Baked Milk and Egg Diets for Milk and Egg Allergy Management

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KEYWORDS

• Cow's milk allergy • Hen's egg allergy • Baked milk • Baked egg
• Extensively heated milk • Extensively heated egg • Milk allergy • Egg allergy

KEY POINTS

- Baked milk and egg are well tolerated in the diets of a majority of milk- and egg-allergic children.
- Inclusion of baked milk and egg in the diet of children who are tolerant of these baked forms may accelerate the resolution of milk and egg allergy.
- Clinical factors and biomarkers for predicting baked milk and egg tolerability or reactivity are lacking, and further research is needed.
- Tolerance to baked milk and egg may be a marker of a milder and transient milk and egg allergy.
- Anaphylaxis to baked milk and egg can occur, thus physician-supervised introduction is recommended.

INTRODUCTION

Cow's milk (CM) and egg allergies are some of the most common food allergies in young children. It is estimated that up to 3.8% and 2% of children less than 5 years of age have CM and egg allergy, respectively.[1] CM and egg are a large part of diets in many cultures. These allergens are commonly found in baked goods and are an important source of protein and calories, particularly in young children. Strict elimination of all CM and egg products may put children at risk for nutritional deficiencies as well as have a psychosocial impact. Studies show that the baked form of CM and egg is less allergenic and tolerated by a majority of CM- and egg-allergic children. The

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ability to add baked CM and egg products to the diets of CM- and egg-allergic children can improve the nutritional content of their diet and increase quality of life. In addition, data suggest that including baked CM and egg in the diet may accelerate resolution of CM and egg allergy. The goal of this review is to examine our current understanding of the effects of baked CM and egg in the management of CM and egg allergy.

PREVALENCE OF BAKED MILK AND EGG TOLERANCE

A CM allergy natural history study in a multi-site US population by Wood and colleagues,[2] which followed 293 infants, found that 21% (32 of 155) of subjects with CM allergy at the 5-year time point tolerated some baked milk products. An egg allergy natural history study in the same population by Sicherer and colleagues,[3] which followed 213 infants, found that 38% (43 of 113) of subjects with egg allergy at the 6-year time point tolerated some baked egg products. Percentages are typically higher in studies in which baked CM and egg tolerance are proactively evaluated with oral food challenges. For example, in a large population study in Australia by Peters and colleagues[4] in which baked egg challenges were offered at age 1 and 2 years of age to challenge-proven raw egg–reactive children, 80% (n = 126 of 157) of subjects tolerated baked egg at baseline.

Overall, studies show that between 69% and 83% of CM-allergic children can tolerate baked CM, and between 63% and 83% of egg-allergic children can tolerated baked egg, as detailed in **Tables 1** and **2**, **Box 1**. The studies that were reviewed used similar methods for baking CM and egg. In baked CM studies, a serving size was the equivalent of 0.5 to 2.6 g of CM protein in a muffin or cupcake baked at 350°F (180°C) for 20 to 30 minutes.[5–8] In baked egg studies, a serving size was the equivalent of 1 to 3 g egg protein in a muffin or cupcake baked at 350°F to 375°F (180°C–190°C) for 20 to 30 minutes.[9–16]

Not many studies have examined the tolerance of baked milk or egg in patients with eosinophilic esophagitis (EoE). One study examined 15 patients with EoE who were electively ingesting baked milk. Eleven patients (73%) showed tolerance of baked CM ingestion, and 4 patients showed a relapse of EoE disease on esophageal biopsy ($\geq$10 eosinophils per high-power field).[17] This small study suggests that baked milk and egg proteins may be tolerated most patients with EoE and warrant further investigation.

FOOD PROCESSING

Proteins possess both sequential and conformational epitopes that immunoglobulin E (IgE) antibodies may recognize and bind to. Heating alters conformational epitopes and induces other protein structural changes so that IgE antibodies may no longer bind.[18] Interaction of food proteins with one another (such as CM and egg with a wheat matrix) may also alter allergenicity.[19]

Casein makes up 80% of CM protein and is immunodominant, whereas whey makes up 20% and consists primarily of α-lactalbumin and β-lactoglobulin.[20] Casein and α-lactalbumin are more heat stable than β-lactoglobulin.[18] In one study, most children older than 9 years with persistent CM allergy had IgE binding to sequential (linear) casein epitopes as compared with patients younger than 3 years who are likely to outgrow CM allergy.[21]

Ovalbumin makes up 54% of egg white (EW) protein, however, ovomucoid (OM), which makes up 11%, is considered the immunodominant protein.[22] Compared with ovalbumin, OM is stable to both heat and digestive enzymes.[23] Children with persistent egg allergy have had higher levels of OM-specific IgE, specifically to sequential (linear) OM epitopes.[22,24]

Table 1
Prevalence of baked milk tolerance in studies using baked milk challenges

	Number of Subjects	Median Age (y) (Unless Indicated)	Unbaked Milk OFC?	Median CM IgE (kU_A/L) of BM Tolerant	Median CM IgE (kU_A/L) of BM Reactive	Median CM SPT Wheal (mm) of BM Tolerant	Median CM SPT Wheal (mm) of BM Reactive	Proportion Tolerant to BM (%)
Nowak-Wegrzyn et al,[5] 2008	91	Mean 7.5 (range, 2.1–17.3)	Yes; unless >95% PPV testing[a]	2.43 (range, 0–79.1)	11.6 (range, 0.69–101.0)	7 (range, 2.5–19.0)	9.5 (range, 5–24)	75
Caubet et al,[6] 2013[b]	121	BM tolerant: 7.5 (range, 4–11); BM reactive: 8.0 (range, 4.4–10.9)	Yes; unless >95% PPV testing[a]	4.0 (range, 0.2–42.3)	11.9 (range, 0.8–50.5)	—	—	69
Bartnikas et al,[7] 2012	35	BM tolerant: 8.9 (range, 3.9–18.1); BM reactive: 3.7 (range, 3.1–11.0)	No	1.93 (range, <0.35–20.6)	2.39 (range, <0.35–31.0)	10 (range, 0–20)	15 (range, 7–20)	83
Mehr et al,[8] 2014	70	BM tolerant: 4.5 (IQR, 2.5–8.0); BM reactive: 7.3 (IQR, 4.9–9.6)	No	—	—	8 (IQR, 7–10)	8.5 (IQR, 7.5–10)	73

Abbreviations: BM, baked milk; IgE, immunoglobulin E; IQR, interquartile range; OFC, oral food challenge; PPV, positive predictive value; SPT, skin prick test.
[a] Greater than 95% positive predictive value CM immunoglobulin E for milk allergy: greater than 5 kU_A/L in children 2 years of age or younger or greater than 15 kU_A/L in children older than 2 years; greater than 95% positive predictive value CM skin prick test wheal diameter of 8 mm or greater.
[b] Second cohort only; first cohort is already described in Nowak-Wegrzyn and colleagues.[5]

Table 2
Prevalence of baked egg tolerance in studies using baked egg challenges

	Number of Subjects	Median Age (y) (Unless Indicated)	Unbaked Egg OFC?	Median EW IgE (kU_A/L) of BE Tolerant	Median EW IgE (kU_A/L) of BE Reactive	Median EW SPT Wheal (mm) of BE Tolerant	Median EW SPT Wheal (mm) of BE Reactive	Proportion Tolerant to BE (%)
Lemon-Mule et al,[9] 2008	91	Mean 6.9 (range, 1.6–18.6)	Yes; unless >95% PPV testing[a]	1.3 (25%–75% IQR, 0.6–4.3)	5.1 (25%–75% IQR, 1.9–11.1)	6 (IQR, 5–8)	8 (IQR, 6.3–9)	70
Clark et al,[10] 2011	95	4.6 (IQR, 2.7–7.3)	Yes	2.2 (IQR, 0.7–7.7)	5.1 (IQR, 2.6–16.6)	4 (IQR, 3–5)	6 (IQR, 4–7.5)	66 (by 6 y of age)
Lieberman et al,[11] 2012	100	5.9 (range, 1.2–19.8)	No	2.81	5.85	7	7	66
Cortot et al,[12] 2012	52	7.2 (range, 2.2–18); BE tolerant: 8.8; BE reactive: 7.0	No	2.02 (range, <0.35–13.00)	1.52 (range, 0.51–6.10)	12 (range, 0–35)	17 (range, 10–30)	83
Turner et al,[13] 2013	236	BE tolerant: 3.2 (IQR, 1.8–5.8); BE mild-moderate symptoms: 4.7 (IQR, 1.9–6.8); BE anaphylaxis: 4.8 (range, 3.0–5.9)	No	—	—	8 (IQR, 7–10)	Mild-moderate symptoms: 9 (range, 6–11); anaphylaxis: 9 (range, 8.0–11.5)	64

Tan et al,[14] 2013	143	3.8 (IQR, 1.8–6.7)	No	—	—	8 (IQR, 7–11)	9 (IQR, 8–11)	63
Bartnikas et al,[15] 2013	169	BE tolerant: 5.22 (range, 0.84–17.07); BE reactive: 6.18 (range, 2.02–12.93)	No	1.31 (range, <0.35–42.00)	6.00 (range, <0.35–17.10)	9 (range, 0–35)	13 (range, 3–20)	84
Turner et al,[16] 2014	186	BE tolerant: 5.1 (IQR, 3.8–8.8); BE reactive: 5.6 (IQR, 2.7–10.6)	No	—	—	5 (IQR, 4–7)	8 (IQR, 5–10)	66

Abbreviations: BE, baked egg; EW, egg white; IgE, immunoglobulin E; IQR, interquartile range; OFC, oral food challenge; PPV, positive predictive value; SPT, skin prick test.

[a] Greater than 95% positive predictive value egg white immunoglobulin E for egg allergy: greater than 2 kU_A/L in children 2 years of age or younger or greater than 7 kU_A/L in children older than 2 years.

Box 1
Baked milk and egg challenge protocol

Preparation

- Provide baked milk or egg recipe to family.
- For children older than 2 years: If using recipes published in Leonard and colleagues,[33] ask the family to bring in 1 muffin if the recipe made 6 muffins or 2 to 3 muffins if it made greater than 6.
- For younger children less than 2 years of age and picky eaters, the total serving size should be adjusted, for example, one-half muffin.
- Schedule the challenge when other atopic conditions are stable (eczema, asthma, allergic rhinitis, urticaria/angioedema, and so forth).
- Medications that may interfere with the challenge should be discontinued at the appropriate time before the challenge.[36]
  - Antihistamines: 5 half-lives
  - H2-blockers: 12 hours
  - Oral/IM/IV steroids: 3 days to 2 weeks
  - Leukotriene antagonist: 24 hours
  - Short- and long-acting bronchodilators: 8 hours
- Consider delaying the challenge if patients have had a significant clinical reaction to the challenge food within the past 6 to 12 months.

Challenge day

- Ensure medications have been discontinued for the appropriate length of time.
- Obtain baseline vitals, including weight for medication dosing. Consider the pulmonary function test or peak flow in patients older than 5 years with a history of asthma.
- Perform a thorough physical examination. Patients should be free of fever, significant rash, upper or lower respiratory symptoms, abdominal symptoms, or vomiting and diarrhea within the past 48 hours.
- Calculate doses of emergency medications.

Challenge procedure

- Administer doses 15 to 20 minutes apart. Perform a brief physical examination between each dose. If there is a suspicion that a reaction may be developing, consider delaying the next dose, repeating the last dose, or stopping the challenge.
- Divide 1 muffin (containing 1.3 g milk protein or 2.2 g of egg protein) into
  - Dose 1: one-eighth muffin
  - Dose 2: one-eighth muffin
  - Dose 3: one-quarter muffin
  - Dose 4: one-half muffin
- With a higher-risk challenge, muffins may be divided into more doses.

Treatment of reactions

- Antihistamines
  - Cetirizine 0.25 mg/kg by mouth (max 10 mg)
  - Diphenhydramine 1.0 to 1.5 mg/kg by mouth/IM/IV (max 50 mg)
- Epinephrine 1:1000 concentration
  - 0.01 mL/kg (maximum 0.5 mL) IM anterolateral thigh
  - Auto-injector 0.15 mg (<25 kg) or 0.3 mg (>25 kg) anterolateral IM thigh
- Steroids: prednisolone by mouth or methylprednisolone (Solumedrol) IM/IV 1 to 2 mg/kg (max 60 mg)
- H2-antagonists: raniditine 2 mg/kg by mouth or IV (max 50 mg)

- Albuterol: nebulization 2.5 to 5.0 mg × 3 doses
- Oxygen: 8 to 10 L/min via face mask
- IV fluids: 10 to 15 mL/kg bolus normal saline/lactated ringer bolus (max 1000 mL per bolus)

Discharge instructions

- Passed challenge:
  - Starting the following day, offer 1 to 3 servings of the baked foods daily, at minimum 3 times per week, using home-baked muffins or equivalents (eg, bread rolls or cupcakes) or store-bought baked foods with milk or egg listed as third ingredient or further down on the ingredient list.[33]
  - Continue avoidance of not well-baked foods with milk or egg ingredients.
  - Provide an emergency plan and prescription for epinephrine auto-injector in case of reactions to unbaked milk/egg.
  - Consider scheduling pizza challenge for baked-milk, muffin-tolerant patients.
  - Reevaluate skin prick tests and serum CM/egg white–specific IgE levels in 6 to 12 months and consider challenges to regular unbaked milk or egg based on the declining immunologic parameters.
- Failed challenge:
  - Continue strict avoidance of all forms of milk or egg.
  - Provide an emergency plan and prescription for epinephrine auto-injector.
  - Milk: Consider repeating the baked milk challenge in 1 to 3 years, with longer time intervals for the patients who had anaphylaxis during the baked milk challenge.
  - Egg: Consider repeating the baked egg challenge in 1 year.

Abbreviations: IM, intramuscular; IV, intravenous; max, maximum; min, minimum.

A recent study by Bloom and colleagues[25] using gel electrophoresis showed that the casein bands persisted for up to 60 minutes of heating, whereas β-lactoglobulin and α-lactalbumin bands were undetectable after 15 to 20 minutes of heating.[25] Immunoblotting using pooled serum from baked milk–reactive subjects showed preserved IgE binding to casein even with extended heating time. Similarly, the OM band persisted after 25 minutes of heating, whereas the ovalbumin band gradually weakened in the same amount of time. Immunoblotting using pooled serum from baked egg–reactive subjects showed stronger binding to scrambled EW, hardboiled EW, waffles and muffins containing egg, compared with baked egg or regular egg–tolerant subjects.

Previously it was shown that heating OM in a wheat matrix makes OM insoluble, likely from polymerization of wheat with OM via disulfide bonds.[19,26] Bloom and colleagues[25] also found that the presence of a wheat matrix during heating reduced IgE binding to CM proteins.

PREDICTIVE BIOMARKERS

As compared with evaluation of regular egg allergy, skin prick test (SPT) or specific IgE levels to CM or EW proteins have not been reliable in predicting baked milk or egg tolerance. Different patient populations and variability in methods of baking or heating CM and EW have resulted in varied proposed cutoffs.

Nowak-Wegrzyn and colleagues[5] found that only very high CM IgE levels had substantial positive predictive values (PPVs). A CM IgE level of 35 kU_A/L or greater only had a greater than 50% PPV, whereas CM IgE less than 0.35 kU_A/L had a 100% negative predictive value (NPV). A cutoff of CM IgE 5.0 kU_A/L was suggested for performing baked milk oral food challenge (OFC). Caubet and colleagues[6] evaluated data from 225 prospective baked milk OFCs, including 100 from Nowak-Wegrzyn and

colleagues[5] and suggested cutoffs of casein IgE 4.95 kU_A/L (89% NPV, 54% PPV) and CM IgE 9.97 kU_A/L (86% NPV, 60% PPV). Bartnikas and colleagues[7] retrospectively studied physician-diagnosed milk-allergic children and found that a casein IgE of 0.9 kU_A/L and CM IgE of 1.0 kU_A/L had a greater than 90% NPV, while all subjects with casein IgE of greater than 10.3 kU_A/L and CM IgE greater than 20.6 kU_A/L had were baked milk reactive.

In regards to skin testing, Nowak-Wegrzyn and colleagues[5] found that a CM SPT of 14 mm had a greater than 50% PPV and a CM SPT less than 5 mm had a 100% NPV, with high sensitivity but poor specificity. Bartnikas and colleagues[7] found that all subjects with a CM SPT of less than 7 mm were baked milk tolerance, and all subjects with a casein SPT mm of greater than 15 mm were baked milk reactive. Conversely, Mehr and colleagues[8] found that CM or muffin SPT wheal was not predictive of baked milk tolerance.

In the natural history study by Sicherer and colleagues,[3] the baseline egg-specific IgE level did not predict who would go on to tolerate baked egg. Similarly, Cortot and colleagues[12] found no difference in EW-specific IgE levels between baked egg–tolerant and baked egg–reactive patients. Lemon-Mule and colleagues[9] found that only very high levels of OM-specific and EW-specific IgE had substantial PPVs. OM-specific IgE of 50 kU_A/L had a 90% PPV, and EW-specific IgE of 75 kU_A/L had greater than 50% PPV. An undetectable OM-specific IgE still had 10% PPV for baked egg reactivity. In the same population, Lieberman and colleagues[11] retrospectively studied baked egg tolerance in a clinical setting and found that an EW-specific IgE of 10 kU_A/L had a 60% PPV with high specificity but low sensitivity. Bartnikas and colleagues[15] found that OM-specific IgE was not superior to EW-specific IgE in predicting baked egg reactivity and suggested the following cutoffs with greater than 90% NPV for performing a baked-egg challenge: OM-specific IgE 0.35 kU_A/L and EW-specific IgE 6.0 kU_A/L.

In a large Japanese study, 108 children (median age, 34.5 months) with suspected egg allergy underwent double-blind, placebo-controlled food challenges with raw and heated egg.[27] Heated egg was prepared by heating liquid EW at 194°F (90°C) for 60 minutes, then freeze drying and homogenizing into a powder. The outcomes of the challenges were compared with the serum concentration of specific IgE antibodies and total IgE by using ImmunoCAP (Phadia AB, Uppsala, Sweden). Reactions to heated EW were observed in 38 children, considered allergic to raw and heated egg; 29 children reacted only to raw EW, and 41 children were heated and raw egg tolerant. Receiver operating characteristic analysis showed that EW-IgE was most accurate in the diagnosis of allergy to raw EW. The positive decision point, based on 95% clinical specificity, was 7.4 kU_A/L; the negative decision point, based on 95% clinical sensitivity, was 0.6 kU_A/L. For reaction to heated EW, OM-IgE was superior. The positive decision point was 10.8 kU_A/L, and the negative decision point was 1.2 kU_A/L. Collectively, data from various studies suggest that egg-allergic children with low levels of OM-specific IgE antibodies have the best odds of tolerating baked egg. In a research setting, a model that included the interactions between IgE and IgG_4 to ovalbumin and OM had enhanced accuracy in predicting reactivity to baked egg.[28]

With regard to skin testing, Lemon-Mule et al[9] found that a large EW SPT wheal of 15 mm only had a 60% PPV for baked egg reactivity and a negative EW SPT wheal had less than a 5% PPV. Bartnikas and colleagues[15] suggested an EW SPT cutoff of 11 mm with greater than 90% NPV. Tan and colleagues[14] studied baked egg tolerance in egg-allergic children less than 7 years old and found that a large OM SPT of 11 mm or greater had a 100% PPV and a muffin SPT of 2 mm or less had a 88% NPV. In the study by Lieberman and colleagues,[11] EW SPT was not found to be significant.

Similarly, Turner and colleagues[16] retrospectively studied the ability of egg extract and raw egg SPT to predict baked egg tolerance in physician-diagnosed, egg-allergic children. Neither SPT nor the ratio of egg extract/raw egg SPT was helpful in predicting baked egg challenge outcomes.

INFLUENCE ON REGULAR COW'S MILK AND EGG TOLERANCE

In the natural history study by Wood and colleagues,[2] CM allergy resolution was 4 times more likely in subjects who tolerated baked milk ($P<.0001$). In the natural history study by Sicherer and colleagues,[3] egg allergy resolution rate was 70.8% in those consuming baked egg at an early 6-month follow-up, compared with 45.2% in those not consuming baked egg and 57.1% in those who reported a reaction to baked egg. This finding gave an instantaneous risk ratio of 3.4 for egg allergy resolution in the baked egg–consuming group versus the nonconsumption group ($P<.001$). In the natural history study by Peters and colleagues,[4] subjects reactive to baked egg at 1 year of age compared with subjects who were tolerant were 5 times more likely to have persistent egg allergy at age 2 years (13% vs 56%, respectively; adjusted odds ratio 5.27; $P = .02$).

Shorter time to regular CM and egg tolerance in patients who tolerate baked milk and egg may indicate a milder allergy phenotype. However, in Sicherer and colleagues,[3] the type of regular egg reaction and baseline egg IgE level did not predict who would go on to tolerate baked egg. Alternatively, higher rates of regular CM and egg tolerance in baked milk– and egg-tolerant patients may reflect a more proactive approach to evaluation for CM and egg allergy resolution when baked milk or egg is already tolerated. Adding baked milk and egg to the diet was the protocol for subjects who were tolerant in the baked milk study by Nowak-Wegrzyn and colleagues[5] and in the baked egg study by Lemon-Mule and colleagues[9]; however, it was not mandated in the CM and egg allergy natural history studies by Sicherer and colleagues[3] and Wood and colleagues,[2] which reported lower baked milk and egg tolerance. In Peters and colleagues,[4] it was noted that baked egg–tolerant subjects who frequently ($\geq$5 times per month) ingested baked egg versus infrequently or not at all were 3 times more likely to develop regular egg tolerance (adjusted odds ratio 3.52; $P = .009$).

Lastly, there are data suggesting that ingestion of baked milk and egg results in immune modulation and may actively lead to earlier tolerance of regular CM and egg, in a sense acting as a form of immunotherapy. In Nowak-Wegrzyn and colleagues[5], Kim and colleagues[29] and Leonard and colleagues,[30] ingesting baked milk and egg was associated with a significant decrease in CM- and EW- specific SPT wheal diameter and EW- and OM- specific IgE levels, and an increase in specific IgG4 levels to casein and OM. This finding is commonly seen in allergen immunotherapy, such as subcutaneous immunotherapy for allergic rhinitis or oral immunotherapy for food allergy. In Kim and colleagues,[29] subjects ingesting baked milk were 16 times more likely than the comparison group to become regular milk tolerant ($P<.001$). In Leonard and colleagues,[30] subjects ingesting baked egg were 14.6 times more likely than the comparison group to develop regular egg tolerance, and they developed tolerance earlier ($P<.0001$).

SAFETY

Inclusion of baked milk and egg into the diets of milk- and egg-allergic children who are tolerant appears to be very safe and well tolerated. In Kim and colleagues[29] and Leonard and colleagues,[30] no acute allergic reactions to properly baked milk and egg were reported at home. In addition, there was no worsening of underlying eczema,

asthma, or allergic rhinitis. One baked milk–tolerant subject continued to tolerate baked milk after developing EoE.[29] A baked milk–reactive subject and 5 subjects in the comparison group also developed EoE while strictly avoiding milk. One baked egg–tolerant subject developed atypical food protein–induced enterocolitis syndrome to egg and subsequently removed all forms of egg from the diet.[30] In two other studies, acute reactions to baked milk (n = 3) and egg (n = 1) were reported at home, one to baked milk that required epinephrine.[7,13]

Anaphylaxis to baked milk and egg does occur.[5,9,12,14,16,31] In Nowak-Wegrzyn and colleagues,[5] reactivity to baked milk was a marker of a more severe CM allergy as only the baked milk–reactive subjects experienced anaphylaxis during OFC, compared with none of the baked milk–tolerant subjects who reacted to unheated milk. The following were not found to be predictors of baked milk anaphylaxis: age, history of asthma, respiratory symptoms at first reaction to milk or CM-induced anaphylaxis, elapsed time since last anaphylaxis, SPT size, or lifetime peak CM-specific IgE levels. In Mehr and colleagues,[8] 4 out of 19 positive baked milk OFCs required adrenaline, including one subject after ingesting one-sixteenth of a muffin (approximately 3 mg of baked CM protein). Baked milk reactivity predictors were found to include a history of CM-induced anaphylaxis, food allergies to greater than 3 food groups, asthma, and requiring asthma preventive therapy. Age at OFC, time since the last clinical reaction, previous anaphylaxis to other foods, and/or other atopic condition (eczema) were not predictive. In Turner and colleagues,[13] of the 86 children who were baked egg reactive, 12 (14%) developed anaphylaxis, including 4 to less than 100 mg baked egg protein. Adrenaline was given in 5 children, and a second dose was used for persistent hypotension in one child. Food allergy to 3 or more food groups was found to be predictive of baked egg reactivity; but SPT, prior EW-induced anaphylaxis, asthma on preventer therapy, history of another atopic condition, or a history of anaphylaxis to foods other than egg were not.

Conversely, in Clark and colleagues,[10] adrenaline was not required for any of the 28 of 77 (37%) positive baked egg challenges, when included gastrointestinal symptoms in 68% OFCs. The investigators suggested that reintroduction of baked egg in children aged 2 to 3 years with a history of previous mild reaction to egg and no asthma could be done at home. In general, however, because of the risk of anaphylaxis, it is recommended that evaluation of baked milk and egg tolerance be done under physician supervision in children who do not have a reliable history of already regularly tolerating them in clinically relevant amounts.[32]

DIETARY GUIDELINES

Published recipes and dietary guidelines for baked milk and egg can be found in the recent Leonard and colleagues[33] review. Although the exact frequency of baked milk and egg ingestion to be the most beneficial is not yet known, ingestion a few times a week seems reasonable.[33] Baked egg and milk tolerance may develop over time and in older children; therefore, rechallenging should be considered in those children who are initially baked milk or egg reactive.[5,9,10,34]

Although baked milk and egg may accelerate the resolution the milk and egg allergy, data do not support the use of baked milk and egg in the prevention of food allergy. In a study investigating associations between egg allergy at 12 months of age and age of introducing different forms of egg, Koplin and colleagues[35] found that between 4 and 6 months of age, first exposure to cooked egg (boiled, scrambled, fried, or poached) reduced the risk of egg allergy compared with first exposure to egg in baked good. Thus, more intact egg protein may be necessary for the prevention of egg allergy as

compared to the use of modified egg protein in the possible treatment of the established allergy.

SUMMARY

Baked milk and egg appears to be well tolerated by most milk- and egg-allergic children. There is evidence that inclusion of baked milk and egg in the diets of children who are tolerant may accelerate the resolution of milk and egg allergy. Although further research is needed on biomarkers that can predict baked milk or egg reactivity, in general, the higher the specific IgE level or SPT, the less likely that baked milk and egg will be tolerated. Some data suggest that casein- and ovomucoid-specific IgE levels may be useful in predicting reactivity. Physician-supervised introduction of baked milk and egg is recommended since anaphylaxis to baked milk and egg has occurred and is difficult to predict. Tolerance of baked milk is a marker of a mild and transient milk allergy, whereas tolerance to baked egg is not as predictive of a milder phenotype of egg allergy. Children reactive to baked milk and egg have a more persistent milk and egg allergy and are in need of treatments that accelerate tolerance development.

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