

IgE-mediated food allergy—diagnosis and management in New Zealand children

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Abstract

Aim To summarise the diagnosis and management of IgE-mediated food allergy (FA) in New Zealand children.

Method A review of the scientific literature and subsequent consensus development.

Results FA is a common problem in New Zealand children with management necessitating accurate diagnosis, appropriate risk management, and reassessment over time.

Conclusion This paper highlights the importance of a structured approach to diagnosis and management of FA in New Zealand children, guided by appropriately skilled health professionals.

Key points

- Food allergy is a common paediatric condition.
- The history of an immediate allergic reaction is critical in interpretation of skin-prick test (SPT) or serum specific IgE (ssIgE, also referred to as RAST or EAST).
- Specialist paediatric referral should occur in any child with anaphylaxis, allergy to more than one food allergen, or where the primary care practitioner is not confident about diagnosis, test interpretation, or management.
- Children and young people with food allergy should have advice about allergen avoidance and a written management plan detailing the signs, symptoms and management of allergic reactions.
- Children with IgE-mediated food allergy require regular follow-up. Many food allergies are not persistent and need reassessment over time.

Introduction

IgE-mediated food allergy (FA) is common, affecting up to 10% of children under the age of 5 years.¹ Parental perception is that up to 30% of pre-schoolers may be affected.² Management of FA involves accurate diagnosis of the specific allergen(s), advice on allergen avoidance, risk assessment with provision of an appropriate action plan, and follow-up.

Many children grow out of FA. Reassessment, often including cautious reintroduction of the offending allergen, is an important part of ongoing management.

Recent evidence based reviews^{3,4} have reinforced the paucity of quality evidence on which to base decisions about diagnosis and management of FA. However FA is a common paediatric condition and regardless of poor evidence clinical care needs to be offered to these patients.

This consensus document has been developed by the Allergy Special Interest Group of the Paediatric Society of New Zealand, providing a current guide to managing children with IgE-mediated FA in New Zealand (NZ).

Definitions

FA is defined as an adverse immunologic reaction to a food protein.³ Many FA are IgE-mediated immediate hypersensitivity reactions, while immunological mechanisms other than IgE also occur. Food intolerance does not have an immunological mechanism. Some food intolerance is clearly defined (e.g. lactose intolerance) but much is not; non IgE-mediated food allergy and food intolerance will not be considered further in this document.

Sensitisation is defined as the presence of specific IgE detected on SPT or ssIgE.

Epidemiology

There are no data on rates of FA in NZ children. In Australia up to 10% of 1 year olds have proven food allergy.⁵ Milk, egg and peanut allergy account for about 75% of early food allergies.⁶ Other common allergens include fish, shellfish, tree nuts, kiwifruit, sesame, and also wheat and soy.

Atopy is a risk factor for FA, with most children with FA having eczema. There is often a family history of atopy and sometimes of FA. While atopy is inherited, allergy to a specific allergen is not and importantly IgE sensitisation to specific allergens does not necessarily imply causation of eczema.

Prevention

It is poorly understood why some children develop FA while most develop tolerance. Maternal allergen avoidance during pregnancy or breast feeding does not prevent FA in the infant.³ Later introduction of peanut, egg, and cow's milk to the infant's diet is associated with an increased rate of allergy to that food.^{1,7,8}

Prospective studies are currently evaluating early introduction of common food proteins as a strategy to prevent FA. While general infant feeding guidelines often suggest introduction of solids at about 6 months of age, allergy prevention advice is that solids can be introduced to the infant's diet from 4 months onwards, with no role for avoidance of commonly allergenic foods.^{9,10}

Diagnosis

Clinical Features of IgE-mediated allergy—The history of an allergic reaction is important in assessing possible FA.¹¹ Factors to consider include:

- Signs and symptoms of IgE-mediated allergic reactions are varied with no single feature always present (Table 1).

- Onset of symptoms in IgE-mediated FA is often within minutes of exposure to an allergen. Delay of symptom onset more than two hours after ingestion is uncommon.¹²
- Most allergic reactions occur after ingestion of an allergen, with patients having different thresholds to trigger reaction. Skin contact with an allergen may result in local reactions but seldom causes severe reactions. Inhalation in the vicinity of peanut butter is unlikely to cause a reaction.¹³ Reactions following inhalation in other situations (e.g. cooking fish) can occur.
- Most IgE-mediated reactions resolve quickly. Anaphylaxis can be biphasic, with recurrence of symptoms after initial apparent resolution.¹⁴ Persistence of urticaria beyond 6-8 hours makes FA a less likely cause unless there is ongoing allergen exposure.
- Many reactions occur with the first known ingestion of an allergen. If a food allergen is regularly consumed and tolerated then development of allergy to that food is uncommon.

Table 1. Signs and symptoms of an IgE-mediated allergic reaction

Cutaneous	Urticaria Angioedema Flushing / erythema Itch
Respiratory	Watery rhinorrhoea Sneezing Tongue swelling * Hoarseness / laryngeal oedema * Cough * Wheeze * Stridor *
Gastrointestinal tract	Vomiting Abdominal pain Diarrhoea
Cardiovascular / general	Pallor * Dizziness * Collapse *

* Features of anaphylaxis, defined as a severe allergic reaction with involvement of cardiovascular and/or respiratory systems.

Anaphylaxis—Anaphylaxis is a severe, systemic allergic reaction with circulatory or respiratory compromise.¹⁵ Anaphylaxis due to food allergic reactions most often involves respiratory features rather than cardiovascular, and a history suggestive of respiratory involvement as part of a reaction should be sought.

Eczema—Most young children with FA have a history of eczema. Young infants with severe eczema have an increased likelihood of also having FA.¹⁶ In breast fed infants transfer of food allergens via breast milk may contribute to eczema.

Most children with eczema are atopic and thus often sensitised to multiple foods on testing, but in the absence of a suspicious history this may not translate into specific

foods being triggers for eczema flares. Screening with large panels of allergens is not recommended in eczema.^{3,17} There has been little benefit from food exclusions for treatment of eczema in trials.³

Table 2. Food allergy testing

Test	Pro	Con	Caveat
Skin prick test	Immediate result Inexpensive Can test using food in question if no commercial allergen test available Strongly positive results likely to indicate clinical allergy	Operator and reagent dependent Extremely rarely associated with severe allergic reaction Unreliable with concomitant antihistamine use or dermographism Weakly positive results may or may not indicate clinical allergy	For both SPT and food ssIgE it is possible to have weakly positive tests associated with clinical allergy and strongly positive tests to foods that are clinically tolerated. Neither SPT nor ssIgE predict the severity of allergic reaction
ssIgE	Change in level over time may predict development of tolerance Strongly positive results likely to indicate clinical allergy	Results not immediately available Relatively expensive Not available for all potential allergens Requires venipuncture Weakly positive results may or may not indicate clinical allergy	

In the absence of an immediate IgE-mediated reaction, the potential benefits of food exclusion for management of eczema should be weighed carefully against the potential risks (e.g. failure to thrive, cost). Any food exclusion for eczema should be considered a trial, with the intent being to reintroduce the food after a period of weeks.

Good skin care is the basis of eczema treatment, regardless of potential food triggers. Education needs to be provided including advice on avoidance of irritants, use of moisturisers, and use of topical steroids as appropriate.

Investigations—The first purpose of allergy testing is to confirm the cause of an allergic reaction. Even a convincing history suggesting IgE-mediated FA will not always be confirmed on investigation. Testing for specific IgE can help avoid unnecessary or prolonged periods of dietary restriction. Confirming IgE-mediated FA aids ongoing management and helps predict natural history.

In addition there may be a role for testing where there may be other potentially significant allergens, acknowledging that this may identify clinically unimportant sensitisation in some children. However children presenting after one food allergic reaction may have other food allergies; in one study 40% of infants presenting with cow's milk allergy had egg allergy.¹⁸

Screening for large groups of allergens is not recommended, but testing a small range of common allergens may be considered (e.g. testing peanut in a one year old

presenting with egg allergy who is already ingesting milk and wheat). Importantly foods that are already tolerated should not be tested.

Investigation will be either by SPT or ssIgE¹⁹ (Table 2). SPT are reported as millimetre of wheal, with 3mm taken to indicate presence of specific IgE. Historically ssIgE have been reported as a grade (e.g. 1+ to 6+), but more commonly now the result is reported as KIU(A)/L. As described below the interpretation of test results is highly dependent on the patient's history.

Other tests are not valid for investigation of IgE-mediated FA. Which test is used will depend on availability of the test and the food in question. Where one test is negative despite a suggestive history, undertaking the other test is appropriate. Routine testing with both SPT and ssIgE is not necessary.

For some foods predictive SPT and ssIgE results have been published; strongly positive results indicate a higher likelihood of allergic reaction on supervised food challenge (Table 3).¹¹

Table 3. Allergy tests and food challenge outcomes

ssIgE results predicting chance of reaction at challenge >95%^{29, 30}	
Egg	> 7kU/l
Egg in infants under 2 years	> 2kU/l
Milk	15kU/l
Peanut	14kU/l
Allergy skin prick test results predicting chance of reaction at challenge >95%³¹	
Egg	8mm
In infants under 2 years	6mm
Milk	7mm
In infants under 2 years	5mm
Peanut	8mm
In infants under 2 years	4mm

The key to interpretation of investigations is the patient's history. The pre-test probability influences interpretation of test results.²⁰ Where a child has had symptoms highly suggestive of an IgE-mediated reaction then any positive ssIgE/SPT test may be taken as confirmation of diagnosis. Where the history is less clear or where there is no history of exposure (i.e. a lower pre-test probability) then a more strongly positive test result will be needed to confirm a diagnosis, and may need to be combined with a supervised food challenge for confirmation. The threshold results in Table 3 apply to a selected population with high pre-test probability, and may not have the same applicability in a more general population.

Molecular allergy tests (Component Resolved Diagnostics, CRD) are becoming more readily available.²¹ For example in some populations ssIgE to Ara h 2 helps predict outcome of peanut challenge.²² The range of CRD will evolve with time, and their use in other situations (e.g. to determine tolerance of heat treated forms of cow's milk and egg) will also expand with further data.

Management

Referral guidelines—Specialist paediatric referral is recommended for children with FA with

- Definite or possible anaphylaxis.
- Allergy to cow's milk or multiple food allergies, where expert advice is needed.
- Where there is uncertainty about the diagnosis or interpretation of results.
- Food sensitisation on ssIgE / SPT, where supervised challenge may be necessary to clarify whether there is clinical allergy.
- Allergy to foods such as peanut and nut where the risk of severe allergic reactions is higher.
- Children with asthma and FA, with asthma a risk factor for severe food allergic reaction on accidental exposure.
- Children whose FA persists past 5 years of age.

Some children with FA may be looked after in primary care. Management needs to include advice on allergen avoidance, provision of an action plan and follow-up for possible resolution of FA. Eventual referral for specialist supervised food challenge may be necessary.

Allergen avoidance—Management of FA involves avoidance of known allergens to minimise reactions on accidental exposure. Commercially packaged food from NZ declares the presence of common allergens. Caution is needed with food packaged in other countries.

For some allergens (e.g. egg and milk) total avoidance is not always necessary. Up to 75% of egg or milk allergic children may tolerate these as an ingredient in well cooked foods (e.g. baked foods).^{23,24} This is sometimes apparent on the initial history (e.g. a child who reacted to scrambled egg but tolerates cake containing egg). At other times this tolerance may develop as the allergy is resolving. There are published guidelines for liberalising egg as an ingredient in baking at home in selected patients.²⁵

Many families and doctors are confused by labels that warn about potential traces of an allergen. While avoiding all of these products will be the least risky option, this is difficult to achieve. Risk management decisions about these products should be made by families in discussion with their doctor and dietitian. It is our experience that most children tolerate some products with “may contain traces” warnings without signs or symptoms of allergic reaction.

Risk management—Anaphylaxis may be the initial presentation of children with IgE-mediated FA. Children with less severe initial reaction can have anaphylaxis on further accidental allergen ingestion.¹⁷

Factors that increase the risk of severe allergic reaction include:

- Age, with life-threatening and fatal food allergic reactions more commonly reported in older children, adolescents and young adults.
- Asthma, as almost all patients who die of food allergy also have asthma.
- Peanut/Nut allergy as these are responsible for a significant proportion of fatal food allergic reactions. Cashew nut anaphylaxis is often severe.²⁶

Other factors to consider as part of risk management include:

- Access to emergency care.
- Ability to comply with allergen avoidance.
- Comorbidities and other medications.

Action plan—All children and young people with FA should have a written plan detailing the signs and symptoms of allergic reactions and what action should be taken. The plan needs to be available to all caregivers.

- A variety of plans are available for download on www.allergy.org.au (the website for ASCIA—Australasian Society of Clinical Immunology and Allergy). Use of standardised plans is recommended to minimise confusion amongst caregivers.
- The history and risk assessment will determine whether the plan includes an adrenaline autoinjector (EpiPen®, Anapen®). Guidelines on who should have an adrenaline autoinjector are available on www.allergy.org.au. Use of adrenaline ampoules with a needle and syringe is not a safe alternative.²⁷
- Antihistamines may be part of the plan, used for symptom relief. Antihistamine use does not prevent or treat anaphylaxis. Use of a non-sedating antihistamine is preferred.²⁸
- Referral for education of carers at schools and preschools should be made to local providers, often local Public Health Nurses.
- For children with asthma the action plan may include instructions on the use of bronchodilators, to be used after intramuscular adrenaline for any FA reaction with respiratory symptoms.
- MedicAlert should be considered particularly for older children and adolescents.

Dietetic support—Dietetic input is important for children with cow’s milk allergy, with multiple food allergies, or with allergy to foods that are hard to avoid such as wheat and soy. If maternal allergen avoidance is advised, maternal dietetic advice will be needed.

Cow’s milk alternatives in infancy—Infants with cow’s milk allergy need an alternative for weaning or for supplementation of breast feeding. Goat’s milk is not an option as there is extensive cross reactivity. Special authority funding is available for extensively hydrolysed formula (eHF) and amino acid formula (AAF) for infants meeting PHARMAC criteria, with requirements for regular re-evaluation, and a “step

down” from the more expensive AAF to alternatives as possible. Many infants with cow’s milk allergy can tolerate soy.⁸

Follow up—Children with IgE-mediated FA need follow up to determine whether the allergy is persistent, to consider retesting and food challenge if appropriate, and to ensure that action plans remain up to date, with review of adrenaline autoinjector use as needed.

The natural history of FA is often of resolution. Overall most milk (80% by age 5 years), egg (66% by age 7 years), wheat and soy allergies will resolve. For most children, peanut (80%), nut (90%) and fish allergy will be persistent.³ Follow-up testing frequency depends on the food in question and the interval history of reactions; intervals of less than 12 months are generally unnecessary.¹⁹

During follow-up there needs to be age-appropriate transition of responsibility for managing the FA. Some older children may develop troublesome food aversion and fear of trying new foods; anxiety about FA should be actively sought and managed.

Food challenge—Double-blind, placebo-controlled food challenge (DBPCFC) is the gold standard for diagnosis of FA in clinical studies, but it is rarely part of clinical practice. Supervised open food challenge may be used to clarify diagnosis, determine whether sensitisation is clinically relevant, or to determine resolution.

The decision to undertake a food challenge will depend on:

- Reactions – recent reactions indicate persistent allergy.
- Investigations—strongly positive SPT or ssIgE make tolerance unlikely.
- Family preference and chance of resolution – for some families a 50% chance that an allergy has resolved may mean they are keen to pursue challenge, while others may prefer to wait until the chances of resolution are higher.

Supervised food challenges should be carried out using established protocols with access to immediate medical back-up and resuscitation, in case a severe reaction occurs.

In NZ most food challenges will be done in hospital settings with paediatric specialist supervision. Food challenge does not necessarily inform as to on-going risk—a mild reaction at a small dose indicates persistent FA and a challenge is stopped, with the result not precluding a more severe reaction on subsequent exposure.

Resources

www.allergy.org.au (ASCIA website) with allergic reaction plans, adrenaline autoinjector guidelines, eczema management plans and patient information sheets. ASCIA provides open access online e learning courses for education on food allergy and anaphylaxis.

www.allergy.org.nz is an organisation providing support, information and advocacy, plus education kits for schools and preschools.

Conclusion

Food allergy is a common problem for NZ children. Management necessitates:

- Accurate diagnosis with appropriate investigation
- Education about allergen avoidance, with dietetic assistance as appropriate
- Risk assessment and provision of an appropriate allergic reaction action plan
- Supervised challenges where appropriate
- Follow up for possible resolution and ongoing risk assessment.

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