Alimentary Myths

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Primary food allergy is acquired in early childhood.
Food allergy in adults is mediated by primary sensitisation to inhalant allergens.

High sensitivity and high negative predictive value of extract based diagnostic tests in primary food allergy and a low sensitivity of extract based diagnostic tests particularly in birch pollen related food allergy.
Allergen Recognition Patterns in Walnut Allergy Are Age Dependent and Correlate with the Severity of Allergic Reactions

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JACI in pract 2019
Identification and implication of an allergenic PR-10 protein from walnut in birch pollen associated walnut allergy

Andrea Wangorsch¹, Annette Jamin¹, Jonas Lidholm², Nora Gräni³, Claudia Lang³, Barbara Ballmer-Weber³,⁴, Stefan Vieths¹ and Stephan Scheurer¹

Mol Nutr Food Res 2017

- Walnut Tris-HCl-Extract
- 1. BB 11 without inhibitor
- 2. BB 11 + 10µg/ml rJug s PR10
- 3. BB 11 + 50µg/ml rJug s PR10
- 4. BB 11 + 1mg/ml walnut extract (25mM Tris-HCl, 150mM NaCl)
- 5. BB 11 + 50µg/ml BSA
- 6. Ab control

15 CH patients with positive OFC with walnut sensitisation to walnut extract: 40%
sensitisation to rJug r 5: 93%

AA sequence identity: 67% with Bet v 1.01
74% with Mal d 1
14 allergenic ingredients must be declared

<table>
<thead>
<tr>
<th>Cereals</th>
<th>Nuts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crustaceans</td>
<td>Celeriac</td>
</tr>
<tr>
<td>Fish</td>
<td>Mustard</td>
</tr>
<tr>
<td>Egg</td>
<td>Sesame seed</td>
</tr>
<tr>
<td>Peanut</td>
<td>Sulphur dioxide/sulphites</td>
</tr>
<tr>
<td>Soybean</td>
<td>Lupin</td>
</tr>
<tr>
<td>Milk</td>
<td>Molluscs</td>
</tr>
</tbody>
</table>

*and products thereof
Prevalence of sensitization to foods in Europa (adults)

- Any: 24%
- Hazelnut: 18%
- Peach: 12%
- Celeriac: 9%
- Apple: 7%
- Carrot: 8%
- Kiwi: 7%
- Wheat: 8%
- Tomato: 7%
- Sesame: 8%
- Shrimp: 7%

IgE
Cyclophilin – a novel cross-reactive determinant in PN

Analysis of 15 sera with IgE to peanut but not to Ara h 1,2,3,6,8,9, CCD, profilin

IgE to PN extract inhibited by grass pollen

identification and characterisation: peanut cyclophilin
new pollen-related peanut allergen

Birch pollen (Bet v 7), olive pollen (Ole e 15) molds (Asp f 11,27, Mala s 6), mites (Der f 29) carrot, tomato (Sola a 11),......

Mattsson, Lidholm et al., abstract EAACI 2018
Molecular allergy guide, PAI 2016
Accidental food allergy reactions: Products and undeclared ingredients

157 food allergics
n=73 patients with 151 accidental reactions/y
51 food samples analysed
- Milk
- Peanut
- Sesame
- Hazelnut
- Pecan nut
- Walnut
- Hen’s egg
- Celeriac
Relevance of Oleosins?

Schematic model of an oil body

peanut: Ara h 10/11/14/15
sesame: Ses i 4/5
hazelnut: Cor a 12/13

Uta Jappe et al. Curr Allergy Asthma Rep 2017
Oleosins are lipophilic proteins and may not be well represented in aqueous extracts.

Immunoblot with rabbit-anti-OAP:
1: natural HN-OAP-Fraktion
2: HN-extract, not defatted
4-12: commercial HN-extract
Cor a 12: 17kDa
Cor a 13: 14 kDa

Zuidmeer et al. Clinical and translational Allergy 2014
Double blind placebo controlled food challenge is the gold standard of food allergy diagnosis.
Accurate oral FC requires a cumulative dose on a subsequent day

Niggemann et al. JACI 2012

490 challenges
7 doses
30 min interval

DBPCFC
(n=151)

1d
cumulative dose
blinded

open FC
(n=339)

1d
cumulative dose
open

490 challenges
positive
(n=251, 51%)

1d
positive (n=38, 16%)
with cumulative dose

negative
(n=239, 49%)
Cumulatived threshold for objective symptoms in 6 allergics with hazelnut or peanut allergy

- Higher threshold with chocolate bars than dessert matrix
- Lower gastric emptying with chocolate bars (MRI)
Positive reaction to placebo in children

Placebo challenges
n = 740

Placebo negative
n = 719 (97%)

Placebo positive
n = 21 (3%)

early reactions
urticaria
n=5 (24%)
GI
n=3 (14%)

combined reactions
eczema, urticaria
n=1 (5%)

late reactions
eczema
n=12 (57%)

Graph showing mean (±SEM) for different reaction types:
- Respiratory
- Gastrointestinal
- Skin
Positive reaction to placebo

**Placebo challenges in children (n = 132)**

- Placebo negative: n = 115 (87.1%)
- Placebo positive: n = 17 (12.9%)

Vlieg-Boerstra et al. Allergy 2007

**Placebo challenges (n = 436)**

- Placebo negative: n = 393 (90%)
- Placebo positive: n = 43 (10%)

Ballmer-Weber et al. JACI 2015
196 patients, investigating for drug allergy
Hospital anxiety and depression sale (questionnaire with 2x7 questions)
Drug provocation: placebo-4doses of drugs

60 patients abnormal HADS score (90% females)
54 patients (28%) placebo reaction (pruritus, asthenia, dyspnea)

Placebo reaction correlated significantly with
- history of severe reaction (p<0.001)
- abnormal HADS score (p<0.001): OR 117.
Is food challenge, in particular DBPCFC the gold standard of food allergy diagnosis?

False negative food challenges:
- drugs
- missing cofactors
- blinding/matrix
- induction of short term non-reactivity

False positive food challenges:
- reaction to a matrix component
- placebo reactions
Bet v 1 mediated food allergy is always mild
<table>
<thead>
<tr>
<th>rMal d 1 dose (mg)</th>
<th>patient 1</th>
<th>patient 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01</td>
<td>neg</td>
<td>OAS 10</td>
</tr>
<tr>
<td>0.10</td>
<td>OAS 10</td>
<td>OAS 25</td>
</tr>
<tr>
<td>1.00</td>
<td>OAS 60</td>
<td>OAS 60</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pf↓ 50% hoarsness, cough</td>
</tr>
</tbody>
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DBPCFC with rMal d 1
Bolhaar et al. Clin Exp Allergy 2005
Anaphylactic reactions to apple in a birch-endemic area
Le et al. Int Arch Allergy Immunol 2013
Europrevall: CRD hazelnut allergy

87 patients DBPCFC+ve & 22 anaphylaxis cases

<table>
<thead>
<tr>
<th>Protein</th>
<th>OR</th>
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<tbody>
<tr>
<td>Glycinin</td>
<td>10.5</td>
</tr>
<tr>
<td>2S-Albumin</td>
<td>10.1</td>
</tr>
</tbody>
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Datema et al. Allergy 2017
Sensitisation pattern in severe reaction

- Cor a 9 or Cor a 14: associated with severe symptoms
- Subgroup of patients with severe reactions
- Cor a 1 “only”: 34%

Datema et al. Allergy 2017
Soybean allergy in patients allergic to birch pollen: Clinical investigation and molecular characterization of allergens

Diana Mittag, MS, Stefan Vieths, PhD, Lothar Vogel, PhD, Wolf-Meinhard Becker, PhD, Hans-Peter Rihs, PhD, Arthur Helbling, MD, Brunello Wüthrich, MD, and Barbara K. Ballmer-Weber, MD

Zurich and Bern, Switzerland, and Langen, Borstel, and Bochum, Germany
Empty stomach with rapid rise of gastric pH and low protein content in food (apple 0.3%) → absorption of large amounts of IgE-reactive Bet v 1 related food allergens

Schulten et al. Mol Nutr Food Res 2011
Sensitisation to Bet v 1 homologous food proteins often silent or associated with symptoms localised to the oral mucosa.

But more severe reactions observed in Bet v 1 related food allergy when consumed on an empty stomach with a high amount. Particularly observed: Gly m 4, Api g 1, Cor a 1.