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VIEWPOINT

Top 10 food allergy myths

Claire Nickolls[1] and Dianne E Campbell[1,2]

[1]Department of Allergy and Immunology, Children's Hospital Westmead, and [2]Discipline of Paediatrics and Child Health, University of Sydney, Sydney, New South Wales, Australia

Myth Number 1

A positive allergy test means a clinical allergy.

Mythbuster

Immunoglobulin E (IgE) production to a food allergen by allergen skin prick test (SPT) or serum specific IgE (ssIgE) does NOT reliably determine or predict a clinical allergy.

The why?

A positive SPT (i.e. wheal ≥3 mm) or ssIgE (>0.35 KU/L) indicates that allergen specific IgE is being produced. This is known as being sensitised to the allergen. It does not prove that the patient is clinically reactive to the allergen or will have an IgE-mediated allergic reaction to that food.[1–3] For some common food allergens including egg, cows milk and peanut, the size of the SPT and/or level of ssIgE correlates with an increased likelihood of a clinical IgE-mediated allergic reaction to that food. Positive predictive values (PPVs) for common allergens can assist in ruling a food allergy in, and in decreasing the need for a confirmatory oral food challenge (OFC), where the level of IgE is above the 95% PPV for that food. PPVs have been more difficult to establish for wheat, soy, tree nuts and fish.[4] Moreover, many children's SPT size or ssIgE levels fall between the lower limit of positive and these high cut-off points.

Approximately 30–50% of children with sensitisation to food allergens do not react with IgE-mediated symptoms (urticaria, angiooedema, stridor, vomiting, bronchospasm, cardiovascular compromise, etc.) on exposure to the allergen and are clinically tolerant to the food in question.[1,5]

A positive SPT or ssIgE should be interpreted in the context of the patient's history, particularly previous exposures to an allergen. Because of the high false positive rate of these tests, 'fishing expeditions' where large panels of testing are performed to screen for potential food allergies are not recommended. Targeted screening for few (three or less) very common food allergens in children at very high risk may be indicated in some circumstances.

An individual sensitised to a food on SPT or ssIgE who has a history of regular ingestion of that food without IgE-mediated allergic symptoms is *not* allergic to that food via a IgE-mediated mechanism and should *not* be advised to exclude it from their diet on the basis of the positive test. Allergen exclusion in these circumstances for periods of greater than 3 months under can result in severe allergic reactions on re-exposure to the previously tolerated foods.[6,7] In rare circumstances where a food needs to be removed from the diet, where sensitisation is present, and the child is clinically tolerant, extreme caution should be taken in reintroduction of that food.

Correspondence: Professor Dianne E Campbell, Children's Hospital at Westmead, Corner Hawsbury Road and Hainsworth Street, Lock Bag 4001, Westmead, Sydney, NSW 2145, Australia. Fax: 0298453421; email: diannec3@chw.edu.au

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Myth Number 2

Allergy tests can predict anaphylaxis.

Mythbuster

The size or level of IgE response *cannot* predict which individuals will have anaphylaxis to a food.

The why?

There is no current test, including an OFC that can reliably determine whether and at what dose of allergen an individual will have anaphylaxis to a food to which they are allergic. Moreover, severity of reactions varies between exposures in individuals but does not necessarily escalate with every exposure or reaction over time. Factors that influence severity of any given allergic reaction in a given individual include dose, food matrix, which the allergen is ingested in, exercise, concurrent illness and use of medications[8] (see below – myth 4).

The size of the SPT and/or level of ssIgE correlates with an increased likelihood of a clinical IgE-mediated allergic reaction to that food[3] but not generally to the potential severity of an allergic reaction to that food.

A medically supervised OFC is performed to confirm a patient has a diagnosis of a food allergy where the diagnosis is in doubt (e.g. unclear history or sensitisation on SPT with no prior history of ingestion) or to determine if a food allergy has been outgrown. OFC are performed with incremental doses of allergen (often semi-logarithmic) at staged intervals and are designed to determine whether any clinical allergy is present.[9] Anaphylaxis at OFC represent between 11% and 22% of positive challenges.[10,11] At the onset of a definitive allergic reaction, the OFC is generally stopped, according to preset stopping criteria to minimise the risk of anaphylaxis. Unless (and even when) the child reacts with anaphylaxis as the first symptom on OFC, it is not always possible to accurately determine subsequent risk of anaphylaxis. A child who has a mild allergic reaction during an OFC is still at potential risk of anaphylaxis to that same allergen on subsequent exposures at higher dose and/or under different conditions (exercise, illness, asthma

exacerbation). Likewise a child who has anaphylaxis at OFC may have a milder reaction subsequently and this is particularly so for foods to which children may acquire tolerance over time, such as milk and egg.

Myth Number 3

You cannot have an allergic reaction on the first known oral exposure to a food allergen.

Mythbuster

Over one-third of IgE-mediated allergic reactions occur to a food with no known prior ingestion.

The why?

It is immunologically required to be exposed to antigen/allergen in order to switch B cells from IgM to IgE production and for affinity maturation of B cell responses. This initial exposure (and sensitisation in allergic individuals) to an allergen may occur through the gut via allergens in breast milk,[12] the skin particularly in children with a breakdown in the normal skin barrier such as those infants with eczema,[13] or more rarely via the respiratory tract without any apparent ingestion of the food in question.

Myth Number 4

Allergic reactions get worse with each subsequent oral exposure.

Mythbuster

Food allergic reactions are variable and unpredictable from exposure to exposure.

The why?

The severity of an allergic reaction on any given oral exposure depends on many risk factors. Therefore, allergic reactions do not get predictably worse with each subsequent oral exposure. Individual factors influencing anaphylaxis on any given exposure include underlying disorders (e.g. asthma, arrhythmia and mastocytosis), acute asthma exacerbations, concurrent viral infection, medication use and exercise.[8] Mortality related to food anaphylaxis is associated both with known asthma and a delay in administration of intramuscular injection of adrenaline.[14]

Allergen factors that may influence the severity of a reaction include cooking (e.g. raw, baked and roasted) and the food matrix that may affect how quickly allergen is absorbed via the gastrointestinal tract.

Myth Number 5

Only children who have had a history of anaphylaxis need an adrenaline autoinjector.

Mythbuster

It is not necessary for a child to have previously experienced anaphylaxis in order to be assessed as being 'at risk of anaphylaxis'.

The why?

Whether or not a child with an IgE-mediated food allergy is at risk of anaphylaxis is a clinical judgment that must be considered for all individuals presenting with an IgE-mediated food allergy. There is no current test (skin test and OFC or other) that can reliably determine this risk.

The Australasian Society of Clinical Immunology and Allergy (ASCIA) guidelines state that an adrenaline autoinjector (AAI) prescription is recommended for individuals with a history of anaphylaxis and may also be recommended if there are other known risk factors for more severe or fatal reactions. This includes children with a history of a generalised allergic reaction and any one of the following: adolescent age group, nut allergy, comorbid conditions (e.g. asthma and arrhythmia) or limited access to emergency medical care.

Although not specified in the ASCIA Guidelines, common practice frequently includes prescribing AAI to children with multiple food allergies, a history of reaction to an extremely small amount of the food and allergies to foods associated with higher rates of severe allergic reactions such as nuts and seafood. Guidelines for the provision of AAI vary significantly around the world and are affected by multiple factors including disease prevalence, healthcare resources and government/specialist society and health insurance policies.[15]

Myth Number 6

Hypotension and collapse are common signs of anaphylaxis in children with food allergy.

Mythbuster

Respiratory symptoms are the most common symptoms of food-related anaphylaxis in children.

The why?

Food-related anaphylaxis is the most common trigger for anaphylaxis in children aged 0–19 years.[16] Anaphylaxis in infants and children most commonly presents with respiratory symptoms[17,18] with fatal anaphylaxis primarily due to respiratory compromise.[19] Hypotension is a very late and rare sign of anaphylaxis in children. Because anaphylaxis in children often present with persistent cough and wheeze, it is often incorrectly initially treated with salbutamol and corticosteroids as first-line therapy,[20] which delays the administration of intramuscular adrenaline, with risk of increased morbidity and mortality.[21] Adrenaline is the only first-line therapy for anaphylaxis. Any additional therapy should be given only after adrenaline administration.

Myth Number 7

Antihistamines and/or steroids if used quickly at the first sign of an allergic reaction can prevent food anaphylaxis.

Mythbuster

Antihistamine and steroids have *no role* in the acute first-line management of anaphylaxis.

The why?

Administration of other medications in the treatment of anaphylaxis delays the administration of adrenaline, which is the current best available first-line therapy for anaphylaxis.

Anti-histamines are H1 receptor antagonists and are a generally effective treatment for urticaria and itch caused by release of histamine from mast cells. They do not prevent progression to, or treat, airway obstruction, hypotension or shock. Non-sedating oral antihistamines *should not* be used as first-line treatment for anaphylaxis because they delay the administration of adrenaline but can be useful adjunctive therapy once adrenaline has been administered. There is no evidence that prophylaxis with oral antihistamines decreases the risk of severe allergic reactions on subsequent exposure to food allergens.[22,23] The use of intravenous antihistamines such as promethazine are contraindicated in management of anaphylaxis because they are associated with hypotension[24] and may paradoxically worsen the clinical state.

Corticosteroids have many suppressive actions on mediators of the inflammatory and immune responses. Their known anti-inflammatory mechanism of action requires binding to nuclear receptors and modifying gene transcription, hence the onset of action is several hours. Corticosteroids have not been shown to be effective for the prevention of progression to, or acute treatment of anaphylaxis.[25] They may occasionally have a role as a second-line agent in biphasic or prolonged anaphylactic reactions, which are both rare in paediatric food anaphylaxis.[26–28]

Myth Number 8

Ara h2 is a good test to determine whether or not a child with a positive peanut allergy test has definite clinical peanut allergy and/or is at risk of anaphylaxis.

Mythbuster

Ara h2 or peanut other component testing *is not* useful in ruling out a clinical peanut allergy or in identifying children at risk of severe reactions.

The why?

Not all children with a positive SPT or ssIgE to peanut are allergic to peanut. The reported rates of clinical allergy to peanut in peanut sensitised children vary from 34% to 55%.[24,29,30] Currently, the only way to definitely determine which children are allergic as opposed to sensitised, where there is no clear history of allergic reaction on exposure, is by OFC.

Ara h2 is one of the 11 major peanut proteins. In peanut allergy, anti-Arah2 IgE levels above a particular cut-off point have good predictive value for clinical peanut allergy, but levels below this cut-off point do not rule peanut allergy in or out. In terms of a 95% PPV, Ara h2 performs only slightly better than standard SPT or ssIgE in most reported studies to date.[31] Importantly, a negative Arah2 does not exclude peanut allergy, demonstrated by the Australian-based healthnuts study results where 20% of challenge proven peanut allergic infants had a negative Arah2.[32]

High anti-Ara h2 IgE levels do not in general predict severity of allergic reactions or risk of anaphylaxis. In northern European populations where birch pollinosis and clinical birch pollen allergy is common, sensitisation to Ara h8 alone may be able to identify individuals with pollen food allergy syndrome, who are at lower risk of severe systemic reactions to peanut.[33] The meaning of Ara h8 sensitisation in the Australian context is currently unknown. The combination of sensitisation to multiple components (Ara h1,2,3) may be more useful in this respect, but performs better for whole of population risks than for individual risk assessment.[34]

Myth Number 9

IgE based allergy tests are useful to identify food triggers in childhood eczema.

Mythbuster

Immune-mediated allergic reactions (presumed T cell-mediated) that manifest as atopic eczema, chronic enteropathy and gastrointestinal eosinophilic disorders are not primarily mediated by IgE and therefore SPT and ssIgE are not generally helpful in their investigation and/or management.

The why?

Atopic dermatitis (AD) is common in Australian infants and young children, affecting up to 20%,[35] with a significant proportion of children with eczema have coexistent IgE-mediated food allergy and 40–90% of infants with mod-severe eczema are reported to have food allergen sensitisation to one or more common food allergens, such as egg, milk, peanut, wheat, potato, soy or fish.[36,37] IgE testing is useful in establishing a diagnosis of IgE-mediated immediate food allergy in children with eczema, but not in identifying foods t trigger eczema via a delayed, non-IgE-mediated mechanism. Symptoms of IgE-mediated food allergy are similar in children with and without eczema. IgE testing identifies the allergen specific IgE and is particularly helpful in identifying trigger allergens in disorders where IgE is the principle driver of disease causation, such as IgE-mediated food allergy, insect allergy and acute allergic rhinitis. The principal mechanism of disease in AD is skin barrier defect coupled with dysregulation of T cell and cytokine responses (reviewed in Campbell[38]).

The likelihood of a child with AD reacting with either an immediate or delayed reaction in an observed food challenge (OFC) is reported to be only 27–60% of IgE-sensitised children.[5,39,40] Thus, there is poor correlation between IgE food allergen sensitisation and both immediate and delayed eczematous reactions in childhood AD making the predictive value of SPT and ssIgE in determining which foods cause flaring of or worsening of eczema poor.[5] There are no good tests (either in vivo or in vitro) currently available which can reliably identify food/s which cause non-IgE-mediated eczema reactions – this includes allergy patch testing and allergen specific IgG.

Because of the risk of severe allergic reactions on re-exposure following dietary elimination of foods to which the child is sensitised[6,7] and removal of such food should be done with extreme caution and under the supervision of an experienced specialist and dietician.

Myth No 10

Oral desensitisation is a cure for food allergy.

Mythbuster

Although small studies suggest that desensitisation with a daily dose of allergen can be achieved for a majority of children with egg, milk and peanut allergy, the majority of children remain allergic once the daily therapy is ceased with current oral immunotherapy regimes and both minor and serious side effects are common.

The why?

Recent studies have reported successful desensitisation with oral immunotherapy (OIT) to peanut, milk and egg. This therapy is generally based upon daily administration of gradually increases allergen doses allergen with up-dosing and maintenances phases. These have shown a capacity to induce desensitisation in allergic individuals, albeit with both mild and severe allergic symptoms during therapy in a significant proportion of patients. However, the proportion of children reported to maintain sustained tolerance once regular daily administration of the allergen is ceased is disappointing low at less than 25% with high rates of side effects.[41,42]

The current state of OIT has been comprehensively reviewed by several leading food allergy experts, voicing concerns about the premature uptake of OIT into routine clinical practice.[43–45] Furthermore, a recent meta-analysis concluded that OIT cannot currently be recommended for routine clinical practice and that larger, better designed randomised controlled trials are required.[46]

Overall, oral desensitisation is a promising treatment for children with food allergies, but further research is needed before it is ready for routine clinical use.

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