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What’s New in Allergy

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What’s New in Allergy

• BSACI Nut Allergy Guidelines
• BSACI AAI Guidance
• MHRA AAI Guidance
• AAI attitudes to AAI carriage in young people
• New Epipen technique
• IMAP Guidelines
• BSACI Milk allergy Algorithm
• TRACE Study
• LEAP-ON results
• EAT Study
Summary

Peanut nut and tree nut allergy are characterised by IgE mediated reactions to nut proteins. Nut allergy is a global disease. Limited epidemiological data suggest varying prevalence in different geographical areas. Primary nut allergy affects over 2% of children and 0.5% of adults in the UK. Infants with severe eczema and/or egg allergy have a higher risk of peanut allergy. Primary nut allergy presents most commonly in the first five years of life, often after the first known ingestion with typical rapid onset IgE-mediated symptoms. The clinical diagnosis of primary nut allergy can be made by the combination of a typical clinical presentation and evidence of nut specific IgE shown by a positive skin prick test (SPT) or specific IgE (sIgE) test. Pollen food syndrome is a distinct disorder, usually mild, with oral/pharyngeal symptoms, in the context of hay fever or pollen sensitisation, which can be triggered by nuts. It can usually be distinguish clinically from primary nut allergy. The magnitude of a SPT or sIgE relates to the probability of clinical allergy, but does not relate to clinical severity. SPT of > 8 mm or sIgE > 15 KU/L to peanut is
What is in the Nut Allergy Guidelines?

• Improvements in diagnosing and managing nut allergy.

• Recognises impact on QOL for total nut avoidance and constant vigilance required in everyday life.

• Need for identifying and prioritising the most at risk individuals

• Prevention of development of nut allergy
What is in the Nut Allergy Guidelines
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• Severe eczema, egg allergic, siblings of nut allergic children identified as high risk and need careful assessment.

• Systematic management involving the all care givers, not just parents.

• Comprehensive management plans about specific avoidance advice and management of allergic reactions – including the role of the dietitian.

• Weaning advice and immunotherapy.
Fig. 1. Suggested algorithm for the diagnosis of peanut allergy. 1) In infants and young children with a typical history, a SPT weal of 2 mm may indicate clinical allergy; 2) Either sIgE or SPT should be negative on two occasions or both sIgE and SPT negative; 3) This may include mild or OAS/FPS symptoms; 4) sIgE components do appear to be more sensitive and specific than peanut sIgE. Data in children suggest that sIgE components are no better than SPT. Consider performing Ara h 1, 3 & 9 as it is possible for one of Ara h 1, 3 or 9 to be positive as well as Ara h 8 positive and Ara h2 negative. This indicates an increased likelihood of primary peanut allergy; 5) Consider food challenge.
Fig. 2. Suggested algorithm for the diagnosis of tree nut allergy.  

1) In infants and young children with a typical history, a SPT weal of 2 mm may indicate clinical allergy;  
2) Either slgE or SPT should be negative on two occasions or both slgE and SPT negative;  
3) This may include mild/OAS symptoms or poor recall;  
4) It may not be possible to differentiate between pollen food syndrome (PFS) and primary tree nut allergy based on SPT/slG. slgE components and food challenges may be able to differentiate between the two better;  
5) slgE components for hazelnut should be considered. Evidence for other tree nuts is lacking;  
6) A decision to perform a challenge will depend on the clinical context;  
7) Consider component testing for hazelnut and consider food challenge.
The dilemma of avoidance in nut allergy

Clinical reaction

Allergy testing

Avoidance

Co-sensitization

Cross-reactivity

Peanut or tree nut allergy

Sesame or hazelnut

Pistachio or walnut

Eigenmann et al, 2017 The Journal of Clinical Allergy and Immunology Pract;5:296-300
### Primary Peanut Allergy

- Infants with severe eczema and/or egg allergy most at risk.
- Usually presents in before age 5 years after 1\(^{st}\) ingestion.
- Immediate onset of IgE mediated symptoms
- Positive SPT >3mm or specific IgE tests

### Pollen Food Syndrome (PFS)

- Mild oral pharangeal symptoms.
- Usually older child reporting seasonal A/R
- Usually reports OAS to fruits veg or nuts
- Careful diagnosis necessary as can coexist with primary peanut allergy
- If consumed during high pollen season can cause anaphylaxis (rare)
- Do not necessarily need an AAI unless severe reaction reported or other indication
Total Nut Avoidance

- Children with one nut allergy have a significant chance of being allergic to other nuts even though they may not have reacted or ingested them.
- SPT with > 8mm is useful to advise patients about avoidance.
- SPT between 3-7 mm positive consider challenging
Total Nut Avoidance

Risks

• Very difficult to achieve in reality
• Significant restriction of a wide variety of foods
• Reduces QoL due to anxiety

Benefits

• Safest approach if followed – results in 3% risk of accidental reaction.
• Simplifies message
• Improves avoidance when eating out and for schools/nurseries
Single Nut Avoidance

**Risks**
- Need to be cautious about contamination.
- Higher risk of accidental exposure due to misidentification of unsafe nuts.
- Confusion about which are the safe nuts for each individual among carers i.e. schools/nurseries
- Relies on accurate diagnosis
- Need to challenge more children?

**Benefits**
- Improved QoL
- Nutritional benefits in diet
- Cultural benefits and inclusion
- Possibility of immunological benefits but long term study data needed.
Component Tests

- Using Immunocap – More sensitive and specific than specific than IgE tests alone.
- **Ara h2** Primary peanut allergen associated with risk of severe systemic reactions in over 90% of people with a life threatening peanut allergy.
- Ara h8 associated with OAS and PFS
- **Hazelnut Cor a 9 and Cor a 14 (SPs)** Primary hazelnut allergens
- Hazelnut Cor a 8 (LTP) indicates lower risk of symptoms.
- Profillin PR-10 positive and Bet V 1 Birch pollen positive suggests OAS and PFS

- In infants and young children component tests are considered to be no better than SPTs.
Lipid Transfer Proteins (LTPs)

• Stable to heat and digestion
• Associated with allergic reactions to fruits and vegetables
• Associated with systemic and severe reactions as well as OAS
• Fruits, vegetables, nuts weed, pollen
• (Cor a 8 - hazelnut, Ara h 9 - peanut : Mal d 3 - apple )
Storage Proteins

- Essential protein stores for all living cells.
- Not destroyed by heat or digestive enzymes.
- Responsible for severe systemic reactions
- Ara h 1, Ara h 2 Ara h 3 – Peanuts
- Cor a 9, Cor a 14 - Hazelnuts
Profilin’s

- Very cross reactive and in most plants
- Mostly responsible for mild reactions, but can occasionally cause severe reactions in certain individuals.
- Tree pollen, fruits, vegetables, nuts, grass pollen, weed pollen
- (Bet v 2 - birch: Pru p 4 - peach: Phl p 12 - timothy grass: Hev b 8 - latex)
PR-10 Proteins

• Found in pollen and in pulp of fruits
• Bet v PR-10 is the main birch pollen allergen but is very similar in structure to other PR-10 proteins found in nuts, legumes, rosacea fruits i.e cherries, peaches, apples leading to cross reactions OAS and hay-fever type symptoms. The severity of the reaction depends on the amount of cross reactive protein.
Indicators that Increase Risk of Severe Reactions

- Asthma – present in 78% of fatal anaphylaxis
- Amount of food/allergen ingested
- Teenagers/young adults – due to failure to carry AAs, alcohol, risk taking, failure to avoid triggers.
Fatal Anaphylaxis 2017

- 4 in under 18 year olds
- 2 occurred in school
- 2 following take away food.
- 3/4 episodes involved milk allergy
- 1 involved peanut.
Comprehensive Individualised Management Plan

• Based on individual preferences and needs
• Risk assessment
• Education
• Challenges
• Role of dietitian crucial
Under changes to the Human Medicines (Amendment) Regulations 2017 with MHRA, from 1 October 2017, schools can purchase AAIs for use in children having anaphylaxis, where both medical and parental consent has been obtained.
Guidance on the use of adrenaline auto-injectors in schools
2. Guidance on the use of adrenaline auto-injectors in schools

Schools may administer their “spare” adrenaline auto-injector (AAI), obtained, without prescription, for use in emergencies, if available, but only to a pupil at risk of anaphylaxis, where both medical authorisation and written parental consent for use of the spare AAI has been provided.

The school’s spare AAI can be administered to a pupil whose own prescribed AAI cannot be administered correctly without delay.

AAIs can be used through clothes and should be injected into the upper outer thigh in line with the instructions provided by the manufacturer.

If someone appears to be having a severe allergic reaction (anaphylaxis), you MUST call 999 without delay, even if they have already used their own AAI device, or a spare AAI.

In the event of a possible severe allergic reaction in a pupil who does not meet these criteria, emergency services (999) should be contacted and advice sought from them as to whether administration of the spare emergency AAI is appropriate.

Practical points:

- When dialling 999, give clear and precise directions to the emergency operator, including the postcode of your location.

- If the pupil’s condition deteriorates and a second dose adrenaline is administered after making the initial 999 call, make a second call to the emergency services to confirm
Revised Allergy Action Plans

• Individual Healthcare Plans for children with food allergies, provide medical and parental consent for schools to administer medicines in the event of an allergic reaction.

• This includes consent to administer "spare" back-up adrenaline auto-injector device.
In addition to consent, the revised plans incorporate:

Advice relating to body posture during anaphylaxis

• Emphasis that anaphylaxis can occur without mild symptoms such as skin rash, and adrenaline auto-injectors should be used BEFORE salbutamol to treat respiratory reactions

• Fields to electronically complete Parent details, if desired

• The new plans are available on the BSACI website:

http://www.bsaci.org/about/download-paediatric-allergy-action-plans
www. Spare Pens In Schools

As of October 2017, schools will be able to purchase spare adrenaline autoinjectors (AAIs) for emergency use. AAIs deliver a potentially life-saving dose of adrenaline in the event of a severe allergic reaction (anaphylaxis).

Adrenaline is the first-line emergency treatment for anaphylaxis.

This website is currently under development to support schools and families of children at risk of anaphylaxis.

In the meantime, the following links can be used to access:
- Department of Health guidance on the use of AAIs in schools
- BSACI Allergy Action Plans for children at risk of anaphylaxis

Or click on a logo below:
AllergyWise anaphylaxis online training for Schools

https://www.anaphylaxis.org.uk/information-training/allergywise-training/for-schools/

Now free access for schools thanks to ALK sponsorship.
Changes to instructions on the administration of EpiPen® and EpiPen® Junior adrenaline autoinjector

5th October 2017

Reduced injection time from 10 seconds to 3 seconds
Removal of massage step

Aims to simplify process of giving Epipen
Reassures that efficacy will not be altered if using the 10 second technique on device with 3 second instructions and visa versa.

Expect to see devices in pharmacies with 3 second technique instructions from November 2017.
Prevention of development of Food Allergy

• There is no evidence to support the delayed introduction of peanut into the infant’s diet.

• LEAP - Learning Early About Peanut Allergy (LEAP) study randomised controlled trial (RCT), showed that early high dose introduction of peanuts reduced the risk of peanut allergy at age 5 years by 81% among high-risk children.

CONCLUSIONS:

• Among high risk children in whom peanuts had been introduced in the first year of life and continued until 5 years of age, a 12-month period of peanut avoidance was not associated with an increase in the prevalence of peanut allergy. Sustained unresponsiveness.

• Longer-term effects are not known.

Enquiring About Tolerance (EAT)

- Enrolled exclusively breast fed infants from the general population, not high risk at 3 months of age.
- Randomised to early introduction of 6 major food allergens (milk, egg, peanut, sesame, fish and wheat) from 3 months to before 6 months of age.
- Or, introduction of the six foods after age 6 months, along with breastfeeding.
- Did not show the efficacy of early introduction of allergenic foods in an intention-to-treat analysis.
- Per-protocol analysis showed earlier introduction significantly reduced prevalence of peanut and egg allergies, but depends on dose given and adherence. Needs to be interpreted with caution due to bias.

- Although it was safe to introduce these major allergens, it was not very feasible at the frequency and dose required for the study.

Addendum guidelines for the prevention of peanut allergy in the United States: Report of the National Institute of Allergy and Infectious Diseases–sponsored expert panel

Alkis Togias, MD, Susan F. Cooper, MSc, Maria L. Acebal, JD, Amal Assa’ad, MD, James R. Baker, MD, Lisa A. Beck, MD, Julie Block, Carol Byrd-Bredbenner, PhD, RD, FAND, Edmond S. Chan, MD, FRCPC, Lawrence F. Eichenfield, MD, David M. Fleischer, MD, George J. Fuchs, MD, Glenn T. Furuta, MD, Matthew J. Greenhawt, MD, MBA, MSc, Ruchi S. Gupta, MD, MPH, Michele Habich, DNP, APN/CNS, CPN, Stacie M. Jones, MD, Kari Keaton, Antonella Muraro, MD, PhD, Marshall Plaut, MD, Lanny J. Rosenwasser, MD, Daniel Rotrosen, MD, Hugh A. Sampson, MD, Lynda C. Schneider, MD, Scott H. Sicherer, MD, Robert Sidbury, MD, MPH, Jonathan Spergel, MD, PhD, David R. Stukus, MD, Carina Venter, PhD, RD, Joshua A. Boyce, MD

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Summary of addendum guidelines 1, 2, and 3

Addendum guideline

1 Severe eczema and/or egg allergy  Strongly consider evaluation by sIgE measurement and/or SPT and, if necessary, an OFC. Based on test results, introduce peanut-containing foods. 4-6 months

2 Mild-to-moderate eczema  Introduce peanut-containing foods  Around 6 months

3 No eczema or any food allergy  Introduce peanut-containing foods  Age appropriate and in accordance with family preferences and cultural practices
Recommended approaches for evaluation of children with severe eczema and/or egg allergy before peanut introduction.

![Diagram showing recommended approaches](image)

*To minimize a delay in peanut introduction for children who may test negative, testing for peanut-specific IgE may be the preferred initial approach in certain health care settings. Food allergen panel testing or the addition of sIgE testing for foods other than peanut is not recommended due to poor positive predictive value.*
TRACE Study

- One-hundred adults with a diagnosed peanut allergy recruited to four (peanut) challenges at 12 week intervals
- A baseline peanut double-blind placebo controlled food challenge, followed by three further challenges comprising one repeat baseline challenge, and two further challenges with different extrinsic factors exercise and stress thought to have a possible influence on the thresholds and/or severity of reaction.
- The TRACE study aims to help improve “may contain” labelling, by limiting warnings to foods where the peanut levels are likely to be above the threshold.
- Mills, C University of Manchester, Imperial College London, Cambridge University
### iMAP Guideline for Primary Care and ‘First Contact’ Clinicians

### Presentation of Suspected Cow’s Milk Allergy (CMA) in the 1st Year of Life

**Having taken an Allergy-focused Clinical History and Physically Examined**

**Dec 2016**

#### Mild to Moderate Non-IgE-mediated CMA
- Mostly 2-72 hrs. after ingestion of Cow’s Milk Protein (CMP)
- Formula fed, exclusively breast fed or at onset of mixed feeding

**Usually several of these symptoms will be present**
- Treatment resistance e.g. to atopic dermatitis or reflux, increases likelihood of allergy

**Gastrointestinal**
- Irritability - ‘Colic’
- Vomiting - ‘Reflex’ - GORD
- Food refusal or aversion
- Diarrhoea-like stools
  - loose and/or more frequent
- Constipation – especially soft stools, with excessive straining
- Abdominal discomfort, painful flatus
- Blood and/or mucus in stools in an otherwise well infant

**Skin**
- Pruritus (itching), Erythema (flushing)
- Non-specific rashes
- Moderate persistent atopic dermatitis

**Cow’s Milk Free Diet**
- Extensively Hydrolysed Formula – eHF
  - Or - Advise exclusively breast feeding mother to exclude all CMP from her own diet and to take daily Calcium and Vit D
  - See Management Algorithm

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#### Severe

**Non-IgE-mediated CMA**
- Mostly 2-72 hrs. after ingestion of Cow’s Milk Protein (CMP)
- Formula fed, exclusively breast fed or at onset of mixed feeding

**One or more of these Severe and Persisting symptoms:**

**Gastrointestinal**
- Diarrhoea, vomiting, abdominal pain, food refusal or food aversion, significant blood and/or mucus in stools, irregular or uncomfortable stools
  - +/- Faltering growth

**Skin**
- Severe atopic dermatitis
  - +/- Faltering Growth

**Cow’s Milk Free Diet**
- Amino Acid Formula - AAF
  - Or - Advise exclusively breast feeding mother to exclude all Cow’s Milk Protein from her own diet and to take daily supplementary calcium and Vit D according to local recommendations

**Ensure:**
- Urgent referral to local paediatric allergy service
- Urgent dietetic referral

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#### Severe

**IgE CMA**

**ANAPHYLAXIS**
- Immediate reaction with severe respiratory and/or CVS signs and symptoms.
  - (Rarely a severe gastrointestinal presentation)

**Emergency Treatment and Admission**

**Cow’s Milk Free Diet**
- Initial 1st choice

**Extensively Hydrolysed Formula – eHF**
- Soy may be used in some settings if not sensitised

**Or - Advise exclusively breast feeding mother to exclude all Cow’s Milk Protein from her own diet and to take daily supplements of calcium and Vit D according to local recommendations**

**Initial IgE testing needed**

**If diagnosis confirmed** (which may require a Supervised Challenge in a minority of cases):
- Follow-up with serial IgE testing and later Planned Challenge to test for acquired tolerance

**Dietetic referral required**

**If competencies to arrange and interpret testing are not in place - early referral to local paediatric allergy service is advised**
BSACI guideline: prescribing an adrenaline auto-injector

Pamela Ewan, Nicola Brathwaite, Susan Leech, David Luyt, Richard Powell, Stephen Till, Shuaib Nasser, Andrew Clark

First published: 29 September 2016
DOI: 10.1111/cea.12788

Summary

This guidance for the prescription of an adrenaline auto-injector has been prepared by the Standards of Care Committee (SOCC) of the British Society for Allergy and Clinical Immunology (BSACI) to improve the prescribing of adrenaline auto-injectors. It has been developed in response to insufficient quality evidence-based data in some areas, including the question of how often adrenaline auto-injector dose is required, and the optimal dose and absorption after subcutaneous vs. intramuscular injection. Thus, indications for adrenaline (which are partly opinion based) in guidelines from other countries are less applicable to the UK.
BSACI guideline: prescribing an adrenaline auto-injector

Diagnosis of anaphylaxis and identification of putative triggers
OR
Assessment of allergic reactions with anaphylaxis risk

Continuing risk of anaphylaxis*

‘Avoidable’
e.g. parenteral drug, oral prescription-only drug, some occupational, some foods

Not [reliably] avoidable
Risk of further episode, e.g. with food, sting, latex, idiopathic, mastocytosis

Severity grading & risk assessment

Mild, e.g. urticaria without airway involvement ± lip swelling

Moderate*,
e.g. generalised urticaria with mild airway involvement

Severe, e.g. airway involvement or hypotension

No asthma and more than trace exposure

With risk factor e.g. asthma, trace exposure, raised baseline tryptase

No asthma and more than trace exposure

With risk factor e.g. asthma, trace exposure, raised baseline tryptase

AAI not required

AAI recommended

Consider AAI

AAI recommended
BSACI guideline: prescribing an adrenaline auto-injector

Provisional diagnosis of Anaphylaxis (+/- AAI prescribed)

Refer to allergist

Allergy diagnosis
Determine cause or type of anaphylaxis

Allergen or trigger avoidance*

Risk assessment for anaphylaxis

Minimal or no risk

Adrenaline not required

Continuing risk

Adrenaline required

Oral AH + Adrenaline auto-injector

Written treatment plan

Training patients/parents/school staff/carers

Excellent asthma control
Treat other allergies

Follow up + retraining
Adrenaline auto-injectors: updated advice after European review

From: Medicines and Healthcare products Regulatory Agency
Published: 15 August 2017
Therapeutic area: Paediatrics and neonatology and Respiratory disease and allergy

It is recommended that 2 adrenaline auto-injectors are prescribed, which patients should carry at all times.

Contents
— Results of European review
— Patient and carer instructions
— Anaphylaxis

Advice for healthcare professionals
— it is recommended that 2 adrenaline auto-injectors are prescribed, which patients should carry at all times.
Results of European review

The European Medicines Agency (EMA) has completed a review of all adrenaline auto-injectors approved in the EU. The review concluded that:

- due to uncertainties about the site of drug delivery and the speed of adrenaline action within the body, it is recommended that healthcare professionals prescribe 2 auto-injectors, which patients should carry at all times
- the needle length of the device is now stated in the product information because this may be an important factor for the prescriber to consider when choosing a suitable auto-injector
- the training of patients and their carers in the correct use of the product is important and manufacturers were required to update their educational materials – see table below
- manufacturers should carry out studies in humans to more fully understand when and how much adrenaline reaches the bloodstream, and how quickly and effectively it acts on body tissues when given through an auto-injector

These studies have started and will help to inform future recommendations for adrenaline auto-injectors.
Advice for healthcare professionals:

- it is recommended that 2 adrenaline auto-injectors are prescribed, which patients should carry at all times
- ensure that people with allergies and their carers have been trained to use the particular auto-injector that they have been prescribed—technique varies between injectors
- encourage people with allergies and their carers to obtain and practise using a trainer device (available for free from the manufacturers’ websites)

Advice to give to people with allergies and their carers:

- it is recommended that you carry 2 adrenaline auto-injectors at all times; this is particularly important for people who also have allergic asthma because they are at increased risk of a severe anaphylactic reaction
- use the adrenaline auto-injector at the first signs of a severe allergic reaction
- take the following actions immediately after every use of an adrenaline auto-injector:
  - seek help immediately
  - take medicines that your doctor has prescribed for you
  - call 112 or your local emergency number immediately and stay with the person until help arrives
  - stay with the person until medical help arrives
  - give any further help that the person needs
Audit of AAI Use and Prescription
BSACI Nurses committee and members

• 1/3 of AAIs not being carried at all times, out of date, wrong dose.

• Training in Primary care lacking compared to allergy clinic settings (e.g. 41 GP prescriptions 50% had training or given Action plan).

• Additional devices kept in schools, cars, grandparents, second homes

• Schools demanding 2 AAIs for each child.