

Fifteen-minute consultation: The EATERS method for the diagnosis of food allergies

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ABSTRACT

The EATERS mnemonic is a novel method for taking an allergy focused clinical history. It provides a degree of certainty for diagnosing food allergy and can be used in both IgE and non IgE mediated reactions. EATERS will allow health care professionals to use their existing clinical skills to interpret the history of an allergic reaction, and by doing so will help to make sense of allergy test results.

INTRODUCTION

Food allergy is common, affecting up to 5% of infants in the UK.¹ Many of the symptoms are non-specific leading to the diagnosis being overlooked or dismissed. In 2003, the Royal College of Physicians saw the 'unmet need' of the burden of atopic diseases in the UK. A generation later, despite the best efforts of specialists and patient support groups, we are still no closer to providing the care that our patients require. 'Patients need accurate diagnosis, state of the art management and expert clinicians who can distinguish what is and what is not allergy.'²

Allergy tests are notoriously difficult to interpret. The accurate diagnosis of food allergy is beyond the scope of most clinicians without training. Several methods have been proposed to make interpretation easier for the non-specialist, including the use of predictive algorithms.³ In clinical practice, most specialists interpret allergy test results in the light of an allergy-focused clinical history (AFCH)⁴; they then use their clinical experience to formulate a pretest probability to interpret allergy test results.^{5,6} This is only possible because the clinician is able to apply their prior experience to the case. However, without prior experience and training it is impossible to gain the clinical acumen to make an accurate assessment from an

AFCH. How can we expect untrained clinicians to manage when faced with an epidemic of allergic disease? One answer is to resource front-line staff with clinical tools that enable diagnosis and treatment at point of care.

The EATERS history is a novel method for taking an AFCH that allows interpretation of the case and provides a degree of diagnostic certainty. It allows clinicians to use their existing clinical skills to interpret the clinical history, and will help to make sense of allergy test results. No prior training or experience is required.

THE EATERS HISTORY

All allergic reactions have these key elements in their history:

- *Exposure* by consumption of a food allergen.
- *Allergen*, a common known food allergen.
- *Timing* between exposure and onset of symptoms.
- *Environment* where food allergic reactions are more common.
- *Reproducible* symptoms' previous and future exposures to the same allergen.
- *Symptoms* typical for an allergic reaction involving multiple organ systems.

In addition, an AFCH also has⁴:

- Information about the medical history of the child, in particular the presence of other allergic comorbidities such as eczema, asthma, food allergy and allergic rhinitis.
- An immediate family history for atopic disease.

Most children with food allergy will have a clear history that involves these six elements. The carer should be asked to describe each suspected food reaction and the EATERS mnemonic completed for every reaction. Supplementary questions are needed to fill in the gaps left in the history from the presenting description. These questions are important as they will reveal other parts of the history that will



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either support or refute a food allergic reaction. Due to the nature of allergen recognition and the inflammatory hypersensitive response, there are some differences in the history between IgE and non-IgE-mediated allergic reactions, but the same elements of allergic reaction apply. We will first look at IgE-mediated food allergies before considering non-IgE reactions.

The EATERS history in IgE-mediated food allergy

Although the first part of the mnemonic is Exposure, we will discuss Symptoms first as these are normally the presenting complaint of a food allergic reaction. Parents will focus on those symptoms which they consider to be most severe and may ignore other possibilities until their concerns surrounding these symptoms have been directly addressed.

Symptoms

IgE-mediated symptoms involve multiple organ systems that include:

- ▶ Skin: hives, swelling, redness, itch.
- ▶ Gut: vomiting, abdominal pain, diarrhoea.
- ▶ Respiratory tract: rhinorrhoea, cough, wheeze, hoarseness, stridor.
- ▶ Neurological: change in behaviour, sleepiness, feeling of doom.
- ▶ Cardiovascular: shock and collapse.

There are some important features of food allergic symptoms that distinguish them from acute urticaria. First, symptoms tend to rapidly progress and then fade over several hours. Unlike an acute urticaria, they do not wax and wane for days. Second, symptoms tend to start where there has been direct contact with the allergen and spread out or generalise from there. With food allergy hives start around the mouth and on hands if it has been handled, rather than on the trunk or lower limbs, which is more of a feature of acute urticaria. Similarly, with airborne allergies the eyes and nose are often first affected before exposed skin and then other covered parts of the body.

Exposure

Food allergies occur when the food has been eaten. That may sound obvious but many parents believe that other contacts with food, such as being in the same room, can cause an allergic reaction. Misinterpretation of symptoms is one of the reasons why there is concern about suspected food allergies in a quarter of infants, compared with a diagnostic rate of 5%.¹ Other exposures that occasionally will trigger a food allergy include handling raw food, being kissed by a parent who has just eaten, or when in proximity to frying food where aerosolised food allergen may be formed.⁷

Allergens

Common food allergens include milk, egg and nuts (table 1); in adults and older children, shellfish (prawns, and so on) is also common.⁸ Common food allergens are covered by food labelling laws in the UK.

Table 1 Common food allergens in the UK

Common food allergens covered by UK labelling law	Rare food allergens covered by UK labelling law	Common food allergens not covered by UK labelling law
Milk	Soya	Lentil
Eggs	Lupin	Chickpea
Peanut	Mustard	Kiwi
Tree nuts	Celery	
Wheat (gluten)	(Sulfites)*	
Sesame		
Fish		
Shellfish and molluscs		

*Not a food allergy but covered by same labelling laws.

Other common food allergens not covered by these laws are kiwi fruit, lentil and chickpea. Children with unusual food allergens often have multiple food allergies which include the common foods as well. It is rare to have an isolated unusual food allergy. For instance, rare lupin allergy is normally seen associated with common peanut allergy in the UK.⁹

Symptoms associated with raw fruits are normally due to pollen food syndrome. This is caused by cross-reactivity to birch pollen (in the UK and Northern Europe). There are three elements needed to make a diagnosis: symptoms with raw fruit, tolerance to cooked fruit and signs of birch pollen allergy.

Timing

Most *IgE-mediated* food allergies occur immediately on exposure to the allergen. This is because contact with the allergen causes immediate degranulation of mast cells leading to the release of histamine into the skin and tissues. Occasionally, the reaction may be delayed for up to an hour but this is an exception, and tends to occur only when the allergen has been consumed in a fatty food, which may slow its release.¹⁰

Environment

The environment where the reaction took place is also important as there are some typical scenarios related to food allergy. The introduction of solid foods in infancy (also known as weaning) is by far the most common scenario for food allergic reactions, as many new foods are introduced to the infant. Most infants react at the first serving of a new food; this is because a child has been sensitised by a non-oral route (skin most likely), leading to a reaction at the first serving.¹¹ Outside of weaning, food allergies tend to happen when eating away from home in restaurants, in child care or nursery, on holiday, or at parties, where new foods may be tried and there is less parental control over what foods are eaten.

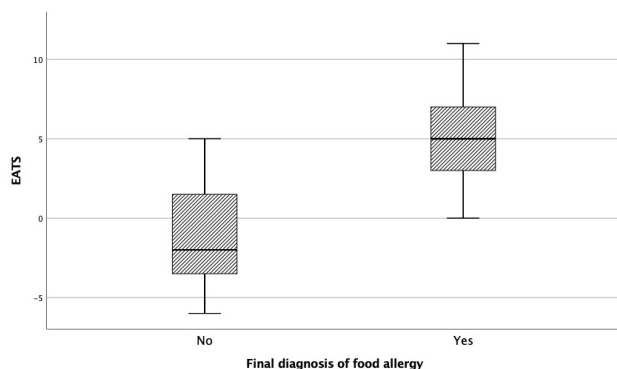


Figure 1 Prediction of food allergy in clinical practice. Box and whisker plot showing the performance of the EATS score in clinic practice. Boxes show median and IQR, ranges whiskers.

Reproducibility

Food allergies are strictly reproducible and will occur at all exposures to the food. Most food allergic reactions occur in infancy on the first introduction of the food. For many, this first reaction is clear and so the child is not offered the food again. It is not appropriate to suggest a repeat exposure to make a diagnosis of IgE-mediated allergy, outside of a formal diagnostic food challenge in hospital, as repeat exposure may lead to a severe or generalised allergic reaction. In practice, diagnostic food challenges are rarely required. If there has been more than one serving the child will react at each and subsequent exposure.

Occasionally, a child will have tolerated the food before *but not since* the index reaction. Normally this occurs only in infancy. The infant will have moderate to

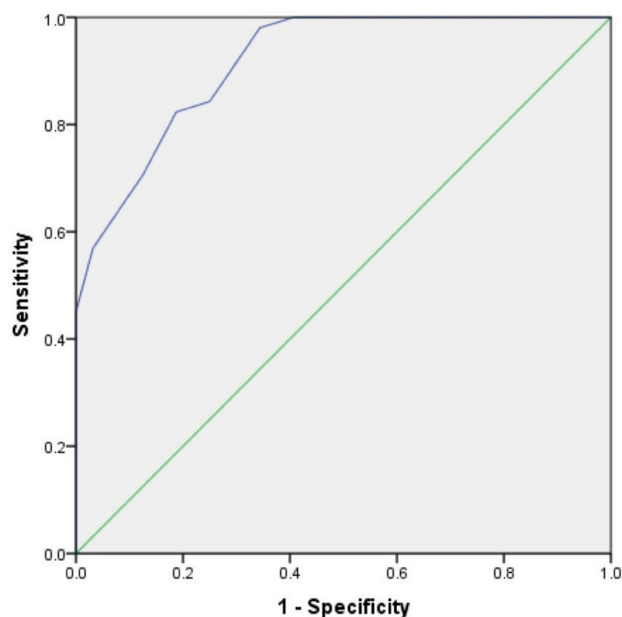


Figure 2 Diagnostic performance in clinical practice. A receiver operator curve showing the performance of the EATS questionnaire with a cut-off value of +2. This value approximated to the highest value of Youden's index (J). The area under the curve (AUC) was 0.917 (95% CI 0.859 to 0.975).

severe eczema and will have become sensitised during a gap in regular consumption. This is most commonly seen in egg allergy in infancy but also occurs with peanut in children with severe eczema in infancy.¹²

The EATERS history in non-IgE-mediated food allergies

Symptoms of non-IgE-mediated food allergy still follow an EATERS pattern. Non-IgE-mediated food allergies require a slightly different approach; whereas in IgE-mediated food allergy the carer will present with concerns about an allergic reaction, with non-IgE this is normally not the case. This presenting complaint tends to be related to symptoms and unlike IgE-mediated symptoms, a connection with food may not have been considered. The practitioner should be alert to the diagnoses in infants who present with a range of the common non-specific symptoms that can occur in cow's milk allergy (CMA).¹³ Once again, the presence of symptoms across multiple organ systems should raise the possibility of food allergy.

Exposure

Unlike IgE-mediated allergy where the culprit is often a new food, in non-IgE-mediated disease the food will be a regular part of the child's diet (or mother's diet if breast fed). Food allergens are passed relatively intact from the maternal gut to human milk.^{14 15} However, it may also lead to symptoms of non-IgE-mediated CMA in breastfed infants.¹³

Allergens

Cow's milk is by far the most common non-IgE-mediated allergen either present in cow's milk infant formula or through maternal breast milk. Soya is also a common allergen but tends to occur in children with pre-existing CMA due to cross-reactivity.¹⁶ Other allergens are rare in isolation but may occur as part of a mixed picture where both IgE and non-IgE recognition occurs to the same allergen.¹ In practice, this mixed picture is more often seen in infants with severe eczema.

Timing

Due to the nature of the hypersensitivity response, symptoms do not occur immediately on exposure. Because of this, the connection between allergen and symptoms is more difficult to establish. There may be hours or days before the onset of symptoms which may also take time to clear on removal of allergen during an elimination diet.^{4 13}

Reproducibility

Like IgE-mediated allergy, non-IgE-mediated symptoms are also strictly reproducible. Symptoms should abate during a period of dietary elimination. However, in order to establish the diagnosis once symptoms have resolved on an elimination diet the infant should be re-exposed.¹³ This may not be popular with parents

Table 2 Summary of symptoms of food allergic reactions using the EATERS history

Non-IgE mediated	Eaters	IgE mediated
Cow's milk formula fed, or Breast fed with dairy exposure through mother's diet	Exposure	Eating, or Occasionally by skin contact, or Rarely as an inhaled food aerosol
Milk and soya are most common.	Allergen	Milk, egg, peanut and tree nuts are most common.
Symptoms occur 1–24 hours after ingestion. Reaction occurs in the first year of life. Onset can be insidious.	Timing	Symptoms occur within an hour of ingestion. Reaction occurs during weaning, or At first known exposure
The allergen is a regular part of the diet or of mother's diet if breast fed.	Environment	The allergen is a new part of the diet.
Symptoms may take time to settle on an exclusion diet. Normally take 2–14 days to improve. Symptoms return on reintroduction of allergen to diet within 6 weeks of exclusion.	Reproducibility	Always has symptoms with exposure In infancy, it may have been tolerated before but there may be a 'gap' in regular consumption leading to allergy.
Skin—eczema Foregut—vomiting, reflux, dysphagia, food bolus impaction Mid-gut—colic, abdominal pain behaviour Hindgut—diarrhoea or constipation, mucous and/or bloody stools, erythema around anus Respiratory—chronic catarrh, cough, or persistent clear rhinorrhoea	Symptoms (Multisystem)	Skin—urticaria and angioedema Gut—vomiting and abdominal pain, diarrhoea Respiratory—acute onset of cough, wheeze, stridor, acute clear rhinorrhoea Neurological—sleepiness, impending doom, anxiety Cardiovascular—shock and collapse
Cardiovascular—vomiting and diarrhoea leading to shock and collapse Skin—pitting oedema Poor growth	(Red flags)	Anaphylaxis—multisystem ABC symptoms

when a return of symptoms may lead to days of unsettled sleep patterns and flare of chronic symptoms. However, there are no other tests available. A child with red flag non-IgE symptoms should not undergo rechallenge except under specialist care.¹³

Symptoms

Non-IgE-mediated food allergies have multisystem symptoms. Many symptoms are non-specific such as vomiting, colic and gastro-oesophageal reflux. The presence of symptoms in other organ systems makes the diagnosis of food allergy more likely.¹⁷ With this in mind, one should consider the gut as a separate system matching their embryological development to the foregut, mid-gut and hindgut. Colic and gastro-oesophageal reflux do not affect the lower gut, similarly constipation is not an upper gut problem unless severe. For example, the presence of colic with loose mucous stool in a formula-fed infant is a typical presentation for non-IgE-mediated CMA, and involves both mid-gut and lower gut. By considering the gut as a separate organ system the need for a trial elimination diet can be readily identified by the history.

EVIDENCE SUPPORTING THE EATERS METHOD

We have used an earlier version of the EATERS method as a diagnostic questionnaire in clinical practice. We sought to assess the diagnostic accuracy of this questionnaire in both a primary and secondary care paediatric allergy clinic. The Exposure Allergen

Timing Symptoms (EATS) questionnaire consisted of 13 questions with answers that favoured either food allergy or spontaneous urticaria (online supplementary table). Answers favouring food allergy were scored as +1 and urticaria favouring answers as −1, so that the total EATS score ranged from +13 to −13. The EATS score was compared with the clinical diagnosis of IgE-mediated food allergy based on a clinical history and positive skin prick tests or specific IgE (sIgE) blood tests to the suspected food allergen as a gold standard. EATS was used prospectively in clinic by primary and secondary care physicians and allied healthcare professionals, and a sample of retrospective cases presenting to allergy clinic with food allergy or urticaria was also scored based on reported history in the clinical notes.

We reviewed 51 cases where food allergy was the clinical diagnosis and 32 cases where it was not. The median EATS score was higher in food allergy (5.0 (IQR 4)) compared with non-food allergic cases (−2.0 (IQR 6); (Mann-Whitney U test, $p < 0.001$)) (figure 1). We estimated the optimal cut-off threshold as +2 giving an area under the curve as 0.917 (figure 2). Using this cut-off gave the questionnaire a sensitivity of 82.4% and a specificity of 81.3%.

The EATS questionnaire compared favourably with other methods of diagnosis and appears to be successful at identifying cases of IgE-mediated food allergy with high sensitivity and specificity.³ It is yet to be validated in non-IgE food allergy but multisystem disease and reproducible symptoms on

reintroduction are stringent requirements for diagnosis. In one study of non-IgE CMA 6/27 infants (22%) presented with isolated colic and would not meet EATERS requirements for multisystem disease.¹⁸ However, demonstrating reproducible symptoms with reintroduction of dairy once symptoms have abated is in line with best practice and would confirm the diagnosis in those with isolated symptoms.¹³

INTERPRETATION OF THE EATERS HISTORY

The presence of several elements of an EATERS history should alert the clinician to the possibility of food allergy in the differential diagnosis (table 2). IgE-mediated food allergy should be confirmed by skin prick or sIgE testing. It will allow sensitivity to be monitored over time, as some food allergies are outgrown. There is no diagnostic test for non-IgE-mediated food allergy other than the removal of the allergen (normally) cow's milk from the infant diet (and maternal diet if breast fed) for 2–6 weeks with review for resolution of symptoms.

While taking an EATERS history alternative diagnoses often become apparent. It also becomes clear to the family that there are many aspects missing from a typical food allergy history and the detail of the process will often provide alternative explanations for the symptoms.

EXAMPLE CASE

A 4-year-old girl developed hives over her face a trunk while at a family party. The family were concerned that she may have a peanut allergy:

- ▶ Environment: Buffet food was being served including peanuts—higher risk away from home.
- ▶ Allergen: Peanut—a common food allergen.
- ▶ Symptoms: Skin symptoms—one system only, but occurred over face where allergen contact may have occurred.

This by itself is not sufficient to make a diagnosis. Further questions are required:

- ▶ Timing: Symptoms first noticed several hours later once the family had returned home.
- ▶ Exposure: She had eaten some buffet food, peanuts were being served but she did not have any of them—however, she may have still encountered peanut allergen due to cross-contamination.
- ▶ Reproducibility: She had never eaten peanuts before, the family had actively avoided nuts due to concerns about allergy.
- ▶ Symptoms: She woke the next day with a return of generalised hives and facial swelling, it took 5 days to settle. There were no other organ system symptoms.
- ▶ Past medical history: She is otherwise well, no other atopic diseases.
- ▶ Family History: Mum has hay fever and asthma and is allergic to cats.

This case illustrates the nuance of an AFCH: The lack of clear timing, uncertain exposure (although

to a known common food allergen) and prolonged single organ system symptoms go against a diagnosis of peanut allergy and point to an acute urticaria as the more likely diagnosis.

It would be reasonable to check sIgE to peanut (or skin prick test if available to the clinician) although some may feel that there is enough non-supporting information to proceed making a diagnosis of acute urticaria without testing. In this example, these tests are negative and the diagnosis of acute urticaria is most likely. There were no red flag symptoms and she does not have asthma so reintroduction of peanut should be considered assuming that the family accept the diagnosis of acute urticaria.

CONCLUSIONS

The EATERS history is a novel method for taking an AFCH. It requires no additional training or prior experience to interpret the results. As such it can be used by a range of healthcare professionals for making a diagnosis of food allergy and permits an interpretation of allergy test results. The EATERS method allows the prospect of a diagnosis of food allergy without specialist intervention. Combined with an assessment of future risk of severe allergic reaction, and information, advice and support for the family, the EATERS history offers diagnosis and treatment for the child with food allergy.⁴

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Contributors MEL wrote the article. TW conducted the service evaluation as a medical student project with supervision from LB, HH, JR, EGA and CP who were involved in all phases of the project, design recruitment and interpretation of results. All authors have read and commented on the final manuscript.

Competing interests MEL is a member of the Milk Allergy in Primary Care (MAP guidelines) group. He has received speaker fees from Danone Nutricia, Mead Johnson, Nestle and Novartis, has undertaken commercial research with Danone Nutricia, Nestle and Almmune and is a scientific advisor for DBV Technologies. HH has received speaker fees from Danone Nutricia, Mead Johnson, Nestle and Thermo Fisher. CP has received speaker fees from Danone Nutricia and has undertaken commercial research with Nestle. TW, LB, EGA and JR have nothing to disclose.

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