Hot topics in paediatric immunology: IgE-mediated food allergy and allergic rhinitis

Background
The epidemic of allergic disease is a major public health crisis. The greatest burden of allergies is in childhood, when rapidly rising rates of disease are also most evident. General practitioners (GP) have a key role in recognising and addressing allergy-related problems and identifying whether a child requires referral to a paediatric allergist.

Objective
This article focuses on IgE-mediated food allergies and allergic rhinitis, the most commonly seen conditions in paediatric immunology. We will discuss prevention, diagnosis, management and treatment strategies.

Discussion
Currently there is no cure for food allergy. Oral tolerance induction continues to be a significant focus of research. All children with a possible food allergy should be referred to an allergist for further testing and advice. Children who develop allergic rhinitis need a regular review by their GP. Immunotherapy should be discussed early in the disease process and needs to be commenced by an allergist.

How common is IgE-mediated food allergy and what are the potential risk factors?
There has been a marked increase in food allergies over the past two decades, particularly in westernised countries. Indeed, it has been shown that up to 10% of infants aged 1 year in Australia have a challenge-proven IgE-mediated food allergy.\(^1\) Prevalence rates of admissions for food-induced anaphylaxis in Australia increased by 350% between 1994 and 2005. In children, the most common reason for anaphylaxis is food allergy. The cause of this epidemic remains elusive.\(^2\)

A number of risk factors associated with a more westernised lifestyle have been linked to this dramatic change. Potentially rectifiable causes such as increased hygiene, an unhealthy fatty diet, obesity, vitamin D deficiency (less ultraviolet B exposure)\(^3\) and the timing of exposure to foods have been suggested.\(^4\)

How can food allergy be prevented?
Exclusive breastfeeding for the first 4–6 months is highly recommended because of its many beneficial aspects, including protection against early allergic disease; however, long-term benefits remain uncertain. There might be some advantage in using hydrolysed infant formulae instead of cow’s milk formula in at-risk infants (ie those whose parents or older siblings are diagnosed with allergies) who are not exclusively breastfed.\(^5\)–\(^7\)

Currently, there is no evidence to indicate that women should modify their diet or take any supplements such as prebiotics or probiotics during pregnancy or breastfeeding. Prebiotics or probiotics in infants have also not shown to prevent food allergy.\(^6\)–\(^7\) The infant feeding guidelines from the Australasian Society of Clinical Immunology recommend introducing solid foods at 4–6 month, including potentially allergenic foods, irrespective of whether the child is at risk or has co-existing eczema.\(^5\)
When should we suspect IgE-mediated food allergy?

At least 170 foods have been reported to cause IgE-mediated food allergies; however, more than 90% of allergic reactions in children are related to eight items: peanuts, tree nuts, eggs, milk, fish, crustacean shellfish, wheat and soy. Diagnosis of food allergy requires a detailed history regarding atopy and diet. The acute onset of symptoms is usually within 2 hours after ingestion of or exposure to the trigger.

Allergen-specific IgE can be detected by skin prick testing (SPT) or serum-specific IgE levels. Children can have allergic sensitisation (production of IgE) without having clinical symptoms. A diagnosis of an IgE-mediated food allergy requires both: the presence of sensitisation to and the development of specific signs and symptoms on exposure of that food5 (Table 1). Children should not eliminate any food in the absence of clinical symptoms based on sensitisation alone.

Very recent studies have addressed the utility of component testing for allergies to different allergens. The predictive value of component-resolved diagnostics is best characterised for peanuts.4 Any child with a suspected food allergy should be referred to an allergist for further testing, advice and management. An oral food challenge might be required to make the final diagnosis.

How can food allergy be treated?

Primary therapy for food allergy is strict avoidance of the causal food(s) (Table 2). Patients need to be educated on how to read ingredient labels and under which circumstances (eg eating away from home, risk of cross-contact) caution might need to be taken.

Histamine H1 receptor antagonists (antihistamines) may address symptoms of a mild-to-moderate allergic reaction, but do not alter the course of a potentially fatal anaphylaxis. Here adrenaline is urgently required (Table 1). All children weighing ≥10 kg who have a history of an anaphylaxis need an adrenaline autoinjector and education on how to use the device. It is important to review and reinforce annually the criteria that would prompt the need for administration of an adrenaline autoinjector.

Food allergies that start in childhood are often outgrown. Allergy to cow’s milk, egg, soy or wheat is more likely to be outgrown than allergy to peanuts, tree-nuts and shellfish.5

Currently, there is no cure for food allergies. Baked food is generally a less allergenic form of the food because the heating process alters the protein structure. There is some evidence that regular ingestion of baked products may accelerate the development of tolerance to the uncooked form of the protein. Oral immunotherapy (OIT) or sublingual immunotherapy continues to be a significant focus of food allergy research.8–10

When should allergic rhinitis be suspected?

Allergic rhinitis is defined as inflammation of the nasal mucosa and is characterised by nasal discharge, blockage, sneezing and itch, with two or more symptoms occurring for more than 1 hour on most days. The traditional differentiation between perennial and seasonal rhinitis has been replaced by a more useful classification, developed by Allergic Rhinitis and its Impact on Asthma (ARIA),11 which is based on symptoms: intermittent or persistent allergic rhinitis (Table 3).

Allergic rhinitis has early- and late-phase responses. The immediate allergic response to antigen is called the early-phase response. Symptoms such as watery rhinorrhea, sneezing and itching occur within 5–15 minutes of allergen exposure. This is followed 3–12 hours later by the late-phase response when congestion of the nose predominates.12

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**Table 1. Symptoms of IgE-mediated food allergy**

<table>
<thead>
<tr>
<th>Mild-to-moderate allergic reaction</th>
<th>Anaphylaxis</th>
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<tbody>
<tr>
<td>• Angioedema</td>
<td>• Shortness of breath</td>
</tr>
<tr>
<td>• Urticaria</td>
<td>• Swelling of the tongue</td>
</tr>
<tr>
<td>• Tingling in mouth or throat</td>
<td>• Swelling/tightness in throat</td>
</tr>
<tr>
<td>• Abdominal pain/vomiting</td>
<td>• Difficulty talking/hoarse voice</td>
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</tbody>
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Note: Patients do not always have cutaneous symptoms before developing anaphylaxis. One of the symptoms listed is sufficient to diagnose anaphylaxis in a patient

**Table 2. Food avoidance recommendations**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Recommendation</th>
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<tbody>
<tr>
<td>Infants with cow’s milk allergy, co-existing eczema or being an at-risk child</td>
<td>Regardless of milk allergy introduce solid foods at 4–6 month including potentially allergenic foods</td>
</tr>
<tr>
<td>Proven IgE mediated allergy to an identified food</td>
<td>Elimination of the identified food only (unless in peanut or tree nut allergy, see below). Avoid unnecessary elimination diets to potentially allergenic food</td>
</tr>
<tr>
<td>Proven IgE mediated allergy to peanuts or tree nuts</td>
<td>Avoid all peanuts and tree nuts (unless tolerated in the past or advised otherwise by Immunologist) due to a risk of contamination and a cross reactivity of at least 30%</td>
</tr>
<tr>
<td>Proven IgE mediated allergy to multiple foods</td>
<td>Consider referral to dietitian</td>
</tr>
</tbody>
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8–10
Diagnosis of allergic rhinitis requires a detailed history of other atopic disease in the patient or family members, as well as potential triggers. The allergic march refers to the development of different allergies at different ages: eczema and food allergy are dominant in early childhood, whereas asthma and allergic rhinitis are more common later. The sensitisation pattern changes from food allergy to environmental allergens.13

Allergic rhinitis is also associated with inflammatory disorders of upper and lower airways, including asthma, rhinosinusitis, conjunctivitis, nasal polypsis and other comorbidities such as sleep disturbances and otitis.12 The physical examination includes nose, throat, eyes, ears, chest and skin. Allergen testing for environmental allergens (house dust mite [HDM], grasses, pollen, animal dander, mould) should be initiated via SPT or serum-specific IgE.

**How do we manage allergic rhinitis?**

Allergic rhinitis is underdiagnosed and undertreated. Although often perceived as trivial, allergic rhinitis is a major chronic respiratory disease, which can have a significant impact on quality of life, productivity and sleep.14 Because of its burden on children’s lives and its impact on asthma,15 allergic rhinitis must be treated properly with effective and safe treatments. Currently, there are several novel treatments under evaluation.12 However, allergen avoidance, antihistamines and intranasal corticosteroids (INCS) are considered the cornerstone of first-line therapy, which should be initiated by a general practitioner (GP).

Allergen avoidance can be difficult. Some strategies are in place for HDM allergy which is the most common allergen source in humid towns. There is a dose-response relationship between HDM levels in the home and sensitisation to HDM.16 A combination of stringent environmental control measurements (Table 4) can markedly reduce HDM levels.17 Interventions that achieve substantial reductions in HDM load may offer some benefit in reducing allergic rhinitis symptoms.18

Second-generation antihistamines are useful where mild or intermittent symptoms are present, although they are not as effective in congestion. They can induce immediate relief of symptoms and, if required, they can be taken on a daily basis. First-generation antihistamines are still available but should be strictly avoided in children because of central nervous system effects.19

INCS reduce inflammation of the nasal obstruction. They are useful in children with moderate-to-severe or persistent symptoms and start to be effective after 1–2 weeks and need to be taken on a daily basis for at least 6 weeks. INCS are not suitable for acute symptom relief. Topical side effects are minimal with INCS.20 Concerns that INCS cause systemic side effects such as suppression of growth and bone metabolism have been allayed.21 However, there are major differences in formulations, volumes and vehicles. GPs need to be aware of these differences to try to match patients’ preferences in order to achieve better adherence and outcomes.20 In cases of severe nasal blockage, nasal decongestions can be used for 3 days, but overuse can result in severe rebound congestion.

Chromones (administration every 4–6 hours) are well tolerated and can be used for symptom relief and prevention; however, their short half-life, limits their application and therefore they are rarely prescribed. Leukotriene receptor antagonists have a role in the treatment of patients with rhinitis and concomitant asthma but are not used for allergic rhinitis only.12

In summary, allergen avoidances, antihistamines and INCS are used as first-line therapy for symptomatic treatment of allergic rhinitis.

### Table 3. ARIA classification of allergic rhinitis

<table>
<thead>
<tr>
<th>Disease subdivision</th>
<th>Symptom duration</th>
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<tbody>
<tr>
<td>Intermittent</td>
<td>&lt;4 days/week OR &lt;4 consecutive weeks</td>
</tr>
<tr>
<td>Persistent</td>
<td>&gt;4 days/week AND &gt;4 consecutive weeks</td>
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### Table 4. Recommendations for HDM avoidance in all rooms

**Recommendations for HDM avoidance in the bedroom**

- Cover mattress, pillow and quilt with HDM resistant covers (suppliers include Allergend, Allerseach and Miteguard). Covers must be washed every 2 months
- Wash sheets and pillow cases weekly in water hotter than 55°C
- Remove sheepskin and woolen underlays
- Remove all soft toys. Replace them with wooden or plastic toys which can be washed. If a soft toy is allowed it should be hot washed weekly. Freezing overnight kills mites but does not remove allergen

- Consider replacing carpets with hard floors
- Damp dust or use electrostatic cloths to clean hard surfaces weekly
- Vacuum carpets weekly
- Reduce humidity
- Avoid heavy curtains
Immunotherapy offers the only curative and specific approach. It has been proven to be effective against grass, pollen and HDM allergy. New data suggest that immunotherapy should be started early, even in children with well controlled symptoms because it has a preventive effect on the progression from rhinitis to asthma. The GP should discuss immunotherapy early in the disease process. If a family considers immunotherapy as a treatment option, the child needs to be referred to an allergist. Asthma can become worse while the child is on immunotherapy and therefore it needs to be adequately controlled before commencement of immunotherapy.

Subcutaneous (SCIT) and sublingual (SLIT) immunotherapy are used in Australia and have a good safety profile. Fatal and near-fatal reactions to SCIT are very rare in children. SCIT needs to be given in a surgery with adequate resuscitation facilities by clinicians with training in this form of treatment. A full course of immunotherapy takes 3–5 years. The allergen extract is given in increasing concentrations, initially weekly, then on a monthly basis to induce tolerance. SLIT is safe for home administration and needs to be taken on a daily basis. First effects of SCIT/SLIT are expected after a few months of treatment. The clinical effects may be sustained for years.

Recombinant anti-IgE antibody (omalizumab) has been applied with success in the treatment of allergic rhinitis, particularly in combination with SCIT. However, it is very expensive and not widely used in routine practice. Also, Toll-like receptor agonists have proved to be beneficial.

**Case 1**

Jenny was referred to the paediatric immunology outpatient clinic by her GP following a possible allergic reaction to eggs. Jenny was born at term after an uneventful pregnancy. She was fully breastfed for 6 months and started on solids within 5 months. Dairy products were introduced without any problems.

When Jenny was 8 months of age her mother gave her a teaspoon of scrambled egg. Within 5 minutes Jenny developed lip swelling and a widespread rash. Her mother took her to the local pharmacist who dispensed 1.5 ml of a second-generation antihistamine (desloratidine can be given to children ≥6 months). By the time they returned home Jenny had become pale and floppy. Her mother rushed to the nearest GP. On arrival at the surgery Jenny was breathing heavily. On examination there was widespread wheeze. Her blood pressure was normal but she had tachycardia (180 beats/min) and tachypnoea (58 breaths/min). The GP placed her in a supported sitting position and administered 0.01 mg/kg adrenaline 1:1000 intramuscular into her lateral thigh. She responded quickly and within 10 minutes symptoms of anaphylaxis had resolved, although she still had some residual rash. The GP called an ambulance and Jenny was transferred to the nearest emergency department for further observation. After 2 hours her rash had resolved and she was free of symptoms. The emergency doctor explained to the parents that children need to be monitored in the emergency department for at least 4 hours after an anaphylactic reaction. Prior to discharge an anaphylaxis action plan was discussed. As Jenny weighed only 8.4 kg, the team followed the recommendation and did not send her home with an adrenaline autoinjector. She was referred to a paediatric immunologist for further investigation and management.

In the paediatric immunology clinic, Jenny’s SPT was positive for egg white (weal size 8 x 9 mm) and egg yolk (6 x 6 mm). Jenny’s parents were advised not to give her foods containing eggs; however, foods labelled ‘may contain traces of egg’ could be eaten without significant concern. The allergist booked Jenny in for a baked egg (egg in muffin) challenge and reviewed and reinforced the anaphylaxis action plan. Given Jenny’s severe adverse reaction (anaphylaxis) adrenaline autoinjector was prescribed, despite her weighing <10 kg. The allergist explained that, generally, children who weigh 10–20 kg have an adrenaline autoinjector junior.

Six weeks later, Jenny tolerated the baked egg challenge without any reaction. Her parents were instructed to give Jenny egg-containing muffins 2–3 times/week to induce tolerance to less well-cooked forms of eggs in the longer term.

One year later Jenny was seen for review. The SPT weal size was smaller but still positive for egg white (6 x 6 mm) and egg yolk (3 x 4 mm). Jenny was deemed to have a good chance of outgrowing her egg allergy. Her mother was instructed to continue giving her baked egg, but to avoid raw or other cooked forms of egg (such as scrambled or boiled eggs). The anaphylaxis action plan was reviewed and Jenny was booked in for a review appointment in 1 year.

At the subsequent appointment her SPT weal size was significantly reduced for egg white (3 x 3 mm) egg yolk (2 x 2 mm). Serum testing for specific IgE levels revealed a mildly elevated IgE for egg white and undetectable levels for egg yolk. The paediatric allergist recommended a challenge for cooked (scrambled) egg. Her mother was comfortable with this and Jenny was booked in for a day admission at the hospital.

Jenny tolerated this egg challenge and is now eating all forms of egg without any reaction. She eats eggs at least twice weekly and is considered to have outgrown her egg allergy. She no longer requires an adrenaline autoinjector and has been discharged from the immunology clinic.

**Case 2**

Kirk, 10 years of age, presented to the paediatric immunology outpatient clinic because he had a continuously blocked nose and persistent cough at night. Kirk was diagnosed with severe eczema when he was a baby but has now largely outgrown this. The immunologist noted that Kirk had been sensitised to hazelnut, although his clinical reactivity was initially not known. Kirk tolerated a subsequent challenge to hazelnut and tolerates all tree-nuts.
At the age of 4 years Kirk had been diagnosed with asthma and required prophylactic inhaled corticosteroid until the age of 6 years to control his symptoms. For the past 2 years his asthma has been well controlled without any treatment. Kirk’s parents were atopic (mother eczema, father asthma).

For almost 2 years Kirk has been complaining of a blocked nose most of the year round. In the mornings he had frequent sneezing and occasionally was waking with red and itchy eyes. His mother had noticed that he snored and coughed at night.

Six months earlier, Kirk’s GP had prescribed daily nasal steroid spray and recommended the use of antihistamines as required. Kirk disliked the nasal spray as it caused a dry nose and repeated nose bleeds. He also found it difficult remembering to take the spray every day. Antihistamines improved his symptoms only slightly.

He presented to his GP because of these ongoing symptoms. On examination his inferior turbinates were swollen bilaterally but tonsils were of normal size. His skin was dry and his chest clear. The remaining examination was unremarkable.

Testing for IgE-specific environmental allergens revealed a high specificity for house dust mite (*Dermatophagoides pteronyssinus* and *D. farinae*). Other IgEs, specific for different grasses and animal dander were not detected.

The GP discussed environmental changes (Table 4) such as protective bedding against house dust mite and mentioned that Kirk might be a candidate for desensitisation using immunotherapy. Kirk’s mother was interested in exploring this option and he was referred to a paediatric allergist.

Kirk was assessed and examined in the immunology outpatient clinic, where his SPT revealed significant sensitisation to house dust mite (*D. pteronyssinus* weal size 19 x 14 mm and *D. farinae* weal size 10 x 5 mm). Testing for all other environmental allergens was negative.

The allergist concluded that house dust mite allergy was likely to be a significant contributing factor to Kirk’s symptoms of allergic rhinitis and residual asthma (coughing at night time). Kirk and his mother agreed to the recommended 3-5-year course of subcutaneous immunotherapy for house dust mite.

Prior to commencement, lung function testing indicated that Kirk’s asthma was well controlled. Kirk received his first injection of immunotherapy in the immunology outpatient clinic and after liaison to confirm appropriate facilities, subsequent injections were given by his GP. The clinical nurse specialist from the immunology clinic was in regular contact with the family by telephone, and Kirk had an appointment after 6 months at the nurse-led clinic. At this time he was already showing symptomatic improvement. His nose did not feel as blocked and he no longer required antihistamines. However, the nurse specialist recommended taking antihistamines prior to each visit for his injections as he had a large localized swelling at the injection side.

Since Kirk has been taking antihistamines prior to the injections he tolerates immunotherapy very well. His symptoms of allergic rhinitis have improved significantly and coughing at night has subsided.

At his 3-year appointment with the specialist, Kirk and his mother said that his symptoms of allergic rhinitis had largely resolved and he no longer had night time coughing. Kirk was discharged from the immunology service.

### Key points

- Diagnosis of IgE-mediated allergy requires presence of symptoms on exposure to the allergen and detection of allergen-specific IgE.
- Children often outgrow their milk, egg or wheat allergy, whereas peanut or tree nut allergies tend to persist into adulthood.
- Currently there is no cure for IgE-mediated food allergies and immunotherapy continues to be a significant area of research.
- Allergic rhinitis is underdiagnosed and undertreated, although it has a significant impact on quality of life.
- Immunotherapy offers the only curative and specific approach to managing allergic rhinitis.
- Immunotherapy should be considered early in the disease process because of its potential preventive effect on the progression from allergic rhinitis to asthma.

### Authors

Kristina Rueter FRACP, MD, FRACP, Paediatric Immunologist, General Paediatrician and Emergency Physician, Princess Margaret Hospital, Perth, and Clinical Senior Lecturer, School of Paediatrics and Child Health, University of Western Australia, Perth, WA. Kristina.Rueter@health.wa.gov.au

Susan Prescott MBBS, FRACP, PhD, Paediatric Immunologist, Princess Margaret Hospital, Perth, Winthrop Professor, School of Paediatrics and Child Health, University of Western Australia, and Research Strategy Leader, Telethon Kids Institute, Perth, WA

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### References


