

Egg allergy: Are all childhood food allergies the same?

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Abstract: Egg allergy is one of the most common food allergies in childhood affecting about 1–2% of preschool children and differs in a number of ways from other common childhood food allergies such as cows milk and peanut. Common egg allergens are altered both by heat and gastric enzymes. Compared with peanuts/tree nuts and milk, egg allergy appears less likely to cause severe life-threatening reactions or fatal anaphylaxis. Children are much more likely to outgrow egg allergy by school age as compared with peanut allergy. While the MMR vaccine is no longer contraindicated in egg allergy, influenza vaccine is contraindicated in children with anaphylaxis to egg. An understanding of the similarities and differences in these common food allergies of childhood is helpful in the management of these common and increasing problems.

Key words: anaphylaxis; egg hypersensitivity; egg protein; milk hypersensitivity; peanut hypersensitivity.

Egg allergy is one of the most common food allergies in childhood and a significant issue for paediatricians. There has been confusion and controversy surrounding vaccine contraindications in the presence of known egg allergy. In this review we examine the nature of egg allergy and attempt to assess its risks in comparison to the other most common childhood food allergies, cows milk and peanut.

Prevalence

Eighty per cent of food allergies in children are caused by peanut, milk and egg.¹ The prevalence of IgE-mediated reactions to egg in a population-based study of 2-year-olds was 1.6%.² However, at 7 years only 0.2% of children had positive skin prick test to egg as compared with 1.4% to peanut, 1.0% to tree nut and 0.4% to cows milk.³ The figures in 7-year-olds relate to sensitisation and only a proportion of these children (around 1/3) would be likely to develop clinical reactions. There is no Australian-based population data for the prevalence of

sensitisation or clinical reactions to egg in preschool children. In an Australian community-based population of 8- to 9-year-olds, none of 456 Tasmanian children had a positive skin prick test to egg.⁴

Clinical Presentation and Diagnosis

Clinical reactions to egg are predominantly IgE-mediated immediate reactions characterised by urticaria, angioedema, vomiting, diarrhoea and wheeze. Contrary to popular opinion, repeated reactions to foods do not necessarily escalate in severity. Ewan *et al.* followed up a cohort of 747 peanut-allergic children for a median duration of 39 months.⁵ Of children with a mild initial reaction and a repeat reaction only 18% of the repeat reactions were more severe. Of children with a moderate to severe initial reaction 98% of the repeat reactions were less severe. Although comparable data are not available for egg allergy, it is likely that similar considerations would apply.⁵ In general, children will most likely react in a similar manner to their previous reaction although there have been reports of severe reactions with previous mild reactions to all common food allergens.

Some children with atopic dermatitis have a delayed reaction causing a worsening of their dermatitis 1–2 days after exposure to egg. These delayed reactions are generally not IgE-mediated and are probably caused by T-cell sensitisation. There are currently no routine skin or blood tests which are useful in the diagnosis of these delayed reactions. Patch testing with food allergens offers the possibility of further clarifying the diagnosis of delayed reactions. However, this form of testing while having a high degree of specificity (95%) has a low degree of sensitivity (approximately 10%).⁶

Skin prick tests and RASTs are sensitive indicators that a child has food-specific IgE, however, are not necessarily predictive of

Key Points

- 1 Egg allergy predominantly affects preschool children.
- 2 Severe life-threatening reactions are less common in egg allergy than in peanut/tree nut allergy.
- 3 Heat and digestion alter the allergenicity of egg proteins.

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likelihood or severity of clinical reactions. A strongly positive SPT to egg (wheal > 7 mm) was found to be strongly predictive of adverse reaction on formal food challenge and a wheal of <3 mm is useful in excluding egg allergy.⁷ Quantitative levels of IgE have been determined for egg allergy which can identify patients who are highly likely to have a reaction to egg.⁸ Utilising the Pharmacia CAP RAST system (Pharmacia, Uppsala, Sweden), egg-specific IgE antibody levels of 7 kUA/L or greater identified patients with ≥95% probability of reacting to an egg challenge. The levels of IgE utilised to determine clinical reactivity to egg are strongly age dependent particularly in children under 1 year of age.⁹ The remainder of this review will focus on IgE-mediated reactions.

What Are the Differences in Natural Exposure?

There is a significant difference in the timing and relative quantities of egg, milk and peanut exposure in early childhood. Egg is usually introduced after 6 months in varying quantities and in various forms; as cooked whole egg, egg white in cooked foods such as cakes or noodles, or through contact with egg yolk in custard. On average, Australian mothers offer their infants one egg per week.¹⁰ In general, the amount of cows milk protein ingested is greater than egg or peanut. Infants ingest peanut at a later age with peanut butter being the commonest form of exposure.¹¹ The relative portion sizes consumed by 1- to 2-year-old children were 226 g milk (7.2 g protein), 43 g egg (4.3 g protein) and 14 g peanut butter (3 g protein).¹² Most infants are exposed to large quantities of cows milk allergens from an early age with exposure occurring in about half the Australian population by 4 months of age.¹³ The mean daily intake of milk in 2- to 4-year-olds is approximately 350 mL (11.9 g protein). The lesser exposure to egg and peanut allergens in the first year of life may reduce the occurrence of significant clinical reactions but not necessarily sensitisation.

How Much Food Allergen Is Needed to Trigger a Reaction?

The threshold doses of allergen for clinical reactivity in children with a previous reaction to a food are comparable for egg, milk and peanut.¹⁴ In addition, the amount of food required to provoke a reaction in 50% of allergic children was approximately 1/20 (2000 mg) of an egg white, 30 mL milk (965 mg milk protein) or 1½ peanuts (500 mg).^{15,16} In relation to the average portion size consumed by a 1- to 2-year-old child,¹² these represent lesser amounts of peanut (1/27) and egg (1/20) as compared with cows milk (1/7).

How Do Children Become Sensitised to Egg?

Children are frequently found to be sensitised without having a previous history of egg ingestion. Significant reactions can therefore occur on first known ingestion or skin contact with egg. In one study of 107 infants with atopic dermatitis and no known egg ingestion, 67% had evidence of IgE sensitivity to egg and positive reactions to an oral food challenge.¹⁷ Sensiti-

sation may theoretically occur either by transplacental transfer of egg allergen¹⁸ or through breast milk.¹⁹ There is no evidence that egg avoidance in pregnancy decreases sensitisation in the infant.²⁰

What Are the Differences in the Natural History?

Egg and milk allergy generally remit in childhood in contrast to peanut allergy which usually persists into adult life. Approximately two-thirds of egg-allergic children outgrow their allergy by 5 years of age and 85–90% of children with milk allergy are tolerant by 3 years.^{21,22} In comparison, only 20% of children with peanut allergy become tolerant by 6 years.²³ In egg allergy, the median time from appearance of first symptoms to tolerance is 35 months. Smaller SPT wheal size, cutaneous reactions and lower specific IgE antibody levels are positive prognostic factors for tolerance.²¹ It has been postulated that once tolerance is established regular intake of the food may help to maintain the tolerance.²⁴

What Components of the Egg Are Allergenic?

Clinically relevant allergens are found in both egg white and yolk; however, egg white allergy is more common. Egg white allergens include ovalbumin, ovomucoid, ovomucin, ovotransferrin and lysozyme. An Australian study of IgE egg allergen binding in egg-allergic children suggested that there were four distinct groups of sera reacting with discrete sets of proteins.²⁵ The allergenic proteins of the four groups were: group 1 lysozyme and ovalbumin, group 2 ovomucoid and group 3 ovomucin. All these are egg white proteins. The fourth group showed binding to all the egg white proteins and to the egg yolk proteins apovitellenins I and VI and phosvitin as well. The frequency of reaction of sera from egg-allergic adult patients to ovotransferrin is 53%, ovomucoid 38%, ovalbumin 32% and lysozyme 15%.²⁶ Ovalbumin comprises of >50% of egg white protein, but ovotransferrin and ovomucoid were the most frequently identified relevant allergens in adults with positive clinical reactions. There are also multiple allergenic proteins in egg yolk, with the commonest being alpha-livitin.²⁷

Alteration of Allergenicity

There is variability in the stability of food allergens to heat, proteolysis and digestion.¹ Food allergens may be altered by heat and acidity. An epitope is that portion of the antigen which binds with antibody. Many epitopes on proteins involve amino acids from regions of the polypeptides that are distant from one another in the primary structure. These are called conformational epitopes and denaturation of the secondary structure of a protein by heat or acidity can destroy the allergenicity. Heating reduces the allergenicity of ovomucoid and ovalbumin, but does not affect lysozyme.²⁸ Boiling egg noodles reduced the amount of detectable egg white protein by greater than 99%.²⁹ Heating also reduces the allergenicity of cows milk whey but not casein

proteins.³⁰ The temperatures required for dry roasting increase the allergenicity of peanut proteins.³¹

Ovomucoid may also be reduced in allergenicity by gastric pH.³² The reduction in allergenicity by heat or gastric digestion provides an explanation for those children with who react to uncooked but not cooked egg³³ and for subjects who react to egg after cutaneous contact but not after ingestion.³⁴ Subjects who are sensitised to the egg allergens which are resistant to gastrointestinal degradation appear to be less likely to outgrow their sensitivity.³⁵ It is possible that the use of inhibitors of gastric acid secretion in young children may be a factor which promotes food sensitisation.³⁶

Anaphylaxis and Deaths

Severe life-threatening events and fatal anaphylaxis to egg in children are less common than to peanut and milk. Over the 15-year period of 1990–2005, there have been six published series of food-related anaphylaxis in children from four different countries (UK, USA, Sweden and Germany) recording 31 deaths and 132 severe life-threatening reactions. The triggers of fatal reactions were egg 7%, milk 17%, peanut 48% and peanut or tree nut 62%. It is of note that both the fatalities to egg occurred in young children (3 months and 2 years) which contrasts with those to peanut which were all in children over 5 years of age. With cows milk, the fatalities were in children of all ages. Foods involved in severe life-threatening reaction were egg 7%, milk 12%, peanut 20% and peanut or tree nut 45%. Thus, the number of fatal reactions was nine times, and the number of severe life-threatening reaction seven times greater to peanut or tree nuts as compared with egg.^{37–42}

MMR Vaccines and Influenza

Measles vaccines are produced in a culture of chick embryo fibroblasts. In the past, MMR vaccine for children with egg allergy has been controversial; however, now it is agreed that

MMR vaccine is not contraindicated in egg allergy. A study in Melbourne gave 410 egg-allergic children MMR vaccine and only four children had minor reactions that did not require any intervention.⁴³ Recent evidence suggests that allergic reactions to MMR vaccines have been caused by sensitisation to gelatin.⁴⁴

Anaphylaxis has been reported after administration of influenza vaccine. In 1976 in the USA, there were 11 episodes of non-fatal anaphylaxis in 48 million doses.⁴⁵ Fatal anaphylaxis has also been documented in an egg-allergic child following influenza immunisation.⁴⁶ The influenza vaccine is derived from egg embryo fluid. An egg protein content of less than 1.2 µg/mL of egg protein is standard for influenza vaccine used in Australia. Egg-allergic children have been safely given influenza vaccine with a 2-dose injection protocol (1/10, followed 30 min later by 9/10 dose) with vaccines containing less than 1.2 µg/mL egg protein.⁴⁷ The Australian Immunisation Handbook recommends that a severe reaction to egg is a contraindication to influenza immunisation. The American Association of Paediatrics recommends that children with reactions less severe than anaphylaxis can be immunised with the influenza vaccine after performing a skin prick test followed by intradermal testing with the vaccine. If the SPT is positive, and the vaccine is indicated, a multidose protocol can be used. The issue of influenza vaccination of egg-allergic children would become a significant issue if a mass vaccination campaign were required for avian influenza.

Are There Issues Related to Dietary Exclusion?

Childhood IgE-mediated food allergy has a significant effect on quality of life for the children and their families. Families with food-allergic children have reduced scores for general health perception, emotional impact on the parent and limitation of family activities.⁴⁸ It is likely that dietary allergen avoidance contributes to the decreased quality of life. Parents obtain dietary advice from a variety of places, not all of which are

Table 1 Comparison of egg, milk and peanut and other tree nut allergies

	Egg	Milk	Peanut
Prevalence of sensitisation in 2- to 4-year-olds ^{22,51,52}	1.0%	2.2–7.5%†	3.3%
Prevalence of clinical reaction in 2- to 4-year-olds ^{2,53}	1.6%	1.1%	1.5%
Prevalence of sensitisation in 7-year-olds (SPT+) ³	0.4%	0.2%	1.4%
Natural history ^{21–23}	67% resolved by 5 years	85–90% resolved by 3 years	20% outgrown at median age 6 years
% allergic children reacting to 15 mg solid food or 0.3 mL milk ¹⁴	5.6%	1.7%	3.9%
Relative amounts of the average portion size 50% of allergic children will react to ¹⁵	1/20	1/7	1/27
Relative incidence of fatal reaction ^{37–42}	7%	17%	48% (62% including other nuts)
Relative incidence of severe life-threatening reaction ^{37–42}	7%	12%	20% (45% including other nuts)
Effect of heat ^{30,31}	Decreased reactivity for some proteins	Decreased reactivity for some proteins	Unchanged or increased if roasted
Effect of digestive enzymes – proteolysis ^{54,55}	Decreased reactivity	Decreased reactivity	Unchanged

†Incidence of allergy in first year of life.

evidence based or sound. In a study by Eggesbo, up to 20% of children whose parents perceive they had an allergy to egg or milk were on overly restrictive diets. On the other hand, up to 50% of children who have confirmed allergy that should be on strict diets lacked appropriate dietary restrictions.⁴⁹

It remains controversial as to whether stringent egg exclusion is required in those children who tolerate small amounts of cooked egg in prepared foods without clinical symptoms. There is no good evidence that this practice lessens the sensitisation period or alters the natural history of tolerance. It is also postulated, but as yet unproven that exposure to small amounts of allergen below a threshold that produces symptoms might actually promote the development of tolerance²⁴ and that some food allergen exposure might actually promote rather than hinder recovery from a food allergy.⁵⁰

Conclusion

As one of the most common childhood food allergies, egg allergy is an important paediatric issue particularly in preschool children. There are significant differences between egg, milk and peanut allergies (Table 1). The majority of children will outgrow their egg allergy by school age. The number of fatal and severe life-threatening events in egg allergy appears to be less than that found in allergy to milk and peanut. The reduction in allergenicity of egg allergens by cooking and gastric ingestion may explain why a number of egg-allergic children appear to tolerate some egg in prepared foods. An understanding of the similarities and differences in the common IgE-mediated food allergies of childhood is helpful in the management of these common and increasing problems.

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