

# EIGHT MYTHS FROM THE FOOD ALLERGY CLINIC

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## ABSTRACT

There are a number of areas of controversy and dogma surrounding food allergy that are widely believed by both parents of children with food allergy and the health professionals who care for them. Consequences of these misconceptions include heightened anxiety, risk taking, inappropriate food exclusion with nutritional consequences and unnecessary omission of vaccination because of fear of an allergic reaction. New research is improving our understanding of the development of allergies and their management. This article aims to address a few of the common myths in paediatric food allergy.

Allergy and allergic conditions are common, but there are a number of areas of controversy and dogma that are widely believed by both parents of children with allergies and the health professionals who care for them. The consequences of these misconceptions may impact significantly on the child's health and the family's lifestyle. For a child or adolescent with a food allergy, risk taking, whether deliberate or unintentional, may result in a potentially life-threatening allergic reaction. However for some children with food allergy and their families, heightened anxiety about this risk can lead to significant restriction of normal activities. Many children with eczema are sensitised to multiple foods on specific IgE or skin-prick tests (SPTs). Not all of these foods will necessarily result in allergic symptoms. Parents may exclude certain foods because of an inaccurate belief that the food is causing their child's symptoms. Inappropriate food exclusion can have significant nutritional consequences such as iron deficiency, rickets or protein-energy malnutrition. Where allergy to a major food group is confirmed, it is important to ensure a suitable alternative in the diet. Children with egg allergy may be exposed to risk of infection with measles because of a widespread misconception among health professionals and the public that the vaccine is contraindicated in children with egg allergy. It is the role of the clinician to ensure accurate diagnosis and appropriate advice on avoidance of the foods to which the child is allergic, to provide appropriate medication and training on the management of allergic reactions and to empower the child and family to lead as normal a life as possible while ensuring the health and safety of the child.

## MYTHS

The following myths are frequently encountered in the food allergy clinic.

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### *Myth: The larger the SPT wheal, the more severe the allergy*

SPTs involve the introduction of minute amounts of an allergen into the epidermis, eliciting a wheal and flare response which is then measured in millimetres.<sup>1,2</sup>

While the size of the SPT wheal helps ascertain the likelihood of an allergy, it does not predict the severity of a reaction. For example, a person with a 2 mm SPT wheal has less probability of clinical allergy than one with an 8 mm wheal, but if the person is allergic, the smaller wheal does not necessarily mean he or she will have a less severe reaction.

Food allergens eliciting an SPT wheal size >3 mm are generally considered to be positive, suggesting the child is sensitised to that allergen.<sup>1</sup> However the positive predictive value of a positive SPT based on this definition is <50%. It is therefore not uncommon for a child with a wheal >3 mm to be able to eat the food tested without adverse reaction. Similarly, a child with a wheal <3 mm may have an allergic reaction following ingestion of that food. It is therefore essential that SPTs are considered in the context of clinical history and not in isolation.

However, as the wheal size increases, the likelihood of clinical reactivity to that food also does. For some common food allergens, validated studies have demonstrated that a wheal above a certain size has a 95%<sup>3</sup> or greater predictive value that the patient is clinically allergic. Results vary between study populations and must be generalised with caution.<sup>1,4</sup> See Table 1 for an example of >95% specificity of SPT size in predicting a positive food challenge in a group of children where there was a strong clinical suspicion of food allergy.

Table 1. SPT wheal diameters giving >95% specificity in predicting the outcome of food challenges<sup>1</sup>

Allergen	Size of wheal in children >2 years	Size of wheal in children <2 years
Cow's milk	8 mm	6 mm
Hen's egg	7 mm	5 mm
Peanut	8 mm	4 mm

By considering the likelihood ratio<sup>3</sup> of the test result, a combination of history and SPT result can be used to reach a diagnosis in the outpatient clinic with minimal requirement for oral provocation challenges.

If clinical history and SPT results in an equivocal diagnosis, specific IgE blood testing may aid diagnosis.<sup>4</sup> If the result is inconclusive a supervised incremental oral challenge is warranted.<sup>2</sup> Double-blind placebo-controlled food challenges remain the gold standard for the diagnosis of food allergy, but are time-consuming and may be difficult to perform with limited resources; therefore open challenges are often used in practice.

There are no current tests to reliably predict the severity of an allergic reaction, although in the future using protein microarray technology to measure individual patterns of specific IgE epitope binding or the diversity of IgE binding to different allergen epitopes may be of value.<sup>5-8</sup>

*Myth: The severity of past allergic reactions predicts the severity of future reactions*

Common misconceptions in IgE-mediated food allergy include the belief that the severity of allergic reactions increases with subsequent exposure, and that an individual who has previously experienced mild reactions will only experience mild reactions in future.

The unpredictable nature of allergy means the severity of a reaction is difficult to anticipate and depends on multiple factors including: amount of allergen ingested; state of the allergen, e.g. raw or cooked egg; intercurrent illness, e.g. the presence of active asthma; concomitant medication; consumption of alcohol; and exercise after exposure.<sup>2</sup>

Several studies have attempted to clarify whether the severity of previous allergic reactions predicts the severity of a future allergic episode.<sup>9,10</sup> A previous severe reaction is a predictor of risk of future anaphylaxis, and a history of asthma is an important risk factor for life-threatening reactions. However the converse, that individuals who have only experienced mild reactions are unlikely to have a severe reaction, is not true<sup>11</sup> and the absence of asthma does not ensure that the child is in a low-risk category.<sup>12</sup>

The European Academy of Allergology and Clinical Immunology (EAACI) taskforce for anaphylaxis in children have identified criteria which help clinicians categorise children who may be at higher risk of anaphylaxis (Table II).<sup>13</sup>

Table II. Identification of children at higher risk of an anaphylaxis<sup>13</sup>

Absolute risk of anaphylaxis
Coexistent asthma
Previous anaphylaxis to food, drug or insect sting
Food-dependent exercise-induced anaphylaxis (FDEIA)
Idiopathic anaphylaxis
Relative risk of anaphylaxis
Reacted to trace quantities of allergen, i.e. vapour or topical contact
Peanut or tree nut allergy
Teenager with a food allergy
Living in a remote area, far from medical services

*Myth: An adrenaline auto-injector should be prescribed for all children with food allergy*

Adrenaline auto-injector devices (Anaguard, Epipen and Anapen) are syringes and needles preloaded with adrenaline. Adrenaline is the drug of choice for anaphylaxis. To ensure the best outcome it should be given at the first sign of an anaphylaxis.<sup>13</sup> There are a number of issues to consider when deciding who should be prescribed an adrenaline auto-injector.

As discussed previously the severity of an allergic reaction can be difficult to predict. Those children in the 'absolute risk of anaphylaxis' category (Table II) should always be prescribed an adrenaline auto-injector device. Those in the 'relative risk' category should be considered individually.<sup>9</sup>

The prescription of an auto-injector should always be given in conjunction with training in its use, a clear emergency management plan and advice on allergen avoidance.<sup>13</sup> The likelihood of a subsequent severe

allergic reaction is much reduced in nut allergic children followed up in a specialist allergy clinic.<sup>14</sup> Although adrenaline auto-injectors are widely prescribed in the UK, many parents fail to administer them when their child has anaphylaxis.<sup>15</sup>

The Epipen and Anapen devices contain a single dose of adrenaline. It is recommended that two devices are carried at all times, including while children are at school. These devices are available in a paediatric dose for children weighing between 15 kg and 30 kg. The Anaguard is pre-loaded with two doses of adrenaline, but is only available in an adult dose.

A second dose of adrenaline is only required by 20% of children with anaphylaxis; however, this may be life-saving for those living in remote areas, when a device malfunctions or if the first dose is accidentally injected into the administering caregiver.<sup>9</sup>

The cost of an adrenaline auto-injector ranges from US\$30 to US\$110 which may be prohibitive. In some countries there is limited or no availability<sup>16</sup> in which case allergen avoidance advice and education of recognition of signs of an allergic reaction is particularly important so that medical help can be sought at the earliest opportunity.<sup>17</sup>

*Myth: Soya milk infant formula is a suitable alternative to cow's milk formula in infants who are allergic to cow's milk*

Soya infant formula has historically been used as an alternative to the universally standard cow's milk formula. An alternative formula may be sought for a number of reasons including cultural and religious beliefs, following a vegetarian or vegan diet, as well as the diagnosis of a cow's milk protein allergy (CMPA). Despite fairly limited indications for its use, soya formula accounts for approximately 20% of the formula market in the USA<sup>18</sup> and is used by 2% of infants in the UK.<sup>19</sup>

In recent years concerns have arisen regarding the safety of its use because of the high phyto-oestrogen content. The structural similarity of isoflavones (a member of the phyto-oestrogen family) in soya and oestrogen has prompted studies exploring the potential negative impact the consumption of soya at an early age may have on sexual development and reproduction. The majority of research thus far has been carried out on animals and there is little evidence relating to human infants.<sup>19,20</sup>

The general consensus is that current evidence does not give rise to major concern; however, further studies are needed. As a precaution the Department of Health in the UK recommends soya formulas should only be used when clinically indicated.<sup>19,21</sup> This advice is echoed by the UK Chief Medical Officer, who states they should only be used in exceptional circumstances, and the British Dietetic Association (BDA) Paediatric Group<sup>22</sup> and the ESPGHAN committee on Nutrition who recommend use of soya formula be discouraged, particularly before 6 months when it is the sole source of nutrition.<sup>23</sup>

There are also concerns regarding the use of soya infant formula as a first-line treatment in CMPA, as some milk-allergic infants will also be soya-allergic. Estimates of cross-reactivity vary considerably.<sup>24,25</sup> Up to 60% of children with cow's milk protein-induced enterocolitis (non-IgE-mediated) will be sensitive to soya,<sup>18</sup> while this appears less likely in children with IgE-mediated allergy.

Soya formulas continue to play a role for older infants (>6 months) with IgE-mediated CMPA who refuse extensively hydrolysed formulas (EHF). They do offer

distinct advantages over EHF with regard to palatability and cost and may also be useful where EHF and/or elemental formulas are not available.

*Myth: Goat's milk infant formula can be used as an alternative to cow's milk infant formula in cow's-milk-allergic infants*

Goat's milk has also long been used as an alternative to cow's milk as many people mistakenly believe it is suitable for use in CMPA. Despite often being advocated for this purpose in lay publications, these claims have not been substantiated.

There is close homology between proteins in goat's milk and cow's milk, and in fact all mammalian milk including sheep and buffalo milk, and clinically significant cross-allergenicity has been observed.<sup>26</sup> Up to 90% of infants with CMPA show IgE cross-reactivity with the protein in goat's milk;<sup>27,28</sup> therefore goat's milk and goat's milk infant formula are not recommended in CMPA.<sup>29</sup> Goat's milk infant formula has been banned from sale in the UK since March 2007, following a recommendation by the European Food Safety Authority (EFSA) that there is insufficient data to establish adequacy and nutritional safety of goat's milk protein as a protein source in infants.<sup>30</sup>

Unmodified goat's milk is contraindicated in infants because of its nutritional inadequacy, e.g. low folate content, high renal solute load and doubtful microbial safety.<sup>30</sup>

First-line treatment for infants with CMPA is usually EHF, an elemental formula or soya formula after 6 months. Soya, rice and oat milk are often used for older children (over 2 years) with CMPA, but are not nutritionally adequate for infants. While some studies suggest that donkey, mare or camel milk may be well tolerated in CMPA, these are not widely available.<sup>31</sup>

*Myth: Mothers of infants at high risk of developing allergy should avoid high-risk foods during pregnancy and lactation*

Infants with family history of allergic disease are at greater risk of developing allergies.<sup>32</sup> Most allergy prevention advice focuses specifically on this high-risk group. There is no convincing evidence at present for the protective effect of maternal allergen avoidance during pregnancy or lactation. Several studies indicate maternal avoidance of potential allergens during breastfeeding may reduce atopic dermatitis; however other studies do not confirm this.<sup>33</sup>

The American Academy of Pediatrics (AAP) previously recommended elimination of peanuts and consideration of elimination of eggs, cow's milk and fish during lactation in mothers of high-risk infants.<sup>34</sup> This advice has recently been withdrawn and the new guidelines<sup>35</sup> now concur with the EAACI advice that there is no evidence for maternal dietary intervention during pregnancy and/or lactation and that this intervention may nutritionally compromise the mother and child.<sup>36</sup>

An area of particular contention is peanut allergy, given its dramatic rise over the past 2 decades. In 1998 the Department of Health in the UK issued recommendations aiming to reduce the incidence of peanut allergy.<sup>37</sup> Because of the possibility that sensitisation to peanut may be occurring *in utero* or during lactation, they suggested that pregnant or breastfeeding women might wish to avoid eating peanuts should they or their partner have an allergic condition. This guidance is currently under review. In recent years a new concept has emerged – peanut sensitisation occurring through different routes, including through the skin.<sup>38</sup> We still

don't know the best strategy to prevent development of peanut allergy,<sup>39</sup> but it is clear that in countries where exposure to peanut protein at an early age is the norm there appears to be low incidence of peanut allergy.<sup>40</sup> The hypothesis that early introduction of peanuts into infants' diet is protective is currently being tested in a randomised interventional trial (LEAP study).

*Myth: Everyone who has a peanut allergy must avoid all types of nuts*

Peanuts and tree nuts such as cashew, pistachio, hazelnuts and almonds are often discussed interchangeably although they do not belong to the same botanical family. While the nuts are unrelated botanically, up to 60% of children with peanut allergy will also be sensitised to one or more tree nuts.<sup>40</sup> Considering the potential severity of the allergy and issues with accurate identification, peanut-allergic children are often advised to avoid all peanuts and tree nuts. However, many will tolerate one or more types of tree nuts and do safely continue to consume them.<sup>41</sup> If some nuts are eaten while others are avoided as they may cause a fatal reaction, the risk of cross-contamination is an important issue.

Cross-contamination occurs when a safe food comes into contact with a food allergen, e.g. when different nuts are stored together, where nuts and nut-free products share the same factory line, or where utensils and equipment used to prepare a nut-containing food contaminate another food.<sup>41</sup> A further issue is adulteration, where one nut is sold as another; for example, almond desserts sold in restaurants which actually contain peanuts.

If a peanut-allergic child continues eating other nuts, parents must be educated on how to minimise risk. This may include advice to offer only plain, not processed, nuts in the home environment only when the child is well and with a management plan of how to avoid an allergic reaction and medication close at hand. Many children unnecessarily avoid other foods associated with peanut allergy, where there is risk of co-reactivity, e.g. sesame, pine nut, legumes and lupin.<sup>37,42</sup> Allergy tests can help to guide advice. Avoidance of these foods is not routinely advised unless previous reactions are reported.

Some foods are avoided unnecessarily because their name contains the word nut, e.g. butternut, nutmeg, coconut. Although allergies to these foods have been reported they are rare and do not appear to be more common in children with nut allergies.

Refined peanut oil will not cause allergic reactions in the majority of peanut-allergic individuals and if anyone does suffer a reaction, it is likely to be mild. Unrefined (crude) peanut oil is more likely to cause symptoms.<sup>43</sup>

*Myth: Children allergic to hen's egg can not have the measles or MMR vaccine as it contains egg*

The measles vaccine is part of the routine vaccination programme for children across the world.<sup>44</sup> In South Africa and other countries, it is given as a monovalent vaccine at 9 and 18 months of age, whereas in Europe, Australia and the USA it is given as a combined vaccine: mumps, measles and rubella (MMR).<sup>44,45</sup> A common misconception that these vaccines contain egg and may cause an allergic reaction in those children allergic to egg, alongside unfounded concerns relating to autism, was partly to blame for the dip in the immunisation rate for MMR in the UK in the late 1990s to less than 80%.<sup>46</sup>

A Cochrane review examined the safety and efficacy of the MMR vaccine but did not focus on egg allergy and the MMR.<sup>47</sup> Egg allergy and the administration of the measles or MMR vaccine was the primary outcome of a study by Baxter<sup>48</sup> and a review by James *et al.*<sup>49</sup> In these studies children with confirmed egg allergy were given the measles or MMR vaccine and the number of children reacting to the vaccine was low. Both vaccines are grown on cultured chick fibroblasts and do not contain hen's egg protein. Reactions to these vaccines are usually due to another component of the vaccine, such as neomycin or gelatine, and the measles or MMR vaccine should not pose a risk to children who are allergic to hen's egg,<sup>46-49</sup> unlike the influenza vaccine and yellow fever vaccines which are prepared in hen's eggs and are contraindicated in severe egg allergy.

The WHO recommends that all children be immunised with the measles or MMR vaccine as appropriate to their geographical location. The current recommendation of the British Society of Allergy and Clinical Immunology Paediatric Allergy Group is that the MMR vaccine may be administered to all egg-allergic children in a routine primary care setting.<sup>50</sup>

#### Declaration of conflict of interest

The authors declare no conflict of interest.

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