After cow’s milk, hen’s egg allergy is the second most common food allergy in infants and young children. The estimated prevalence of egg allergy varies depending on method of data collection or definition. A recent meta-analysis of the prevalence of food allergy estimated that egg allergy affects 0.5% to 2.5% of young children. The major limitation of this meta-analysis was significant variability in study design that made direct comparisons difficult. Most studies included in the meta-analysis were based on self-reports of food allergy, which tend to overestimate the prevalence. Some studies used skin prick test and food-specific IgE levels to confirm sensitization to the allergen; however, only 3 studies used double-blind, placebo-controlled food challenges, the gold standard, to confirm the diagnosis of food allergy. In these 3 studies of unselected populations, the prevalence of egg allergy ranged from 0.0004% in a cohort of German children aged up to 17 years, to 0.6% in nursery school children in Mexico, to 1.6% in 3-year-old Danish children. From Norway, Eggesbo and colleagues reported an estimated point prevalence of allergy to egg in children aged 2.5 years of 1.6% (confidence interval [CI] 1.3%–2.0%), with an upper estimate of the cumulative incidence by this age calculated roughly at 2.6% (CI 1.6%–3.6). A similar prevalence of 1.3% was reported from the United States. Although prevalence depends primarily on nutritional habits in different population, the heterogeneity in egg allergy prevalence may not reflect genuine difference between populations but may be related only to difference in the design and conduct of the primary studies. Egg allergy is closely associated with atopic dermatitis and was found to be present in about two-thirds of children with positive oral food challenges (OFC)
performed for allergy evaluation of atopic dermatitis. The risks of sensitization to aeroallergens and asthma are also increased in children with egg allergy.

**PATHOGENESIS**

Egg allergy may be defined as an adverse reaction of immunologic nature induced by egg proteins, and includes IgE antibody–mediated allergy as well as other allergic syndromes such as atopic dermatitis and eosinophilic esophagitis, which are mixed IgE-mediated and cell-mediated disorders. IgE-mediated food allergy, also known as type I food allergy, accounts for most of the food-induced responses and is characterized by the presence of allergen-specific IgE antibodies. Five major allergenic proteins from the egg of the domestic chicken (*Gallus domesticus*) have been identified; these are designated Gal d 1 to Gal d 5. Most of the allergenic egg proteins are found in egg white (*Table 1*), including ovomucoid (Gal d 1, 11%), ovalbumin (Gal d 2, 54%), ovotransferrin (Gal d 3, 12%), and lysozyme (Gal d 4, 3.4%). Although ovalbumin (OVA) is the most abundant protein in hen’s egg white, ovomucoid (OVM) has been shown to be the dominant allergen in egg.

The allergenicity of proteins depends mostly, but not exclusively, on their resistance to heat and digestive enzymes, reflecting their capacity to stimulate a specific immune response. To elicit a sustained immune response, the immunogen should ideally stimulate both T and B cells. The portion of the immunogen that binds specifically with membrane receptors on T or B cells is called an epitope, which can be sequential or conformational. Sequential epitopes are determined by contiguous amino acids, whereas conformational epitopes contain amino acids from different regions of the protein that are in close proximity because of the folding of the protein. Conformational epitopes can be destroyed with heating or partial hydrolysis, which alters the tertiary structure of the protein. Egg-specific IgE molecules that identify sequential or conformational epitopes of OVM and OVA can distinguish different clinical phenotypes of egg allergy. It has been shown that patients with egg allergy with IgE antibodies reacting against sequential epitopes tend to have persistent allergy, whereas those with IgE antibodies primarily to conformational epitopes tend to have transient allergy.

Egg proteins differ in their physical properties and can be related to different clinical patterns of egg allergy. The importance of OVM may be because of its unique characteristics such as relative stability against heat and digestion with proteinases, and its strong allergenicity, compared with other egg white components. These characteristics are possibly related to the presence of strong disulfide bonds that stabilize this highly glycosylated protein. In 2 different studies, children with persistent egg allergy had significantly higher specific IgE levels to OVM than children who outgrew their egg allergy. In the report by Jarvinen and colleagues, 7 patients with persistent egg allergy had IgE that recognized 4 sequential epitopes of OVM. In contrast, none of the 11 children with transient egg allergy had specific IgE to these epitopes. Gastric digestion has been shown to reduce the allergenicity of OVM, which can explain why some patients have skin contact reactions to egg, but not ingestion reactions.

In contrast, OVA epitopes are heat labile, suggesting that children who have specific IgE primarily to OVA are likely to tolerate heat-denatured forms of egg. However, using the sera from patients with egg allergy, reports have shown that the antigenicity of OVA could resist heat treatment in certain conditions. By using OVA, a recent study investigated the T-cell immunogenicity of chemically glycated proteins termed advanced glycation end products (AGEs), produced by the Maillard reaction that occurs between reducing sugars and proteins during thermal processing of foods. The glycation structures of AGEs are suggested to function as pathogenesis-
### Table 1
**Major egg white allergens**

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Common Name</th>
<th>Content (%)</th>
<th>Mw (kDa)</th>
<th>Carbohydrate (%)</th>
<th>Digestive</th>
<th>Heat Treated</th>
<th>Enzyme Treated</th>
<th>Allergenic Activity</th>
<th>Test Code (In Vitro Tests)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gal d 1</td>
<td>Ovomucoid</td>
<td>11</td>
<td>28</td>
<td>25</td>
<td>Stable</td>
<td>Stable</td>
<td>Stable</td>
<td>+++</td>
<td>f233</td>
</tr>
<tr>
<td>Gal d 2</td>
<td>Ovalbumin</td>
<td>54</td>
<td>45</td>
<td>3</td>
<td>Unstable</td>
<td>Unstable</td>
<td>Unstable</td>
<td>++</td>
<td>f232</td>
</tr>
<tr>
<td>Gal d 3</td>
<td>Ovotransferrin/</td>
<td>12</td>
<td>76.6</td>
<td>2.6</td>
<td>Unstable</td>
<td>Unstable</td>
<td>+</td>
<td>f323</td>
<td></td>
</tr>
<tr>
<td></td>
<td>conalbumin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gal d 4</td>
<td>Lysozyme</td>
<td>3.4</td>
<td>14.3</td>
<td>0</td>
<td>Unstable</td>
<td>Unstable</td>
<td>++</td>
<td>k208</td>
<td></td>
</tr>
</tbody>
</table>

*Data from Benhamou AH. State of the art for egg allergy. Allergy 2010;65:283–9.*
related immune epitopes in food allergy. They showed that T-cell immunogenicity of
OVA can be enhanced by the Maillard reaction, indicating a critical role for thermal
processing in the allergenicity of OVA.

In egg yolk, α-livetin (Gal d 5) is the major allergen and is involved in the bird-egg
syndrome, which is described later.28,29 Several other allergens have been identified
in egg yolk, including vitellenin (apovitellenin I) and apoprotein B (apovitellenin VI),
although their roles in food allergy remain unclear. Manufactured food products often
contain trace amounts of egg lecithin as emulsifiers, but ingestion of trace amounts of
egg lecithin is probably insufficient to elicit allergic reactions.14

Regarding non–IgE-mediated as well as mixed IgE-mediated and non–IgE-medi-
ated egg allergy, the pathogenesis is less clear. Egg allergy has been implicated as
a trigger for atopic dermatitis and allergic eosinophilic esophagitis. Only few cases
of enteropathy induced by egg are reported in the literature.

CLINICAL FEATURES

Allergy to hen’s egg usually presents in the second half of the first year of life, with
a median age of presentation of 10 months.30 This reflects the typical age of the first
dietary exposure to egg. It has been shown that most reactions occur on first known
exposure to egg, particularly in sensitized children with atopic dermatitis.31,32 The
development of sensitization in these patients may be caused by exposure in utero
33 or via exposure to egg proteins through maternal breast milk.34,35 Mouse models
suggest that sensitization may also occur via epicutaneous exposure (before gut
mucosa exposure) and may play a role in the development of atopic dermatitis and
asthma.36,37

IgE-mediated Reactions

IgE-mediated reactions are the most common type of allergic reactions to egg. Chil-
dren typically present with rapid onset of urticaria or angioedema, usually within
minutes to 2 hours after ingestion. Although cutaneous symptoms are most common,
immediate reactions involving the gastrointestinal or respiratory tracts are reported as
well. The severity of reactions can be unpredictable, potentially life threatening, and
can vary from episode to episode. Anaphylaxis can occur with exposure to egg,
and asthmatics, in particular, are at high risk for severe allergic reactions.38–40 Egg
accounted for 7% of severe anaphylactic reactions in infants and children in a German
survey.41 Fatal reactions to egg are rare, but have been reported.42 Ingestion of raw or
undercooked egg may trigger more severe clinical reactions than well-cooked egg.43

Egg allergy is also associated with other types of IgE-mediated allergies, mostly in
the adult population. Occupational asthma has been reported in bakery workers who
are frequently exposed to aerosolized egg and in people who work in factories that
process eggs.44 In bird-egg syndrome, the primary sensitization is to airborne bird
allergens and there is secondary sensitization or cross-reactivity with albumin in
egg yolk (Gal d 5). These patients experience respiratory symptoms such as rhinitis
and/or asthma with bird exposure and allergic symptoms when egg is ingested.29,45

Food-dependent, exercise-induced anaphylaxis with egg as the trigger has also
been reported.46

Mixed and Non–IgE-mediated Reactions

Egg proteins not only trigger IgE-mediated allergy, but can also be involved in non–
IgE-mediated and mixed IgE-mediated and non–IgE-mediated reactions. These disor-
ders include atopic dermatitis and the eosinophilic gastroenteropathies.
Atopic dermatitis
Egg allergy can manifest as atopic dermatitis, especially in infants and young children. In an international multicenter study of children with atopic dermatitis, egg sensitization was found to be closely associated with early-onset, moderate-to-severe atopic dermatitis. A small randomized trial of egg avoidance in children with egg sensitization and atopic dermatitis found that egg elimination decreases the extent and severity of the skin symptoms, showing the clinical relevance of egg sensitization in these patients. Isolated delayed reactions (i.e., flares of atopic dermatitis usually after 6 to 48 hours) are suggestive of non–IgE-mediated reactions and are likely caused by T-cell-mediated mechanisms. Late reactions are more difficult to identify. A combination of immediate allergy symptoms and delayed skin reactions is also described in a significant proportion of children. More than 10% of the children who reacted to an OFC developed isolated atopic dermatitis flares after 16 hours or later.

The combination of egg allergy and atopic dermatitis is a risk factor for asthma. In a small cohort of children with both these allergic conditions, 80% also suffered from asthma. Children with asthma are at increased risk for more severe allergic reactions to foods.

Gastroenteropathies
A small number of children with egg allergy present with gastrointestinal symptoms, including allergic eosinophilic esophagitis (EoE). This inflammatory disorder is characterized by high numbers of intraepithelial eosinophils in the esophagus and is mediated by mixed IgE-mediated and non–IgE-mediated processes. Egg was found to be the second most common allergen triggering symptoms in a series of more than 500 patients with EoE. This was confirmed on endoscopy after allergy evaluation with skin prick testing and patch testing. Elimination of food triggers has been found to be an effective treatment of EoE.

Food protein–induced enteropathy caused by egg has been reported. A 5-month-old boy developed protein-losing enteropathy and hypogammaglobulinemia, which was triggered by egg exposure in maternal breast milk. After maternal elimination of egg, resolution of symptoms occurred. Furthermore, reintroduction of egg into the maternal diet caused recurrence of symptoms. Recently, food protein–induced enterocolitis syndrome to egg has also been reported.

DIAGNOSIS
The diagnostic workup of suspected food allergy should start with a detailed history and physical examination of the patients. The next step may include in vitro and/or in vivo allergy tests that are used to support the diagnosis of egg allergy. These tests may include measurement of food-specific IgE antibodies, skin prick tests, atopy patch test, diagnostic elimination diet, and/or OFC. These different diagnostic tools are discussed later, with a focus on the diagnosis of egg allergy.

IgE-mediated Reactions
The history of an immediate reaction consistent with typical allergic symptoms, supported by evidence of specific IgE antibodies, establishes the diagnosis. Either skin prick tests or in vitro tests for IgE are usually performed initially.

Skin prick testing is a quick, useful test for determining the presence of specific IgE antibodies to egg. Traditionally, taken with a good clinical history, cutoff levels for skin prick test wheal size of 3 mm or greater than the negative saline control have been used to support a clinical diagnosis. Higher cutoff levels have been proposed, which are associated with higher specificity and positive predictive values, although in
younger children (<2 years) smaller skin prick test wheals are more likely to be predictive of egg allergy than in older children. Specifically, a wheal size of 5 mm or greater has been reported to provide a 100% positive predictive value (PPV) for children less than 2 years of age, whereas for older children, a wheal size of 7 mm has a reported 100% PPV. (Table 2). Children with test results greater than these cutoffs are presumed to be clinically reactive, and OFC are avoided in these cases. Because of a high negative predictive value (91% for skin prick test <3 mm), a negative prick test can be helpful to rule out an allergy to egg. Skin prick testing has low specificity, therefore isolated positive tests in the absence of clinical suspicion may not indicate clinical allergy.

Egg white–specific IgE can be measured using standardized, in vitro IgE assays providing a quantitative measurement. There is a positive correlation between increasing levels of egg white–specific IgE and the likelihood of clinical reactivity to egg. A range of predictive cutoff values for the diagnosis of egg allergy have been proposed. Studies using the ImmunoCAP (Phadia, Uppsala, Sweden) have shown that an IgE level of 7 kUA/L to egg has a 95% PPV for clinical reactivity to egg for children more than 2 years of age; for children 2 years of age or less, a level of 2 kUA/L has a 95% PPV. Although there is a demonstrable relationship between serum IgE levels and challenge outcome, there is poor agreement between cutoff levels identified by different centers. This may be because of differences in inclusion criteria, significance level, challenge method and outcome criteria, subject age, and prevalence of egg allergy and eczema between studies. These variables should be taken into account when interpreting cutoff levels for any given patient population. Similar to skin prick testing, the measurement of specific IgE to egg in the absence of a history of egg ingestion is discouraged because the test has poor sensitivity and low negative predictive value. The presence of undetectable IgE levels to egg (<0.35 kUA/L) does not exclude clinical reactivity to egg.

It has been suggested that quantification of OVM antibodies could be useful in guiding the physician in deciding whether to perform an OFC. Recently published data suggest that a concentration of IgE antibodies to OVM higher than approximately 11 kUA/L (positive decision point) indicates a high risk of reacting to heated (as well as

<table>
<thead>
<tr>
<th>References</th>
<th>Year</th>
<th>Age Group (y)</th>
<th>Number of Patients</th>
<th>PPV</th>
<th>SPT Wheal Diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sampson and Ho</td>
<td>1997</td>
<td>Children and adolescents</td>
<td>100</td>
<td>85</td>
<td>≥3</td>
</tr>
<tr>
<td>Sporik et al</td>
<td>2000</td>
<td>&lt;2</td>
<td>39</td>
<td>100</td>
<td>≥5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;2</td>
<td>82</td>
<td>≥7</td>
<td></td>
</tr>
<tr>
<td>Boyano-Martinez et al</td>
<td>2001</td>
<td>&lt;2</td>
<td>81</td>
<td>93</td>
<td>≥3</td>
</tr>
<tr>
<td>Hill et al</td>
<td>2004</td>
<td>&lt;2</td>
<td>90</td>
<td>100</td>
<td>≥5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;2</td>
<td>555</td>
<td>≥7</td>
<td></td>
</tr>
<tr>
<td>Verstege et al</td>
<td>2005</td>
<td>All children (range 0.3–14.5)</td>
<td>160</td>
<td>95</td>
<td>≥13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;1</td>
<td>26</td>
<td>≥11.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;1</td>
<td>134</td>
<td>≥13.3</td>
<td></td>
</tr>
</tbody>
</table>

less-heated or undercooked) egg. A concentration lower than approximately 1 kUA/L (negative decision point) suggests that there is a low risk of reaction to heated egg, even if the patients might well react to less-heated or undercooked egg. Further studies are required to confirm these data in other populations, and this test is not currently used in practice.

Although these tests provide an indication of likelihood of clinical reactivity to egg, neither is able to predict the severity of allergic reactions that may occur with each individual, nor the natural history of the allergy. However, the rate of decline of specific IgE levels with time is a prognostic indicator for the development of tolerance.

Standardized, double-blind, placebo-controlled OFCs remain the gold standard for the diagnosis of food allergy. A physician-supervised OFC is required if the history and/or IgE test results do not clearly indicate an allergy. OFC should always be performed by well-trained physicians and health personnel, and emergency equipment must be readily available. The food is gradually administered with increasing doses because it may cause immediate, potentially severe, symptoms.

**Asthma**

The diagnosis of suspected occupational asthma caused by egg allergy, which is also IgE mediated, involves skin prick testing, pulmonary function testing, and possible bronchoprovocation challenge.

**Mixed IgE-mediated and Non–IgE-mediated Disorders**

Skin prick test and specific IgE test are useful for detecting an IgE-mediated sensitization, but do not provide information regarding non–IgE-mediated mechanisms of allergy. For mixed IgE-mediated disorders, including atopic dermatitis or allergic gastrointestinal disorders, the results need to be correlated with the clinical picture.

---

**Table 3**

Diagnostic decision points for egg-specific serum IgE levels (Pharmacia ImmunoCAP)

<table>
<thead>
<tr>
<th>References</th>
<th>Year</th>
<th>Age Group (y)</th>
<th>Challenge</th>
<th>PPV</th>
<th>Egg-Specific IgE (kUA/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sampson and Ho&lt;sup&gt;64&lt;/sup&gt;</td>
<td>1997</td>
<td>Children and adolescents</td>
<td>126</td>
<td>95</td>
<td>6.0</td>
</tr>
<tr>
<td>Boyano-Martinez et al&lt;sup&gt;30&lt;/sup&gt;</td>
<td>2001</td>
<td>0–2</td>
<td>94</td>
<td>94</td>
<td>&gt;0.35</td>
</tr>
<tr>
<td>Roehr et al&lt;sup&gt;63&lt;/sup&gt;</td>
<td>2001</td>
<td>2 mo–11.2</td>
<td>42</td>
<td>100</td>
<td>17.5</td>
</tr>
<tr>
<td>Osterballe and Bindslev-Jensen&lt;sup&gt;56&lt;/sup&gt;</td>
<td>2003</td>
<td>0.5–4.9</td>
<td>56</td>
<td>95</td>
<td>1.5</td>
</tr>
<tr>
<td>Celik-Bilgili et al&lt;sup&gt;65&lt;/sup&gt;</td>
<td>2005</td>
<td>All children</td>
<td>227</td>
<td>95</td>
<td>12.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(range 0.1–16.1)</td>
<td>41</td>
<td></td>
<td>10.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≤1</td>
<td>186</td>
<td></td>
<td>13.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Komata et al&lt;sup&gt;67&lt;/sup&gt;</td>
<td>2007</td>
<td>All children</td>
<td>764</td>
<td>95</td>
<td>25.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(range 0.2–14.6)</td>
<td>N/A</td>
<td></td>
<td>13.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≤1</td>
<td></td>
<td>N/A</td>
<td>23.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1–2</td>
<td></td>
<td>N/A</td>
<td>30.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt;2</td>
<td></td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Benhamou et al&lt;sup&gt;68&lt;/sup&gt;</td>
<td>2008</td>
<td>Median 47 mo</td>
<td>51</td>
<td>100</td>
<td>7</td>
</tr>
</tbody>
</table>

*Data from Tey D. Egg allergy in childhood: an update. Current Opinion in Allergy and Clinical Immunology 2009;9:244–50.*
and, when necessary, confirmed with a positive challenge. Atopy patch tests with egg white may provide additional information in these cases.52

**Differential Diagnosis**

Gastrointestinal symptoms, such as vomiting and diarrhea, occurring after ingestion of undercooked egg can be caused by food poisoning, such as salmonella or campylobacter infection, rather than allergy. Unlike food allergy reactions, symptoms are generally delayed and occur 8 to 72 hours after exposure. Allergies to foods other than egg should also be considered in the differential diagnosis, especially if the reactions occurred to foods that contained multiple ingredients.

**Cross-reactivity**

Serologic and clinical cross-reactivity with other bird eggs (turkey, duck, goose, seagull, and quail) have been reported.71,72 A minority of patients with allergy to egg are reactive to chicken meat as well. Chicken serum albumin (Gal d 5) is responsible for this cross-reactivity.28

**MANAGEMENT**

The management of egg allergy is similar to that of other food allergies. It requires education on avoidance and management of allergic reactions in the event of accidental exposure. Hen’s egg is a versatile ingredient used in food from many cultures, including a wide range of manufactured food products (Table 4). The dietary avoidance of egg can thus be challenging73 and can pose significant quality-of-life concerns. To ensure that elimination of egg does not result in nutritional deficiency, and in particular for those who have additional dietary limitations (eg, vegetarian diet or multiple food allergies), a dietician should be involved in the care of the patient.

Patients must be counseled about the potential for accidental exposure to food allergens via cross-contamination. This exposure can occur wherever food is being prepared or served, including restaurants and bakeries. In addition, egg whites and shells are used as clarifying agents and can be found in soup stocks, consommés, wine, alcohol-based beverages, and coffee drinks. Egg white is also used as a wash for bread products. Counseling should also include a discussion about egg

<table>
<thead>
<tr>
<th>Avoid Foods that Contain Eggs or Any of these Ingredients:</th>
<th>Egg Protein is Sometimes Found in the Following:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin (also spelled as albumen)</td>
<td>Baked goods</td>
</tr>
<tr>
<td>Egg (dried, powdered, solids, white, yolk)</td>
<td>Egg substitutes</td>
</tr>
<tr>
<td>Eggnog</td>
<td>Lecithin</td>
</tr>
<tr>
<td>Globulin</td>
<td>Macaroni</td>
</tr>
<tr>
<td>Lysozyme</td>
<td>Marzipan</td>
</tr>
<tr>
<td>Mayonnaise</td>
<td>Marshmallows</td>
</tr>
<tr>
<td>Meringue (meringue powder)</td>
<td>Nougat</td>
</tr>
<tr>
<td>Ovalbumin</td>
<td>Pasta</td>
</tr>
<tr>
<td>Ovovitellin</td>
<td></td>
</tr>
<tr>
<td>Surimi</td>
<td></td>
</tr>
</tbody>
</table>

Data from The Food Allergy and Anaphylaxis Network.
alternatives and substitutes because commercial products marketed as egg substitutes may have egg ingredients (Box 1).

Careful reading of ingredient labels is essential and legislation has been enacted in the United States mandating clear labeling of food packages to identify the presence of the 8 major food allergens, including egg (as well as milk, tree nuts, peanuts, wheat, soybeans, fish, and crustacean shellfish). Some products in the United States may have advisory labeling, such as “may contain egg.” This type of labeling is not currently regulated. Based on a recent study, avoidance of advisory-labeled products should be recommended because they present a small, but real, risk of allergic reactions, especially products from small companies. Other countries are addressing issues of food labeling as well. Since November 2005, prepackaged food sold within the European Union have been required by law to list egg in the ingredient panel if it is a deliberately added component of the product, however little the amount.

Several studies have found that most individuals with egg allergy can tolerate extensively heated or baked egg. However, identification of these patients remains difficult and the only currently available diagnostic test to determine which patients can tolerate extensively heated egg (unless it is currently in their diet) is an OFC. Patients may be allowed to continue to eat egg in more processed forms than what triggered their reaction(s) if they have eaten egg in these forms regularly and in the recent past (similar to passing an oral food challenge). In most cases, this involves patients who reacted to lightly cooked egg (eg, scrambled egg, French toast), but have a history of tolerating extensively heated egg (eg, muffins, waffles). However, patients should avoid more intermediate forms of cooked egg, such as meatballs/meatloaf, breaded foods, casseroles, custard, mayonnaise, and hardboiled egg.

There are several caveats that should be discussed with patients when considering inclusion of certain heated forms of egg in the diet. It is possible that a patient may have a reaction caused by ingestion of a larger amount of egg or more lightly cooked egg than usual (eg, undercooked muffins or cookies). Furthermore, the effect of including heated egg in the diet on the natural history of egg allergy is unknown. However, patients who have reacted to intermediately cooked or extensively heated egg should avoid all forms of egg. An OFC to extensively heated egg may be considered by an allergy specialist if a patient is not currently eating egg in this form but the patient (or parents of the patient) wishes to introduce it into the diet. Caution is needed, because severe reactions can occur from this type of oral food challenge.

<table>
<thead>
<tr>
<th>Box 1</th>
<th>Substitutions for egg in recipes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two tablespoons of fruit puree (binding only)</td>
<td></td>
</tr>
<tr>
<td>One tablespoon of ground flax seeds, 3 tablespoons water (binding only)</td>
<td></td>
</tr>
<tr>
<td>One and one-half tablespoons water, 1.5 tablespoons oil, 1 teaspoon baking powder (leavening and binding)</td>
<td></td>
</tr>
<tr>
<td>One teaspoon baking powder, 1 tablespoon liquid, 1 tablespoons vinegar (leavening and binding)</td>
<td></td>
</tr>
<tr>
<td>Potato-based commercial egg substitute from Ener-G foods (leavening and binding)</td>
<td></td>
</tr>
<tr>
<td>One packet of gelatin, 2 tablespoons warm water; mix when ready to use (leavening and binding)</td>
<td></td>
</tr>
<tr>
<td>One teaspoon yeast dissolved in one-quarter cup water (leavening and binding)</td>
<td></td>
</tr>
</tbody>
</table>

Data from The Food Allergy and Anaphylaxis Network.
In addition, the effect of ingesting heated egg on the course of the allergy is not yet understood. However, it has been recently shown that ingestion of extensively heated egg in children with egg allergy is associated with favorable immunologic changes. Continued ingestion of extensively heated egg for tolerant children showed a decrease in OVA-IgE/IgG4 and OVM-IgE/IgG4 ratios from baseline at 3, 6, and 12 months. These results suggest that ingestion of extensively heated egg by tolerant children might hasten the development of tolerance to unheated egg.

**Egg Proteins in Medications and Vaccines**

Medications and vaccines may have ingredients derived from egg. Patients should ensure that the clinicians and pharmacists caring for them are aware of their egg allergy, especially before receiving any new medication or vaccine. Influenza vaccines are derived from the extraembryonic fluid of chicken embryos inoculated with specific types of influenza virus. The vaccines typically contain measurable quantities of residual OVA. OVA levels in influenza vaccines vary between manufacturers and also between batches from the same manufacturer; from barely detectable to as high as 42 μg/mL. There are few published data on the risk of allergic reaction to influenza vaccine in individuals with egg allergy. Immediate allergic reactions, including anaphylaxis, have been reported in patients with egg allergy after influenza vaccination. In a population survey of 48 million people undergoing influenza vaccination, there were only 11 reports of anaphylaxis, although none had a known prior history of egg allergy, suggesting an alternative allergen. Several procedures have been proposed to safely vaccinate patients with a history of a severe hypersensitivity reaction to egg.

The yellow fever vaccine is prepared in egg embryos, and allergic reactions to this vaccine have been reported. This vaccination is required for travelers entering several countries in areas where yellow fever is endemic. In a small study, a reduced intradermal dose of the yellow fever vaccine induced protective antibody responses in individuals with egg allergy.

In contrast, the measles, mumps, and rubella (MMR) vaccine is not contraindicated for children with egg allergy, although the measles vaccine is produced in a culture of chicken embryo fibroblasts. Three large trials have shown the safety of the MMR vaccine in children with egg allergy. Allergic reactions to these vaccines have been primarily attributed to the gelatin component.

Two other areas of concern are lipid emulsions that contain egg (eg, propofol and intralipid) and use of egg lysozyme, an enzyme found in egg white, in pharmaceutical products. There are case reports of anaphylaxis to these products.

**Provision of Emergency Treatment**

Identification of individuals with IgE-mediated egg allergy is important, because these patients are at risk for severe reactions. As with other forms of food allergy, the severity of symptoms in a given individual with egg allergy may vary considerably between reactions. In addition, the severity of an initial reaction does not predict the severity of subsequent reactions. Children with egg allergy are more likely to develop asthma, and concomitant asthma places patients at higher risk for severe allergic reactions to foods. In a small study investigating whether children with egg allergy of varying severity could tolerate extensively heated forms of egg, 18% of children who reacted to extensively heated egg and 23% who reacted to lightly cooked egg required treatment with epinephrine. In another series of 167 children that examined dietary advice and adherence in patients with egg allergy, the initial episode was a local reaction in 29%, a mild to moderate systemic reaction in 31%, and a severe systemic
reaction in 18%.\textsuperscript{98} Twenty percent of the children in this study had a subsequent reaction to egg that was more severe than the initial event. Children whose only apparent clinical manifestation of food allergy is atopic dermatitis may be at risk of an acute systemic reaction on reintroduction of that food after a period of elimination because atopic dermatitis may have IgE-mediated triggers.\textsuperscript{4,5,13}

Accordingly, we suggest that individuals diagnosed with IgE-mediated egg allergy have an epinephrine autoinjector(s) available at all times.\textsuperscript{6} In addition, these patients should have written anaphylaxis emergency action plans.

**NATURAL HISTORY**

Earlier studies indicated that tolerance to egg is achieved by most children with egg allergy, with resolution in 50% by age 3 years and in 66% by age 5 years.\textsuperscript{99} However, a more recent study suggested that egg allergy is more persistent, predicting resolution in 4% by age 4 years, 12% by age 6 years, 37% by age 10 years, and 68% by age 16 years.\textsuperscript{100} Whether these differing results are caused by population differences or a change in the natural history of egg allergy is unclear. Because most children do outgrow their egg allergy, periodic reevaluation is recommended.

Several prognostic indicators for the development of tolerance to egg have been identified. These indicators include lower level of egg-specific IgE,\textsuperscript{70} faster rate of decline of egg-specific IgE level with time,\textsuperscript{70} earlier age at diagnosis,\textsuperscript{70} milder symptoms,\textsuperscript{79,101} and smaller skin test wheal sizes.\textsuperscript{99} Moreover, people who are tolerant to extensively heated egg may be more likely to outgrow the egg allergy. However, those who are allergic to extensively heated egg are more likely to have severe, and maybe lifelong, egg allergy.

**FUTURE TREATMENTS**

Currently, there are no treatments that can cure or provide long-term remission from food allergy. However, several treatment strategies are being investigated. These approaches are either allergen-specific or aimed at modulating the overall allergic response. Oral tolerance induction studies to food allergens are still experimental\textsuperscript{102,103} and a few studies show promising results.\textsuperscript{103–106} However, adverse reactions are common.\textsuperscript{102,103} There is still uncertainty about whether oral immunotherapy (OIT) achieves true tolerance or transient desensitization (with recurrence of symptoms after discontinuation of therapy). There is a high probability of spontaneous tolerance development to egg, so it is unclear whether OIT changes the time course to the development of tolerance.

With recent reports indicating that extensively heated egg is tolerated by most patients with egg allergy and that the associated immunologic changes with continued ingestion of extensively heated egg seem favorable, incorporation of extensively heated egg in the diet may present a more natural form of immunotherapy. At this point, OIT is still considered investigational, and therefore is not recommended in routine clinical practice.

**SUMMARY**

Egg allergy is one of the most common food allergies in childhood and can induce a range of IgE-mediated and non–IgE-mediated disorders. A recent study has suggested that egg allergy is more persistent than was previously believed. Avoidance and preparation in case of allergic reactions caused by accidental exposures remain
the cornerstones of management. Although there are currently no cures for food allergy, ongoing studies of OIT are showing promise.

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