

Baked egg food challenges – clinical utility of skin test to baked egg and ovomucoid in children with egg allergy

J. W.-L. Tan^{1,2}, D. E. Campbell^{1,2}, P. J. Turner², A. Kakakios^{1,2}, M. Wong^{1,2}, S. Mehr^{1,2} and P. Joshi^{1,2}

¹Children's Hospital at Westmead, Sydney, Australia and ²University of Sydney, Sydney, Australia

Clinical & Experimental Allergy

Summary

Background Many children with IgE-mediated egg allergy can tolerate products containing extensively heated (baked) egg. Aside from food challenge, there are no tests which reliably predict tolerance to baked egg in egg-allergic individuals.

Objectives To determine if skin prick test (SPT) to baked egg (muffin) and ovomucoid can predict the outcome of baked egg challenges in egg allergic patients.

Methods In this prospective study, children with a recent history of immediate allergic reactions to egg [and corroborative positive SPT or serum-specific IgE (ssIgE) to egg] or those with SPT/ssIgE > 95% PPV for egg allergy were invited to undergo an open standardized baked egg (muffin) challenge. SPT to egg white, ovomucoid, and fresh muffin were performed immediately prior to challenge.

Results One hundred and forty-three egg allergic children underwent baked egg challenge and of these, 90 (63%) tolerated 1 g of egg protein in a baked muffin. Of the 53 positive challenges, eight (15%) had respiratory and/or cardiovascular symptoms. The median SPT diameters in positive challenges compared with negative challenges were baked muffin – 6.0 mm/4.0 mm and ovomucoid 7.5 mm/5.0 mm respectively. Receiver operating characteristic (ROC) curves were generated for SPT to baked egg and ovomucoid. The area under the curve was 0.68 for baked egg, and 0.67 for ovomucoid. A muffin SPT of < 2 mm had a negative predictive value of 88% and an ovomucoid SPT ≥ 11 mm had a positive predictive value of 100%.

Conclusions and Clinical Relevance A SPT of < 2 mm to muffin had a high negative predictive value to baked egg challenge. Ovomucoid SPT ≥ 11 mm was very likely to predict a reaction to baked egg. In these children, deferring the challenge would be appropriate.

Keywords baked egg, egg allergy, food challenge, ovomucoid

Submitted 1 November 2012; revised 7 May 2013; accepted 2 June 2013

Correspondence:

John Wei-Liang Tan, Children's Hospital at Westmead and University of Sydney, Sydney, Australia.

E-mail: john.tan@health.nsw.gov.au

Cite this as: J. W.-L. Tan,

D. E. Campbell, P. J. Turner, A. Kakakios, M. Wong, S. Mehr and P. Joshi, *Clinical & Experimental Allergy*, 2013 (43) 1189–1195.

Introduction

Egg is the most common cause of IgE-mediated food allergy in Australian infants, with a prevalence of 9% [1]. Egg is a ubiquitous ingredient in many commercially available foods, therefore strict avoidance of egg can be difficult and burdensome. Previous studies have shown that many children with IgE-mediated allergy to egg can tolerate extensively heated (baked) egg and that strict avoidance of egg in all forms may not be necessary for all egg allergic children [2, 3]. The ability to include egg in baked products significantly liberalizes the diet of the egg allergic child and may help to reduce anxiety about accidental ingestion and allergic reactions. Furthermore, introduction of baked egg into a child's diet may be

associated with accelerated resolution of egg allergy [4, 5]. Skin prick test (SPTs) and/or serum-specific IgE (ssIgE) to whole egg or egg white extract are not particularly helpful in predicting tolerance to baked egg in an egg allergic individual [2, 6, 7]. Currently, the only safe and effective way to determine if an egg allergic child can tolerate baked egg is via a supervised open food challenge (OFC). Formal OFC generally takes several hours to complete and may lead to a severe reaction with all the associated risks. In many countries, wait lists for OFC are long with limited resources available. The ability to identify children who are suitable or unsuitable for OFC to baked egg would help to resolve these issues.

We therefore sought to determine if SPT to baked egg (fresh muffin) and ovomucoid is useful in predicting the

clinical outcomes in OFC to baked egg in children with highly probable egg allergy.

Methods

Egg allergy was defined as children with highly probable egg allergy on the basis of a clinical reaction to any form of egg within the past 12 months and current positive SPT/ssIgE to egg white (≥ 3 mm, ≥ 0.35 kU/L) OR, in children who had never ingested egg, a positive SPT/ssIgE to egg white $> 95\%$ PPV, (defined as SPT to egg white > 7 mm or ssIgE of ≥ 6 KUa/L for children over 2 years and > 5 mm and ≥ 2 KUa/L in those children under 2 years [8, 9]. OFC to whole egg was not performed prior to baked muffin observed standardized food challenge (OFC). Children were recruited from the allergy clinics at the Children's Hospital at Westmead, Sydney, a tertiary referral centre. All egg allergic children who met inclusion criteria were invited to undergo an open OFC to baked egg in a muffin at the Children's Hospital at Westmead. Recruitment and challenges were conducted over a 2-year period from January 2010 until December 2011. A standard recipe was used (see Appendix). One muffin was estimated to contain 1/6th of an egg (~ 1 g of egg protein) and was baked at 180°C for 20 min in a wheat-based matrix.

Children were assessed and examined prior to OFC to ensure suitability. SPT was performed on the day of challenge using commercial extracts to egg white, ovomucoid (Australasian Medical and Scientific, ALK Abello Spain), and to muffin. For SPT to muffin, a small portion of muffin (containing baked egg) was mixed with an equal volume of normal saline and homogenized; this solution was then applied to the skin using a small applicator. SPT was performed according to standard guidelines, with single use lancet, using histamine 10 mg/mL as a positive control (Hollister Stier Laboratories, Washington, DC, USA) [10]. A positive SPT was defined as a weal size of at least 3 mm greater than a saline control read at 15 min.

The OFC protocol involved incremental doses of muffin at 20 min intervals; 1/16 muffin, 1/8 muffin, 1/4 muffin, 1/4 muffin, and the remainder of muffin. The OFC was considered positive with an objective clinical reaction (angioedema, urticaria, persistent cough, wheeze, vomit, and hypotension) or with persisting subjective symptoms (chest tightness and throat tightness) as per PRACTALL criteria [11]. Patients were considered to have passed the OFC if they had no symptoms of IgE-mediated allergy at any time up to 2 h after the last dose. After the observation period, children are discharged home with instructions not to have any egg in the following 24 h. Families were contacted by telephone within 1 week of OFC to assess for any

delayed reactions. Delayed reactions were not included as positive reactions for this study. The study personnel performing OFC were blinded as to the result of the SPT to ovomucoid and fresh muffin.

Severe reactors were defined as those having cardiovascular or respiratory involvement [with or without involvement of skin and/or gastrointestinal tract (GIT) symptoms] consistent with WAO [12] and ASCIA criteria [13]. Patients with reactions involving either skin and/or GIT symptoms alone were classified as mild reactors. Children who failed to complete the challenge by ingesting less than a whole muffin, but remained asymptomatic were deemed incomplete challenges and excluded from the analysis.

The local Research Ethics Committee approved the study (HREC/10/CHW/3, SSA/10/CHW/71) and informed consent was obtained.

Statistical analysis

The utility of SPT to baked egg and ovomucoid SPT were assessed for their ability to predict response to baked egg challenge. SPT to egg white was analysed only for children included on the basis of clinical history. In children without a recent history of clinical reaction to egg, SPT to egg white was an inclusion criteria and to analyse this variable as an outcome measure would be statistically confounding. For each level of SPT measurement, sensitivity, specificity, likelihood ratios, positive predictive value, and negative predictive value were calculated and ROC curves constructed using GraphPad Prism 6 software (GraphPad Software Inc, La Jolla, CA, USA). Mann–Whitney *U*-test was used to compare SPT size between groups. Subgroup analyses of ROC curves were performed according to the method of Hanley & McNeil [14]. A *P*-value of < 0.05 was considered significant.

Results

Challenge outcome

One hundred and forty-three patients underwent OFC to baked egg in a muffin during the study period. Patient demographics are described in Table 1. Eighty-five children (59%) were avoiding all egg on the basis of previous clinical reactions, while 58 (41%) children were avoiding egg on the basis of sensitization alone. Of the 143 challenges performed, 90 passed (63%). In children with a history of prior anaphylaxis to egg, 14/19 (74%) passed the muffin OFC. Of the 53 positive challenges, eight children had a severe allergic reaction on muffin OFC challenge (according to WAO and ASCIA criteria) and three received intramuscular adrenaline (Table 2). The remaining 45 children with a positive muffin OFC

Table 1. Patient demographics

Characteristic	
Age at challenge to baked egg, median (interquartile range)	3.8 years (1.8–6.7 years)
Gender, no. (%)	
Male	78 (55%)
Female	65 (45%)
Other atopy, no. (%)	
Asthma (physician diagnosed)	48 (34%)
Asthma (on preventer therapy)	25 (17%)
Allergic rhinitis	42 (29%)
Eczema	93 (65%)
Previous reaction to egg, no. (%)	
Anaphylaxis	19 (13%)
Mild-moderate symptoms	66 (46%)
Prior reaction to baked egg	3 (2%)

SPT, skin prick test; OFC, oral food challenge.

had mild allergic reactions with skin and/or gut symptoms. Two children were reported to have delayed reactions (abdominal pain and diarrhoea) > 8 h after the challenge.

The median SPT measurements to baked egg ($P = 0.0003$), ovomucoid ($P = 0.0073$) and egg white were significantly higher in those with a positive OFC

compared with negative OFC (Table 3). Those with a severe reaction on OFC did not have a higher median SPT to ovomucoid (7.5 mm) compared with those with mild reactions (8.0 mm; Table 3).

Of the eight children with a severe reaction to muffin, three reacted to less than 1/8th of a muffin (equivalent to < 150 mg extensively heated egg protein). Only one of these eight children had a history of severe reaction to whole egg; four had previously experienced only mild symptoms whereas three were avoiding egg on the basis of IgE sensitization alone (Table 2).

Test characteristics

ROC curves were generated and area under curve calculated for SPT to muffin (0.68, $P = 0.0003$) and ovomucoid (0.67, $P = 0.008$; Fig. 1a). Negative and positive predictive values (NPV, PPV) for fresh muffin and ovomucoid SPT were calculated for cut-off points (Table 4).

Seventeen subjects (15%) had a SPT of less than 2 mm to muffin, of whom 15 passed the muffin OFC. Thus, a SPT of < 2 mm to baked egg had 88% NPV. Median SPT to egg white and ovomucoid for these individuals with a muffin SPT < 2 mm was 8 mm (IQR

Table 2. Details of individuals who had severe systemic reactions on baked egg challenge

Age (years), gender	Other atopy	Other food allergy	Age at first reaction	Worst historical reaction to egg	SPT prior to OFC (mm)	Reaction at OFC	Adrenaline
4 F	Eczema, Asthma AR	Yes	n/a	Never exposed	EW: 8 Muffin: 8 OVM: 4	Sudden lethargy, rhinitis, urticaria & angioedema	No
4 F	Eczema, Asthma AR	Yes	23 months	Generalized urticaria	EW: 13 Muffin: 8 OVM: 9	Wheeze, cough, urticaria, diarrhoea	Yes
3 F	Eczema,	Yes	6 months	Generalized urticaria to < 1 tsp of hard boiled egg	EW: 13 Muffin: 8 OVM: 7	Hypotension, pallor, urticaria, vomit	Yes
8 F	Eczema, AR	Yes	6 months	Anaphylaxis after eating a slice of cake	EW: 10 Muffin: 7 OVM: 8	Wheeze, urticaria, itchy throat	Yes
1 M	Eczema, Asthma	No	n/a	Never exposed	EW: 15 Muffin: 8	Wheeze, cough, rhinitis, oral itch	No
3 M	Eczema, AR	No	n/a	Never exposed	EW: 8 Muffin: 9 OVM: 0	Wheeze, cough, vomit, diarrhoea	No
7 M	Eczema, asthma	Yes	12 months	Generalized urticaria and angioedema after eating egg in chicken nuggets	EW: 8 Muffin: 3 OVM: 8	Sore throat, urticaria, persistent abdominal pain	No
12 M	Eczema, Asthma, AR	Yes	2 years	Generalized urticarial and vomiting after one fried egg	EW: 9 Muffin: 8 OVM: 8	Sore throat, urticaria, persistent abdominal pain	No

OFC, open food challenge; SPT, skin prick test; EW, egg white; OVM, ovomucoid.

Table 3. Median skin prick test (SPT) values (with interquartile ranges) for baked egg in muffin, ovomucoid and egg white, by challenge outcome

Challenge outcome	Muffin (mm)	Ovomucoid (mm)	Egg white (mm)
Negative	4.0 (2.6–6.0)	5.0 (3.0–7.0)	8.0 (7.0–11.0)
Positive	6.0 (4.5–7.5)	7.5 (5.0–10.0)	9.0 (8.0–11.0)
Mild reactions	5.5 (4.5–7.5)	8.0 (5.0–10.0)	9.0 (7.5–11.0)
Severe reactions	7.5 (5.3–7.8)	7.5 (7.4–7.6)	9.0 (8.0–13.0)

5–10.5 mm) and 3 mm (95% IQR 0–8 mm) respectively. SPT ≥ 11 mm to ovomucoid had PPV of 100% (Table 4).

To determine whether the inclusion of egg-sensitized children had influenced the test characteristics of SPT to muffin and ovomucoid, ROC curves were generated for each group of children (convincing clinical history and sensitization to egg only) and analysed according to the method of Hanley & McNeil [14]. No significant differences were observed in the cut-off points for PPV ovomucoid and NPV fresh muffin ($P > 0.05$, Figs 1b,c).

Discussion

Predicting the outcome of food challenges in children with food allergy remains elusive. Although cut-off points in sIgE and SPT have been established for predicting the likelihood of clinical reactivity to some common foods [8, 9, 15], there is no current reliable method for determining a challenge outcome for food allergy which performs well across the whole range of the testing scale. This is because many individuals with food allergy have SPT or sIgE which falls between highly predictive cut-off points (e.g. a peanut sIgE of 2 KUa/L or a SPT of 5 mm). In this study, we have attempted to define cut-off points to determine clinical reactivity to extensively heated egg in muffin. Although, the SPT to ovomucoid extract and fresh muffin did not perform well across the whole measurement scale, we were able to determine useful cut-off points for predicting the outcome of muffin OFC in our population of children with egg allergy.

Recent studies have demonstrated that the majority of children with IgE-mediated egg allergy can tolerate egg in a baked product (70–80.3%) [2, 4–7, 16]. These

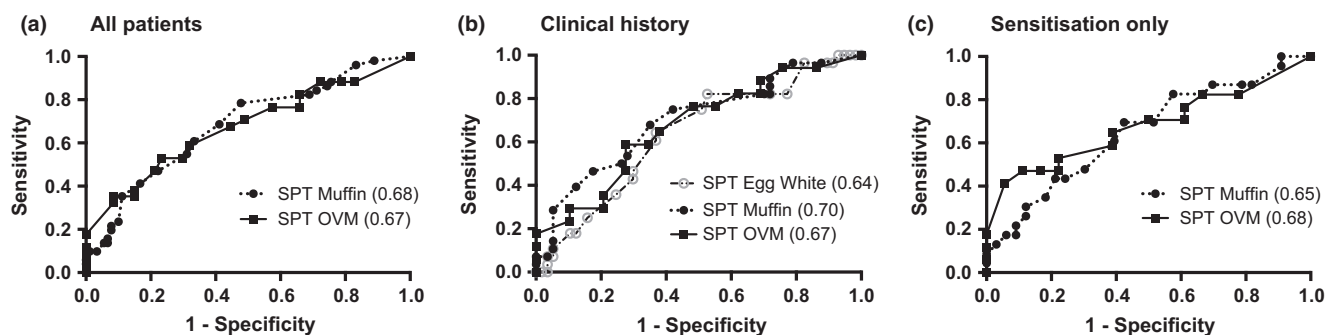


Fig. 1. Receiver operating characteristic curves (AUC in parentheses within figure legends) for skin prick test (SPT) to baked egg (homogenized muffin) and ovomucoid in predicting tolerance to baked egg in the study cohort (a) as well as subgroups of children included on the basis of clinical history (b) or sensitization alone (c). SPT to egg white is shown in b but not a or c, where cases were included on the basis of SPT to egg white alone.

Table 4. Test performance characteristics for SPT to muffin and ovomucoid

SPT reagent	SPT cut-off (mm)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR+	LR–
Muffin	< 2	96	17	40	88	1.15	0.24
	≤ 2	88	24	40	79	1.17	0.48
	≤ 3	84	29	40	76	1.19	0.54
	≤ 4	78	52	48	81	1.64	0.41
	≤ 5	61	67	51	75	1.82	0.59
Ovomucoid	≥ 7	53	70	56	67	1.78	0.67
	≥ 8	47	79	62	67	2.21	0.67
	≥ 9	35	85	63	65	2.37	0.76
	≥ 10	32	91	73	65	3.80	0.74
	≥ 11	18	100	100	63	∞	0.82

reports are consistent with our current study, where 63% of egg allergic children were able to tolerate egg in a baked muffin product.

There are several advantages of skin testing over ssIgE in the setting of baked egg challenge in egg allergic children. Firstly, ssIgE to a compounded food with allergen suspended in a matrix such as baked egg muffin is currently not possible. Secondly, a point-of-care investigation, which can be performed quickly, cheaply, and relatively painlessly has obvious advantages over ssIgE which requires venesection and laboratory processing, resulting in an inability to make immediate point-of-care decisions about whether to proceed with a food challenge. SPT utilizing fresh food have been widely used, particularly in the setting of fruit and vegetable allergy, where heat labile allergens are not well preserved in commercial extracts [10]. We hypothesize that SPT to fresh muffin reflects the degree to which allergenic modification has occurred during the baking process and is therefore a good candidate for a point-of-care skin test reagent in the setting of baked egg OFC.

There are well accepted predictive cut-off points for egg white SPT for whole egg OFC [8]; however, there have been few previous reports of similar SPT cut-off points for baked egg OFC, or other heat-modified allergens such as baked milk OFC. Cortot et al. conducted a retrospective analysis and found that SPT to egg white was not predictive of outcome of baked egg challenge [7]. Although median egg white SPT is reported as often lower in baked egg tolerant than baked egg reactive subjects, there has been no useful cut point established for egg white SPT in determining baked egg OFC outcome [2, 6, 7]. We did find significant differences between the median SPT for baked egg and ovomucoid in baked egg reactive and tolerant subjects and useful cut-off points. Furthermore, our results which show a high NPV of SPT (< 2 mm) to baked muffin confirm a recent publication from Faraj and Kim who report a high NPV (95%) for fresh skin testing with baked egg and baked milk product in a smaller cohort of egg and milk allergic children [17].

The mechanism by which egg allergic children may tolerate baked egg (but not lightly cooked egg) is likely complex and related to several factors, including the denaturation of proteins with conformational changes in the major allergenic epitopes and on the food matrix in which the egg is incorporated [3]. Egg contains in excess of 20 different proteins, including ovalbumin and ovomucoid. Ovalbumin is present in greater quantity than ovomucoid, but is readily undergoes conformational change with heat, which reduces its allergenicity as well as increases the access of gastrointestinal proteases to ovalbumin resulting in complete degradation [2, 3]. Ovomucoid, on the other hand, is

heat stable because it is a highly glycosylated protein with three protein domains stabilized by disulphide bonds [18]. Due to this quality, ovomucoid IgE has been studied as a more accurate predictor for reactions in egg allergic individuals [19–21]. Ovomucoid-specific IgE has recently been shown to perform better than egg-white-specific IgE in the prediction of boiled egg OFC outcome in egg sensitized children, where the ovomucoid-specific IgE was greater than 10 kUA/L (97% PPV) [19]. It has also been shown to be predictive of baked egg OFC at very high ovomucoid ssIgE levels of greater than 50 kUA/L [2]. We confirm the potential utility of high ovomucoid IgE production in predicting allergy to baked egg, reporting that a SPT > 11 mm was highly predictive of baked egg allergy in our cohort. Ando et al. reported specific IgE to ovomucoid of > 11 kUA/L indicate a high risk of reaction to whole egg, and < 1 kUA/L suggest a low risk of reaction to egg heated to 90°C for 60 min [20]. Lemon-Mule et al. did not find a useful negative predictive cut-off point for ovomucoid ssIgE [2], also consistent with our finding for ovomucoid SPT.

In our study, egg was baked at high temperature (180°C) for a short duration (20 min). It is possible that baked products which have undergone less heat processing or have a different matrix may have different test characteristics from our muffin used in this study. This requires further exploration; however, ovomucoid does appear to be a useful marker for baked egg allergy. Recently, it has been shown that wheat in a baked egg matrix decreases the allergenicity of ovomucoid *in vitro* [22]. Solubility of ovomucoid was shown to be decreased in a process that mimicked baking [23] suggesting that interaction of baked egg with a protein matrix can slow the absorption of intact allergens and decrease accessibility to digestion, potentially rendering it less allergenic. These observations may account for the tolerance to baked egg of some individuals with a moderately raised IgE to ovomucoid.

While tolerance to extensively heated egg might be in part due to the lower dose of egg allergen consumed, there are certainly egg allergic children who are able to tolerate extensively heated egg, but not the same dose of egg protein in a less-heated form. Lemon-Mule et al. reported 30 subjects who were able to tolerate 1/3 of an egg when baked in a muffin, but reacted to a lower dose of protein when challenged with lightly cooked scrambled egg [2]. We have reviewed the case notes of children within our service who have undergone OFC to lightly cooked egg over the past year. Of those children who reacted to lightly cooked egg at a total dose of egg protein under 300 mg, 45% were tolerating baked egg in muffin in their diet (containing 1 g of egg protein) on a regular basis.

A potential limitation of this study is that individuals were not all formally challenged to egg to establish clinical reactivity to egg prior to OFC to extensively heated egg. We considered the cohort to be highly probable egg allergy rather than challenge proven. Although OFC to whole egg as an inclusion criteria would have strengthened the study, it was considered unethical to challenge children with a very high probability of clinical reaction (PPV > 95% SPT/ssIgE), including 16% with a past history of anaphylaxis to egg. We performed subgroup analyses to demonstrate that children included on the basis of sensitization alone (with a > 95% likelihood of clinical egg allergy) were neither significantly different to those children with a convincing previous reaction to egg, nor was there any significant difference in the test performance characteristics of SPT to muffin and ovomucoid between these two groups.

Clinical judgement is needed in deciding when total elimination of egg product is no longer necessary. To date, the only way of determining if an egg allergic individual can tolerate baked egg is by formal OFC. Challenges are time consuming and are of significant cost. On average, a formal challenge takes approximately 5–6 h and often requires a day admission in a hospital, resulting in long waiting lists and significant costs. We have identified a group of children in our cohort who were at very low risk of reacting to baked egg on the basis of a small SPT to fresh muffin. These children may be suitable for a less intensive observed introduction. We have piloted an in-hospital nurse supervised, parent led OFC protocol for these at 'low risk' egg allergic children in our institution (with SPT muffin < 2 mm) using a two-dose OFC (¼ muffin followed by the remainder 20 min later, with a 1-h observation period), and this may be applicable to other populations of egg allergic children with negative SPT to fresh muffin. We also demonstrated that a past history of anaphylaxis to egg is not a contraindication to muffin OFC, and that a large proportion of such children can successfully tolerate baked egg in their diet.

In our egg allergic population, an SPT of ≥ 11 mm to ovomucoid had a 100% positive predictive value. We suggest that a large SPT to ovomucoid may be useful in selecting those patients likely to react to extensively heated egg and therefore not appropriate for muffin OFC. This would benefit patients by avoiding the induction of a food allergic reaction. However, these findings require confirmation in other cohorts and lower risk populations, to determine a clinically useful cut-off for differential severity prediction.

Appendix

Recipe for preparation of baked egg in muffin

Ingredients:

- ½ cup (125 g) butter or margarine
- ⅔ cup (160 g) sugar
- 1¾ cup (220 g) plain flour or gluten free flour
- ½ cup (125 mL) cow's milk or milk substitute
- Two level teaspoons baking powder
- Two large eggs (egg size ~ 50 g)

Preparation instructions:

- 1 Pre-heat conventional oven to 180°C.
- 2 Mix flour, baking powder and sugar together.
- 3 Add softened butter/margarine and mix until a crumbly mixture is formed.
- 4 Whisk or beat the eggs and milk together and stir into the flour mix.
- 5 Stir ingredients until just combined.
- 6 Place muffin paper cases into a muffin tray.
- 7 Distribute batter evenly into each muffin cup.
- 8 Bake for 20 min, until golden brown and slightly firm to touch.

References

- 1 Osborne NJ, Koplin JJ, Martin PE *et al*. Prevalence of challenge-proven IgE-mediated food allergy using population-based sampling and predetermined challenge criteria in infants. *J Allergy Clin Immunol* 2011; 127:668–76, e1–2.
- 2 Lemon-Mule H, Sampson HA, Sicherer SH, Shreffler WG, Noone S, Nowak-Węgrzyn A. Immunologic changes in children with egg allergy ingesting extensively heated egg. *J Allergy Clin Immunol* 2008; 122:977–83, e1.
- 3 Martos G, Lopez-Exposito I, Bencharti-wong R, Berin MC, Nowak-Węgrzyn A. Mechanisms underlying differential food allergy response to heated egg. *J Allergy Clin Immunol* 2011; 127:990–7, e1–2.
- 4 Clark A, Islam S, King Y *et al*. A longitudinal study of resolution of allergy to well-cooked and uncooked egg. *Clin Exp Allergy* 2011; 41:706–12.
- 5 Leonard SA, Sampson HA, Sicherer SH *et al*. Dietary baked egg accelerates resolution of egg allergy in children. *J Allergy Clin Immunol* 2012; 130:473–80, e1.
- 6 Lieberman JA, Huang FR, Sampson HA, Nowak-Węgrzyn A. Outcomes of 100 consecutive open, baked-egg oral food challenges in the allergy office. *J Allergy Clin Immunol* 2012; 129:1682–4, e2.
- 7 Cortot CF, Sheehan WJ, Permaul P *et al*. Role of specific IgE and skin-prick testing in predicting food challenge results to baked egg. *Allergy Asthma Proc* 2012; 33:275–81.
- 8 Sporik R, Hill DJ, Hosking CS. Specificity of allergen skin testing in predicting positive open food challenges to milk, egg and peanut in children. *Clin Exp Allergy* 2000; 30:1540–6.

- 9 Sampson HA. Utility of food-specific IgE concentrations in predicting symptomatic food allergy. *J Allergy Clin Immunol* 2001; **107**:891–6.
- 10 Bernstein IL, Li JT, Bernstein DI *et al*. Allergy diagnostic testing: an updated practice parameter. *Ann Allergy Asthma Immunol* 2008; **100**(Suppl. 3):S1–148.
- 11 Sampson HA, Gerth van Wijk R, Bindslev-Jensen C *et al*. Standardizing double-blind, placebo-controlled oral food challenges: American Academy of Allergy, Asthma & Immunology-European Academy of Allergy and Clinical Immunology PRACTALL consensus report. *J Allergy Clin Immunol* 2012; **130**:1260–74.
- 12 WAO. Guidelines for the assessment and management of anaphylaxis. *WAO Journal* 2011; **4**:13–37.
- 13 Allergy ASoCia. Health professional information paper: Anaphylaxis. ASCIA; 2013; Available at: http://www.allergy.org.au/images/stories/anaphylaxis/ASCIA_HPIP_Anaphylaxis_2013.pdf. (Accessed 6 April 2013).
- 14 Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. *Radiology* 1982; **143**:29–36.
- 15 Sampson HA, Ho DG. Relationship between food-specific IgE concentrations and the risk of positive food challenges in children and adolescents. *J Allergy Clin Immunol* 1997; **100**:444–51.
- 16 Koplin JJ, Osborne NJ, Wake M *et al*. Can early introduction of egg prevent egg allergy in infants? A population-based study. *J Allergy Clin Immunol* 2010; **126**:807–13.
- 17 Faraj Z, Kim HL. Skin prick testing with extensively heated milk or egg products helps predict the outcome of an oral food challenge: a retrospective analysis. *Allergy Asthma Clin Immunol* 2012; **8**:5.
- 18 Djurtoft R, Pedersen HS, Aabin B, Barkholt V. Studies of food allergens: soybean and egg proteins. *Adv Exp Med Biol* 1991; **289**:281–93.
- 19 Haneda Y, Kando N, Yasui M *et al*. Ovomucoids IgE is a better marker than egg white-specific IgE to diagnose boiled egg allergy. *J Allergy Clin Immunol* 2012; **129**:1681–2.
- 20 Ando H, Moverare R, Kondo Y *et al*. Utility of ovomucoid-specific IgE concentrations in predicting symptomatic egg allergy. *J Allergy Clin Immunol* 2008; **122**:583–8.
- 21 Caubet JC, Bencharitiwong R, Moshier E, Godbold JH, Sampson HA, Nowak-Wegrzyn A. Significance of ovomucoid- and ovalbumin-specific IgE/IgG (4) ratios in egg allergy. *J Allergy Clin Immunol* 2012; **129**:739–47.
- 22 Shin M, Lee J, Ahn K, Lee SI, Han Y. The influence of the presence of wheat flour on the antigenic activities of egg white proteins. *Allergy Asthma Immunol Res* 2013; **5**:42–7.
- 23 Kato Y, Oozawa E, Matsuda T. Decrease in antigenic and allergenic potentials of ovomucoid by heating in the presence of wheat flour: dependence on wheat variety and intermolecular disulfide bridges. *J Agric Food Chem* 2001; **49**:3661–5.