Position Paper - Oral Food Allergen Challenges

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Oral food allergen challenges are standardised procedures where incremental amounts of a particular food are fed to a patient, usually over a period of two to three hours. This does not involve testing the food on skin.

The patient is monitored to determine if the food being tested causes an allergic reaction, and observed for a minimum of one hour after the last dose or reaction. Observation can be longer (two to four hours), depending on the clinical situation and food being challenged.

Oral food allergen challenges are performed under medical supervision by a clinical immunology/allergy specialist or an experienced paediatrician or physician with postgraduate allergy training.

They generally involve nursing support staff and take place in a clinic with immediate access to emergency treatment for a severe allergic reaction (anaphylaxis).

Clinical justification for oral food allergen challenges

Food allergy is common, with prevalence of around 5% in children and 2% in adults. The most common food allergens are egg, cow's milk, peanut, tree nuts, sesame, soy, fish, shellfish and wheat. Currently the only treatment is avoidance of the food/s.

Peanut, tree nut, seed and seafood allergies are much less likely to be outgrown and can be lifelong allergies.

Severity of allergic reactions to foods cannot be predicted, so people with food allergy and their carers need to:

- Maintain a high level of dietary vigilance.
- Be prepared to treat potentially life-threatening severe allergic reactions (anaphylaxis), following accidental exposure.

Oral food allergen challenges are regarded as the gold standard procedures for the diagnosis of food allergy, are standard of care in managing food allergy, and appear in practice guidelines worldwide.

Oral food allergen challenges are medical procedures that are mainly used to determine if a person with:

- Confirmed food allergy (who has had a previous allergic reaction to a food), has outgrown that allergy.
- Positive food allergy test results (who is sensitised to a food), but has never previously eaten or reacted to that food, has a food allergy.
- Suspected food allergy is actually allergic, when clinical history or allergy tests are unclear.
- Confirmed food allergy can safely eat a particular form of the food.

Oral food allergen challenges play a pivotal role in ongoing management of food allergies for the following reasons:

- Food allergies can cause potentially life-threatening severe allergic reactions known as anaphylaxis.
- Food allergies can cause growth issues particularly in young children, anxiety around accidental allergic reactions, and unnecessary avoidance of foods.
- Food allergies have been consistently demonstrated to impair quality of life for patients and their families.
- Fear of having an allergic reaction can have significant negative impact on the learning and socialisation of children with food allergies, for example, by causing them to avoid school excursions and camps.

Other tests for food allergies

In people with food allergies, immunoglobulin E (IgE) antibodies to allergens are usually raised. This is why immediate type allergies (which can result in anaphylaxis), are called IgE mediated allergies.

Whilst food allergy testing using skin prick tests (SPT) or blood tests for allergen specific IgE (ssIgE) may be used in conjunction with oral food allergen challenges, they are not considered as substitute tests for challenges, as they are significantly less accurate.

A positive food allergy test using SPT or blood tests means that a patient's immune system has produced an antibody response to that food, known as being sensitised to an allergen:

- The positive predictive value (PPV) of SPT and ssIgE varies between foods, and the level of the test (magnitude of sensitisation) does not correlate with severity of reactions.
- False positives frequently occur, which means that while the test is positive, the person can eat the food without any symptoms.
- False negative SPT and ssIgE are less common with most food allergens than false positive tests.

For the reasons stated above, it is important in some circumstances to confirm the significance of a positive (or negative) allergy test with an oral food allergen challenge, to prevent unnecessary avoidance of food and unnecessary prescription of adrenaline autoinjectors.

Medically supervised food allergen challenges are also performed in some people who have Food Protein-Induced Enterocolitis Syndrome (FPIES):

- FPIES is an adverse food reaction involving the immune system that mainly affects infants and young children. It is caused by an allergic reaction to one or more ingested foods which results in inflammation of the small and large intestine.
- Typically FPIES causes reproducible profuse vomiting around two hours after ingesting the offending food.
- FPIES is not IgE mediated and therefore does not result in raised IgE levels, so SPT or blood tests are not useful. This is why oral food allergen challenges are often required for people with FPIES, to confirm diagnosis or to determine if the food can be tolerated, to prevent unnecessary avoidance of food, with significant developmental and growth implications.

Oral food allergen challenge protocols

ASCIA oral food allergen challenge protocols have been developed to provide standardised protocols used by clinical immunology/allergy specialists in Australia and New Zealand. The protocols are peer reviewed and based on expert opinion and published literature.

The ASCIA protocols are similar to published protocols used worldwide for food allergen challenges:

- First doses of a food challenge typically contain 1-10mg of food protein.
- Subsequent doses then contain semi-logarithmically increasing or doubling quantities of protein, given at 15-20 minute intervals.

Most oral food allergen challenges require approximately two hours to eat the required doses of food, followed by a minimum one hour of observation (or longer if an allergic reaction occurs during the challenge):

- For most foods, symptom-free ingestion of a total cumulative dose of up to 4-6 grams of food protein is considered sufficient to rule out a food allergy to that specific food.
- Where symptoms consistent with allergy appear, the food challenge is stopped and treatment for the allergic reaction is provided by the nursing and medical staff supervising the challenge.
- If the oral food allergen challenge is completed without an allergic reaction, it is 'negative'.
- If an allergic reaction occurs, the challenge is 'positive' and the diagnosis of a food allergy is confirmed.

Benefits of negative oral food allergen challenge results (without allergic reactions)

One of the main purposes of oral food allergen challenges is to 'de-label' patients by confirming that they no longer have a food allergy. This has significant effects on quality of life for the patient, their family and other carers, developmental implications, and cost savings.

For example, a negative oral food allergen challenge can result in:

- Improved quality of life for patients, their families and other carers, due to patients no longer having to restrict that food in their diet, and elimination of anxiety around the risk of accidental ingestion of that food. Food restriction has significant social, developmental and growth implications, particularly in children.
- Cost savings due to patients no longer needing to carry an adrenaline (epinephrine) injector (EpiPen® or Anapen®). This is particularly significant when oral food allergen challenges are performed in children prior to starting school, thus avoiding years of prescriptions and associated health care visits.

After a negative result for an oral food allergen challenge, the challenge food/s needs to be regularly included in the diet (at least once a week) to maintain tolerance.

Some people who do not eat the food for long periods may become sensitised to the food and have allergic reactions again when they consume the food.

Benefits of positive oral food allergen challenge results (with allergic reactions)

If an allergic reaction occurs during the challenge it will be treated with medications (including adrenaline if indicated), and any other medical measures as needed.

It is also necessary for the patient to stay under medical supervision for at least four hours after the challenge.

Confirming a suspected food allergy is important for the following reasons:

- To educate about avoidance and preparedness for anaphylaxis. This can be important for teenagers and adults who have avoided a particular food since early infancy with no ongoing inadvertent reactions, as they may have difficulty appreciating the seriousness of their food allergy.
- It improves the preparedness of patients with a food allergy (and their family and school or children's education/care service) to treat anaphylaxis. Preparedness is important as the severity of severe reactions over time is unpredictable, and timely treatment of anaphylaxis substantially reduces the risk of fatality.
- Studies have shown improvement in quality of life for patients with a positive challenge result, possibly due to decreased 'fear of the unknown' and improved understanding of management.

Clinical management pathway for oral food allergen challenges

Oral food allergen challenges are conducted in clinics where resources are available to manage the risk of anaphylaxis, which requires emergency treatment and resuscitation facilities.

Reasons a patient may require a medically supervised oral food allergen challenge, due to medium to high risk or probability of allergic reactions, include:

- A history of allergic reactions to the proposed challenge food.
- SPT result equal to or greater than 3mm.
- An attempt to introduce a less allergenic form of a known allergen such as baked milk or baked egg challenges in cases of confirmed milk or egg allergy, respectively.

Where the likelihood of a reaction is considered very high, based upon the clinical history and complementary allergy testing, a food challenge is deemed unnecessary, and the person is considered to be food allergic.

An oral food allergen challenge should <u>not</u> be conducted if a patient or their family does not intend to include the food regularly in the diet following a negative challenge, as this is a waste of resources, irrespective of the likelihood of allergic reactions.

Oral food allergen challenge precautions

Oral food allergen challenges should only be used in:

- Patients who have been carefully selected by clinical immunology/allergy specialists or appropriately qualified and experienced medical practitioners in consultation with clinical immunology/allergy specialists.
- Patients who are well on the day of the challenge, to ensure that the challenge can be performed as safely as possible and that the patient's illness is not mistaken for an allergic reaction to the challenge food. If a patient has an infection, fever, active eczema flare, active asthma exacerbation or any other illness, the challenge should be postponed. If asthma is present, it must be stable with no recent wheezing.
- A controlled medical environment with medical and nursing staff experienced in treating anaphylaxis, with immediate access to emergency treatment for anaphylaxis. This includes experienced nursing staff and supervision by a clinical immunology/allergy specialist or appropriately qualified and experienced medical practitioners, in consultation with a clinical immunology/allergy specialist.

If the patient being challenged has a prescribed adrenaline injector this should be brought to the food allergen challenge. If a severe allergic reaction occurs, it may be an opportunity for the person (if old enough and well enough), or parent to administer the adrenaline injector in a controlled setting.

Medical and nursing staff supervising the food challenge should always have a supply of adrenaline available even if the patient has their own adrenaline injector with them.

Current limitations of oral food allergen challenges

In Australia and New Zealand clinical immunology/allergy specialists work in public and private hospital clinics as well as private consulting rooms. Whilst oral food allergen challenges are currently routinely conducted in all of these settings, access is limited by several factors:

- High demand for oral food allergen challenges, commensurate with the high prevalence of food allergy (around 5% in children and 2% in adults).
- The 'hidden waiting list', whereby patients are subjected to long waiting times in both public and private allergy clinics to simply consult with a clinical immunology/allergy specialist, even before they are referred for challenge.
- Insufficient trained medical and nursing staff who are skilled in the procedure for conducting oral food allergen challenges (including the ability to perform multiple challenges simultaneously to different foods on different people in the same clinic without cross-contamination occurring) and the management of allergic reactions.
- Currently there is no Medicare Benefits Schedule (MBS) item number for medical practitioners who perform oral food allergen challenges in Australia. In contrast, oral food allergen challenges attract reimbursement for provision of the procedure in many countries, including the US and UK.
- No MBS item number means that it is not feasible for oral food allergen challenges to be conducted in private clinics in Australia unless the patient pays for this service.

Improved access to food allergen challenges will be required to confirm the patient's food allergy prior to new food allergy treatments, such as Oral Immunotherapy (OIT), which is already used in many countries. This will become a significant challenge once OIT is routinely available in Australia and New Zealand.

The introduction of a MBS item number or code for oral food allergen challenges to be conducted in private and hospital clinics would greatly assist in improving timely access to oral food allergen challenges, which are the gold standard tests for diagnosing food allergy.

Improved access to food allergen challenges will result in considerable improvements in quality of life and cost savings, mainly due to many patients who are de-labeled of their food allergy no longer needing to:

- Restrict foods, which may have significant developmental, growth and mental health implications.
- Carry prescribed adrenaline (epinephrine) injectors (EpiPen® or Anapen®).

Summary of key points

- Oral food allergen challenges are regarded as the gold standard procedures for the diagnosis of food allergy, are standard of care in managing food allergy, and appear in practice guidelines worldwide.
- Oral food allergen challenges are performed under medical supervision by a clinical immunology/allergy specialist or an experienced paediatrician or physician with postgraduate allergy training.
- Most oral food allergen challenges require approximately two hours to eat the required doses of food, followed by a minimum one hour of observation (or longer if an allergic reaction occurs during the challenge). They generally involve nursing support staff and take place in a clinic with immediate access to emergency treatment for a severe allergic reaction (anaphylaxis).
- Benefits of negative oral food allergen challenge results (without allergic reactions), include:
  - Improved quality of life for patients, families and carers, due to patients no longer having to restrict that food in their diet, with significant developmental and growth implications, and elimination of anxiety around the risk of accidental ingestion of that food.
  - Cost savings due to patients no longer needing to carry an adrenaline injector (EpiPen® or Anapen®).
- Benefits of positive oral food allergen challenge results (with allergic reactions), include:
  - Improved quality of life for patients due to decreased 'fear of the unknown' and improved understanding of management, through education about avoidance and preparedness for anaphylaxis.
  - Preparedness of patients with a food allergy (and their family, school or children's education/care service) to treat anaphylaxis. Preparedness is important as the severity of severe reactions over time is unpredictable, and timely treatment of anaphylaxis substantially reduces the risk of fatality.
- Whilst food allergy testing using skin prick tests (SPT) or blood tests for allergen specific IgE (ssIgE) may be used in conjunction with oral food allergen challenges, they are not considered as substitute tests for challenges, as they are significantly less accurate.
- There is a high demand for oral food allergen challenges, commensurate with the high prevalence of food allergy (around 5% in children and 2% in adults) combined with lack of less resource-intensive tests of comparable accuracy, and patients are subjected to long waiting times in both public and private allergy clinics.
- There is currently no MBS Item number for medical practitioners who perform oral food allergen challenges in Australia, which means that it is not feasible for these to be conducted in private clinics unless the patient pays for this service. The introduction of an MBS item number or code for food allergen challenges to be conducted in private and hospital clinics would greatly assist in improving timely access to oral food allergen challenges. This would improve health outcomes through timely and improved diagnosis and management of food allergy.

Further information

References: www.allergy.org.au/hp/papers/references-food-allergen-challenges

Consent Form: www.allergy.org.au/hp/papers/ascia-consent-form-food-allergen-challenges

ASCIA patient information: www.allergy.org.au/patients/food-allergy

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