

Universiteit Antwerpen belspo

# Food allergy: pathogenesis & clinics

Didier EBO  
Immunology - Allergology - Rheumatology

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## Content

1. Definitions
2. Pathogenesis (IgE-mediated)
3. Causes
4. Clinics & natural course
5. Diagnosis
6. Therapy

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## 1. Definitions

- Babylonian speech confusion
- Classification (Ortolani C, Allergy 1995;50(S20)8-13)

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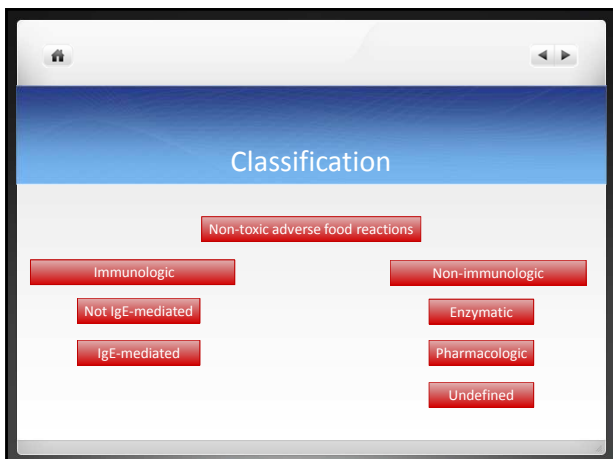
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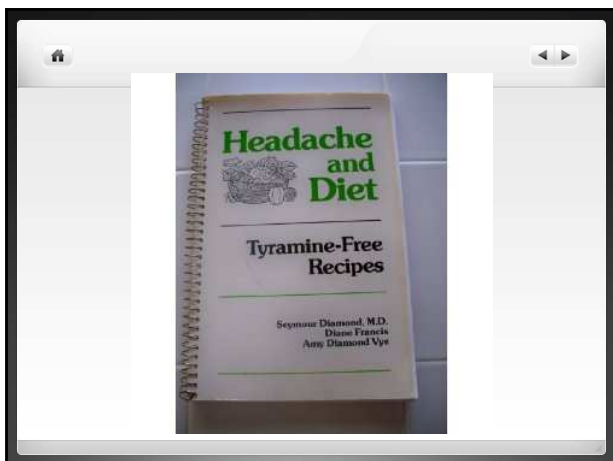
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**IgE-mediated food allergy**

- Most prevalent, increasing
- Most severe (fatalities)
- Changing (geographical and age-related patterns > prognostic)

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**Prevalence and distribution of sensitization to foods in the European Community Respiratory Health Survey: a EuroPrevall analysis**

P. Burney<sup>1</sup>, C. Summers<sup>2</sup>, S. Chinn<sup>1</sup>, R. Hooper<sup>1</sup>, R. van Ree<sup>3</sup> & J. Lidholm<sup>4</sup>

<sup>1</sup>Respiratory Epidemiology and Public Health, Imperial College, London, UK; <sup>2</sup>Corporate Development and Performance, Greater Manchester Police Headquarters, Manchester, UK; <sup>3</sup>Department of Experimental Immunology and Department of Otorhinolaryngology, Academic Medical Centre, Amsterdam, The Netherlands; <sup>4</sup>Phadia AB, Uppsala, Sweden

To cite this article: Burney P, Summers C, Chinn S, Hooper R, van Ree R, Lidholm J. Prevalence and distribution of sensitization to foods in the European Community Respiratory Health Survey: a EuroPrevall analysis. *Allergy* 2010; **65**: 1182-1188.

- 24 foods
- 7,7% Iceland > 16,8% Belgium > 24,6% Portland (USA)

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	Germany (%)	Italy (%)	France (%)	Belgium (%)	USA (%)	Australia (%)	Spain (%)	Norway (%)	Sweden (%)	Kingdom (%)	Iceland (%)	Switzerland (%)	Estonia (%)	Overall (%)
Fish	0.9	0.0	0.0	0.0	0.0	0.0	0.5	0.3	0.3	0.2	0.0	-	0.0	0.2
Egg	0.3	0.0	0.1	0.6	0.0	0.5	0.3	1.5	0.5	0.5	0.4	-	0.0	0.4
Cow's milk	1.3	2.1	0.1	0.6	2.3	1.1	0.1	1.3	1.3	0.5	0.0	-	0.0	0.8
Mustard	2.2	0.6	2.6	0.0	0.0	1.0	0.9	0.3	0.4	0.6	0.3	0.0	0.0	0.9
Melon	1.8	2.8	3.6	3.4	0.0	2.1	1.2	0.6	0.5	0.5	0.0	0.0	0.0	1.6
Pipsey seed	3.2	3.6	4.1	0.9	2.0	1.9	1.1	0.7	0.6	0.5	0.0	0.0	0.0	1.8
Soy	3.3	3.0	3.2	1.7	4.7	1.8	1.9	0.8	0.0	1.0	0.0	-	1.2	3.1
Sunflower	3.7	2.1	4.0	2.0	2.0	1.9	1.9	1.3	1.2	1.5	0.0	0.0	0.0	2.1
Walnut	3.3	3.1	3.7	2.5	2.1	2.1	3.1	0.6	1.1	0.8	0.0	0.0	0.0	2.2
Barnes	3.0	4.2	4.4	4.5	0.0	2.8	2.4	2.2	1.6	1.0	1.0	0.0	0.0	2.5
Peanut	4.2	3.6	3.0	2.0	9.3	3.0	1.9	0.8	1.0	1.5	1.2	-	-	2.6
Buckwheat	3.8	3.7	3.6	2.0	2.5	3.6	2.2	1.8	1.0	1.9	1.0	9.7	-	2.8
Rice	3.8	4.7	3.9	1.7	4.8	2.3	3.0	1.1	0.8	1.9	0.3	4.9	-	2.9
Tomato	5.6	4.5	3.8	3.7	4.7	4.1	3.5	1.6	1.8	7.7	0.8	0.0	-	3.3
Corn	5.7	5.2	3.9	2.9	4.9	3.4	3.2	1.4	1.7	2.0	0.7	3.2	-	3.3
Celery	8.6	6.5	4.3	4.6	4.2	2.1	1.0	2.9	4.0	1.4	0.0	0.0	-	3.5
Kiwifruit	7.9	6.9	6.0	6.2	6.2	4.1	1.8	3.2	3.4	1.6	0.7	0.0	0.0	3.6
Carrot	7.7	6.2	4.4	4.3	2.1	3.1	1.7	3.6	3.1	1.7	0.0	0.0	0.0	3.6
Peanut	5.6	4.1	4.2	3.2	4.9	5.1	3.1	2.2	2.1	2.1	1.0	9.7	-	3.7
Apple	10.3	5.7	4.7	7.0	1.7	2.0	2.2	5.4	5.1	1.0	0.0	4.0	0.0	4.2
Wheat	6.0	6.7	5.5	4.3	6.1	7.9	3.4	3.0	2.3	3.9	0.7	7.3	-	4.6
Strawberry	4.4	10.2	7.0	5.1	0.0	2.4	4.9	6.3	4.8	6.2	2.8	0.0	-	5.4
Almond	11.7	7.5	5.6	8.2	3.5	3.1	3.8	2.7	6.5	2.9	0.3	9.6	0.0	5.4
Cherry	14.7	7.7	5.0	8.0	14.9	4.1	2.6	12.8	11.6	4.9	0.4	12.6	3.9	7.2
Whey food	21.8	21.9	14.1	16.8	24.6	15.4	11.1	21.7	17.2	14.5	7.7	-	-	16.2

\*For each food, each country's prevalence is determined by averaging over centres within that country, and overall prevalence is determined by averaging over all countries.

### Prevalence and distribution of sensitization to foods in the European Community Respiratory Health Survey: a EuroPrevall analysis

P. Burney<sup>1</sup>, C. Summers<sup>2</sup>, S. Chinn<sup>1</sup>, R. Hooper<sup>1</sup>, R. van Ree<sup>3</sup> & J. Lidholm<sup>4</sup>

<sup>1</sup>Respiratory Epidemiology and Public Health, Imperial College, London, UK; <sup>2</sup>Corporate Development and Performance, Greater Manchester Police Headquarters, Manchester, UK; <sup>3</sup>Department of Experimental Immunology and Department of Otorhinolaryngology, Academic Medical Centre, Amsterdam, The Netherlands; <sup>4</sup>Phadia AB, Uppsala, Sweden

To cite this article: Burney P, Summers C, Chinn S, Hooper R, van Ree R, Lidholm J. Prevalence and distribution of sensitization to foods in the European Community Respiratory Health Survey: a EuroPrevall analysis. *Allergy* 2010; **65**: 1182-1188.

- 24 foods
- 7,7% Iceland > 16,8% Belgium > 24,6% Portland (USA)
- Cave sensitization DOES NOT mean allergy !!!

Toxicology 278 (2010) 319–325

Contents lists available at ScienceDirect

**Toxicology**

journal homepage: [www.elsevier.com/locate/toxicol](http://www.elsevier.com/locate/toxicol)

Review

Food allergy – science and policy needs – The UK Food Standards Agency Research Programme

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 Exposure  
 Antibody  
 Prevalence

**ABSTRACT**

Food allergy is a significant health issue in the UK, affecting between 1 and 2% of adults and 5 and 8% of children. The UK Food Standards Agency seeks to ensure the safety of food allergic consumers by providing them with information and guidance on food choices. Since 1995, with the aim of addressing important policy issues and improving the quality of the support and guidance available for food allergic consumers, the Agency (and before that the Ministry of Agriculture, Fisheries and Food), has had a programme of research dedicated to investigating the causes and mechanisms of food allergy and delivering benefits for UK consumers. In this paper, we outline some of the major scientific challenges that the programme has sought to address. We reflect on how the findings have been used as a basis for the development of sound, evidence-based policy and advice for UK consumers, and the current direction of research being supported by the programme.

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**Further fatalities caused by anaphylactic reactions to food, 2001-2006**

*To the Editor:*

In 2001 we reported a group of 32 individuals who died because of food-induced anaphylaxis. The cases were accumulated in a registry kept by members of the American Academy of Allergy, Asthma & Immunology and The Food Allergy and Anaphylaxis Network.<sup>1</sup> The registry,

Bock A et al. J All Clin Imm 2007

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**TABLE I. Food fatalities 2001-2006**

Patient no.	Age (y)	M/F	Date	Culprit	Asthma	Previous history	Food	Location	Timely epinephrine
1	32	M	3/11/2001	Nuts	Yes	Yes	Nut bowl	Restaurant	No
2	16	M	5/9/2001	Walnut	Yes	Yes	Chinese food	School, cooking class	Probably
3	9	M	5/18/2001	Peanut	Yes	Yes	Cookie	School outing	No
4	24	F	11/26/2001	Peanut	Yes	Yes	Chinese food	Home	No
5	25	F	10/30/2001	Nut meats	Yes	Yes	Candy	Home of friends	No
6	16	M	11/5/2002	Milk	Yes	Yes	Bread	Home	Unk
7	31	M	12/13/2002	Peanut	Yes	Yes	Catered food	Office party	No
8	50	M	12/24/2002	Nut	Yes	Yes	Cookie	Home	No
9	12	F	3/14/2003	Peanut	Unk	Unk	Egg roll	Unk	Unk
10	18	M	6/21/2003	Peanut	Unk	Unk	Wrap	Unk	Unk
11	32	M	3/15/2003	Shrimp	Yes	Yes	Meal	Restaurant	No
12	29	M	6/13/2003	Peanut	Yes	Yes	Meal	Restaurant	No
13	29	M	4/24/2000	Almond	Yes	Yes	Candy	Office	Yes
14	17	F	12/26/1986	Nuts	Yes	Yes	Cookie	Home of friends	No
15	21	F	10/9/2003	Peanut	Yes	Yes	Brownie	College	No
16	18	M	1/20/2004	Shrimp roll	Yes	Unk	Shrimp roll	Restaurant	No
17	27	M	2/1/2004	Peanut	Unk	Yes	Baked clam	Home	No
18	17	M	2/8/2004	Hazelnut	Yes	Yes	Candy	Home of friends	No
19	17	F	4/6/2004	Peanut	Yes	Yes	Peanut butter	Camp	No
20	34	F	5/29/2004	Peanut	Unk	Yes	Thai dish	Home	No
21	5	M	8/1/2004	Peanut	Unk	No	Peanuts	Home	No
22	9	M	7/22/2004	Milk	Unk	Unk	Milk	Camp	Yes
23	22	F	10/29/2004	Peanut	Yes	Yes	Dessert	Restaurant	No
24	14	F	1/22/2005	Peanut	Yes	Yes	Egg roll	Restaurant	No
25	36	M	3/21/2001	Peanut	Yes	Yes	Brownie	Work	No
26	17	M	3/5/2005	Milk/whey	Yes	Yes	Protein shake	Home	No
27	7	F	3/22/2005	Milk	Yes	Yes	Chocolate mix	Home	Unk
28	11	F	5/1/2005	Peanut	Unk	Yes	Candied apple	Carnival	Unk
29	40	M	2/8/2006	Tree nut	Unk	Yes	Cookie	Work	Yes
30	13	F	4/13/2006	Peanut	Yes	Yes	Wrap	Fast food in mall	No
31	16	M	8/1/2006	Peanut	Yes	Yes	Cookie	Home of friends	No

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**Further fatal allergic reactions to food in the United Kingdom, 1999-2006**

We report 48 additional deaths meeting these criteria from 1999 to 2006. Ages ranged from 5 months to 85 years, with a median age of 21 years. The age distribution is similar to that in the previous report, with 7 aged 0-10 years, 26 aged 11-30 years, and 15 aged more than 30 years. There were 22 men (46%) reacting to milk (4), peanuts (3), nuts (2), fish (1) shellfish (1), snail (1), sesame (1), egg (1), and uncertain (8); and 26 women reacting to milk (2), peanuts (6), nuts (7), tomato (1), and uncertain (10). The circumstances comprised at home (14), the home of friends or relatives (10) at work (1), at school (2), at nursery (1), in a restaurant (11 of which 4 were abroad), out and about (6, of which 4 were from takeout food), in camp (2), and a wedding

Pumphrey RS et al. J All Clin Imm 2007

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## 2. Pathogenesis of IgE-mediated allergy

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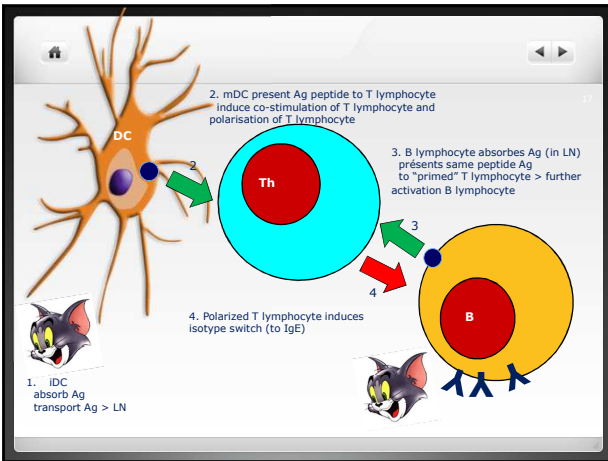
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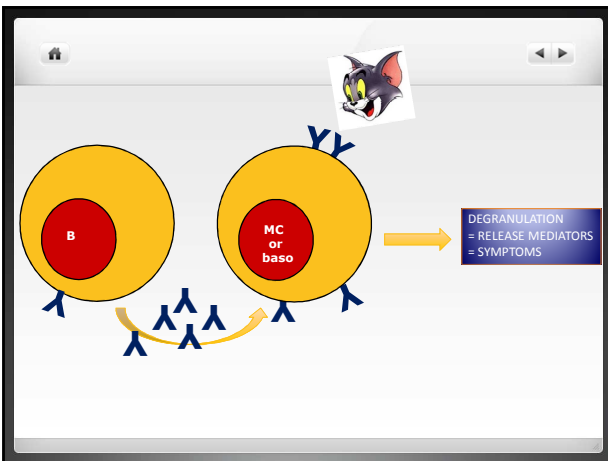
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## 2. Pathogenesis: primary food allergy

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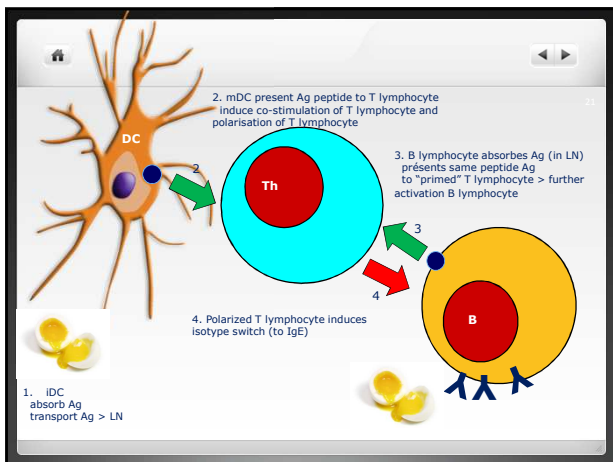
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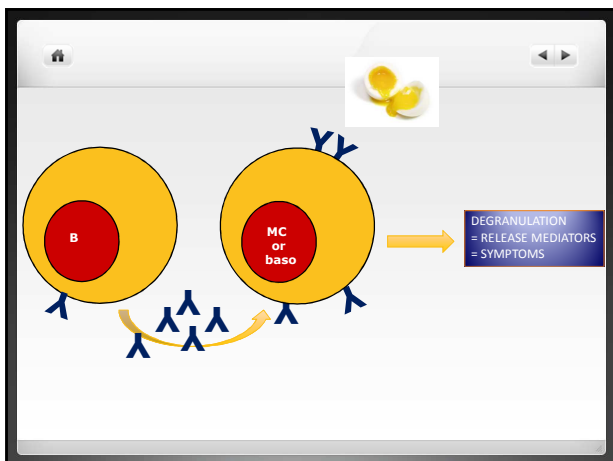
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## 2. Pathogenesis: secondary food allergy

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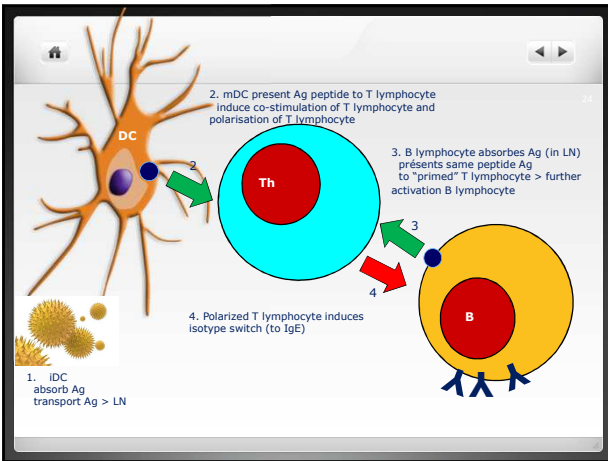
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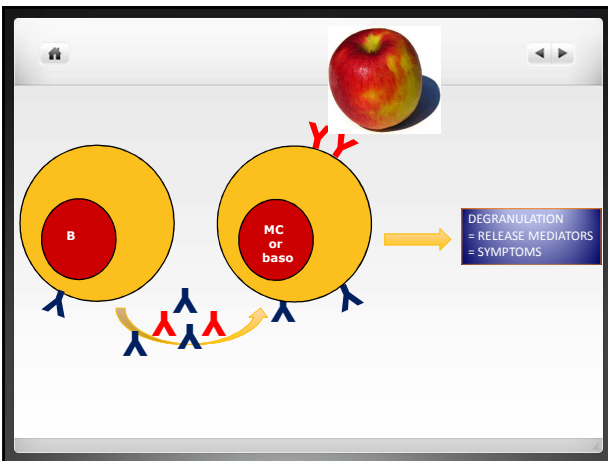
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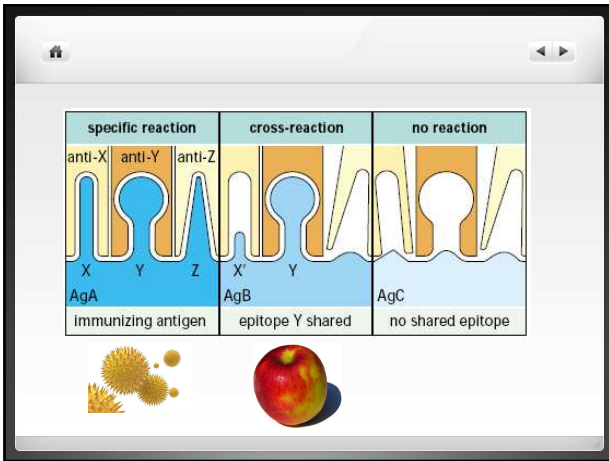
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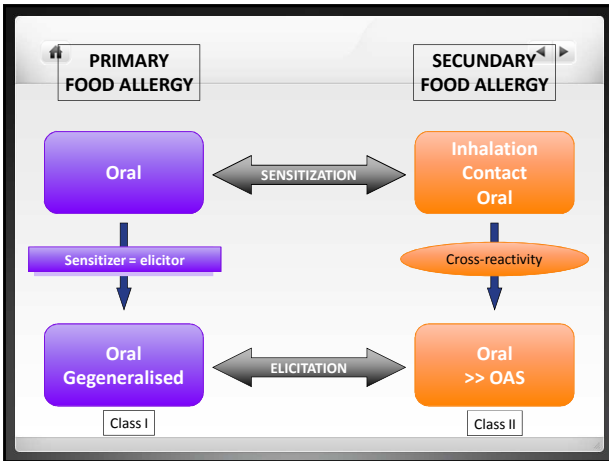
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2. Pathogenesis: components

An allergen = collection of allergen components that can all trigger production of sIgE antibodies

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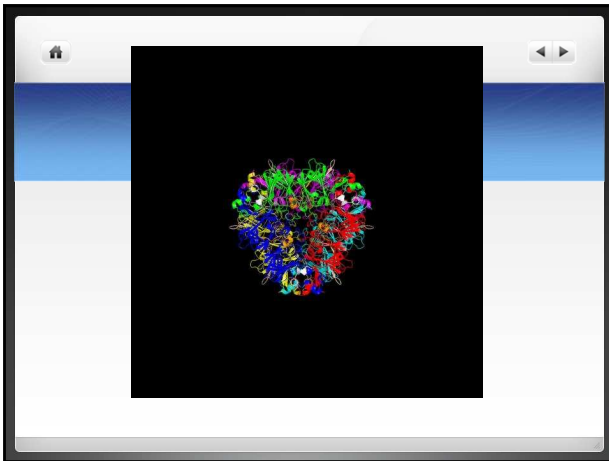
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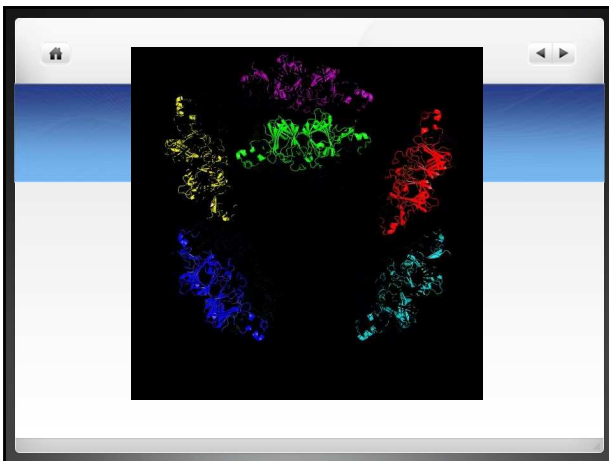
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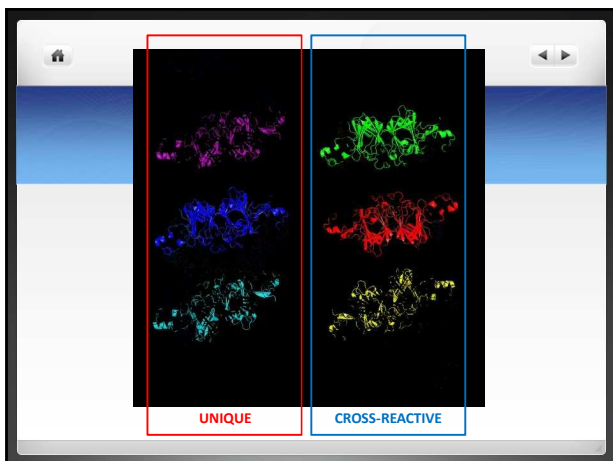
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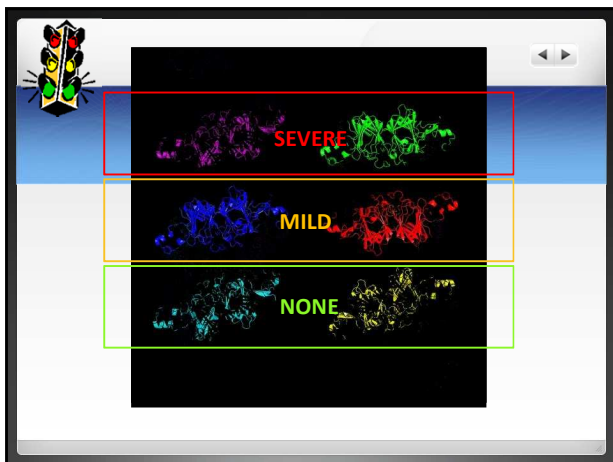
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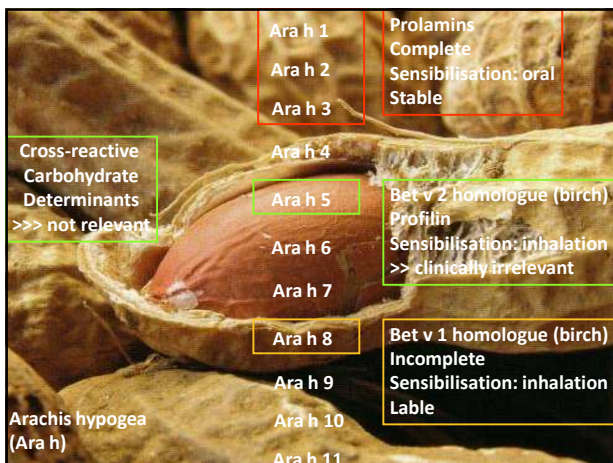
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**3. Causes**

- 7 super families: 65% of all food allergies
- Prognostic sensitization profiles
  - Geographic
  - Age-related

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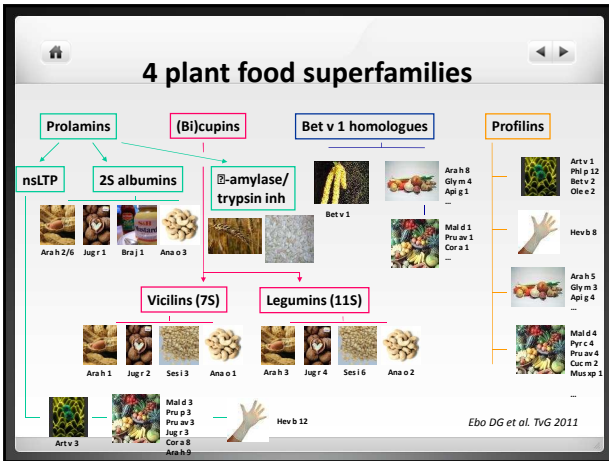
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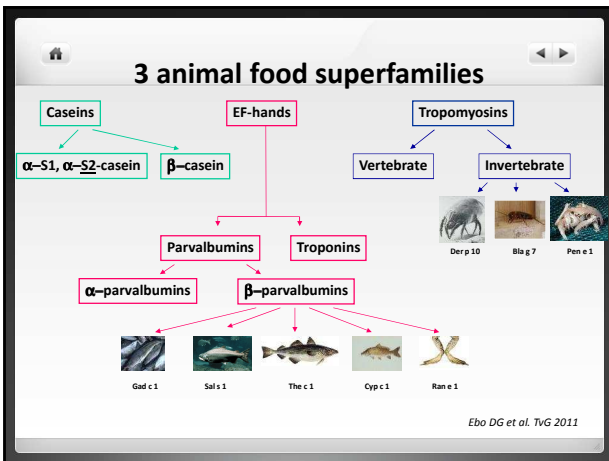
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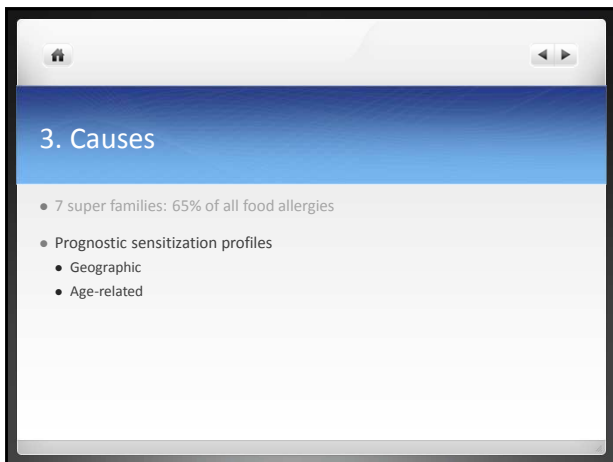
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**CRD hazelnut (UA/UZA)**

**Cor a 1: Bet v 1 homologues**  
 Adults, adolescents  
 Inhalation (birch)  
 Mild (OAS)

**Cor a 9: legumine**  
**Cor a 11: vicillin**  
 (Young) children  
 Route sensitization???  
 Severe

**Cor a 8: ns lipid transfer proteins**  
 Adults

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Verweij MM, Hagendorens MM, De Knop KJ, Bridts CH, De Clerck LS, Stevens WJ, Ebo DG. Young infants with atopic dermatitis can display sensitization to Cor a 9, an 11S legumin-like seed-storage protein from hazelnut (*Corylus avellana*).  
 Pediatr Allergy Immunol 2010.  
 © 2010 John Wiley & Sons A/S

**Submitted:**  
 Verweij MM, Hagendorens MM, Trashin S, Cucu T, De Meulenaer B, Devreese B, Bridts CH, De Clerck LS, Ebo DG  
**Age-dependent sensitization to the 7S-vicilin like protein Cor a 11 from hazelnut (*Corylus avellana*) in a birch endemic region.**

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4. Clinics & natural course

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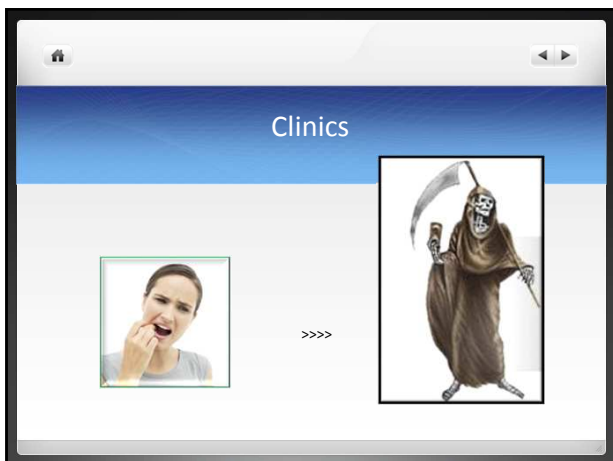
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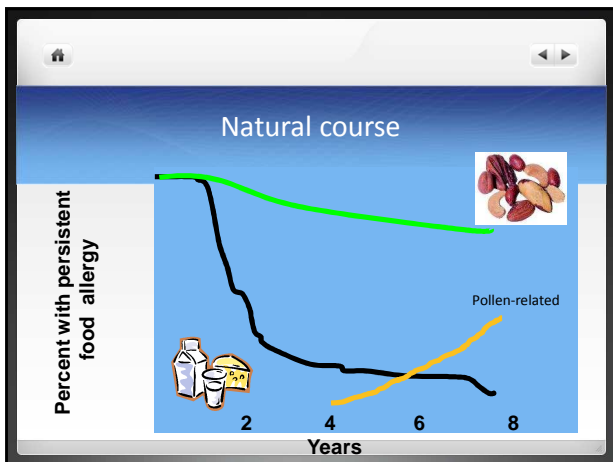
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- A presentation slide titled "5. Diagnosis". It contains a bulleted list of diagnostic methods:
- History
  - Total IgE
  - sIgE + components (prognostic patterns)
  - Skin tests
  - Basophil activation tests
  - Food challenges
    - Double blind placebo controlled (adults)
    - Open (children)

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6. Therapy

- Omalizumab (anti-IgE)
- Immunotherapy
  - Pollen (SCIT, SLIT): pollen-related food allergy
  - Food (oral)

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**A phase II, randomized, double-blind, parallel-group, placebo-controlled oral food challenge trial of Xolair (omalizumab) in peanut allergy**

nut protein. While no firm conclusions can be drawn from these limited data, the results are consistent with findings of a similar anti-IgE preparation, HU-901<sup>5</sup>—that is, although the study was stopped early and most subjects on omalizumab did not reach the predefined study endpoints, omalizumab may increase the tolerability to peanut in a subset of patients with peanut allergy and may deserve further investigation.

Sampson H et al. J All Clin Imm 2011 (May)      ~ 300 mg/2 wk (€ 400 / 150 mg)  
 € 8000 / year (life-long)  
 Not reimbursed

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doi: 10.1111/j.1365-2222.2011.03794.x      Clinical & Experimental Allergy 41, 1177–1200  
 © 2011 Blackwell Publishing Ltd

**BSACI GUIDELINES**

**Immunotherapy for allergic rhinitis**

Although some studies have shown limited improvement of oral allergy symptoms following immunotherapy with birch pollen extracts [74–79] others have disagreed. Improvements appear more likely to occur in patients over 20 years who are monosensitized to birch pollen and with more intense oral symptoms. Resolution is less likely in patients treated with combined grass and tree pollen immunotherapy [75]. Symptoms may become worse [75, 80] and new sensitizations may develop while on treatment [81]. Symptoms may also recur once treatment has been discontinued. On the basis of current evidence, the presence of oral allergy syndrome is neither an indication nor a contra-indication to birch pollen SCIT or SLIT.

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Immunotherapy in food allergy

- SCIT / oral
- Option in controlled trials
- Desensitization (temporary) vs. induction of tolerance (definitive)
  - Partial or total
- Frequent (controllable side effects)
- Need additional studies before entrance in mainstream clinical practice

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6. Therapy

- Omalizumab (anti-IgE)
- Immunotherapy
  - Pollen (SCIT, SLIT): pollen-related food allergy
  - Food (oral, SLIT, SCIT)
- >>> NO CURE (avoidance)



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**TERRIFYING**

poor labels  
hidden allergens  
unawareness  
new allergies

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**TERRIFYING**

poor labels  
hidden allergens  
unawareness  
new allergies

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**% positive test**

	Peanut	Hazelnut
 "May contain"	25	36
"Present in environment"	25	23
No warning	11	25

	Peanut	Hazelnut
 "May contain"	43	79
"Present in environment"	7	60
No warning	25	50

Pele M et al. Food Addit Contam. 2007  
Dec;24(12):1334-44

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**TERRIFYING**

poor labels  
**hidden allergens**  
unawareness  
new allergies

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**Anaphylaxis from Passive Transfer of Peanut Allergen in a Blood Product**

**TO THE EDITOR:** Anaphylactic reactions to blood transfusions are rare and their causes often remain elusive.<sup>1</sup> The inducement of clinically relevant allergic reactions by means of the passive transfer of IgE in blood products has been well documented.<sup>2</sup> In an editorial comment written in 2003, Erick speculated on the possibility that allergic transfusion reactions could be induced by the passive transfer of food allergens.<sup>3</sup> We present such a case.

A 6-year-old boy with acute lymphoblastic leukemia had an anaphylactic reaction while receiving a leukoreduced pooled buffy-coat product with ABO-identical platelets. During transfusion, rash, angioedema, hypotension, and difficult breathing occurred. The patient recovered within 30 minutes after resuscitation with adrenaline. His serum level of mast-cell tryptase, measured directly after the reaction, was 24  $\mu\text{g}$  per liter (normal level, <5), which confirmed the clinical pic-

Jacobs JFM et al. NEJM 2011

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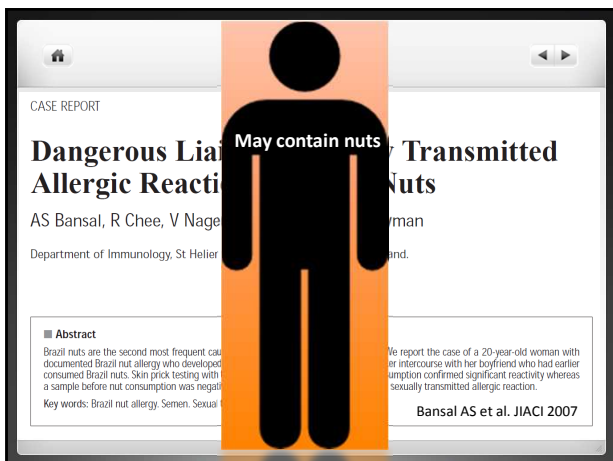
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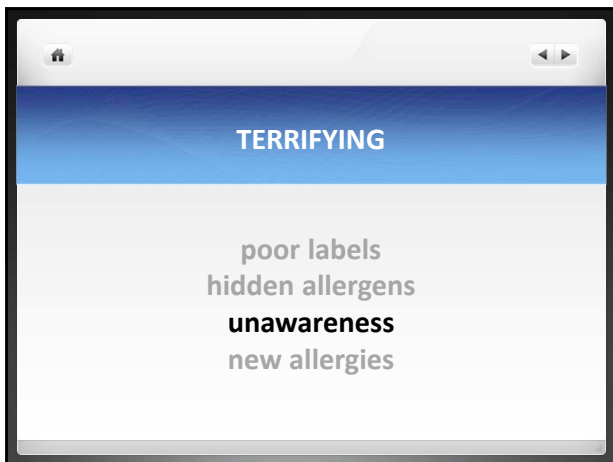
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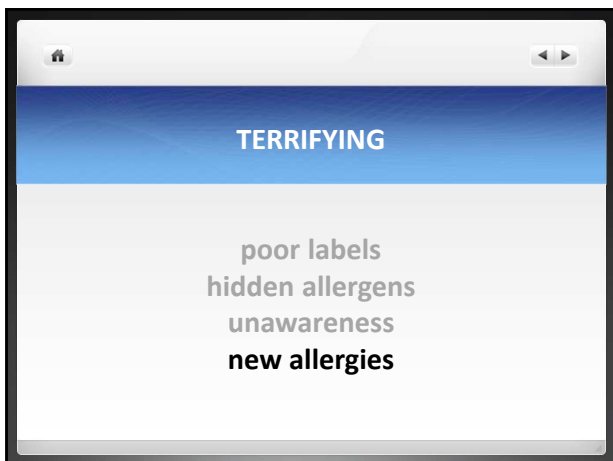
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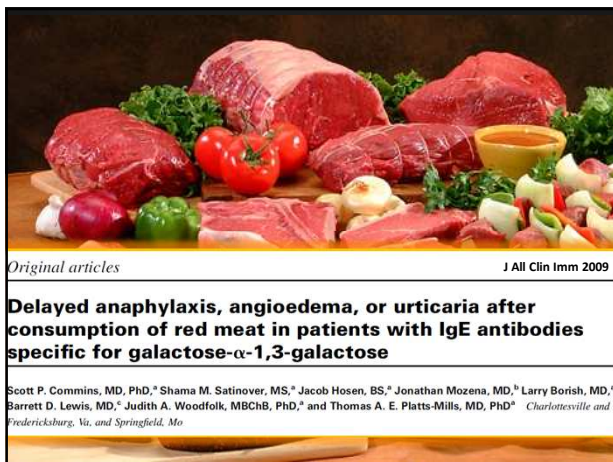
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 Universiteit Antwerpen 

**Thanks for your attention**

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