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Holloway E, Fox A, Fitzsimons R. Diagnosing and managing food allergy in children
Practitioner 2011; 255 (1741):19-22

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Practitioner
Medical Publishing Ltd

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FIGURE 1
Swollen lips and urticaria are typical signs of an IgE-mediated allergic response

What are the common food allergens?

What are the main mechanisms involved?

How should children be managed?

THE PAST FEW DECADES HAVE SEEN A HUGE RISE IN ALLERGIC DISEASE. RECENT STUDIES SUGGEST that the prevalence of food allergy in children in the UK is now around 5%.[1]

The number of children put on restricted diets by their parents because of presumed allergy is likely to be much higher. A recent population-based study in the Isle of Wight found that 33% of mothers thought their child had had an allergic reaction to food by the age of three.[1]

Accurate diagnosis of food allergy is essential in order to ensure that the correct foods are carefully avoided while safe foods are not excluded unnecessarily. [2] Examples of common food allergens are listed in table 1, right.

Central to the successful diagnosis of food allergy is an understanding of the two main mechanisms involved.

Easier to recognise are IgE-mediated (immediate type) reactions which are the result of mast cell degranulation leading to histamine release.[3] The typical signs of lip swelling and urticaria (see figure 1, above) and possible progression to respiratory compromise (anaphylaxis) are usually clearly described, occurring within minutes of exposure to the problem food.

Table 1

Common food allergens

IgE-mediated	Non IgE-mediated
Cow's milk	Cow's milk
Egg	Egg
Peanut	Soya
Tree nuts	Wheat
Sesame	
Fish	
Shellfish	
Wheat	
Soya	
Kiwi	

The second type of allergic reaction to food is a non IgE-mediated (delayed type) response. This tends to start two to six hours, occasionally longer, after exposure and cause less specific signs/symptoms which are less obviously allergic in origin. These include eczema or gastrointestinal symptoms such as gastro-oesophageal reflux, diarrhoea or persistent crying.

Both these types of reaction are explored in the following two cases. »

Table 2

Clinical signs of food allergy

System	IgE-mediated	Non IgE-mediated
Skin	Pruritus Erythema Acute urticaria Acute angioedema	Pruritus Erythema Atopic eczema
Gastrointestinal	Oral pruritus/swelling Nausea/vomiting Colicky abdominal pain	Gastro-oesophageal reflux Diarrhoea/loose stools Blood +/- mucus in stools
Respiratory	Sneezing Itchy nose Rhinorrhoea Wheeze Cough	Abdominal pain Infantile colic Constipation Perianal erythema Faltering growth Food aversion/refusal

Adapted from NICE CG116: Food allergy in children and young people

CASE 1

An eight-month-old girl is brought to the surgery with a history of an acute reaction after having a mouthful of scrambled egg. She had previously tolerated cake made with eggs.

Within a few minutes of eating the egg she developed swollen lips and had hives on her face and chest. She was taken by ambulance to hospital from where she was discharged after being given oral chlorphenamine.

She has had a background of eczema since four months of age.

Diagnosis

The NICE guideline on food allergy in children divides symptoms into IgE- and non IgE-mediated responses according to the system affected, see table 2, above.

With the presence of a clear history of urticaria and lip swelling, this is a typical history for an IgE-mediated allergic response, especially as it occurred immediately after exposure to a common food allergen which had not been tolerated in the plain form in the past. In the case of egg allergy, it is common for children to tolerate well cooked egg, as in this case, as the cooking process denatures the allergenic proteins.[4] These children can be advised to eat baked egg but avoid plain/uncooked forms.

The recent NICE guideline advises that where an immediate type allergic reaction is suspected on clinical history, allergy testing should be performed to confirm the diagnosis. This could involve either skin prick testing or specific IgE blood tests (previously known as RAST). Both tests can help confirm a food allergy.[3] However, the results must be interpreted in the context of the clinical history.

Although the size of the allergy test response indicates the probability of allergy being present, it does not relate to the severity of reactions that may occur.

It may also be important to test for other foods that may be a problem so, for example, in this case, testing for allergy to peanut would be advisable as 20-30% of children who are allergic to egg also have peanut allergy.[5]

In this case, the skin test response to egg was 4 mm. In the context of the history of clinical reactivity, this confirms egg allergy. The peanut skin prick test was 8 mm – large enough to suggest strongly (>95% positive predictive value[3]) allergy to peanut so a presumptive diagnosis could be made without any clear history of previous exposure. This child should therefore also be told to avoid peanut indefinitely unless future skin prick tests are negative and the child is shown to have outgrown the allergy.

Alternative methods currently marketed commercially for use in the diagnosis of allergy have no scientific validity. These include IgG testing, Vega testing and kinesiology. The NICE guideline is quite explicit that these have no place in allergy diagnosis.

Management

The mainstay of management is allergen avoidance, which requires education and advice from a registered dietician. The child and carers also need to know how to recognise and treat any future allergic reactions. This child is at risk of having further reactions, the severity of which cannot be accurately predicted and thus there should be a written emergency plan in place. The plan should include advice to take a fast-acting antihistamine,[6] e.g. chlorphenamine if any accidental exposure and reactions occur.

IgE-mediated reactions are unpredictable but some children seem to be at particular risk of having severe reactions. Where there is a history of anaphylactic reaction or ongoing asthma, adrenaline auto-injectors should be prescribed as these are the major risk factors for future severe reactions.

‘Where there is a history of anaphylactic reaction or ongoing asthma, adrenaline auto-injectors should be prescribed’

Nut allergy, which is known to cause the majority of anaphylactic reactions, living far away from medical help and high parental anxiety are all relative indications for adrenaline auto-injector prescription, see table 3, below. When prescribed, it is advisable that children have two devices to hand at all times[6]

Table 3

Indications for prescribing adrenaline auto-injectors[6]

Absolute indications	Relative indications
● Previous anaphylactic reaction ● History of asthma	● Nut allergy ● Living far away from a medical centre ● Allergic reactions to very small quantities/airborne foods ● Adolescent patients ● Parental anxiety

i.e. two at school and two at home. It is essential that training on how and when to use the adrenaline auto-injectors is given as well as a written emergency plan.

In this particular case it is worth bearing in mind that 80% of children who have both egg allergy and eczema will develop respiratory allergy such as asthma later in childhood[7] so she may also need prescriptions for adrenaline auto-injectors in the future, if not now.

It is essential to keep a close eye on the control of asthma in children with food allergy as they are more likely to have severe asthma attacks and undertreated asthma can predispose to more severe allergic reactions, if they occur.

It should also be noted that egg allergy is not a contraindication to MMR vaccination and no special precautions are required. The MMR vaccine is grown on chick fibroblasts so the hen's egg protein content in the vaccine is negligible and the MMR vaccine has now been deemed safe for administration in primary care to children who are allergic to egg.[8]

Referral

NICE advises that referral to secondary care should be considered in the following cases of suspected IgE-mediated food allergy:

- confirmed IgE-mediated food allergy and concurrent asthma
- allergic reaction involving systemic response
- more than one food allergen involved
- confusion over diagnosis

Prognosis

Egg allergy is outgrown in 68% of children by their 16th birthday.[9] Most improvement is seen in the first few years so regular or intermittent repeat allergy testing can be useful to help identify those children who are outgrowing their allergy. Tolerance can be confirmed with a careful exposure to the food under medical supervision in a hospital setting. Peanut allergy is only outgrown in 20% of patients.

CASE 2

A mother brings her breast-fed five-month-old child to her local surgery for follow-up. He has previously been diagnosed with troublesome gastro-oesophageal reflux disease (GORD) and mild eczema.

His mother noticed a deterioration when she started to introduce additional formula feeds from three months. He is described as 'a miserable baby' who has a very poor sleep pattern and 'lots of colic'. He has never had any symptoms of urticaria/lip swelling/breathing difficulties.

His mother asks for referral to 'a specialist' for allergy tests as she suspects the formula milk is a problem.

Discussion points

GORD and eczema are common diseases of infancy which may be related to allergy. An allergy-focussed clinical history is required to obtain the information that may point to food allergy as the underlying cause.

'If a careful history raises the suspicion of non IgE-mediated allergy then there is no value in IgE allergy tests'

Non IgE-mediated food allergy is most common in early infancy although it often goes undiagnosed for an extended period. The most common causes are milk and soya, and less often egg and wheat.

A past medical or family history of atopy increases the likelihood that chronic symptoms such as reflux may be related to food allergy. The association between increased exposure and worsening symptoms is also important. The presence of clusters of symptoms in different systems e.g. eczema and reflux, also increase the likelihood of underlying food allergy.

If a careful history raises the suspicion of non IgE-mediated allergy then there is no value in IgE allergy tests. The diagnosis of non IgE-mediated food allergy relies on a two-stage process:

1 Strict exclusion of suspected allergen(s) - only one at a time

2 Re-challenge with suspected allergen(s), one at a time, to see if symptoms recur

In the above case, a period of safe exclusion of cow's milk protein (CMP) to see if there is improvement of symptoms is required in the first place. In the case of CMP allergy the infant should have a trial of four to six weeks on a CMP-free diet with extensively hydrolysed formula or amino acid formula.

In the case of a breast-fed infant, his mother should exclude all dairy products from her diet for the same period. This requires the guidance of an experienced dietician.

The second stage of re-challenging with CMP, often resisted by parents, to demonstrate a recurrence of symptoms is important for this child as non-specific symptoms such as colic, eczema etc may simply have resolved with time.

Given that CMP allergy affects infants at a crucial stage in development, prompt diagnosis and exclusion of CMP has an important role in helping these infants to thrive and bond effectively. In some cases of suspected or proven non IgE-mediated food allergy referral to a secondary care setting should be considered. These include:

- faltering growth
- more than one allergen involved
- atopic eczema resistant to routine treatment
- cases of allergic enterocolitis
- confusion over diagnosis

Prognosis

In non IgE-mediated allergy, the prognosis is good with the majority of infants outgrowing allergy to milk, wheat, soya or egg by school age. Given the lack of a diagnostic investigation, a reasonable approach to ongoing management is to advise parents to re-introduce the allergen to the child's diet every six months to see if tolerance has been achieved.

CONCLUSION

These cases illustrate common presentations of childhood food allergy. Careful documentation using a targeted and thorough history usually makes it possible to distinguish suspected IgE-mediated allergy from non IgE-mediated.

Investigations should be tailored to the suspected mechanism of allergy i.e. allergy tests for suspected IgE-mediated allergy and exclusion/re-introduction diets for non IgE-mediated allergy.

Once diagnosed, management requires allergen avoidance guided by a dietician together with education in recognising and treating reactions appropriate to the underlying mechanism.

Food allergy is commonly outgrown so regular reassessment is essential »

key points

SELECTED BY
Dr Peter Saul
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The prevalence of food allergy in children in the UK is now around 5% and the number of children put on restricted diets by their parents because of presumed allergy is likely to be much higher. Accurate diagnosis of food allergy is essential in order to ensure that the correct foods are carefully avoided while safe foods are not excluded unnecessarily.

IgE-mediated (immediate type) reactions are the result of mast cell degranulation leading to histamine release. The typical signs of lip swelling, urticaria and possible progression to respiratory compromise (anaphylaxis) are usually clearly described, occurring within minutes of exposure to the problem food. Non IgE-mediated (delayed type) responses tend to start two to six hours, occasionally longer, after exposure and cause less specific signs/symptoms which are less obviously allergic in origin.

The recent NICE guideline on food allergy in children advises that where an immediate type allergic reaction is suspected on clinical history, allergy testing should be performed to confirm the diagnosis. This could involve either skin prick testing or specific IgE blood tests. Results must be interpreted in the context of the clinical history. Alternative methods currently marketed commercially for use in the diagnosis of allergy such as IgG testing, Vega testing and kinesiology have no scientific validity. The NICE guideline is quite explicit that these have no place in allergy diagnosis.

The mainstay of management is allergen avoidance. The child and carers also need to know how to recognise and treat any future allergic reactions. There should be a written emergency plan in place. The plan should include advice to take a fast-acting antihistamine if any accidental exposure and reactions occur. Where there is a history of anaphylactic reaction or ongoing asthma, adrenaline auto-injectors should be prescribed as these are the major risk factors for future severe reactions. Nut allergy, living far away from medical help and high parental anxiety are all relative indications for adrenaline auto-injector prescription. It is essential that training on how and when to use the auto-injectors is given as well as a written emergency plan. Egg allergy is outgrown in 68% of children by their 16th birthday but peanut allergy is only outgrown in 20% of patients.

GORD and eczema are common diseases of infancy which may be related to allergy. Non IgE-mediated food allergy is most common in early infancy, although it often goes undiagnosed for an extended period. The most common causes are milk and soya, and less often egg and wheat. The diagnosis of non IgE-mediated food allergy relies on a two-stage process: Strict exclusion of suspected allergen(s), only one at a time; re-challenge with suspected allergen(s), one at a time, to see if symptoms recur. The prognosis is good with the majority of infants outgrowing non IgE-mediated allergy by school age.

both to monitor for tolerance and also to look for development of allergic comorbidities.

Further reading

National Institute for Health and Clinical Excellence. CG116: Food allergy in children and young people. NICE. London. 2011
British Society for Allergy and Clinical Immunology (BSACI) guidelines: www.bsaci.org
European Academy of Allergy & Clinical Immunology (EAACI) position papers: www.eaaci.net
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Useful information

British Society for Allergy and Clinical Immunology
www.bsaci.org

The Anaphylaxis Campaign
www.anaphylaxis.org.uk

Allergy UK
www.allergyuk.org

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