Diagnosis and management of food allergy in children

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Abstract

Food allergy (FA) in children is common, affecting about 6% of children in the UK, and is thought to be increasing in prevalence. Presentation varies widely with age, causative food, type of FA (IgE-mediated or non-IgE mediated) and severity. Assessment of suspected FA includes a detailed clinical history and dietary history and appropriate confirmatory allergy testing. The traditional management of complete dietary exclusion of the causative and related foods is evolving to one of limiting exclusion and early reintroduction. Novel treatments under investigation are mechanisms to prevent FA and oral desensitisation in selected cases in an attempt to cure FA. This article aims to give advice to the generalist about how to assess and initiate appropriate investigation a child presenting with possible food allergy.

Keywords Diagnosis; food allergens; food allergy; oral tolerance; treatment

Introduction

Food allergy (FA) in children is common; so all clinicians treating children will regularly encounter children and families living with FA. The focus of management of FA in recent years has shifted from total allergen avoidance to limiting avoidance, earlier reintroduction and attempts to induce oral tolerance and cure the allergy.

Definition and pathogenesis

'What is food allergy'?

The term *food allergy* refers to 'an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food (almost always a food protein)'. The definition for FA encompasses immune responses that are IgE mediated, non-IgE mediated or a combination of both.

Food intolerance is a non-immune reaction that includes metabolic (e.g. lactase or fructase deficiency), toxic (e.g. microbial contamination or Scromboid fish poisoning), pharmacologic (e.g. caffeine), psychological (e.g. panic attacks) and undefined mechanisms. A common misinterpretation that still exists is to refer to non-IgE mediated FA as intolerance, as in cow's milk protein intolerance. The correct term is non-IgE mediated milk allergy.

What are the mechanisms of food allergy?

FA allergy is classified on the basis of the immune mechanisms into IgE-mediated, non-IgE mediated (e.g. cell mediated) or a combination.

IgE-mediated reactions are characterised by early onset symptoms typically within 5–30 minutes of ingestion of the trigger food (and almost always within 2 hours). These reactions classically involve the skin (urticaria, angioedema, pruritus), gastrointestinal tract (nausea, abdominal pain, vomiting, diarrhoea) and respiratory system (runny nose, throat swelling, cough, wheeze and dyspnoea).

In certain at risk individuals, food specific IgE antibodies are produced by plasma cells following prior exposure to the antigen. This is known as 'sensitisation'. These antibodies bind to the surface of mast cells, and when re-exposed to the food, antigenic proteins bind to and cross-link these cell-bound IgE-antibodies and trigger the release of symptom-inducing mediators such as histamine. Individuals can have allergic sensitisation to food allergens without having clinical symptoms on contact with that food. Therefore, sensitisation *per se* (i.e. *having a positive allergy test*) is not sufficient to diagnose IgE-mediated FA. A diagnosis requires typical symptoms on exposure to that food and evidence of sensitisation.

A small proportion of children with hay fever develop 'secondary' IgE-mediated FA called Pollen Food Syndrome (formerly Oral Allergy Syndrome). These pollen allergic individuals develop antibodies to closely related or cross-reacting allergens in fruits and vegetables. Symptoms are limited to areas of direct contact (mouth and throat) and only to unprocessed foods as these allergens are labile and are destroyed by stomach acid and heat.

Non-IgE mediated FA is less clearly defined probably because cases are more difficult to identify as the time delay between food contact and symptoms is prolonged (sometimes up to 48–72 hours) and there is no identifying allergy test. Non-IgE mediated FA usually affects infants and young children with predominantly abdominal symptoms including colic, abdominal cramps, vomiting, diarrhoea, constipation, blood in the stools and failure to thrive. Moderate to severe eczema may be a comorbidity. The only diagnostic test for non-IgE mediated FA is dietary avoidance of the suspected food allergen with demonstration of complete or partial resolution of symptoms followed by reintroduction to elicit symptoms again. Dietary avoidance should be for at least 4 weeks and be under dietetic supervision.

Prevalence and natural history

How commonly does food allergy occur?

FA is said to be common and thought to be increasing in prevalence. It is generally accepted that it affected about 6–8% of children in the UK.

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Cow's milk, egg, peanuts and tree nuts are the most common allergens in children, with an estimated prevalence for each of 2–3%. Shellfish, fruits and vegetables are the most commonly occurring allergens in adults. Although any food can trigger an allergic response, and more than 170 have been reported to cause IgE mediated reactions, only a few foods cause the majority of allergic reactions, with most attributed to peanut, tree nuts, milk, egg, fish, shellfish, wheat, soya, sesame and kiwi fruit.

Can a child grow out of food allergy?

The natural history of FA is variable and influenced by food and patient factors. FA to milk, eggs, wheat and soya typically resolves in childhood, whilst FA to peanuts, tree nuts, fish and shellfish tends to persist into adulthood. Prognosis also varies by disorder as, for example, non-IgE mediated milk allergy has a better outcome than IgE mediated. Persistence is furthermore likely with higher early levels of sIgE, presence of other or multiple food allergies and of co-existing allergic conditions like asthma or rhinitis. Decreases in sIgE over time may signal resolution.

The proportion of children who outgrow FA to specific foods varies between analyses, although as a guide around 50–60% of children with milk or egg allergy should demonstrate tolerance by school age. Recent evidence suggests that the rate of resolution for foods commonly outgrown has slowed, and that it can continue into teenage years or even early adulthood.

Assessment of children with suspected food allergy

The diagnosis of a FA is important as it guides appropriate and safe dietary elimination, or where negative, enables safe dietary expansion. Assessment is based on history and allergy tests.

How to take a food allergy focused history

A detailed clinical history and careful dietary history are fundamental to the diagnosis of FA. They can establish the likelihood of the diagnosis, suggest which immunological mechanism is involved and identify the potential culprit food triggers. The history should capture the possible causal food or foods, form (raw, cooked or baked) and quantity ingested as well as the timing of the reaction, symptoms interrogated by systems, and ancillary factors or activities accompanying the reaction (e.g. intercurrent illness, exercise, medications).

Presenting symptoms and signs vary widely, as described above, and are influenced by a number of factors. Young children, for example, cannot describe subjective symptoms like pruritus, chest tightness, anxiety or dizziness. In addition, in this age group symptoms may be obvious but difficult to interpret, for example vomiting after feeds or choking with feeds. Some foods trigger reactions at first known contact (e.g. peanuts), whilst other may have been ingested for some time before symptoms occur (e.g. milk). Furthermore, baking milk or egg reduces allergenicity and many can tolerate this form but not less well-processed forms. By contrast, heat stable proteins found in fish or nuts cause symptoms in all forms.

The severity of presentation also covers a wide spectrum in both IgE mediated FA, ranging from, localised peri-oral urticaria or angioedema to life-threatening or even fatal cardio-respiratory arrest of generalised anaphylaxis; and non-IgE mediated FA, ranging from localised eczematous rash to hypovolaemic shock from profuse vomiting and watery diarrhoea of food protein-induced enterocolitis syndrome (FPIES). FPIES is an increasingly recognised specific severe form of non-IgE mediated FA. It manifests with profuse emesis and diarrhoea in young infants commonly caused by milk or soya allergy, although any food can cause FPIES.

The history must also identify other atopic conditions such as eczema, asthma, rhinitis and hay fever. These can impact on patient general well-being, as, for example, poorly controlled asthma is a risk factor for anaphylaxis.

Most patients present for an assessment of suspected FA in an outpatient setting quite some time after their suspected reaction. Clinical examination will therefore not reveal these, but is nevertheless important to assess the patient for co-existent allergic conditions e.g. asthma, allergic rhinitis or atopic dermatitis.

How to investigate a child with suspected food allergy

The medical history alone or in combination with the physical examination is not diagnostic of FA. The history is used to estimate the risk of allergy, the causative food or foods and the type of food-induced allergic reaction. This then provides a guide to appropriately select and interpret minimally invasive investigations and arrive at a probability of allergy.

Recommended tests are skin prick tests (SPT), measurement of serum specific IgE (sIgE), elimination diets and oral food challenges. The routine use of total serum IgE measurements, intradermal tests, patch tests and basophil activation tests is not advised. A number of unproved tests including serum allergen specific IgG_4 measurement, hair analysis, iridology, applied kinesiology and electrodermal testing (or the Vega test) are to be specifically discouraged.

IgE-mediated food allergy: determining specific IgE levels in the skin (SPT) or serum (sIgE) are the initial tests used to help in the diagnosis of IgE-mediated FA. SPTs are preferred as results are immediately available.

Non-IgE mediated food allergy: as mentioned (under *Pathogenesis*) there are no validated tests to assist in the diagnosis of non IgE-mediated FA. Diagnosis of these types of food allergies relies on observed reduction in symptoms with dietary elimination and recurrence with reintroduction. In practice, where there is noticeable clinical improvement with dietary elimination, the diagnosis is clear and reintroduction of the offending food is rarely performed. By contrast, where the diagnosis is uncertain, particularly in elimination diets assessing the possibility of delayed onset FA in eczema, reintroduction after a period of elimination is an essential part of the diagnostic assessment.

Food challenges: an oral food challenge (OFC), effectively a supervised exposure to a known allergen, is the gold standard test to assess the presence of IgE-mediated food allergy; with the double blind placebo controlled food challenge as the true gold standard. Oral challenges are most frequently used to make a definitive diagnosis of FA where the history and allergy test conflict, or to assess the development of tolerance. Open challenges are usually used in clinical practice. Blinded challenges,