egg reactivity and anaphylaxis to baked and regular egg during OFC. Low IgE/IgG4 ratios to OVA and OVM are associated with tolerance.

REVIEWER COMMENTS. The implications of the role of specific IgG4 in the mechanism of tolerance is important in our understanding of food allergy. Further evaluation of food-specific IgE/IgG4 ratios is important before this can be used as clinical diagnostic tool, although the possibility is intriguing.

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