

British Society for Allergy and Clinical Immunology guidelines for the management of egg allergy

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Clinical & Experimental Allergy

Summary

This guideline advises on the management of patients with egg allergy. Most commonly, egg allergy presents in infancy, with a prevalence of approximately 2% in children and 0.1% in adults. A clear clinical history and the detection of egg white-specific IgE (by skin prick test or serum assay) will confirm the diagnosis in most cases. Egg avoidance advice is the cornerstone of management. Egg allergy often resolves and re-introduction can be achieved at home if reactions have been mild and there is no asthma. Patients with a history of severe reactions or asthma should have reintroduction guided by a specialist. All children with egg allergy should receive measles, mumps and rubella (MMR) vaccination. Influenza and yellow fever vaccines should only be considered in egg-allergic patients under the guidance of an allergy specialist. This guideline was prepared by the Standards of Care Committee (SOCC) of the British Society for Allergy and Clinical Immunology (BSACI) and is intended for allergists and others with a special interest in allergy. The recommendations are evidence-based but where evidence was lacking consensus was reached by the panel of specialists on the committee. The document encompasses epidemiology, risk factors, diagnosis, treatment, prognosis and co-morbid associations.

Keywords adrenaline, aetiology, allergy, anaphylaxis, BSACI, diagnosis, egg, epinephrine, food, influenza, management, MMR, SOCC, vaccines, yellow fever

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Introduction

The guideline, prepared by an expert group of the Standards of Care Committee (SOCC) of the British Society for Allergy and Clinical Immunology (BSACI), addresses the question of diagnosis and treatment as well as recommending guidance for families with egg-allergic children. During the development of these guidelines, all BSACI members were consulted using a web-based system and their comments and suggestions were carefully considered by the SOCC. Evidence for the recommendations was obtained from electronic literature searches of Medline/PubMed, NICE and the Cochrane library (cut off June 2009) using the following strategy and key words – (allergy OR skin prick test OR anaphylaxis OR contraindications OR immediate adverse reactions) AND (egg OR lecithin OR ovalbumin). The experts' knowledge of the specialist literature and hand searches were used in addition. Where evidence was lacking, a consensus was

reached among the experts on the committee. Conflicts of interests were recorded by the BSACI. None jeopardized unbiased guideline development.

Executive summary

- Egg allergy may be defined as an adverse reaction of an immunological nature induced by egg protein. This guideline focuses predominantly on type-1 IgE-mediated allergy to egg.
- The prevalence of egg allergy is estimated at approximately 2% in children and 0.1% in adults.
- Egg allergy presents most commonly in infancy, often after the first apparent ingestion with rapid onset of urticaria and angio-oedema; severe reactions involving airway narrowing are uncommon.
- The clinical diagnosis is made by the combination of a typical history of urticaria and/or angio-oedema/

vomiting/wheeze with rapid onset (usually within minutes) after ingestion of egg with evidence of sensitization (the presence of specific IgE).

- The reported level of IgE required to support a diagnosis varies between studies. For clinical purposes, an egg white skin prick test (SPT) weal of 5 mm or more is considered adequate to confirm a clinical history in most cases of allergy.
- It is not possible to identify a single cut-off value for egg serum-specific IgE, which is 'diagnostic' for egg allergy at all ages.
- A food challenge may be necessary to confirm or refute a conflicting history and test results but in practice this is not commonly required.
- No cut-off has been identified for SPT weal size or serum-specific IgE, which predicts the overall clinical severity.
- Egg avoidance advice is the cornerstone of management and may require referral to a dietician if there are multiple food allergies or if the patient is already on a restricted diet for other reasons.
- Mild egg allergy often resolves and an attempt to introduce well-cooked egg as an ingredient (e.g. in cake) may be made at a time-point determined on an individual basis.
- Children with a history of a severe egg reaction are more likely to have persistent disease and should have avoidance and reintroduction guided by a specialist.
- Egg allergy in infancy is associated with an increased risk of developing asthma later in life.
- All children with egg allergy should receive mumps and rubella (MMR) vaccination (only children with a documented history of anaphylaxis to the vaccine itself should have further doses administered under hospital supervision).
- Influenza and yellow fever (YF) vaccines contain measurable quantities of egg protein and if these vaccines are required the patient should be referred to an allergy specialist.

Definition and mechanism

Egg allergy may be defined as an adverse reaction of an immunological nature induced by egg protein [usually ovalbumin (OVA) and/or ovomucoid]. Classically, the mechanism is a type-1 (immediate) hypersensitivity reaction mediated by egg white-specific IgE. Late-phase and delayed hypersensitivity reactions also occur, typically in eczema. This guideline will focus predominantly on type 1 reactions.

Background and epidemiology

Food allergy is common and its prevalence in childhood is estimated at between 3–7% [1, 2]. Egg and milk allergies

are the commonest food allergies of infancy. The prevalence of egg allergy confirmed by challenge has been estimated at 1.6% at 2.5 years with a crude cumulative incidence of 2.6% [1]. Another study found a crude cumulative incidence of 2.4% at 2 years [3]. The prevalence in the adult population has been estimated at 0.1% [4].

Aetiology

The onset of egg allergy is usually observed early in life, in children with a history of eczema and atopy. The production of egg white-specific IgE is a prerequisite for developing type-1 hypersensitivity to egg. However, the route, timing and dose of egg protein exposure that result in sensitization and clinical allergy are unknown.

Risk factors

The presence of eczema is a significant risk factor for egg allergy [5]. Sometimes, egg allergy occurs in association with allergies to other foods, such as cow's milk or peanuts. A comparison of the prevalence of food allergies is displayed in Table 1.

Diagnosis

In most cases, the clinical signs will have resolved by the time the patient reaches medical attention. Therefore, the clinical diagnosis is made by the combination of a typical history of urticaria and/or angio-oedema/vomiting/wheeze with rapid onset (usually within minutes) after ingestion of egg with evidence of sensitization (the presence of specific IgE).

Clinical presentation

Egg allergy presents most commonly in infancy, usually after the first apparent ingestion [5, 14]. Clinical reactions include urticaria and/or angio-oedema in 80–90% (within minutes) and gastrointestinal symptoms in 10–44% (within 2 h) [6, 15, 16]. Most reactions are mild, with facial urticaria only. More severe reactions with significant respiratory symptoms are less common (5–10% in challenge studies) [15, 16]. Symptoms or signs such as a hoarse cry, or change in voice pitch, cough, stridor or wheeze all indicate significant involvement of the respiratory tract and hence a more severe reaction. Occasionally, young children will develop pallor and floppiness. Skin contact is most likely to induce local cutaneous reactions although systemic reactions have been reported, when egg white has been empirically applied to nappy rash [17]. Ingestion of raw or undercooked egg may trigger more severe clinical reactions than well-cooked egg [18]. One

Table 1. Food allergy; comparison of egg, milk, peanut and tree nut allergy

Food	% Estimate	Study locality	References
Egg	2.4%	United Kingdom	Tariq <i>et al.</i> [3]
	2.6%	Norway	Eggesbo <i>et al.</i> [6]
	0.6%	France	Calculated from Rance <i>et al.</i> [7]
Peanut	1.8% of children (1 in 50)	United Kingdom	Hourihane <i>et al.</i> [8]
	1.4% of children (1 in 70)	Isle of Wight (UK)	Grundy <i>et al.</i> [9]
	0.6%	France	Calculated from Rance <i>et al.</i> [7]
Tree nuts	0.5%	France	Calculated from Rance 2005 [7]
Milk	2.5–3.8% (0–1 year)	Isle of Wight (UK)	Hide and Guyer [10]
	2.2% (at 2 years)	Europe	Host 2002 [11]
	1.9%	Sweden	Jakobsson and Lindberg [12]
	2.8% (age 0–1 year)	The Netherlands	Schrander 1993 [13]
	0.8%	France	Calculated from Rance <i>et al.</i> [7]
All foods	7%	Several countries	Host 2002 [11]
	6.7% (of these: cows milk 12%, egg 9.4%, kiwi 9%, peanut 8.2%, tree nut 7.8%)	France	Rance 2005 [7]

death due to egg allergy has been reported in the United Kingdom since 1992 [19]. Text box 1.

Skin prick test

Skin testing should only be carried out if there is clinical suspicion of egg allergy and has poor predictive value as a screening tool. Traditionally, taken with a good clinical history, cut-off levels for SPT weal size of ≥ 3 mm [5] or serum-specific IgE > 0.35 kU/L have been used to support a clinical diagnosis. However, if the clinical history is weak, SPT weals of between 3–5 mm, may be clinically irrelevant and low levels of specific IgE may be found in children without clinical egg allergy [16]. Higher cut-off levels have been proposed, which are associated with higher specificity and positive predictive values, although in younger children (<2 years) smaller SPT weals and lower serum-specific IgE are more likely to be predictive of egg allergy than in older children [20]. For SPT to egg white, a weal size of 5 mm or greater is associated with high specificity (Table 2) [21] and in most cases there is no need to undertake oral challenge to confirm diagnosis. SPT weal size does not appear to correlate with clinical severity. The algorithm in Fig. 1 gives a suggested prac-

Text box 1. Who should be referred to an allergy clinic

Children with previous egg allergy symptoms that affected breathing (cough, wheeze or swelling of the throat, e.g. choking), the gut (severe vomiting or diarrhoea) or the circulation (faintness, floppiness or shock)

Children who also receive regular asthma preventative treatment and/or have poorly controlled asthma

Where diagnosis is not clear and needs to be confirmed or excluded

Severe eczema in children on an egg-containing diet

Persistent* or adult-onset egg allergy

Egg allergy with requirement for influenza or yellow fever immunization

Egg allergy with another major food allergy

*Allergy that persists beyond the normal age of resolution (i.e. beyond 6–8 years).

tical clinical approach for the diagnosis of egg allergy based on expert opinion and available data. Skin testing with commercially available standardized egg reagents is recommended. The value of raw egg SPT in predicting the outcome of an oral egg challenge remains unclear.

Serum-specific immunoglobulin E

Egg white-specific IgE can be measured using standardized, *in vitro* IgE assays providing a quantitative measurement. There is a relationship between increasing levels of egg white-specific IgE and the likelihood of clinical reactivity to egg, although many patients with positive tests for IgE lack clinical reactivity. A range of predictive cut-off values for the diagnosis of egg allergy have been proposed (Table 3). Predictive cut-off levels are found to be lower in younger children and increase with age [25, 26]. Although there is a demonstrable relationship between serum IgE levels and challenge outcome, there is poor agreement between cut-off levels identified by different centres (Table 3). This is because of differences in inclusion criteria, significance levels, challenge method and outcome criteria, subject age and prevalence of egg allergy and eczema between studies, the latter two affecting total and specific IgE levels. These variables should be taken into account when interpreting cut-off levels in one's own patient population. The measurement of specific IgE to egg in the absence of a history of egg ingestion is discouraged as in this circumstance the test has poor sensitivity and low negative predictive value; oral challenge will subsequently be required if the specific IgE level is positive but low [5]. Text box 2.

Treatment and prognosis

Avoidance advice

Verbal and written advice on the avoidance of egg products should be provided (see BSACI patient information leaflet, Appendix 3). Ingredients and allergy warning

Table 2. Performance of skin prick testing for egg diagnosis

References	Number	Age	Method of diagnosis	Prevalence of egg allergy (%)	Prevalence of eczema (%)	PPV (%) at stated sIgE cut-off (weal, mm)		Specificity (%) at stated sIgE cut-off (weal, mm)	
						PPV	Cut-off	Specificity	Cut-off
Sampson and Ho [22]	100	Child-adol*	DBC	73	100	85	3	53	3
Boyano-Martinez et al. [16]	81	All <2 yr	OC	79	43	93	EW 3	71	EW 3
		Mean 16 m				96	EY 3	88	EY 3
Monti et al. [5]	107	All <19 m	OC	67	100	100	EW 5	100	EW 5
		Mean 16 m				100	EY 5	100	EY 5
Roehr et al. [23]	42	Median 13 m	DBC	51	100	81	3	57	3
Eigenmann and Sampson [24]	58	Child-adol*	DBC	69		85	3	61	3
Hill et al. [21]	30	All <2 yr Median 13 m	OC			100	<2 yr 5	100	<2 yr 5
Verstege et al. [20]	101	Median 22 m	DBC/OC	63	87	95	<1 yr 11		
						95	≥1 yr 13		
Sporik et al. [15]	121	Median 36 m	OC	77				100	All EW 7
								100	<2 yr EW 5

*Age range unspecified other than child-adolescent. Where results are stratified by age, this is shown in the 'cut-off' column.

PPV, positive predictive value; m, months; yr, years; adol, adolescent; OC, open challenge; DBC, double-blind placebo-controlled food challenge; EY, egg yolk; EW, egg white (unless stated otherwise skin prick test extract is 'hen's egg' or not specified by authors).

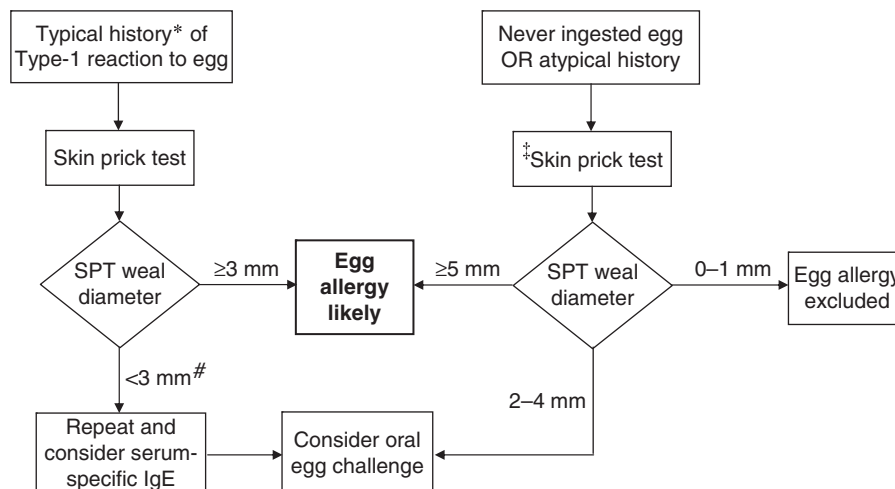


Fig. 1. Algorithm for diagnosis of egg allergy. *A typical history is the rapid onset of symptoms, e.g. urticaria, angio-oedema, vomiting, abdominal pain, wheezing or breathlessness. Skin prick test (SPT) weals should always be given as diameters in excess of the negative control. #Clinical allergy may be found in young infants with an SPT weal diameter of 2 mm particularly if there is an associated flare. †Not recommended as a screening test for egg allergy.

labels should be checked. Where the allergy has begun to resolve, well-cooked egg as an ingredient (e.g. sponge cake) may be tolerated, but not lightly cooked whole egg (e.g. scrambled). In this case, the patient should continue to eat the form of egg previously tolerated ('see Reintroduction of egg' Appendices 1 and 2). Figure 2 shows a classification of egg-containing foods also called 'the egg ladder' to aid reintroduction. Nursery and school staff should receive training in allergen avoidance as well as

recognition and treatment of food-induced allergic reactions.

Avoiding eggs

Eggs served in a recognizable form are easy to avoid, but they are also used in many different types of manufactured foods. An egg-free diet can therefore be difficult to maintain, unless most of the food consumed is cooked

Table 3. Performance of serum-specific IgE by immunocap for the diagnosis of clinical egg allergy

References	Number	Age	Method of diagnosis	Prevalence of egg allergy (%)	Prevalence of eczema (%)	PPV (%) at stated sIgE cut-off (kU/L)		Specificity (%) at stated sIgE cut-off (kU/L)	
						PPV	Cut-off	Specificity	Cut-off
Sampson and Ho [22]	100	Child–adol*	DBC	73	100	95	6		
Sampson [27]	75	Median 46 m	DBC	80	61	96	6	90	6
Celik-Bilgili <i>et al.</i> [28]	178	Median 13 m	OC	67	88	95	> 12.6 < 1 yr 10.9 > 1 yr 13.2		
Boyano-Martinez <i>et al.</i> [16]	81	All < 2 yr Mean 16 m	OC	79	43	94 98	EW 0.35 EY 0.35	77 93	EW 0.35 EY 0.35
Monti <i>et al.</i> [5]	107	All < 19 m Mean 16 m	OC	67	100			100	EY 17.5
Roehr <i>et al.</i> [23]	42	Median 13 m	DBC	51	100	100	17.5	100	17.5
Osterballe and Bindslev-Jensen [29]	56	All < 5 yr Median 26 m	OC	64	100	100	EW 1.5	100	EW 1.5
Komata <i>et al.</i> [25]	764	Median 15 m	OC	49	74	95	All 25.5 < 1 yr 13 1–2 yr 23 > 2 yr 30		
Benhamou <i>et al.</i> [30]	51	Median 47 m	OC/DBC	69		100	7	100	7
Ando <i>et al.</i> [26]	108	Median 35 m	DBC	62		95 (raw egg allergy) 84–88 (heated egg allergy)	EW 7.38 OVA 9.84 OVM 5.21 EW 30.7 OVA 29.3 OVM 10.8	95 (raw egg allergy) 75–80 (heated egg allergy)	EW 7.38 OVA 9.84 OVM 5.21 EW 30.7 OVA 29.3 OVM 10.8

*Age range unspecified other than child–adolescent. Unless stated otherwise serum IgE directed against ‘hen’s egg’ or unspecified by authors. Where results are stratified by age, this is shown in the ‘cut-off’ column.

OC, open challenge; DBC, double-blind placebo-controlled food challenge; EY, egg yolk; EW, egg white; WE, whole egg; OVA, ovalbumin; OVM, ovomucoid; adol, adolescent; m, months; yr, years.

Text box 2. Diagnosis

Most children should receive a clinical diagnosis without resorting to food challenge
 In the absence of a convincing history, a negative skin prick test can be used to exclude egg allergy
 There is no evidence that skin prick test weal size or cut-off value for specific IgE can predict the severity of egg allergy reactions
 The severity of any reaction depends on many other factors such as the amount of allergen ingested, how well it is cooked and concomitant asthma, exercise or illness

from fresh ingredients [32]. From November 2005, pre-packaged foods sold within the European Union (EU) have been required by law to list egg in the ingredients panel where it is a deliberately added component of the product, however tiny the amount. Some food manufacturers now also voluntarily include information about the likelihood of cross-contamination from other egg-containing products manufactured at the same factory.

Not all foods have a food-ingredient label, and those who cannot tolerate any type of cooked or raw egg should

avoid such products. This is particularly important if they are sold loose, for example bread and pastries from open bakeries, as they may have been glazed or cross-contaminated with egg. Foods bought outside the EU will need to have their ingredient label checked for the presence of egg, usually stated as in Text box 3.

Although eggs are stated on the label, it is helpful to know what types of food are more likely to contain egg, which may include foods as listed in Fig. 2.

Breastfeeding

Egg protein from the maternal diet is detectable in breast milk [33]. Therefore, eczema in breastfed babies with egg allergy may improve if their mother avoids eating eggs [34].

Referral to a dietician

Exclusion of eggs does not lead to nutritional deficiency. However, if there are additional dietary limitations, e.g.

1. Well-cooked egg	2. Lightly cooked egg	3. Raw egg
Cakes	Scrambled egg	Fresh mayonnaise
Biscuits	Boiled egg	Fresh mousse and shop-bought mousse which contains egg
Dried egg pasta	Fried egg	Fresh ice cream
Pancakes and Yorkshire pudding	Omelette	Sorbet
Egg in sausages, both vegetarian and meat varieties, and also in other processed meats such as burgers prepared meat dishes	Egg fried rice	Royal icing (both fresh and powdered icing sugar)
Well-cooked fresh egg pasta	Meringues	Home-made marzipan
Quorn	Some marshmallows	Raw egg in cake mix and other dishes awaiting cooking (children of all ages love to taste or lick the spoon!)
Sponges and sponge fingers	Lemon curd	Egg glaze on pastry
Chocolate bars which contain nougat or dried egg, e.g. Milky Way or Mars bar or Crème egg,	Quiche	Horseradish sauce
Some soft-centred chocolates	Poached egg	Tartar sauce
Chewitts	pancakes,	'Frico' edam cheese or other cheeses containing egg white, lysozyme
Egg in some gravy granules	Egg in batter	Mayonnaise
Dried egg noodles, cakes, some biscuits, waffles	Egg in breadcrumbs, e.g. on fish fingers and chicken nuggets	Salad cream
Commercial marzipan	Hollandaise sauce	
	Quiche and flans (fruity and savoury),	
	Egg custard and egg custard tarts	
	Crème caramel	
	Crème Brûlée	
	'Real' custard	
	Yorkshire pudding – some patients who can eat well-cooked egg can tolerate these, but it depends on how well-cooked they are and if they contain any 'sticky' batter inside	
	Tempura batter	

Fig. 2. Classification of egg-containing foods (amended from the Egg Ladder [31]).

Text box 3. Sources of egg antigen

<p>Egg white, egg yolk (because of egg white contamination) Processed egg, e.g. powdered, dried and pasteurized Egg proteins, e.g. albumin, ovalbumin, globulin, ovoglobulin, livetin, ovomucin, vitellin and ovovitellin Where the labelling is in Latin, the words for egg are OVUM or OVO</p>

vegetarian diet or multiple food allergies, a dietician should be involved.

Provision of emergency medication

All families with egg-allergic children should have an appropriate oral antihistamine available and this will be

sufficient to treat mild reactions. The small minority of children who have had severe reactions with evidence of airway narrowing (e.g. wheeze, voice change, choking) or hypotension should be provided with injectable adrenaline [35] and their families reviewed annually by an allergy specialist. Children with egg allergy who have asthma requiring ongoing preventative treatment with inhaled corticosteroids should also be considered for an adrenaline auto-injector. In practice, however, adrenaline auto-injectors are infrequently required in egg allergy. Families should receive training in how to use their emergency medication, including demonstration with a trainer device. Nursery and school staff should receive advice on egg avoidance and training in the use of emergency medication.

Provision of treatment plan

A treatment plan in plain language is required for all children who have been prescribed an adrenaline auto-injector describing the indications, names, doses and routes of any emergency medication that has been recommended. A copy should be forwarded to the person responsible for allergy care in the school or nursery.

Resolution of egg allergy

The natural history of egg allergy is for the majority to undergo spontaneous resolution over time. Two prospective studies examined predictive factors. Boyano-Martinez and colleagues studied 58 egg-allergic children aged <2 years at diagnosis for a median of 32 months. 50% had atopic eczema and all were referred for investigation to an allergy clinic. The median time to tolerance of raw egg was 35 months and 66% resolved after 5 years of follow-up [36]. The likelihood of eventual resolution of allergy was strongly increased in children with only cutaneous reactions after ingestion, an SPT weal to raw egg white <6 mm and/or egg white serum-specific IgE <1.98 kU/L. Another study found that for children diagnosed by 2 years, those with multi-system or respiratory reactions on challenge were more likely to have persistent egg allergy [37]. A study of a tertiary centre population suggested that the level of egg white specific IgE, and the presence of other food allergy or atopic disease were risk factors for persistence [38]. Children with a peak level of egg white-specific IgE <2 kU/L had the fastest rate of resolution. Shek and colleagues studied a group of egg-allergic children and found that a reduction in serum egg white-specific IgE level of 50% over 12 months was associated with a 0.52 probability of egg allergy tolerance [39]. However, levels of specific IgE and resolution of allergy also depend on other factors such as age and eczema severity, which may independently affect specific IgE levels [25]. In clinical practice, it is likely that changes in SPT weal size over time provide similar information.

There has been recent interest in measuring specific IgE directed against major egg allergens, particularly ovomucoid, which is resistant to degradation by heating [26, 40]. Jarvinen *et al.* [41] demonstrated that IgE antibodies against sequential ovomucoid epitopes were found more often in patients with persistent rather than resolved egg allergy. A study of 108 egg-allergic subjects (median age 35 m) showed that low levels of egg white and ovomucoid-specific IgE were associated with tolerance to cooked egg [26]. If confirmed, measurement of specific IgE directed against major allergens may help to predict resolution of egg allergy and the selection of patients for home introduction of cooked egg products.

Reintroduction of egg

Mild egg allergy. Patients with mild egg allergy will often be able to tolerate extensively heated egg products. A recent study of egg-allergic patients aged between 0.5 and 25 years showed that 70% were able to tolerate challenges with well-cooked egg [42]. It is useful to know whether children have achieved tolerance to egg-containing foods by school age, as they no longer need to worry about cooked egg as a hidden ingredient in foods, and allergen avoidance practice becomes less onerous. Resolution of egg allergy occurs in stages starting with tolerance to well-cooked egg (e.g. cake), then lightly cooked egg (e.g. scrambled) followed finally by raw egg (see egg ladder, Fig. 2). Therefore, children who tolerate cooked egg may still react to raw or undercooked egg [18]. As a rule, reactions do not become more severe over time and often become less severe.

The speed with which egg allergy resolves can vary greatly between individuals, and therefore the timing and appropriateness of reintroduction should be individually assessed. Reintroduction should not be attempted within 6 months of a significant reaction to egg. Children who have had only mild symptoms (only cutaneous symptoms) on significant exposure (e.g. a mouthful of scrambled eggs) with no ongoing asthma may have well-cooked egg (e.g. sponge cake) introduced from the age of about 2–3 years at home (Appendix 1). If this is tolerated then reintroduction of lightly cooked egg (e.g. scrambled) may be attempted from about 3–4 years. If there is a reaction at any stage, the previously tolerated diet should be continued and further escalation considered after 6 months. Reintroduction at home should not be attempted if there have been significant gastrointestinal, respiratory or cardiovascular symptoms during previous reactions, only a trace amount has ever been ingested or there is ongoing asthma (see also Text box 4) [42]. A recent publication cautioned against the home introduction of egg, after reporting that injectable adrenaline was administered to a number of children during hospital-based challenges to cooked egg [42]. This study, however, was not designed to answer the issue of practicality and safety of home egg

Text box 4. Consider a supervised challenge (hospital day case) in the following:

<p>Children with previous egg allergy symptoms that affected breathing (cough, wheeze or swelling of the throat, e.g. choking), the gut (severe vomiting or diarrhoea) or the circulation (faintness, floppiness or shock)</p> <p>Children who had a less severe reaction after only trace exposure</p> <p>Children who receive regular asthma preventative inhaler treatment and/or have poorly controlled asthma</p> <p>Children with multiple/complex allergy</p> <p>Children whose parents are unable to comprehend or adhere to protocol</p>

introduction in children with *mild* egg allergy, as recommended in these guidelines. Further, the population studied was significantly skewed by children with severe egg allergy and asthma [42], two factors which would lead one to consider a supervised challenge (Text box 4).

More severe and/or persistent egg allergy. Children with egg allergy, which is either more severe (see Text box 4) or persists beyond the time of usual resolution (6–7 years), should be followed up periodically to assess the likelihood of resolution and to refresh avoidance advice and emergency medication training. A history of any accidental exposure should be sought and SPTs or specific IgE assays repeated. There are no prospective studies based on specific IgE levels, to advise when to challenge these children. However, it would seem reasonable to attempt re-introduction if there has been no significant recent clinical reaction accompanied by a reduction in SPT wheal size or level of serum-specific IgE over time [39]. These children should have a supervised challenge in the hospital and not at home. However, there may be exceptions, for example if a child has had a subsequent mild reaction after significant exposure.

Egg allergy in adults. Egg allergy in adults is likely to be severe and long-lasting and is due either to persistent childhood egg allergy or to true adult-onset egg allergy. Adult-onset egg allergy may be (i) occupational, for example, in workers from the baking industry who develop sensitization by inhalation [43], (ii) part of the bird-egg syndrome with an allergy to egg yolk [44], or (iii) egg-white allergy after eggs have been tolerated for years [45]. A combination of bird-feather sensitization and egg allergy has been named the bird-egg syndrome. Typically, patients develop upper and lower respiratory symptoms on exposure to birds and gastrointestinal symptoms with chicken meat or lightly cooked eggs. The likely allergen is chicken serum albumin Gal d 5 and the egg allergy is due to IgE cross-reactivity with livetin found in egg yolk [46]. Patients should receive egg avoidance advice, emergency medication and training in its use. There is little information on the prognosis for adult egg allergy and patients may be seen periodically to repeat tests for specific IgE and update training in emergency medication.

Vaccinations

There are three vaccines, which are cultured on derivatives of hen's eggs; MMR, influenza and YF. The MMR vaccine is cultured in fibroblasts derived from chick embryos and not on egg and therefore the amount of egg protein is negligible. However, influenza and YF vaccines are cultured in chick embryos and contain measurable amounts of egg protein. Therefore, egg-allergic patients

should be evaluated by an allergy specialist before influenza or YF vaccination is considered.

Measles, mumps and rubella vaccine. All children with egg allergy should receive their normal childhood immunizations, including the MMR vaccination as a routine procedure performed by their family doctor/nurse. This advice should be provided at diagnosis. Studies on large numbers of egg-allergic children show there is no increased risk of severe allergic reactions to the vaccines [47]. Children who have had documented anaphylaxis to the vaccine itself should be assessed by an allergist.

Influenza vaccine. In the United Kingdom, influenza vaccination is currently recommended for all individuals aged >65 years and all individuals aged >6 months in high-risk groups (e.g. chronic respiratory disease including asthma). However, although one study showed a reduction in asthma exacerbations in children who had received the influenza vaccine [48]; most studies failed to show evidence that influenza vaccination reduced the number or severity of asthma exacerbations in asthmatic individuals [49–51]. 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 µg/mL [52].

There are few published data on the risk of allergic reaction to influenza vaccine in egg-allergic individuals [53, 54]. Immediate allergic reactions, including anaphylaxis have been reported in patients with egg allergy after influenza vaccination [55–58]. 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 [53].

According to the BNF, influenza vaccination is contraindicated in patients who have had anaphylaxis to egg. In each case, it is necessary to undertake an analysis of the severity of the egg allergy in order to determine whether and how the vaccine is to be administered. Individuals who eat egg freely can receive the standard dose of influenza vaccine regardless of past history of egg allergy or evidence of sensitization to egg on skin testing or specific IgE. Individuals with more severe egg allergy should be individually assessed to determine whether the benefits of influenza vaccination outweigh the risks.

Several procedures have been proposed to safely vaccinate patients with a history of a severe hypersensitivity reaction to egg. Vaccination with 1/10 dose followed at 30 min with the remaining 9/10 dose was tolerated without any adverse reaction in 83 children (median age, 3

years) (egg allergy was defined by SPT or RAST and history of anaphylaxis or blinded oral challenge). However, the vaccine used in this study contained no more than 1.2 µg/mL egg protein. A single booster injection 1 month after the initial vaccination was tolerated by all 34 recipients who needed a second dose [59]. UK vaccine manufacturers are required to state maximal OVA content in their vaccines. Several show a maximum OVA content of 1 µg per 0.5 mL dose (2 µg/mL), which is higher than the level in the James study [59]. We propose that an influenza vaccine with the lowest OVA content be used in these subjects (<http://www.bsaci.org>). Furthermore although skin testing with vaccine to predict hypersensitivity remains controversial, we suggest that egg-allergic patients undergo skin testing with the vaccine before administration. Vaccines with an OVA content of below 1.2 µg/mL and resulting in a negative skin test may be given in two divided doses (1/10+9/10). If the OVA content of the

vaccine is unknown or >1.2 µg/mL, then a skin prick followed by an intra-dermal test at 1/100 is recommended. If both are negative, the vaccine may be administered in divided doses. Subjects with a positive skin test to egg are more likely to have an allergic reaction on vaccination and the risks should be explained and alternative options discussed with the patient. If influenza vaccination is selected, then depending on the clinical risk the vaccine should be administered using either the two-dose protocol or a multiple graded-dose challenge/desensitization protocol [60, 61]. This procedure should only be undertaken by allergists experienced in treating anaphylaxis, and after informed consent. Figure 3 illustrates the recommended pathway for influenza vaccines for egg-allergic patients.

The intra-nasal live attenuated influenza vaccine contains egg protein and, pending further study, is not currently recommended in patients with egg allergy.

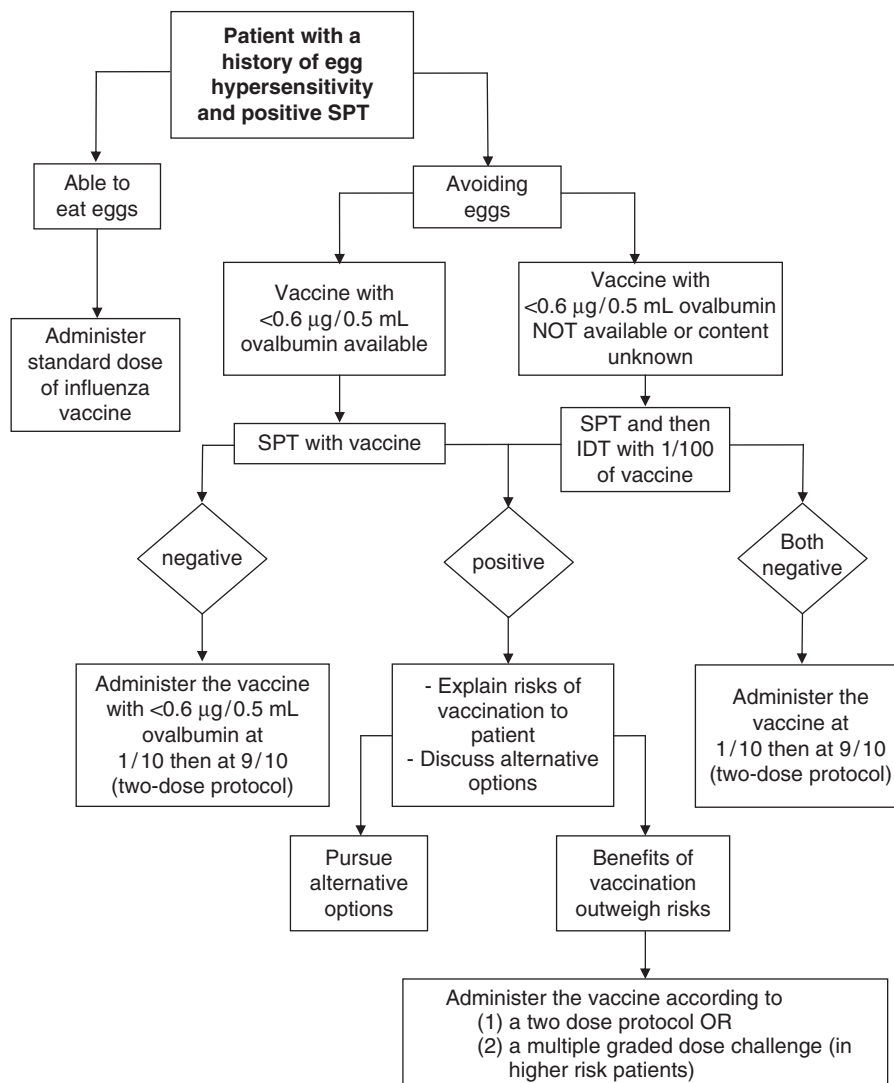


Fig. 3. Influenza vaccination of patients with a history of hypersensitivity to egg.

Yellow fever vaccine. The currently available YF vaccine is not heated and contains live attenuated virus. The vaccine is cultured in chicken embryo and therefore may contain residual chicken and egg proteins. Subjects presenting for YF vaccination should be asked if they have had adverse reactions to previous doses of YF vaccine or other vaccines (containing egg) and if they are allergic to eggs or chicken.

The reported rate of anaphylactic reactions to YF vaccine is 1 in 131000 injections [62]. Some of these reactions were likely to be due to unrecognized allergy to raw egg or other components of the vaccine. In such patients, skin testing with commercial or heated egg extracts were negative but positive with raw egg and YF vaccine [63, 64]. When investigating such patients, a negative IDT to YF vaccine undertaken at 1/100 dilution is likely to predict tolerance [63, 65].

Prospective administration of YF vaccine has not been reported in egg-allergic individuals and therefore the likelihood of severe allergic reactions remains unknown. Reports of anaphylaxis to the YF vaccine may have resulted from either egg or chicken allergy. Allergic reactions occur in some patients who can tolerate well-cooked egg but are allergic to raw egg. Therefore, a detailed history of egg and chicken allergy is required followed by skin prick and intra-dermal testing to egg and the YF vaccine before the decision on whether to vaccinate. If skin testing is positive, desensitization in a specialist allergy clinic should be considered for travellers to countries where vaccination is compulsory [66]. Therefore, all egg- or chicken-allergic individuals needing YF vaccination should be assessed by an allergist.

Co-morbid associations

Asthma and peanut allergy

Children with egg allergy are at an increased risk of other allergic disease especially asthma (odds ratio 5.0) [3] and peanut/nut allergy. A careful history should be taken to enquire about symptoms suggestive of asthma. The presence of asthma may increase the potential severity of accidental egg reactions and excellent asthma control should be a priority. In the absence of a clinical history of peanut allergy, testing for peanut sensitization in egg-allergic children is not currently recommended.

Prevention

There are currently no effective strategies for the primary prevention of egg allergy, although studies are underway examining the effect of early-life introduction of allergenic foods.

Future research

- Investigation of oral immunotherapy for the treatment of egg allergy.
- Development of more robust diagnostic cut-off values relevant to unselected clinic patients especially for serum-specific IgE.
- The value of specific IgE testing to major egg allergens in predicting the resolution of egg allergy and severity of future reactions.
- Auditing the use of egg challenges undertaken at home compared with supervised hospital provocation.

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These *guidelines* inform the management of egg allergy. Adherence to these guidelines does not constitute an automatic defence for negligence and conversely non-adherence is not indicative of negligence. It is anticipated that these guidelines will be reviewed 5 yearly.

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Appendix 1: Home introduction of baked (i.e. well cooked) egg as an ingredient, for children with a history of egg allergy

Background

For children who have had a previous mild reaction to egg (e.g. facial rash or vomiting, but NOT wheezing, throat tightening or floppiness), it is appropriate to try reintroduction of baked egg products at home. Most children with egg allergy grow out of it in early life. Raw or uncooked egg is more likely to cause allergy than cooked egg. As the allergy resolves with time, many children will start to tolerate well cooked (baked egg products) followed by lightly cooked whole egg (e.g. scrambled egg) then finally uncooked whole egg. This protocol informs parents how to perform the egg challenge at home. Children who have had more severe symptoms may need to have a challenge performed under hospital supervision. Your doctor will advise when it is appropriate to try each stage of reintroduction. Use the following information only as a guide. There may be variations for individual children, which your doctor will explain. Text box (A1).

Protocol for cooked egg re-introduction at home

1. Postpone the reintroduction if your child is unwell.
2. Have oral antihistamines available.
3. Bake a fairy cake containing egg, ensure that the other ingredients of the cake are tolerated, e.g. cow's milk. (Suggested recipe: 1 egg, 4 oz self-raising flour, 4 oz margarine, 4 oz caster sugar to make eight cakes).
4. Begin by rubbing a small amount of cake on the inner part of your child's lips.
5. Wait for 30 min and allow your child to continue normal activities.
6. Signs of an allergic reaction may include: Itching, redness, swelling, hives (nettle-sting type rash), tummy pain, vomiting or wheezing.

Text box (A1). The following children will need a supervised challenge in hospital (day case):

Children with previous egg allergy symptoms that affected breathing (cough, wheeze or swelling of the throat, e.g. choking), the gut (severe vomiting or diarrhoea) or the circulation (faintness, floppiness or shock)
Children who also receive regular asthma preventative treatment and/or have poorly controlled asthma

7. If there have been no symptoms, give your child a pea-sized amount of cake to eat.
8. A day or two later, if there have been no symptoms; give your child twice the amount of cake to eat.
9. Repeat stage 8 until the cake is finished. Symptoms usually occur up to 2 h after the last dose (worsening of eczema may occur after some hours, or the next day). This can then be repeated using a two-egg recipe (with 4 oz flour, sugar and margarine).
10. If symptoms occur then, do not give any more cake. Give a dose of antihistamines (according to the label) by mouth. Consider attempting reintroduction again in six months time and discussion with your doctor.
11. If the cake has been tolerated, then your child should eat this regularly. Try other foods containing well-cooked egg, e.g. biscuits, pasta. Do not worry if your child does not like to eat egg products – this is quite common.

Appendix 2: Home introduction of lightly cooked whole egg for children with a history of egg allergy

Background

This information sheet is for children who can already tolerate well-cooked egg as an ingredient (e.g. in cakes) and wish to introduce lightly cooked whole egg at home. Do not use this protocol if your child has had a previous severe reaction to egg. Your doctor will advise you when it is appropriate to try this.

1. Postpone the reintroduction if your child is unwell.
2. Have oral antihistamines available.
3. Cook a portion of scrambled eggs, but ensure that other ingredients are tolerated, e.g. cow's milk.
4. Begin by rubbing a small amount of egg on the inner part of your child's lips.
5. Observe for 30 min, allow the child to continue normal activities.
6. Signs of an allergic reaction may include: Itching, redness, swelling, hives (nettle-sting type rash), tummy pain or vomiting.
7. A day or two later, if there have been no symptoms; give your child a small bite of scrambled egg to eat.
8. Repeat stage 7 with increasing amounts of scrambled egg at intervals of several days until a whole portion is finished. Symptoms usually occur up to 2 h after the last dose (worsening of eczema may occur after some hours, or the next day).
9. If symptoms occur, then do not give any more egg. Give a dose of antihistamines (according to the label) by mouth. Consider attempting reintroduction again in 6 months time and discussion with your doctor.
10. If all of the doses have been tolerated, then your child should continue to eat lightly cooked whole

egg. Try similar foods, e.g. boiled egg. Do not worry if your child does not like to eat eggs – this is quite common.

Appendix 3: Patient information sheet – hen's egg allergy

What is egg allergy?

Egg allergy is caused by an allergic reaction to egg protein. This protein is found mostly in the egg white but also in the yolk. It is common in children under 5 years and usually first noticed in infancy when egg is introduced into the diet for the first time. It is rare for egg allergy to develop in adulthood. Those who develop egg allergy as adults may also be allergic to birds or feathers that contain a protein, which is similar to that found in egg yolk.

What are the symptoms?

Most reactions are mild. Commonly infants refuse the egg-containing food, develop redness and sometimes swelling around the mouth soon after skin contact and then vomit after eating. Stomach ache or diarrhoea may also occur. Rarely, some children also develop a more severe reaction with cough, an asthma-type wheeze or even anaphylaxis. Further reactions do not, as a rule, become increasingly severe unless a greater amount or a less well-cooked form is eaten; accidental reactions are almost always milder than the original. Accidental skin contact usually only causes a rash but no generalized or dangerous symptoms; severe reactions rarely occur unless egg is eaten.

Egg allergy may also be responsible for worsening of eczema, but this is usually more difficult to diagnose given the slower time to onset of symptoms.

Will the allergy resolve?

Egg allergy will resolve in most children, usually by school age. Generally, as they grow out of it, children tolerate well-cooked egg (e.g. cakes) first, followed by lightly cooked (e.g. scrambled eggs) before finally being able to eat raw egg. Children who have had more severe reactions (e.g. with wheezing) may take longer to grow out of their allergy and in some cases egg allergy will persist.

How is egg allergy diagnosed?

The diagnosis of egg allergy is based on the history of previous reactions, and can be confirmed by skin tests or blood tests.

What is the treatment?

The best current treatment is to avoid all food containing egg for 1–2 years, allowing the allergy time to resolve. Egg may be found in a wide range of foods, including: cakes, pastries, desserts, meat products, salad dressings, glazes, pasta, battered and bread crumbed foods, ice cream, chocolates and sweets. It may also be referred to by unusual terms especially on imported foods e.g. egg lecithin or albumen (= egg white). The proteins in eggs from other birds are very similar to those

Text Box (A3). Products useful for an egg-free diet

Egg-free products include	Egg-free mayonnaise Egg-free cakes and muffins Egg-free puddings Egg-free omelette mix
Whole egg replacers	Whole egg replacer (Allergycare) Ener-G egg replacer (General Dietary) Loprofin egg replacer (SHS) No-egg replacer (Orgran)
Egg white replacer	Loprofin egg white replacer (SHS)

in hens' eggs and should be avoided too. This list is not exhaustive and because ingredients can change, food labels must be read carefully every time you shop. Text Box (A3).

Lists of egg-free foods can be obtained directly from many food manufacturers and supermarket chains. They are very helpful in the day-to-day management of the diet.

You should also obtain antihistamine syrup (available without prescription) and keep this available at mealtimes. Your doctor may provide an adrenaline injection, but children with egg allergy would only require this if they were considered to be at high risk of a severe allergic reaction, which is unusual. If you are provided with an adrenaline injection your doctor will show you how to use it and provide a treatment plan. You should keep a copy with your child's medication and also give copies to others, e.g. nursery/school teachers and grandparents. You should also provide emergency medication for your child's school or nursery, which your doctor can prescribe.

After a period, your doctor will provide advice on egg reintroduction. Your doctor may want to perform an allergy test on your child's blood or skin (these tests are safe), or may ask you to begin introducing well-cooked egg at home. Advice sheets are available to help you introduce egg.

If your child has had more severe reactions involving wheezing, the decision whether to reintroduce egg will be made by an allergy specialist.

Can my child have their routine immunizations?

All children with egg allergy should receive their normal childhood immunizations, including the MMR vaccination as a routine procedure performed by their family doctor/nurse. MMR is *not* grown on hen's egg, as widely believed. Studies on large numbers of egg-allergic children show that there is no increased risk of severe allergic reactions to the vaccine.

As with other vaccines, MMR should be postponed if children are unwell. Adrenaline should be readily available at the clinical site in all cases because anaphylaxis, although rare, can occur.

If previous vaccination (MMR or other) resulted in a severe allergic reaction (any breathing problems or collapse), then the child should be seen by an allergy specialist before further immunizations are given.

What about other immunizations?

Influenza vaccine is prepared on hen's egg and may contain small amounts of egg protein. There is a risk of anaphylaxis in people with severe egg allergy and they should see an allergy specialist to assess the risk. People who can eat moderate amounts of egg can have the vaccine even if they have had an allergy to egg in the past and even if their allergy tests for egg are still positive.

Yellow fever vaccine contains measurable amounts of egg protein and people with egg allergy who need it should be seen by an allergy specialist.

Can I continue to breastfeed my baby?

If you are breastfeeding, any food proteins, such as egg, will also be present in your breast milk. If your baby is well, with no allergic symptoms, then it is fine for you to eat egg as normal. If your baby has symptoms, such as eczema or rashes, which may be due to an allergy to the egg in your milk, then it may be worthwhile removing egg from your own diet for a couple of weeks to see whether your baby's symptoms improve. If there is no improvement in your baby's condition, then eggs can be re-introduced back into your diet.

Does egg allergy mean my child is at risk of other allergies?

Most children with egg allergy will already have a history of eczema. Egg allergy also increases the risk of developing asthma later in childhood, but not in all children. Allergies to other foods are more common in egg-allergic children.

I have another child/infant to whom I have not given egg. When should it be introduced into their diet?

The Department of Health recommends that egg should be introduced into the weaning diet from 6 months onwards. There is no evidence to suggest that delaying the introduction of egg beyond 6 months will reduce the chance of your child developing egg allergy.