Managing food allergies in the real world

Paul Turner
MRC Clinician Scientist & Hon. Consultant in Paediatric Allergy & Immunology,
Imperial College London & Clinical Associate Professor, University of Sydney
Acknowledgements:

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Clare Mills (Manchester)

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Andrew Clark
Pam Ewan

**AUSTRALIA**
Dianne Campbell
Katie Allen

**MANCHESTER**
Richard Pumphrey
Is there a Food Allergy epidemic?

Little robust evidence
Best evidence for peanut

Sicherer S et al. JACI 2003
Grundy J et al. JACI 2002
Classification of Reactions

Adverse reaction to food

- Non Toxic
  - Immune mediated (Food Allergy)
    - IgE mediated
    - Non IgE mediated
  - Non-immune mediated (Food Intolerance)
    - Enzymatic
    - Pharmacological
    - Other

Immediate food allergy
Oral Allergy Syndrome
Coeliac Disease
Food Protein Enteropathies
Eosinophilic Gastroenteropathies
## Prevalence of Food Allergy

<table>
<thead>
<tr>
<th>Food</th>
<th>USA</th>
<th>AUS</th>
<th>FRA</th>
<th>NOR</th>
<th>CH</th>
<th>UK</th>
<th>USA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>2.5%</td>
<td>2.7%</td>
<td>1.1%</td>
<td>3.2%</td>
<td>1.7%</td>
<td>2.3%</td>
<td>0.3%</td>
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<tr>
<td>Egg</td>
<td>1.3%</td>
<td>8.9%</td>
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<td>1.3%</td>
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<tr>
<td>Peanut</td>
<td>0.8%</td>
<td>3.0%</td>
<td>0.7%</td>
<td>-</td>
<td>0.3%</td>
<td>1.8%</td>
<td>0.6%</td>
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<tr>
<td>TreeNuts</td>
<td>0.2%</td>
<td>-</td>
<td>0.7%</td>
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<td>0.5%</td>
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<tr>
<td>Fish</td>
<td>0.1%</td>
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<td>0.1%</td>
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<td>1.4%</td>
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<td>2.0%</td>
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<tr>
<td>Sesame</td>
<td>-</td>
<td>0.8%</td>
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<tr>
<td>Overall</td>
<td>6.0%</td>
<td>10%</td>
<td>6.0%</td>
<td>-</td>
<td>5.2%</td>
<td>5.5%</td>
<td>3.7%</td>
</tr>
</tbody>
</table>

*Osbourne N et al. JACI 2011; 127:668-76 (AUS)*
*Eggesbo M et al J.Paed 2001, 139:583 (NOR)*
*Venter C, et al JACI 2006; 117:1118 (UK)*
*Sampson H.A. JACI 2004;13:806. (USA)*
*Rance F et al CEA 2005;35:167.(FRA)*
*Hourihane J et al JACI 2006;119:1197 (UK)*
Adrenaline auto-injector devices

Time trends in the prevalence of peanut allergy: three cohorts of children from the same geographical location in the UK

C. Venter¹,², S. Hasan Arshad¹, J. Grundy¹, B. Pereira¹, C. Bernie Clayton¹, K. Voigt¹, B. Higgins² & T. Dean¹,²

¹The David Hide Asthma and Allergy Research Centre, St. Mary’s Hospital, Newport, Isle of Wight, UK; ²School of Health Sciences and Social Work, University of Portsmouth, Portsmouth, UK

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• Community cohort of children born 1989 vs 1994-96 vs 2001-2 on IoW
• Questionnaire/examination/SPT at 1,2,3 yrs of age
• OFC for any +ve SPT if no Hx of tolerance OR any suspicion of reaction, regardless of SPT
Results

In 2001/2 cohort of 969 children:

- 33.7% of parents reported a food related problem
- 5.3% sensitised to food
- 6% had FA at open OFC
- 5% had FA by DBPCFC

**Figure 1** Comparison of sensitization to peanuts in three cohorts of children aged 3–4 years. *Test for trend: Chi-square (quadratic component) $P = 0.005$.

**Figure 2** Comparison of peanut allergy in three cohorts of children aged 3–4 years. *Test for trend: Chi-square (quadratic component) $P = 0.127$. 
Figure 2 Summary of food allergy prevalence from studies that provided data for children aged 5 years or less. Studies are categorised according to level of evidence; OFC proven food allergy (black bars); food allergy based on symptoms and sensitisation (grey bars) or questionnaires/parental reporting (yellow bars).
Figure 3 Summary of food allergy prevalence from studies that provided data for children older than 5 years. Studies are categorised according to level of evidence; OFC proven food allergy (black bars); food allergy based on symptoms and sensitisation (grey bars) or questionnaires/parental reporting (yellow bars).
## Foods implicated:

- Allspice
- Almond
- Anise seed
- Apple
- Artichoke
- Avocado
- Baker’s yeast
- Banana
- Barley
- Bay leaf
- Beet
- Black Pepper
- Brazil nut
- Brewer’s yeast
- Buckwheat
- Cantaloupe
- Carrot
- Cashew nut
- Castor bean
- Celery
- Chamomile
- Chestnut
- Chicken
- Chicory
- Chilli
- Chocolate
- Cinnamon
- Clam
- Clove
- Coconut
- Cod
- Coriander
- Corn
- Cow’s Milk
- Crab
- Crustaceans
- Cumin Seed
- Cuttlefish
- Dates
- Egg
- Fennel
- Fig
- Flaxseed
- Food additives
- French beans
- Garlic
- Ginger
- Goat’s milk
- Halibut
- Hazelnut
- Honey
- Hops
- Horseradish
- Juniper Berry
- Kiwi
- Lentil
- Lima Bean
- Limpet
- Lobster
- Mango
- Millet
- Mushrooms
- Mustard
- Nutmeg
- Oat
- Orange
- Oyster
- Parsley
- Pea
- Peach
- Peanut
- Pecan nut
- Pine nut
- Pineapple
- Pistachio
- Pomegranate
- Poppy seed
- Potato
- Psyllium seed
- Raspberry
- Royal jelly
- Sage
- Salmon
- Sesame
- Shellfish
- Shrimp
- Soy
- Squash
- Squid
- Sunflower seed
- Sweet Potato
- Tangerine
- Tapioca
- Thyme
- Turmeric
- Vanilla
- Walnut
- Walnut
- Watermelon
- Wheat
Foods that cause more than 90% of IgE-mediated FA in children

Milk
Eggs
Peanuts
Tree nuts and seeds
Fish
Shellfish
Soy
Wheat
Explanations for the increase in PN allergy

- Change in peanut formulation/dietary consumption
- Changes in exposure / skin barrier function
- Impact from other atopic conditions?
Can early exposure alter the risk of food allergy?

- LEAP Study

(N=628)  
P<0.001

A. Intention-to-Treat Population in Primary Trial

B. Intention-to-Treat Population in Follow-up Study
Can early exposure alter the risk of food allergy?

Other studies:

- Egg
- Multiple foods: EAT Study
A (na) phylaxis

Originates from Greek, meaning against or without protection.

vs. prophylaxis, for protection

“A rapidly evolving, generalised multi-system reaction characterized by one or more symptoms or signs of respiratory, cardiovascular and other systems such as the skin and/or GI tract.”
1. Has the incidence of anaphylaxis increased?

2. Has mortality due to anaphylaxis increased?
Fatal food anaphylaxis, UK 1992-2007

points 1992–1999 are plotted below the line
points 2000–2007 are plotted above the line

Data c/o
R Pumphrey
Fatal food anaphylaxis

A

Children (under 16 years)

B

Adults (over 16 years of age)

Turner et al, JACI 2015
Where is the clinical need?

<table>
<thead>
<tr>
<th>‘Perceived’ RISK</th>
<th>** DANGER **</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peanut</td>
<td>Cow’s Milk</td>
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</table>

‘Perceived’ RISK

** DANGER **
<table>
<thead>
<tr>
<th>Pre-packed foods</th>
<th>Catering outlets</th>
</tr>
</thead>
<tbody>
<tr>
<td>27%</td>
<td>59%</td>
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<tr>
<td>(? none to “traces”)</td>
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</tbody>
</table>
FIGURE 1. Annual incidence rate for different events in food-allergic people aged 0–19 years. Data are estimated risk of self-reported/medically coded/fatal food anaphylaxis and hospital admission for food anaphylaxis. Continuous bars represent means with 95% CI, dotted bars represent the range of point estimates from individual studies, in a systematic review undertaken by Umasonthar et al. [4*]. Wherein reference risks vary markedly between European and US populations, they are stated separately. Otherwise, reference risks are for the US population.

83% of (245) teenagers with anaphylaxis don’t use their AAI
Anaphylaxis is not uncommon, but death from anaphylaxis is very rare.
1. Dietary Avoidance
2. Treatment of accidental reactions
3. Desensitisation?
Management

1. Dietary Avoidance

2. Treatment of accidental reactions

3. Desensitisation?
### Table 1 Examples of countries with mandatory disclosure of allergens in pre-packed foods

<table>
<thead>
<tr>
<th></th>
<th>Wheat</th>
<th>Other gluten-containing cereals</th>
<th>Egg</th>
<th>Milk</th>
<th>Peanut</th>
<th>Tree nuts</th>
<th>Soy</th>
<th>Fish</th>
<th>Crustacean</th>
<th>Mollusc</th>
<th>Celery</th>
<th>Mustard</th>
<th>Sesame</th>
<th>Lupin</th>
<th>Sulphur dioxide</th>
<th>Other</th>
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Table adapted from http://farrp.unl.edu/IRChart with reference to national legislation.

*The 28 constituent member states of the European Union (EU) are: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom.

1 Local legislation also requires mandatory disclosure of tartrazine.

2 It is unclear whether disclosure of mollusc is required by local legislation.

3 Local legislation requires mandatory disclosure of eggs, milk, wheat, buckwheat, peanuts, shrimp and crab. In addition, disclosure is recommended (but not required) for the following 18 ingredients: abalone, squid, salmon roe, orange, kiwifruit, beef, walnut, salmon, mackerel, soybean, chicken, banana, pork, Matsutake mushroom, peach, yam, apple, and gelatin.

4 Legislation specifies prawn/shrimp and crab rather than ‘crustacea’.

5 Local legislation requires mandatory disclosure of egg, milk, buckwheat, peanuts, soybeans, wheat, mackerel (but not other finned fish), prawn/shrimp, crab, pork, peaches and tomatoes. There are no allergens for which labelling is optional.

6 Tree nuts in USA include a range of native nuts not included, for example, under EU legislation e.g. Beech, Butternut, Chestnut, Coconut, Ginko nut, Hickory nut, Lychee, Shea nut.
Many people who are allergic to egg or milk may tolerate the allergen in products that have been baked at high temperature for long periods such as cakes or biscuits. Processing and denaturation of the allergen may reduce ambiguity but would further restrict consumer choice. The best solution would be to stop this, suggesting a change in policy. There is a high degree of agreement between published LOAEL data with a recommended cut-off of (low) amounts of soy protein, and most people with soy allergy can tolerate these ingredients. However, most studies, particularly the Euro-PREVALL collaboratory, used double-blind placebo-controlled adverse reactions in sensitive individuals. This allows manufacturers to assess potential cross-contamination quantitatively and to determine the risk of harm from cross-contamination to sensitive individuals, and thus avoid the need to address the issue altogether (Food Standards Agency, personal communication). Although some very sensitive people might react to the smallest amount of allergen, this derives from toxicology, where a safety margin of at least 100:1 is considered to exist. The levels of allergen required to trigger an allergic response in a person can vary from individual to individual, depending on various factors. For example, the same person might be able to tolerate the allergen in products that have been made in a factory that also produces the allergen intentionally adding small amounts of allergen to a product, or in a factory that also produces the allergen but in a clean environment where allergens are present. Regulatory authorities require products made as a raw ingredient, but not those containing refined soy oil.

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Impact on the consumer

- 69% of cereals and 56% of confectionery labelled ‘may contain’ despite not listing nut as an ingredient.¹

- Shopping for a nut-allergic person took:
  - 40% longer
  - cost an average of 11% more

- Adversely impacts on quality of life

<table>
<thead>
<tr>
<th>Product with PAL</th>
<th>Product without PAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Helpful to allergic consumers</strong></td>
<td><strong>Not helpful to allergic consumers</strong></td>
</tr>
</tbody>
</table>
| 1. **Product with PAL** with a real risk of inducing an allergic reaction i.e. unsafe to consume  
  - Proper risk assessment by the food manufacturer  
  - Conclusion that the allergen may be present in the product (despite allergen management and Good Manufacturing Practice). | 5. **Product without PAL**, with unknown risk of inducing an allergic reaction i.e. may be safe or unsafe to consume  
  - Proper risk assessment undertaken  
  - Manufacturer uses PAL nonetheless  
  - No conclusion about allergen presence can be drawn |
| 2. **Product with PAL** with unknown risk of inducing an allergic reaction i.e. may be safe or unsafe to eat  
  - No proper risk assessment  
  - No conclusion about allergen presence can be drawn |  |
Do PALs contribute to anxiety?

• Paediatric food allergy causes more anxiety than other chronic diseases such as DM \(^1\)

• Labelling is a particular concern: \(^2,^3\)

“…considerable confusion over the extent to which parents should exclude allergens… including whether foods labelled “may contain traces” should be avoided…” \(^4\)

\(^1\) Avery et al, PAI 2003;14:378-82
\(^2\) Cummings et al. PAI 2010;21:586-94;
\(^3\) Sheth et al, Ann Allergy Asthma Immunol 2010;104:60-5
\(^4\) Hu et al, Arch Dis Child 2007;92:771-5
So why bother?

- PALs helpful if they provide reliable information, but use is widespread\(^1\)
- Phrasing is confusing

\(^2\)Imamura et al. PAI 2008;19:270-4
### Do allergic individuals heed PAL?

<table>
<thead>
<tr>
<th>Statement</th>
<th>UK (n=184)</th>
<th>Australia (n=246)</th>
</tr>
</thead>
<tbody>
<tr>
<td>“May contain nuts”</td>
<td>80% avoid</td>
<td>75% avoid</td>
</tr>
<tr>
<td>“May contain traces of nuts”</td>
<td>60% avoid</td>
<td>45% avoid</td>
</tr>
<tr>
<td>“Does not contain nuts but made in a factory that uses nuts”</td>
<td>40% avoid</td>
<td>35% avoid</td>
</tr>
</tbody>
</table>

Noimark et al. PAI 2009
Zurzolo et al. MJA 2013

But wording used bears no relation to risk of contamination\(^1,2\)

\(^1\) Pele et al. Food Add Contam 2007; 24:1334-44.  
\(^2\) Hefle et al. JACI 2007; 120:171-6.
The reality:

- Wide inconsistencies in labelling
- Foods can become contaminated with residues of allergenic foods at multiple points:
  - Harvesting on farms
  - Storage & transportation
  - Manufacture: shared equipment
- Measures to reduce cross-contamination not uniform across manufacturers
Not a trace!

- Cow’s milk
- Egg
- Wheat
- Soya
- Peanut

ED_{05}  

ED_{01}  

10mm
### What do consumers want?

<table>
<thead>
<tr>
<th>Label Type</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not suitable for someone with X allergy</td>
<td>1</td>
</tr>
<tr>
<td>May contain traces of X</td>
<td>3</td>
</tr>
<tr>
<td>May contain</td>
<td>3</td>
</tr>
<tr>
<td>Packaged in a facility that also processes X</td>
<td>4</td>
</tr>
<tr>
<td>Manufactured on equipment that process X</td>
<td>5</td>
</tr>
</tbody>
</table>

n=623

DunnGalvin A. Impact of food labelling practices in individuals with food allergy. 2015
Management

1. Dietary Avoidance

2. Treatment of accidental reactions

3. Desensitisation?
Accidental/inadvertent reactions are common:

- 1 in 8 peanut-allergic children experienced at least one accidental reaction every year\(^1\)
- Over 50% of 512 infants had at least one reaction over 3 years follow-up\(^2\)

Avoidance is, therefore, inadequate on its own.

All food-allergic children need:
- Personalised Allergy Management Plan
- Rescue treatment (which may include AAI)

1. Dietary Avoidance

2. Treatment of accidental reactions

3. Desensitisation?
Desensitisation - does it work?

Systematic review with meta-analysis

Effectiveness and safety of orally administered immunotherapy for food allergies: a systematic review and meta-analysis

Ulugbek Numatov¹, Graham Devereux², Allison Worth¹, Laura Healy¹ and Aziz Sheikh¹*

¹Allergy and Respiratory Research Group, Centre for Population Health Sciences, The University of Edinburgh, Medical School, Doorway 3, Teviot Place, Edinburgh EH8 9AG, UK
²Department of Child Health, Royal Aberdeen Children’s Hospital, University of Aberdeen, Aberdeen AB25 2ZP, UK

(Submitted 3 January 2013 – Final revision received 15 May 2013 – Accepted 19 June 2013 – First published online 15 August 2013)
But is it safe as a routine treatment?

- OIT involves an increased risk for allergic reactions, including potentially life-threatening symptoms (bronchial/laryngeal reactions, adrenaline use).

- OIT-related reactions are largely unpredictable (unrelated to cofactors/dose increases).

- GI symptoms are common - no effective treatment available.

- High risk patients: patients with persistent & severe allergy do not fare well on OIT (high sIgE/SPT, asthma, bronchial/laryngeal $).

- Strict long-term commitment & supervision is required to ensure compliance & control of underlying allergic diseases (mainly asthma), especially in teenagers.
What happens after initial desensitisation?

- **Failure to desensitize during build-up phase 10-20%**
- **Partial desensitization**: failure to reach full maintenance dose 10-20%
- **Desensitization**: failure during tolerance food challenge 10-20%
- **Tolerance**: no reactivity during tolerance food challenge 40-60%

**Dosing**
- **Initial modified dose escalation**
- **Weekly / bi-weekly dose escalation**

**Phases**
- **Build-up phase**
- **Maintenance phase**
- **Discontinuation-elimination diet**

Nowak-Wegrzyn & Sampson. JACI 2011; 127(3):558-73
Certificate of Advanced Study and MSc in Allergy

Modules and Short Courses

- **The Scientific Basis of Allergy**
  - Module 1

- **Diagnosis & Treatment**
  - Module 2

- **The Cutting Edge of Allergy**
  - Module 3

- **Allergic Gastrointestinal Disease**
  - Optional Module 1

- **Allergic Airways Disease and Asthma**
  - Optional Module 3

- **Rhinitis and Hayfever**
  - Optional Module 4

- **Allergic Skin Disease**
  - Optional Module 5

- **Paediatric Allergy**
  - Optional Module 6

- **Food Hypersensitivity**
  - Optional Module 2

- **Research Skills**
  - Dissertation Module

https://www.imperial.ac.uk/medicine/study/postgraduate/masters-programmes/msc-pg-cert-allergy/

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