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Current understanding of egg allergy

Jean-Christoph Caubet, MD and Julie Wang, MD

Pediatrics Mount Sinai School of Medicine, Division of Pediatric Allergy and Immunology, New York City, NY, USA

SYNOPSIS

Egg is one of the most important allergens in childhood feeding, and egg allergy can pose quality of life concerns. A clear clinical history and the detection of egg white specific IgE will confirm the diagnosis of IgE-mediated reactions. Non-IgE-mediated symptoms such as in eosinophilic diseases of the gut might also be observed. Egg avoidance and education regarding the treatment of allergic reactions are the cornerstones of management of egg allergy. In this review, we discuss epidemiology, risk factors, diagnosis, treatment and natural history of egg allergy.

Keywords

Egg; allergy; food; children; hypersensitivity; IgE; ovomucoid; ovalbumin

INTRODUCTION

After cow's milk, hen's egg allergy is the second most common food allergy in infants and young children [1–5]. 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 [6]. The major limitation of this meta-analysis was significant variability in study design that made direct comparisons difficult. The majority of studies included in the meta-analysis were based upon 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 three studies used double-blind, placebo-controlled food challenges, the gold standard, to confirm the diagnosis of food allergy [7–9]. In these three studies of unselected populations, the prevalence of egg allergy ranged from 0.0004% in a cohort of German children aged up to 17 years [7], to 0.6% in nursery school children in Mexico [8], to 1.6% in 3 year old Danish children [9]. From Norway, Eggesbo et al. [2] reported an estimated point prevalence of allergy to egg in children aged 2½ years of 1.6% (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 [1]. 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

Correspondence to: Julie Wang, Mount Sinai School of Medicine, Division of Pediatric Allergy and Immunology, One Gustave L. Levy Place, Box 1198, New York City, NY, USA, Phone: 212-241-5548, julie.wang@mssm.edu.

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associated with atopic dermatitis and was found to be present in about 2/3 of children with positive oral food challenges (OFC) performed for allergy evaluation of atopic dermatitis [10]. The risks of sensitization to aeroallergens [11] and asthma [12] are also increased in egg allergic-children.

PATHOGENESIS

Egg allergy may be defined as an adverse reaction of immunological nature induced by egg proteins [13] and includes IgE antibody-mediated allergy as well as other allergic syndromes such as atopic dermatitis and eosinophilic esophagitis, which are mixed IgE- and cell-mediated disorders. IgE-mediated food allergy, also known as type I food allergy, accounts for the majority of 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 1-5 [14]. 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%) [15]. Although ovalbumin (OVA) is the most abundant protein comprising hen's egg white, ovomucoid (OVM) has been shown to be the dominant allergen in egg [16–18,18].

The allergenicity of proteins depends mostly, but not exclusively, on their resistance to heat and digestive enzymes [19], reflecting their capacity to stimulate a specific immune response [14]. 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 due to 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 egg-allergic patients 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 [20].

Egg proteins differ in their physical properties and can be related to different clinical patterns of egg allergy. The importance of OVM may be due to its unique characteristics such as relative stability against heat [21] and digestion with proteinases [22], and its strong allergenicity [15], compared with other egg white components. This is possibly related to the presence of strong disulfide bonds that stabilize this highly glycosylated protein [18]. In 2 different studies, children with persistent egg allergy had significantly higher specific IgE levels to OVM than children who outgrew their egg allergy [15,20]. In the report by Jarvinen et al [20], seven patients with persistent egg allergy had IgE that recognized four sequential epitopes of OVM. In contrast, none of the 11 children with transient egg allergy had specific IgE to these epitopes. Interestingly, gastric digestion has been demonstrated to reduce the allergenicity of OVM [23], which can explain why some patients have skin contact reactions to egg, but not ingestion reactions [24].

In contrast, OVA epitopes are heat labile [25], suggesting that children who have specific IgE primarily to OVA are likely to tolerate heat-denatured forms of egg. Using egg-allergic patients' sera, reports have shown that the antigenicity of OVA could, however, resist heat treatment under certain conditions [26]. By using OVA, a recent study [27] investigate 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-related immune epitopes in food allergy. Interestingly, they showed that T-cell immunogenicity of OVA can be enhanced by the Maillard reaction, indicating a critical role for thermal processing on allergenicity of OVA.

In egg yolk, alpha-livetin (Gal d 5) is the major allergen and is involved in the bird-egg syndrome, which is described below [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- and non-IgE-mediated 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 upon first known exposure to egg, particularly in sensitized children with atopic dermatitis [31,32]. The development of sensitization in these patients may be due to 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 (prior to 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. Children typically present with rapid-onset of urticaria or angioedema, usually within minutes to two hours after ingestion. Although cutaneous symptoms are most common, immediate-type reactions involving the gastrointestinal or respiratory tracts are reported as well. The severity of reactions can be unpredictable, is 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- and non-IgE-mediated reactions. Disorders that fall into these categories 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 [13]. 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, demonstrating the clinical relevance of egg sensitization in these patients [47]. Isolated delayed reactions, that is, flares of atopic dermatitis usually after 6 to 48 hours, are suggestive of non-IgE-mediated reactions and are likely due to T-cell mediated mechanisms. Late reactions are more difficult to ascertain. A combination of immediate allergy symptoms and delayed skin reactions is also described in a significant proportion of children [48]. More than 10% of the children who reacted to an oral food challenge (OFC) developed isolated atopic dermatitis flares after 16 hours or later [49].

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 [50]. 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- and non-IgE-mediated processes [51–53]. Egg was found to be the second most common allergen triggering symptoms in a series of over 500 patients with EoE. This was confirmed on endoscopy after allergy evaluation with skin prick testing and patch testing [54]. Elimination of food triggers has been found to be an effective treatment for EoE.

Food protein-induced enteropathy due to egg has been reported [55]. A five-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 [56].

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 may include measurement of food-specific IgE antibodies, skin-prick tests, atopy patch test (APT), diagnostic elimination diet and/or OFC. We will discuss below these different diagnostic tools 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, cut-off levels for skin prick test wheal size of 3 mm or greater than the negative saline control [31] have been used to support a clinical diagnosis. Higher cut-off 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 [57]. Specifically, a wheal size of 5 mm or greater has been reported to provide a 100% positive predictive value (PPV) for children under 2 years of age, whereas for older children, a wheal size of 7 mm has a reported 100% PPV [58,59] (Table 2). Children with test results above these cutoffs are presumed to be clinically reactive, and oral food challenges (OFC) are avoided in these cases. Due to a high negative predictive value (91% for skin prick test <3 mm [60]), a negative prick test can be helpful to rule out an allergy to egg. It should be noted that skin prick testing has low specificity, therefore isolated positive tests in the absence of clinical suspicion may not be indicative of 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 demonstrated that an IgE level of 7 k_AU/L to egg has a 95% PPV for clinical reactivity to egg for children over 2 years of age; for children two years or under, a level of 2 k_AU/L has a 95% PPV [30,60–63]. Although there is a demonstrable relationship between serum IgE levels and challenge outcome, there is poor agreement between cut-off levels identified by different centers (Table 3) [30,64–68]. This may be due to 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 cut-off levels for one's own 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 k_AU/L) does not exclude clinical reactivity to egg [60–62].

From another point of view, 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 k_AU/L (positive decision point) indicates a high risk of reacting to heated (as well as less heated or undercooked) egg [69]. At the same time, a concentration lower than approximately 1 k_AU/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 over time is a prognostic indicator for the development of tolerance [70].

Finally, standardized double-blind, placebo-controlled oral food challenges (DBPCFC) 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 as it may cause immediate, potentially severe symptoms.

Asthma—The diagnosis of suspected occupational asthma due to egg allergy, which is also IgE-mediated, involves skin prick testing, pulmonary function testing, and possible bronchoprovocation challenge.

Mixed IgE- and non-IgE-mediated disorders—Skin prick test and specific IgE test are useful for detecting a IgE-mediated sensitization, however, 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 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 due to food poisoning, such as salmonella or campylobacter infection, rather than allergy. Unlike food allergy reactions, symptoms are generally delayed and occur 8–72 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 challenging [73] 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, e.g. 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 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 alternatives and substitutes as commercial products marketed as “egg substitutes” may have egg ingredients (Table 5).

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) [74]. 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 [75], 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 (EU) have been required by law to list egg in the ingredient panel where it is a deliberately added component of the product, however little the amount.

Several studies have found that the majority of egg allergic individuals can tolerate extensively heated or baked egg [76–79]. However, identification of these patients remain

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 due to ingestion of a larger amount of egg or more lightly cooked egg than usual (eg, undercooked muffins or cookies). Furthermore, the impact 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.[79]

In addition, the impact 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 [79]. 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 extra-embryonic fluid of chicken embryos inoculated with specific types of influenza virus. The vaccines typically contain measurable quantities of residual egg white protein (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 ug/mL [80]. There are few published data on the risk of allergic reaction to influenza vaccine in egg-allergic individuals [81,82]. Immediate allergic reactions, including anaphylaxis have been reported in patients with egg allergy after influenza vaccination [83–85]. 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 [81]. Several procedures have been proposed to safely vaccinate patients with a history of a severe hypersensitivity reaction to egg [86–88].

The yellow fever vaccine is prepared in egg embryos, and allergic reactions to this vaccine have been reported [89]. This vaccination is required for travelers entering several countries in endemic areas. In a small study, a reduced intradermal dose of the yellow fever vaccine induced protective antibody responses in egg-allergic individuals [90].

In contrast, the measles, mumps and rubella (MMR) vaccine is not contraindicated for egg allergic children, although the measles vaccine is produced in a culture of chick embryo fibroblasts. Three large trials have demonstrated the safety of the MMR vaccine in egg

allergic children [91–93]. Allergic reactions to these vaccines have been primarily attributed to the gelatin component [94].

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 [95–97].

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 [9]. 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 [2]. 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% [98]. Twenty percent of the children in this study had a subsequent reaction to egg that was more severe than the initial event. To be noted, children whose only apparent clinical manifestation of food allergy is atopic dermatitis may be at risk of an acute systemic reaction upon reintroduction of that food after a period of elimination since atopic dermatitis may have IgE-mediated triggers [4,5,13].

Accordingly, we suggest that individuals diagnosed with IgE-mediated egg allergy have an epinephrine autoinjector(s) available at all times [6]. In addition, the patient should have a written anaphylaxis emergency action plan.

NATURAL HISTORY

Earlier studies indicated that tolerance to egg is achieved by the majority of children with egg allergy, with resolution in 50% by age 3 years and in 66% by age 5 years [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 [100]. Whether these differing results are due to population differences or a change in the natural history of egg allergy is unclear. Since the majority of children do outgrow their egg allergy, periodic re-evaluation is recommended.

Several prognostic indicators for the development of tolerance to egg have been identified. These include lower level of egg-specific IgE [70], faster rate of decline of egg-specific IgE level over time [70], earlier age at diagnosis [70], milder symptoms [79,101], and smaller skin test wheal sizes [99]. Moreover, people who are tolerant to extensively heated egg may be the ones who are more likely to outgrow the egg allergy. Those who are allergic to extensively heated egg on the other hand are the ones for whom egg allergy is more likely to be severe and maybe lifelong.

FUTURE TREATMENTS

Currently, there are no treatments that can cure or provide long-term remission from food allergy. However, several treatment strategies are under investigation. These approaches are either allergen-specific or aimed at modulating the overall allergic response. Oral tolerance induction studies to food allergens are still experimental [102,103] and a few studies show

promising results [103–106]. However, adverse reactions are common [102,103]. There is still uncertainty of whether oral immunotherapy (OIT) achieves true tolerance or transient desensitization (with recurrence of symptoms after discontinuation of therapy). In view of a high probability of spontaneous tolerance development to egg it is unclear whether OIT changes the timecourse to the development of tolerance.

With recent reports indicating that extensively heated egg is tolerated by a majority of egg allergic patients and that the associated immunologic changes with continued ingestion of extensively heated egg appear 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- and non-IgE-mediated disorders. A recent study has suggested that egg allergy is more persistent than previously believed. Avoidance and preparation in case of allergic reactions due to accidental exposures remain the cornerstones of management. Although there are currently no cures for food allergy, on-going studies of OIT are showing promise.

Abbreviations

EW	Egg white
OFC	oral food challenge
OVA	Ovalbumin
OVM	Ovomucoid
DBPCFC	double-blind, placebo-controlled oral food challenges

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Table 1

Major egg white allergens (reproduced with authorization from Benhamou AH, state of the art for egg allergy, Allergy 2010, 65:283–289)

Allergen	Common name	Constitute (%)	Mw (kDa)	Carbohydrate (%)	IgE binding activity			Allergenic activity	Test code (in-vitro tests)
					Heat-treated	Digestive	Enzyme-treated		
Gal d 1	Ovomucoid	11	28	25	Stable	Stable	Stable	+++	f233
Gal d 2	Ovalbumin	54	45	3	Unstable	Unstable	Unstable	++	f232
Gal d 3	Ovotransferrin/conalbumin	12	76.6	2.6	Unstable	Unstable	Unstable	+	f323
Gal d 4	Lysosyme	3.4	14.3	0	Unstable	Unstable	Unstable	++	k208

Diagnostic decision points for skin prick test wheal diameter to egg (Pharmacia ImmunoCAP) (adapted with authorization from Tey D, Egg allergy in childhood: an update, Current Opinion in allergy and clinical Immunology 2009, 9:244–250)

Table 2

References	Year	Age group	Number of patients	PPV	Egg-specific IgE (kU _A /l)
Sampson HA and Ho [64]	1997	Children and adolescents	100	85	≥3
Sporik et al [59]	2000	<2 years	39	100	≥5
		>2 years	82		≥7
Boyano-Martinez et al [30]	2001	<2 years	81	93	≥3
Hill et al [58]	2004	<2 years	90	100	≥5
		>2 years	555		≥7
Verstege et al [57]	2005	All children (range 0.3–14.5 years)	160	95	≥13
		<1 year	26		≥11.2
		>1 year	134		≥13.3

Diagnostic decision points for egg-specific serum IgE levels (Pharmacia ImmunoCAP) (adapted with authorization from Tey D, Egg allergy in childhood: an update, Current Opinion in allergy and clinical Immunology 2009, 9:244–250)

Table 3

References	Year	Age group	Challenge	PPV	Egg-specific IgE (kU _A /l)
Sampson and Ho [64]	1997	Children and adolescents	126	95	6.0
Boyano Martinez et al [30]	2001	0–2 years	94	94	>0.35
Roehr et al [63]	2001	2 month–11.2 years	42	100	17.5
Osterballe and Bindslev-Jensen [66]	2003	0.5–4.9 years	56	95	1.5
Celik-Bilgili et al [65]	2005	All children (range 0.1–16.1 years)	227	95	12.6
		≤ 1 year	41		10.9
		>1 year	186		13.2
Komata et al [67]	2007	All children (range 0.2–14.6 years)	764	95	25.5
		≤1 year	N/A		13.0
		1–2 years	N/A		23.0
		>2years	N/A		30.0
Benhamou et al [68]	2008	Median 47 months	51	100	7

Table 4

How to read a label for an egg-free diet. Reproduced with permission from: the Food Allergy and Anaphylaxis Network

Avoid foods that contain eggs or any of these ingredients:	Egg protein is sometimes found in the following:
Albumin (also spelled as « albumen »)	Baked goods
Egg (dried, powdered, solids, white, yolk)	Egg substitutes
Eggnog	Lecithin
Globulin	Macaroni
Lysozyme	Marzipan
Mayonnaise	Mashmallows
Meringue (meringue powder)	Nougat
Ovalbumin	Pasta
Ovovitellin	
Surimi	

Table 5

Substitutions for egg in recipes: reproduced with permission from the Food Allergy and Anaphylaxis Network

2 Tablespoons of fruits puree (binding only)
1 Tablespoon of ground flax seeds, 3 Tablespoons water (binding only)
1 ½ tablespoons water, 1 ½ tablespoons oil, 1 teaspoon baking powder (leavening and binding)
1 teaspoon baking powder, 1 Tablespoon liquid, 1 Tablespoons vinegar (leavening and binding)
Potato based commercial egg substitute from Ener-G foods (leavening and binding)
1 packet of gelatin, 2 Tablespoons warm water – mix when ready to use (leavening and binding)
1 teaspoon yeast dissolved in ¼ cup water (leavening and binding)