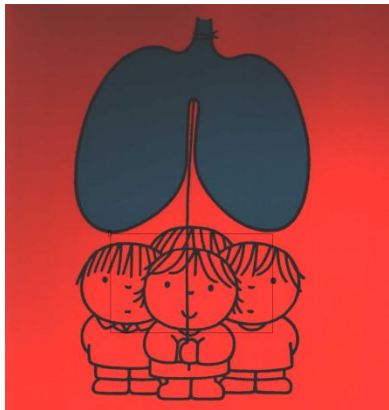


# Food allergy and asthma in children – Comorbidity or coincidence?



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# Learning aims

**At the end of this presentation you will be able to:**

- **Critically review the literature on the relationship between food allergy & asthma**
- **Distinguish between sensitization and allergy**
- **Interpret polysensitization in the clinical context of a child with asthma**

# Current wisdom

**“many allergists will prescribe EpiPen to any patient with both asthma and food allergy”**

## **3.4.1. Asthma.**

**In summary:** Asthma and FA often coexist in pediatric and adult patients. FA is associated with severe asthma.

**Whether or not you agree with this statement depends heavily on how one approaches the diagnosis of food allergy**

Hugh A. Sampson, MD,<sup>h</sup> Robert A. Wood, MD,<sup>i</sup> Marshall Plaut, MD,<sup>j</sup> Susan F. Cooper, MSc,<sup>j</sup> and Matthew J. Fenton, PhD<sup>j</sup>

J Allergy Clin Immunol Dec 2010

# Martin, 8 yrs of age



**History of atopic eczema, current asthma and mild rhinitis**

**Age 1 yr "allergy test": +ve for cow's milk and peanut; referred to dietician**



**Presently uses diet free from peanut, tree nuts, and (shell)fish**



# GP repeated allergy test

- Peanut > 100 kU/I
- Soy 24 kU/I
- Wheat 2 kU/I
  
- also positive for house dust mite, grass pollen, and cat (“polysensitization”)

**Referred for general “allergy management advice”**

- asthma is well controlled on low-dose ICS
- no active eczema
- rhinitis troublesome in episodes



# Parental request

**How should we proceed with respect to his food allergies?**

**Before allergy test 1 yr: no symptoms but eczema  
Strict avoidance**

**Accidental exposures very rare (traces):**

**becomes generally unwell, pale, shaky**

**Martin is afraid to experiment with foods**



# 8 yr old, asthma, strong sensitization to peanut

**What would you do?**

- a. Leave him on the diet; he's doing well
- b. Leave him on the diet; his specific IgE is so high that we can predict the outcome of food challenge
- c. Skin prick testing
- d. (double blind) peanut challenge in hospital



# Double blind peanut challenge

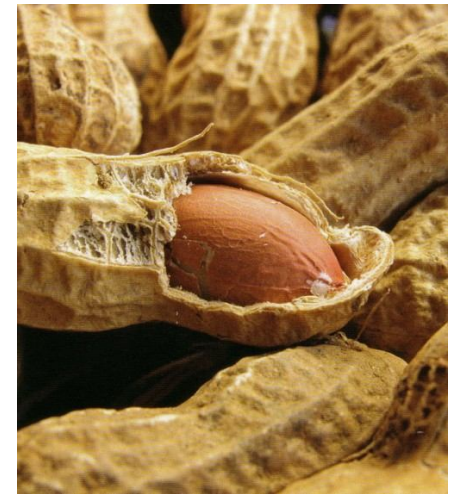
**Day 1: vomiting, mild erythema, rhinitis, teary red eyes**

**Day 2: no symptoms**

**Code: day 1 placebo, day 2 peanut**

**No peanut allergy**

**Peanut introduced without any problem**



# The trouble with food allergies

- **Diagnosis is difficult**
- **Sensitization is not the same as allergy!**
- **People are (being made) scared**
- **If you *really* want to investigate food allergy in individual patients, there's no alternative but DBPCFC**
  - **Confirms or refutes diagnosis**
  - **Gives indication of severity of reaction**
  - **Provides threshold dose**

# Incorrect diagnosis of food allergy

## Oral Food Challenges in Children with a Diagnosis of Food Allergy

David M. Fleischer, MD, S. Allan Rock, MD, Gavle C. Snears, PA-C, Carla G. Wilson, MS, Naomi K. Mizazawa, PA-C.

Table II. OFC results on foods avoided due to immunoassay or PST

Food group	Avoiding on admission	OFC positive result	OFC negative result	Avoiding on discharge	% Negative
Egg	10	1	9	1	90%
Fruits	10	2*	8	2	80%
Meats	13	0	13	0	100%
Milk	9	0	9	0	100%
Oats	4	0	4	0	100%
Peanut	7	1	6	1	86%
Shellfish	2	0	2	0	100%
Soy	19	1	18	1	95%
Vegetables	6	0	6	0	100%
Wheat	13	3	10	3	77%
Other	18	0	18	0	100%
Totals	111	8	103	8	93%

**Diagnosis based on "allergy test" is common**

**Diagnosis based on "allergy test" is usually incorrect**

**Beware of the allergy test!**

# The trouble with “food allergy” in asthma research

- **It's not always asthma**
  - Anaphylaxis or severe asthma exacerbation?
- **It's not always food allergy**
  - Most studies use sensitization, not food challenges

# Asthma or anaphylaxis?

- **Anaphylaxis = systemic allergic reaction with respiratory symptoms (wheeze, stridor, dyspnoea) or shock/hypotension**  
(J Allergy Clin Immunol 2006;117:391-7)
- **Fatal anaphylaxis: most have asthma** (J Allergy Clin Immunol 2001;107:191-3; Ann Allergy Asthma Immunol 2010;104:371-7)
- **Distinguishing the two only through history (Other symptoms? Time relation to food exposure?)**
- **Distinction may be difficult**

# Asthma or anaphylaxis?

## Food allergy as a risk factor for life-threatening asthma in childhood:

### A case-controlled study

J Allergy Clin Immunol 2003;112:168-74

- All 26 PICU admissions (ventilation) for asthma

**Asthma exacerbations or anaphylaxis after all?**

**Difficult to distinguish in retrospect**

- Patients with type 1 allergic symptoms to food in 24 h before admission excluded
- Interviewed about food allergy on re-assessment
- Food allergy = suggestive history + sensitization
  - Significant risk factor for life-threatening asthma (OR 8.6)

# Sensitization or allergy?

**Characteristics of childhood peanut allergy in the Australian Capital Territory, 1995 to 2007** J Allergy Clin Immunol 2009;123:689-93

**Risk of diagnostic confusion**

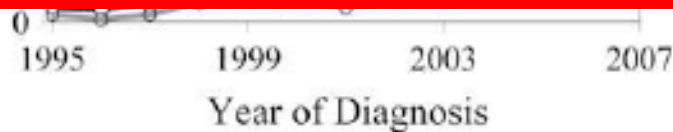
**child with asthma becomes wheezy**

**has had exposure to foods < 2 hrs of wheeze**

**→ potential misclassification as “anaphylaxis”**



ry of  
thin 2  
ood +



no food challenges

**82% of peanut sensitized individuals had peanut allergy**

**34% of peanut allergic patients had anaphylaxis**

**28% of peanut sensitized individuals had anaphylaxis**

# Sensitization or allergy?

## **Allergy or tolerance in children sensitized to peanut: Prevalence and differentiation using component-resolved diagnostics**

J Allergy Clin Immunol 2010;125:191-7

- **Population based cohort n=933 at 8 yrs of age**
- **11.8% peanut sensitized (n=110)**
  - **12 with convincing history + strongly sensitized considered as allergic without challenge**
  - **19 not challenged (no consent)**
  - **79 open food challenges → 7 positive**
  - **Estimated clinical allergy prevalence among sensitized individuals 22.4% (95% CI 15-32%)**



# Prevalence of peanut allergy?

## **Incidence, prevalence, and trends of general practitioner–recorded diagnosis of peanut allergy in England, 2001 to 2005**

J Allergy Clin Immunol 2011;127:623-30

- Large GP database (3 million people, over 5 yrs)
- Diagnosis of peanut allergy recorded by GP
  - 0.08% per patient-year in 2005 (95% CI 0.07-0.08%)

**Prevalence in Australian study: 5.3%**

**Prevalence in Manchester study: 2.6%**

**Prevalence depends on definition and diagnosis**

# Sensitization or allergy?

- Many studies use symptoms + sensitization as basis for diagnosis of food allergy
- This carries a very high risk of overdiagnosis
- History is unreliable: prevalence of *presumed* food allergy is 15-20%, most cannot be confirmed  
(J Allergy Clin Immunol 2006;117:1118-24; Allergy 2001;56:393-402)
- History + high degree of sensitization equally unreliable



**10-fold increase in peanut allergy over 15 years???**

**10-fold increase in tendency to diagnose peanut sensitization as "allergy"**

## Sensitization or allergy?

**F** Not a single study to date has examined the prevalence of food allergy in asthmatic children and its impact on asthma severity by **DBPCFC**

psychologically

- food allergy & asthma increasingly being viewed as a volatile combination
- “many allergists will prescribe EpiPen to any patient with both asthma and food allergy”

# Sensitization or allergy?

Respiratory reactions induced by food challenges in children with pulmonary disease

*Pediatr Allergy Immunol 1992;3:188-94*

- **279 children with asthma referred to national allergy referral centre for evaluation of food allergy**
- **All sensitized to multiple foods**
- **DBPCFC: 64% +ve**
  - **Respiratory symptoms in 65% of +ve challenges**
  - **17% wheeze during DBPCFC**
  - **Wheeze as sole manifestation in 5 patients**



# Sensitization or allergy?

- Sensitization ≠ allergy!
- Most studies look at symptoms to a food plus sensitization to *that* food
- This might make sense if patient is only sensitized to that particular food
- What if patient is sensitized to many foods?

# Sensitization or allergy?

**Reported symptoms to peanut between 4 and 8 years among children sensitized to peanut and birch pollen – results from the BAMSE birth cohort** Allergy 2010;65:213-9

- Birth cohort study n=1928 at age 4 and 8
- Sensitization to peanut 5.5% (age 4) and 7.4% (8)
- Only examined sensitization to peanut & birch
- If sensitized to peanut but not birch pollen (40%):
  - 76% reported symptoms on peanut exposure
- If sensitized to peanut *and* birch pollen (60%):  
**Symptoms more likely if patient is monosensitized**

**How common is monosensitization vs polysensitization?**

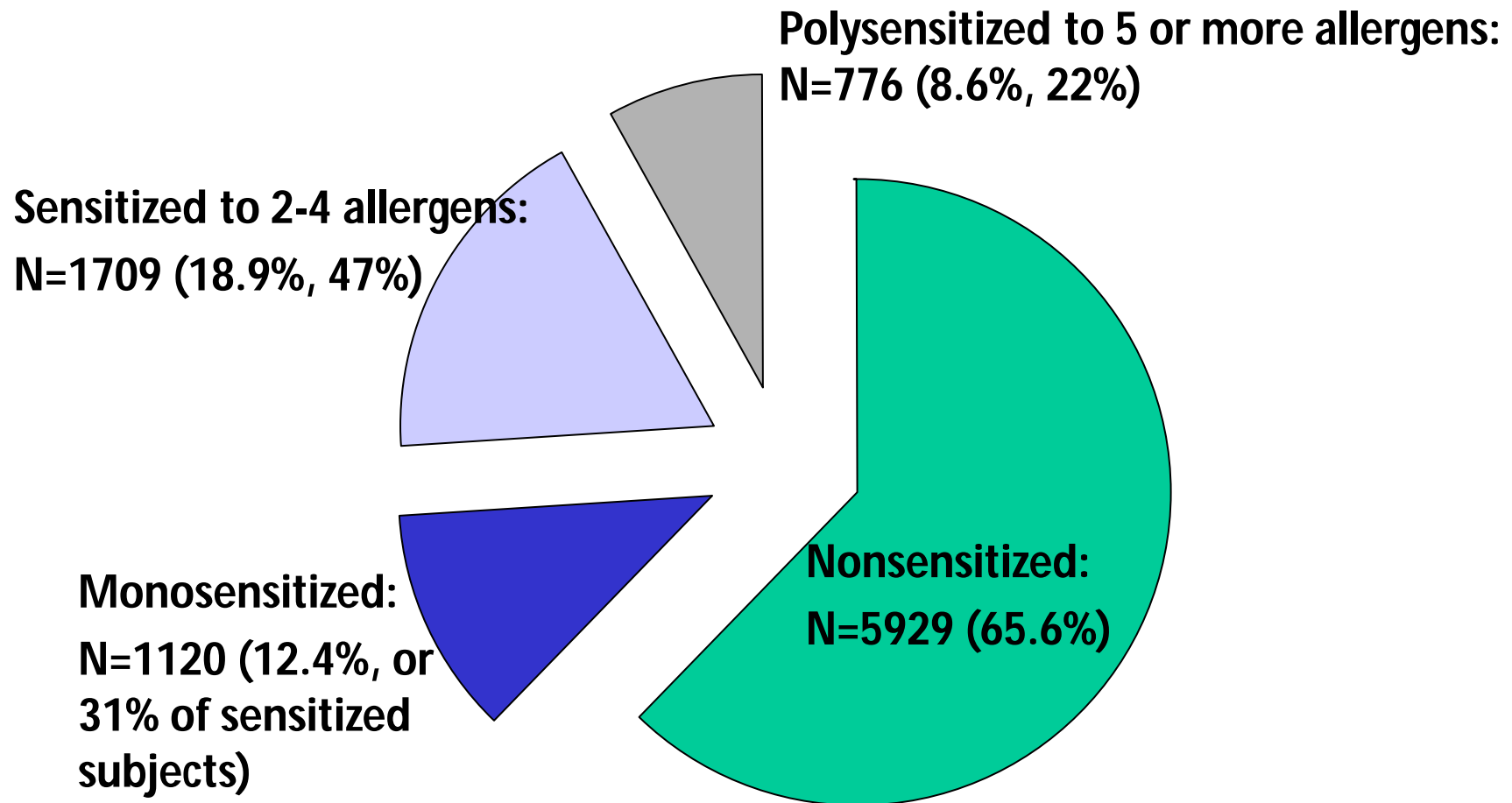
# Mono- or polysensitization?

- **3 population studies: mono- and polysensitization equally common (Isle of Wight, ALSPAC, and BAMSE cohorts)**
- **Relevance to clinical practice?**
- **Need to know distribution of sensitization patterns in patients**

Sensitization patterns to food and inhalant allergens in childhood: A comparison of non-sensitized, monosensitized, and polysensitized children [Pediatr Allergy Immunol 2011;22:166-71](#)

# Mono- or polysensitization?

Review of all 9044 specific IgE tests in children 0-18 yrs of age in our hospital lab (for specialists and GPs) 1990-2003



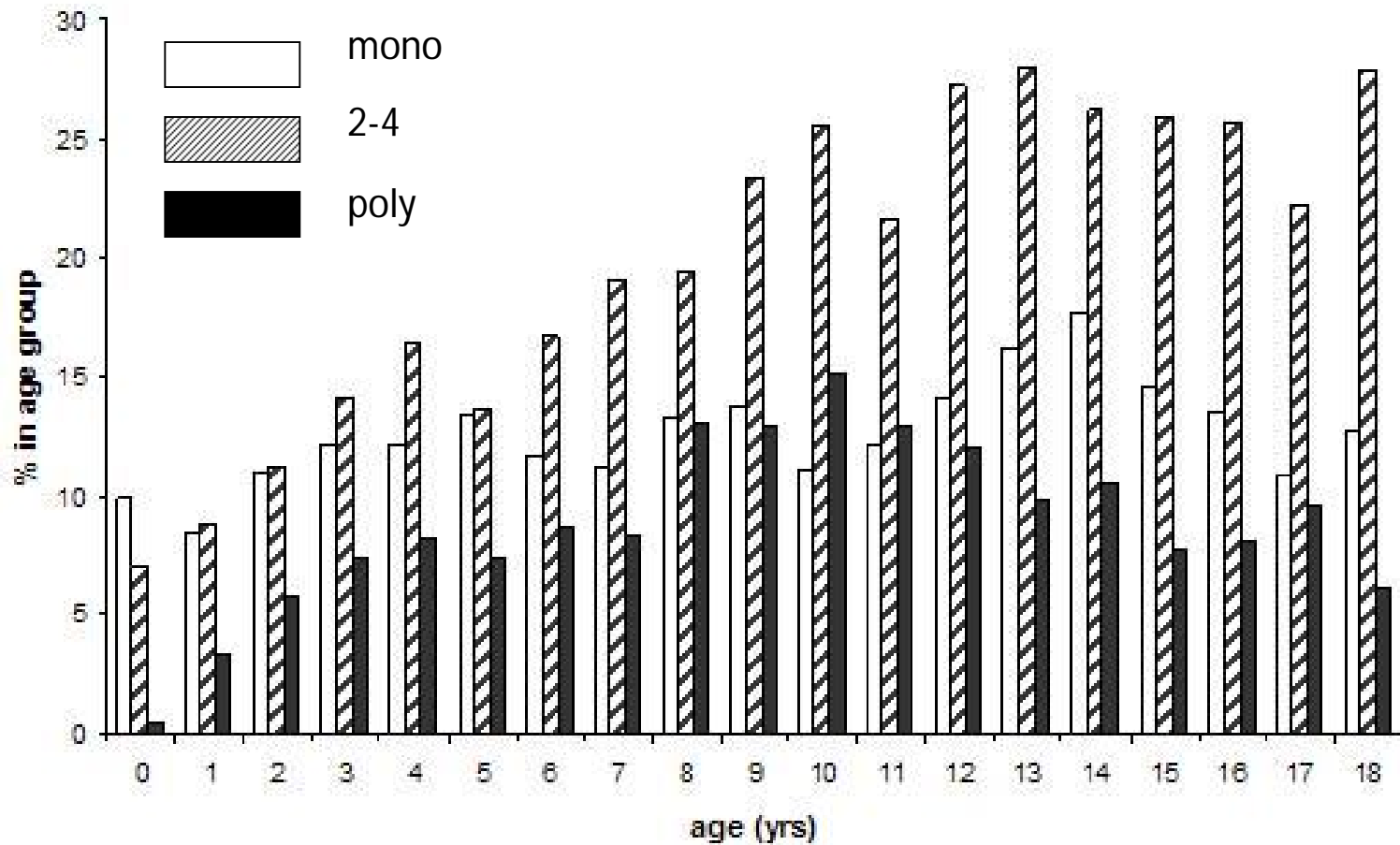
# 1120 monosensitized children

aeroallergens

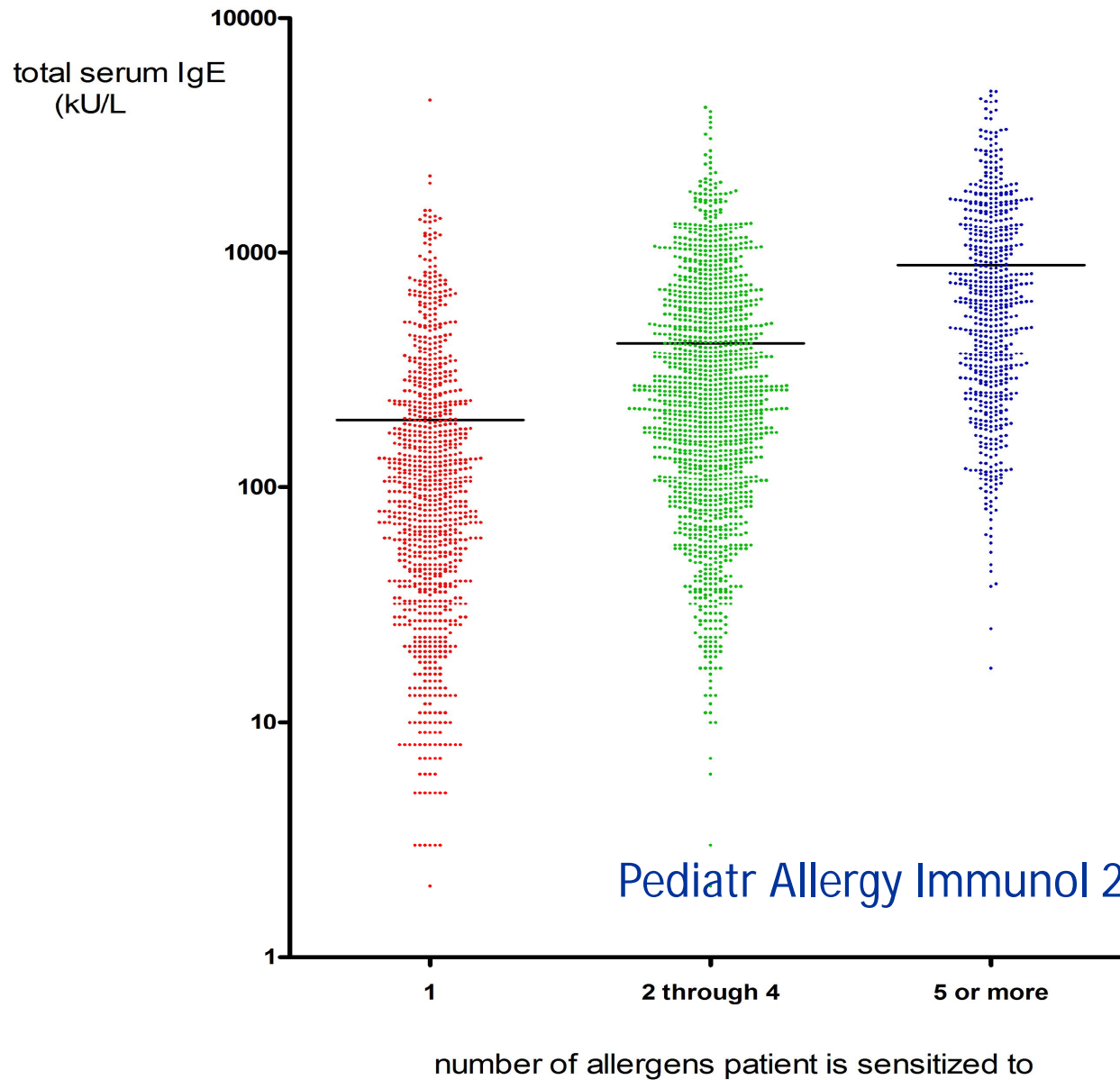
food allergens

Allergen	Number (%)	Allergen	Number (%)
House dust mite	516 (22.2%)	Cow's milk	209 (27.6%)
<b>Peanut sensitized children:                      4.6% monosensitized                      25.6% sensitized to 2-4 allergens                      69.8% polysensitized</b>			
Cat	54 (2.7%)	Wheat	4 (0.8%)
Dog	22 (1.5%)	Soy	3 (0.7%)
<b>Total</b>	<b>820 (73%)</b>	← p<0.0001 →	<b>300 (27%)</b>

# Mono- or polysensitization?



# Mono- or polysensitization?



Pediatr Allergy Immunol 2011;22:166-71

# Mono- or polysensitization?

Table 4. Cosensitization patterns between food allergens and aeroallergens in children sensitized to one or more allergens

Cosensitization to In children sensitized to	House dust, %	Grass pollen, %	Tree pollen, %	Cat dander, %	Dog dander, %	Percentage of children cosensitized to one or more aeroallergens, %
Cow's milk (n = 754)	40.5	36.3	24.0	31.7	37.3	55.7
Hen's egg (n = 545)	49.5	39.4	30.3	39.4	45.5	64.2
Peanut (n = 693)	56.6	62.9	53.7	46.8	61.0	79.2
Wheat (n = 506)	63.6	75.1	64.8	50.6	68.6	85.8
Soy (n = 414)	63.5	74.6	70.3	52.9	70.5	87.9

## **Peanut sensitized children:**

**57% sensitized to house dust mite**

**63% to grass pollen, 54% to tree pollen**

**47% to cat, 61% to dog**

**79% sensitized to at least one aeroallergen**

# Polysensitization

- **Common phenomenon in children**
- **Almost all children sensitized to peanut are cosensitized to other allergens**
- **This is not (only) cross-reactivity to biologically related allergens (pollen)**
- **May indicate a more severe atopic “phenotype”**

# Polysensitization: more severe asthma symptoms?

- **Case control study: severe asthma associated with higher number of +ve SPT to aeroallergens** (J Allergy Clin Immunol 2006;118:1218-25)
- **185 young men: QOL lower in polysensitized individuals** (Ann Allergy Asthma Immunol 2005;94:640-3)
- **Cohort study of inner city children with asthma: linear correlation between number/degree of aeroallergen sensitization and health care/medication use** (Clin Exp Allergy 2009;39:1381-9)

# Conclusions

- Relationship between childhood asthma and food allergy is complex and poorly understood
- Potential misclassification bias severe asthma & anaphylaxis
- Most studies show relationship between peanut **sensitization** (not peanut allergy) and severity of asthma
- Peanut sensitization is almost always accompanied by sensitization to other allergens
- Polysensitization is associated with more severe asthma

# Recommendations

- **Children with asthma: screen for aeroallergen sensitization**
- **Take a good and critical food allergy history**
- **Do not use food allergen sensitization as a diagnostic tool for food allergy (unreliable)**
- **Use DBPCFC to rule in/out relevant food allergy**
- **Sensitized to peanut? → check for polysensitization**
- **Interpret polysensitization cautiously**
  - **Marker for more severe asthma**
  - **Not a marker for multiple food allergies**

# Take home message

- Food allergen sensitization *per se* has no clinical value in children with asthma
  - It does not indicate clinical food allergy
  - May be regarded as a chance finding
- Polysensitization marker for more severe asthma

A man wearing a white bucket hat, a bright pink polo shirt, and blue shorts is climbing a rocky, reddish-brown trail. He has a black backpack and is smiling at the camera. In the background, another person is visible climbing a similar rocky path. The terrain is rugged and appears to be a desert canyon.

**¡ Muchas  
gracias !**

**Valle de la Luna, San Pedro de Atacama, October 2011**

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