

## HOW TO



**FIGURE 1**  
The safety issues surrounding skin-prick testing are similar to routine immunisations  
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**How** are food allergies diagnosed in practice?

**What** emergency care may be needed?

**What** is the role for self-administered adrenaline?

# Managing food allergy in children

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**PROVISION OF SPECIALIST ALLERGY SERVICES IN THE UK IS INADEQUATE,<sup>1</sup> AND SO THE VAST MAJORITY OF**

children with a history of food-induced anaphylaxis are managed entirely in primary care.

The majority of food-induced allergic reactions, although unpredictable, are not life-threatening. However life-threatening and fatal anaphylactic reactions can occur, and are preventable.

The prevalence of food allergy in the UK is increasing and food-induced allergic reactions are the most common cause of anaphylaxis in childhood. The GP must not only be skilled in recognising and managing anaphylaxis, but must also be aware of the importance of the long-term

management of children who have experienced food-induced anaphylaxis.

The emphasis is on providing a personalised management plan focusing on avoidance strategies. The GP should aim to empower patients and caregivers to identify and treat anaphylaxis.

In addition, frequently-associated allergic disorders such as asthma and eczema may require attention to reduce the risk of future reactions and perhaps the likelihood of developing additional food allergen sensitisation.

### THE MEANING OF ANAPHYLAXIS

There is presently no universally-accepted definition, but a recent symposium reached a consensus on the following broad definition: 'anaphylaxis is a serious allergic reaction that is rapid in onset and

may cause death'.<sup>2</sup> In practical terms, this is an allergic reaction with cardiovascular or respiratory involvement and usually due to an IgE-mediated allergic reaction.

Although a pathophysiological distinction exists between anaphylaxis and anaphylactoid reactions this distinction cannot easily be made clinically and the emergency treatments are identical. Table 1 lists agents commonly associated with anaphylactic reactions.

### INCIDENCE

The incidence of anaphylaxis in the UK has risen in the last decade.<sup>3,4</sup> Food allergy remains the most common cause in childhood, and the prevalence of food



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**FIGURE 2**

The increase in food-induced anaphylaxis has been attributed to increased reporting, dietary changes and novel foods such as Macadamia nuts and kiwi fruit

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**Table 1**

### Causes of IgE-mediated anaphylaxis and anaphylactoid reactions

- Foods
- Venoms and saliva
- Antibiotics
- Aspirin and nonsteroidal anti-inflammatory drugs
- Miscellaneous drugs and blood products including: allergy extracts, globulins, antitoxins, insulin, folic acid, iron dextran, mannitol, methylprednisolone, opiates, progesterone, protamine sulphate and streptokinase
- Anaesthetic drugs (for example succinylcholine, thiopental)
- Vaccines, cryoprecipitate, immune globulin, plasma, whole blood
- Natural rubber, latex
- Radiographic contrast media
- Physical factors
- Other such as cold temperatures, exercise, idiopathic

foods such as peanuts and tree nuts), and the availability of novel or previously scarce foods such as Macadamia nuts and kiwi fruit.

It has been suggested that there is a strong association between acute severe asthma and food allergy.<sup>9</sup> The fact that food-induced anaphylaxis in childhood frequently presents with respiratory symptoms that may mimic acute severe asthma suggests that life-threatening, food-induced anaphylaxis events may be misdiagnosed as acute severe asthma.

**Table 2**

### Common food allergies in childhood

	Young children	Older children/ adults	Anaphylaxis ascribed to this food?
Cow and goat milk	X		X
Hen's egg	X		X
Peanut	X	X	X
Tree nuts	X	X	X
Finfish	X	X	X
Shellfish	X	X	X
Fruit (eg kiwi)	X	X*	X (apple)
Vegetables	X	X*	X
Seeds (especially sesame, mustard, poppy)	X		X
Spices	X	X	
Soya	X	X	X
Wheat	X	X	X (FDEIA**)

\*oral allergy syndrome \*\*food-associated, exercise-induced anaphylaxis

allergy in early childhood is 6 per cent to 8 per cent, with evidence to suggest that the prevalence is increasing, at least for peanut allergy.<sup>5</sup>

Table 2 details the common food allergies at different ages. The exact incidence of fatal or near-fatal anaphylaxis to food among children is unknown: however, a prospective survey of hospital admissions in children in the UK and

Ireland (between 1998 to 2000) for food-allergic reactions yielded a rate of hospital admissions of 0.89 per 100,000 children per year. Some 58 cases were severe: three were fatal, six were near-fatal, and eight of these nine had asthma with a wheeze being the life-threatening symptom.<sup>6-8</sup>

The increase in food-induced anaphylaxis has been attributed to a host of factors including increased awareness and reporting, dietary changes (such as the increased consumption of allergenic

### DIAGNOSIS

Anaphylaxis is a clinical syndrome, comprising of one or more of circulatory, respiratory, gastrointestinal and dermatologic manifestations.<sup>2</sup>

Table 3 lists symptoms and signs that are commonly associated with anaphylaxis. It is reassuring that the majority of food-induced allergic reactions are not of life-threatening severity.

The presentation of severe food reactions in childhood involves the respiratory tract, usually in association with angioedema and or urticaria. However anaphylaxis in adults is more commonly associated with hypotension.<sup>5,10</sup> A broad differential diagnosis for the diagnosis of anaphylaxis may need to be entertained, a process that is best approached in a symptom-based manner.

### PATHOPHYSIOLOGY OF IgE-MEDIATED ANAPHYLAXIS

The symptoms and signs that make up anaphylaxis are the result of the interaction between the allergen and >>

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**FIGURE 3**

There is evidence to suggest that peanut-induced anaphylaxis is on the increase

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**Table 3**

### Clinical signs and symptoms of anaphylaxis

- **Cardiovascular** hypotension, tachycardia, arrhythmias, or complete vascular collapse with loss of consciousness
- **Respiratory** oral and pharyngeal swelling, hoarseness, laryngospasm, wheezing, cough, breathlessness, and/or chest tightness
- **Gastrointestinal** diarrhoea, cramping, and vomiting, are not infrequent. (In some females, painful abdominal pain due to uterine contractions may be experienced)
- **Dermatological** although neither universally present nor necessary for a clinical diagnosis, the most common signs of anaphylaxis include macular or urticarial rashes, and angioedema and erythema with or without urticaria

the IgE antibodies specific to it present on the surface of peripheral basophils and tissue-mast cells.

The resulting intracellular signal leads to mast cell and basophil degranulation and the release of vasoactive substances, including histamine, bradykinin, prostaglandin D2 and leukotriene C4.

### FOODS KNOWN TO CAUSE ANAPHYLAXIS

Although all food proteins have the immunological potential to induce severe allergic reactions, food-induced anaphylactic A&E admissions are predominantly due to reactions caused by peanut, tree nut, cow's milk, egg and shellfish.<sup>6</sup>

Studies that review the outcomes of positive food challenges reveal that severe food-induced allergic reactions also occur to foods other than peanut, tree nuts and shellfish.<sup>13</sup> Early concerns over the

increased allergenicity of GM foods through allergen modification or undeclared allergen contamination have not been substantiated, possibly as a consequence of the strict regulation imposed on this industry.<sup>14</sup>

Food allergies manifest soon after ingestion (usually within minutes), but may occasionally be delayed by as long as several hours. Rather than being more benign, delayed anaphylaxis has been shown to be more severe and less likely to respond to conservative measures.<sup>15</sup>

Highly-sensitive patients may experience anaphylaxis after inhalation exposure.<sup>16</sup>

The only-known reliable predictor of future anaphylaxis is a documented, individual history of prior anaphylaxis; however, the majority of children with anaphylaxis have no personal history.

Severe food-induced allergic reactions may occur at low doses, particularly for milk and peanut. Cumulative allergen exposure does not appear to increase the risk of a severe reaction. Exercise may be a co-factor for the development of anaphylaxis; this may occur due to exercise alone, or represent food-associated, exercise-induced anaphylaxis (FDEIA). In FDEIA, the responsible food allergen is tolerated in the absence of exercise. Although a wide variety of food allergens may be

**Rather than being benign delayed anaphylaxis has been shown to be more severe**

associated with FDEIA, wheat is the most common cause.

### DIAGNOSIS

Determining whether an anaphylactic event was caused by a food-induced allergic reaction relies on one or more of the following: a thorough medical history, clinical examination, allergy testing by skin-prick testing (SPT) and specific IgE testing, and food challenges using open- or blinded-oral food challenges and elimination diets. Despite recent diagnostic advances, a thorough history remains the mainstay of allergy diagnosis.

Questions that may facilitate diagnosis of food allergy are listed in table 4.

The history is usually unequivocal as it is in the example of a child who ate peanut butter and shortly thereafter developed anaphylaxis. However, it is not uncommon for the trigger to be unidentified, particularly in older children.

If anaphylaxis has occurred repeatedly and food allergy is suspected, a list of ingredients from foods ingested before these events should be obtained to identify candidate allergens for inclusion in subsequent allergen panels.

### PHYSICAL EXAMINATION

There are usually no active signs unless the child is seen during acute anaphylaxis. The examination should however seek to exclude concomitant allergic (for example asthma) and non-allergic disease (say mastocytosis), which may have facilitated or caused the clinical presentation.

### DIAGNOSTIC ALLERGY TESTING

Allergy testing (SPT or in-vitro specific IgE tests) is helpful in identifying or confirming specific allergic triggers.

All GPs should have access to specific IgE antibody testing. The in-vitro IgE tests, although relatively costly, are safe and highly accurate if correctly interpreted in conjunction with a thorough history. The tests are logistically difficult, however, as the patient will need to attend a lab for testing and will need to return to discuss the results.

There are many reasons why the majority of GP practices do not perform skin testing, including lack of allergy training, time and cost. However, if SPT guidelines are followed, the safety issues that surround testing are no greater than those surrounding routinely-performed immunisations. The rapid availability of skin test results, the low cost and broad choice of allergens, remain distinct advantages.

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## Table 4

### The allergic history

**What is the suspected food allergen? Is the allergen typical for age?** For example allergies to cows milk and egg are common in young children but rare in adulthood

**What is the route of allergen exposure?** Was it ingestion, inhalation or contact? A proportion of patients will react after inhalation or contact with the allergen

**What is the timing of the reaction post-exposure?** IgE mediated allergic reactions usually occur within 20 minutes of the reaction and certainly within two hours

**What is the description of allergic reaction symptoms?** If symptoms are not typical of an immediate-onset food reaction, consider a differential diagnosis. Common confusing scenarios include:

- Eczematous patients who experience peri-oral urticaria and contact irritation provoked by fruit juices and other irritants
- Oral allergy syndrome
- Chronic urticaria – for which food allergy is a rare cause
- Anxiety disorders, vasovagal attacks, mastocytosis, hereditary angioedema and vocal cord dysfunction are all disorders with symptoms that may mimic anaphylaxis

**What is the symptom severity?** A previous severe reaction warrants a more stringent emergency management plan

**Is there a prior history of tolerance to the food or are the symptoms reproducible?** It is rare to have a history of previous tolerance to a food allergen. Reactivity may however be influenced by the amount of exposure, cross reactive allergens or processing of the food; for example, foods that contain raw egg protein may induce reactions in patients who tolerate cooked egg

**Were there associated facilitating factors?** Active asthma, medication use, alcohol intake and exercise may suggest a specific diagnosis such as FDEIA or aspirin sensitivity

Allergens to be tested should include those candidate allergens identified in the history. If no candidate allergens are identified, then panels should be selected that are appropriate to the age of the child as well as the geographic location where the reaction occurred.

Testing should also cover potentially cross-reactive allergens. Panels should also include common food allergens that may not yet have been eaten in the child's diet, as tolerance cannot be assumed (food-allergic children are frequently allergic to more than one food).

Both negative and positive predictive values have been established for many of the common food allergens. The use of these predictive values has been shown to reduce the need for unnecessary oral food challenges.<sup>5</sup>

Given that the majority of children with food allergy will have concomitant allergic disease, allergy testing should also include

allergens that may be relevant to the control of these conditions; for example, pollen allergic children with seasonal asthma may benefit from pollen immunotherapy.<sup>17</sup>

The optimal control of asthma is critical, as active uncontrolled asthma has been associated with severe and fatal food-induced allergic reactions.

### FOOD CHALLENGES

Allergy testing will usually enable the exact identification of the patient's food allergy, and cross-reactive food allergies. However if a definite food allergen has not been identified, or tests of cross-reactive allergens are not conclusive, a food challenge may be necessary.

Food challenges may also be required to assess if the child has outgrown their allergy. These should be performed by experienced physicians and in an appropriate setting. If an anaphylactic reaction has recently occurred to a food, it is wisest to wait for at least a year before considering an oral challenge.

### MANAGEMENT

The GP has a critical role to play in both acute- and long-term management of the child who has experienced a food-induced anaphylactic reaction.<sup>18</sup> The GP may be the first to treat acute food-induced anaphylaxis; for example, a child may be rushed to the surgery during an episode of acute anaphylaxis. GPs should therefore rehearse such scenarios so that the entire team is skilled in the identification and management of acute anaphylaxis. This is also necessary if the practice routinely immunise children, which itself may induce anaphylaxis.

A detailed management protocol for the treatment of acute anaphylaxis is available from the UK Resuscitation Council.<sup>19</sup> Anaphylaxis needs to be treated as a matter of urgency as respiratory compromise and shock can develop rapidly.<sup>18</sup>

Emergency treatment of food-induced anaphylaxis always follows the basic life support ABC principles, with the simultaneous intramuscular injection of adrenaline. Intramuscular injections should be into the muscle of the anterolateral thigh in an attempt to prevent or reverse the respiratory and cardiovascular compromise, which may be associated with anaphylaxis (absorption from the thigh muscle is better than the deltoid).<sup>20</sup>

The administration of intravenous adrenaline (epinephrine), particularly in the setting of anaphylaxis, has been associated with incorrect dose administration and should only be



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performed in exceptional circumstances and by experienced staff.

The subcutaneous route is no longer recommended as absorption is erratic and slow; likewise, adrenaline administration by inhalation proves sub-optimal.<sup>21</sup> The range of commercially available pre-loaded self-injectable adrenaline devices is expanding and physicians now have a choice of EpiPen and Anapen, and the Twinjet is about to be launched.

The sublingual route of administration is under investigation.<sup>22</sup>



**FIGURE 4**  
Testing panels need to be carefully selected and may need to include both ingested and inhaled allergens  
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Initial treatment with adrenaline should be followed by administering a fast-acting antihistamine and a short course of oral steroids in an attempt to prevent wheezing as part of a delayed component of the reaction. Oral or intravenous steroids play no immediate role in anaphylaxis management, as they will take at least two hours to exert their effect. Administering a short-acting  $\beta$ -2 agonist may provide additional relief from airway obstruction if wheezing is present.

For the generalised urticarial rash associated with 'mild' anaphylaxis, a fast-acting oral H1 antihistamine medication should suffice; however, injectable adrenaline should always be available in case a moderate to severe generalised reaction occurs. H2 receptor

blockers (such as ranitidine) offer little additional effect as only a minority of H2 receptors are found in the skin.

Remember that anaphylaxis may recur some hours after the initial treatment in a biphasic response, so all children treated for anaphylaxis should be monitored for at least four hours after their reaction – even if they appear to have made a full recovery.

It is important that A&E departments are aware of this, as many patients may be at risk of premature discharge in order that A&E departments do not incur a 'four-hour breach'.

### THE GP'S ROLE IN THE ONGOING MANAGEMENT OF FOOD-ALLERGIC CHILDREN

The long-term duties of managing the patient and their family after anaphylaxis will usually fall to the GP. To some GPs, this may be a tedious and expensive task as the practice is required to renew the

**Table 5**

#### Indications for the prescription of pre-loaded injectable adrenaline devices\* to children with a history of food-induced allergic reactions

##### Absolute

- Previous severe allergic reaction
- Asthma

##### Probable

- Propensity to obstructive airways disease – for example, prior diagnosis of asthma or the infant with 'wheeze or wheezy-cough' variants, such as asthma yet to be confirmed due to young age
- Anxious patient or family
- Frequent travellers, particularly where the language is not spoken by family or nuts are typically present in the local diet
- Limited access to emergency care (eg in remote areas)
- Age. Adolescents and young adults have a greater risk of fatal food anaphylaxis. The majority of recorded fatal reactions to foods (about 90%) occur in children over the age of five years
- Allergy to peanuts or tree nuts. Most deaths from food anaphylaxis occur from nuts. Generalised allergic reactions can be triggered by exposure to trace or small amounts of nuts, which can be difficult to avoid. Subsequent allergic reactions to nuts may be unpredictable. Nut allergy will only be outgrown in approximately 20% of children<sup>31,32</sup>
- Multiple food-allergic children. It may be difficult to identify and avoid triggers

#### Pre-loaded injectable adrenaline devices are generally not prescribed for

- Non-food allergic asthmatics
- Positive, but not predictive allergy tests if diagnosis is equivocal, oral challenge tests are required
- Family (rather than personal) history of anaphylaxis or allergy
- Resolved food allergy

pre-loaded injectable adrenaline devices. However, many families will be traumatised and worried about future reactions.

Additional input will be required to identify and treat any concomitant atopic disease, such as eczema, rhinosinusitis and asthma. The families may also request screening of their other children to avoid additional food reactions in the family. Indications for the referral of children to an allergy centre are proposed.

Although experimental agents are being trialed, the only available therapy for the management and prevention of food allergic reactions is avoidance, and this should be the focus of ongoing management. This may prove difficult unless patients and their caregivers are trained in the challenging task of successfully identifying, and avoiding, their relevant food allergens.

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# HOW TO MANAGE ALLERGIC REACTIONS

## essential practice points

SELECTED BY

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**Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death**

**Food-induced allergic reactions are the most common cause of anaphylaxis in childhood**

**The greatest number of anaphylactic episodes in children are due to peanut, tree nut, finfish, shellfish, cow's milk, sesame, kiwi and hen's egg exposure.** Allergy testing should be performed to confirm the food allergy, rule out potential cross-reacting allergies or unidentified allergies and assist in the management of concomitant allergic disease, for example asthma and eczema

**Consultation and cooperation between the GP and the allergy clinic will maximise the possibility of a successful outcome for the patient**

**The skills of a dietician are required to successfully prevent subsequent accidental ingestions and to ensure that nutritional deficiencies do not develop**

**All food allergic patients require a personalised management plan**

The expertise of a dietician is invaluable in this task. The patient and caregiver must also be trained to identify common presenting allergic symptoms and empowered to commence early, and appropriate, emergency treatment. All patients with food allergy require a written emergency plan, which clearly identifies the patient and their medical contacts, lists their food allergy and the steps to be taken in the event of an accidental exposure.

There is no clear consensus on the indications for carrying pre-loaded injectable adrenaline and there are numerous quandaries with respect to prescribing an emergency action plan and self-injectable adrenaline for first-aid management of anaphylaxis.<sup>23</sup>

Tables 5 lists a rational approach to the prescription of pre-loaded injectable adrenaline devices, but each case must be considered on the basis of individual factors. The child and their caregiver must be carefully instructed on how to use the pre-loaded injectable adrenaline device and should rehearse administration using a 'trainer' device.

Wheezing is a common food-induced allergic symptom, particularly in children, and all food-allergic asthmatic children

should also have a salbutamol inhaler included in their emergency plan. Steroids may provide some protection against delayed anaphylactic reactions, which typically occur four hours after allergen exposure.

Patients should ideally be registered with Medic Alert and order an identifying bracelet or necklace. This is particularly important for older children who may appear frightening to otherwise helpful strangers as a consequence of food-allergy induced urticaria and angioedema.

Dangerous scenarios for accidental food reactions include school environments, restaurants and commercial air travel. For teenage food allergic patients additional risks include 'kiss-induced' reactions and the ingestion of unfamiliar meals that may contain hidden allergens.

It is important to remember that food allergen inhalation may also result in allergic reactions - this is especially so with inhaled fish and milk vapour.<sup>15</sup>

Educational materials, such as model medication plans, are available through allergy organisations, which also provide guidance for schools and patients who are about to travel.

The ongoing nutritional management of individuals with food allergy is important, particularly in young multiple, food-allergic children who are at risk of nutritional compromise.<sup>24-27</sup>

The ongoing assessment of the food allergic child and family should serve to re-evaluate the patient's allergic status, nutritional status, emergency plan and psychological wellbeing. ●

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### SOURCES OF FURTHER INFORMATION

- 1 Allergy UK [www.allergyuk.org](http://www.allergyuk.org)
- 2 Australasian Society of Immunology and Allergy [www.allergy.org.au](http://www.allergy.org.au)
- 3 British Society of Allergy and Immunology A list of specialist Allergy centres is available from the BSACI. [www.bsaci.org](http://www.bsaci.org)
- 4 Food Allergy and Anaphylaxis Network [www.foodallergy.org](http://www.foodallergy.org)
- 5 UK Anaphylaxis Campaign [www.anaphylaxis.org.uk](http://www.anaphylaxis.org.uk)
- 6 Medic Alert Foundation [www.medicalert.org.uk/default.asp](http://www.medicalert.org.uk/default.asp)
- 7 National Eczema Society [www.eczema.org](http://www.eczema.org)

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Do you have any unique ways to deal with children's food allergies?

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