Prevalence of Food Allergies in Southeast Asia

BW Lee, Dept Paediatrics
National University of Singapore

Food Allergy: A ‘hot’ topic

2nd wave of the allergy epidemic?

Food Allergy

Studies reporting Food Allergy Prevalence in preschool children ≤ 5 years

Published data only available from 16/89 countries (those without data not shown)

- OFC proven food allergy
- Symptoms and sensitisation
- Parental reporting

Is there a Food Allergy Epidemic in Asia?
Summary of Prevalence of Food Allergies in Singapore

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Age group</th>
<th>Prevalence (%)</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shellfish</td>
<td>4-6 yrs</td>
<td>1.19</td>
<td>Shek et al[1]</td>
</tr>
<tr>
<td>Peanut</td>
<td>4-6 yrs</td>
<td>0.64</td>
<td>Shek et al[1]</td>
</tr>
<tr>
<td>Tree nut</td>
<td>4-6 yrs</td>
<td>0.28</td>
<td>Shek et al[1]</td>
</tr>
<tr>
<td>Fish</td>
<td>14-16 yrs</td>
<td>0.30</td>
<td>Shek et al[2]</td>
</tr>
<tr>
<td>Egg</td>
<td>11-30 mths</td>
<td>1.8</td>
<td>Lee et al*</td>
</tr>
<tr>
<td>Cow’s milk</td>
<td>11-30 mths</td>
<td>0.5</td>
<td>Lee et al*</td>
</tr>
</tbody>
</table>

*Preliminary data, 2014, unpublished (n = 2,737).

Lee AJ and Shek LP Singapore Med J 2014

Peanut Allergy and Country of Birth

- **Peanut Allergy and Country of Birth**
- **Odds ratio (Compared vs Asia born Asians)**
  - Born in the West: 5.5
  - Asian: 3.8

Peanut Allergy Around the World

Data From Singapore 1999

Pattern of food-induced anaphylaxis in children of an Asian community

- **Odds ratio (Compared vs Asia born Asians)**
  - Caucasian: 5.5
  - Asian: 3.8

Asian = Chinese, Malay, Indian, Filipino
Western countries = Australia, New Zealand, United Kingdom, North America and Western Europe

Shek et al J Allergy Clin Immunol 2010

Goh DL et al Allergy 1999
Edible “bird’s nest”—induced anaphylaxis: An under-recognized entity?

Denise L. M. Goh, MMed (Paed), MRCP (UK), Fook-Tim Chew, BSc, PhD, Kau-Yan Chua, BSc, PhD, Ob-Moh Chau, MMed (Paed), and Bee-Wah Lee, MD

The Chinese delicacy “bird’s nest” is the most common cause of food-induced anaphylaxis requiring hospitalization among Chinese children in Singapore. This investigation has established an immunoglobulin E-mediated cause and has characterized the major putative allergens.

(J Pediatr 2006;137:277-9)

Singapore (KKH) Paediatric Food Anaphylaxis
Jan 2005 to Dec 2009

Common Food Allergies in Asia
**Shellfish Allergy**
*Population-based Surveys*

![Graph showing Shellfish Allergy prevalence in USA and Singapore/Philippines.]

Sicherer S, J Allergy Clin Immunol 2004
Shek LP, J Allergy Clin Immunol 2010

**Shellfish**
Most Common Cause of Anaphylaxis in Asia

- Thailand: Adults and Children
- Singapore: Adults
- Hongkong: Adults
- Taiwan: Adults and Children

**Food Challenge Provocation Dose**

- **Thai**, children – 1g to 63g, cooked prawn
  Jirapongsananuruk et al Clin Exp Allergy 2008

- **Singapore**, Adolescents and Adults: 2g to 80g, cooked prawn
  Gerez et al, unpublished

- **Canada**, Adult (1 patient): 14g, freeze dried, capsule
  Bernstein et al J Allergy Clin Immunol 1982; 70:205–10
Distribution of symptoms during the most severe reaction to shellfish

- Hives
- Swollen eyes & lips
- Vomiting & Diarrhoea
- Abdominal pain
- Runny nose
- Itchy throat
- Throat tightness & Wheezing
- Feeling faint or dizzy & Loss of consciousness
- Redness of skin

Fig 1. (n=674)

Shek et al, J Allergy Clin Immunol, 2010

2/39 shellfish allergy cases
specific IgE to shrimp
shrimp tropomyosin (Pen a 1, Pen m1, Pen I 1, Lit v 1)
dust mite tropomyosin (Der p 10, Blo t 10)

Mild Crustacean Seafood Allergy
Tropomyosin – A pan-allergen

- **Inhalant-food syndrome**
  - Dust mites as the sensitizing allergen
  - Crustacean shellfish as the cross reactive allergen

<table>
<thead>
<tr>
<th>Challenge</th>
<th>n</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>29 (74.3)</td>
<td>0.891</td>
</tr>
<tr>
<td>Oral</td>
<td>34 (87.1)</td>
<td>0.293</td>
</tr>
<tr>
<td>Upper respiratory tract</td>
<td>15 (38.4)</td>
<td>0.051</td>
</tr>
<tr>
<td>Lower respiratory tract</td>
<td>17 (43.5)</td>
<td>0.905</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>3 (7.6)</td>
<td>0.039</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>11 (28.2)</td>
<td>0.306</td>
</tr>
<tr>
<td>Other symptoms</td>
<td>2 (5.9)</td>
<td>0.326</td>
</tr>
</tbody>
</table>

Thayalasingham M et al, Clin Exp Allergy 2015
Conclusions from reciprocal IgE inhibition Studies:

Mites are the primary sensitizer in humid-climate

15 year Old Girl

- Has asthma and allergic rhinitis
- Ingested home-made tempura prawns – fried coated with Japanese flour
- Developed urticaria, throat discomfort, severe wheezing 20 min later
- Treated at emergency dept for anaphylaxis
  - SaO₂ 77%
**Gross Appearance of Flour**

Areas of light brown discolouration

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**Anaphylaxis from ingestion of mites: Pancake anaphylaxis**

Mario Sánchez-Borges, MD, Raúl Suárez Chacón, MD, Arnaldo Capriles-Hullett, MD, Fernán Caballero-Fonseca, MD, and Enrique Fernández-Calderón, PhD

Caracas, Venezuela, and Madrid, Spain

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**TABLE I. Published cases of CMA until May 31, 2012 (n = 126)**

<table>
<thead>
<tr>
<th>Author (year)</th>
<th>No.</th>
<th>Age (y)</th>
<th>Sex (M/F)</th>
<th>Location</th>
<th>Reactions</th>
<th>Mite Sensitivity</th>
<th>NSAID Hypersensitivity</th>
</tr>
</thead>
</table>

*Note: All cases had symptoms consistent with NSAID hypersensitivity.*
Prebiotic (Carbohydrate) Triggered Anaphylaxis

Anaphylaxis to cow’s milk formula containing short-chain galacto-oligosaccharide (GOS)

Report of 5 Cases

Chiang et al J Allergy Clin Immunol 2012

**SKIN PRICK TEST**

<table>
<thead>
<tr>
<th>A: COW’S MILK FORMULA (numerical refer to diameters weal)</th>
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<tbody>
<tr>
<td>Patient</td>
</tr>
<tr>
<td>Positive Histamine</td>
</tr>
<tr>
<td>Negative Control</td>
</tr>
<tr>
<td>Cow’s Milk</td>
</tr>
<tr>
<td>CMF1 with prebiotics scGOS + lcFOS</td>
</tr>
<tr>
<td>CMF1 without prebiotics</td>
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<tr>
<td>CMF2 with prebiotic scGOS</td>
</tr>
<tr>
<td>Std Vivinal GOS (7.2mg/ml)</td>
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</tbody>
</table>

- SPT to CMF **negative**
- SPT to CMF without PREBIOTICS **negative**
- SPT to CMF containing GOS **positive**

**Basophil Activation Tests**

**CD203c (MFI)**

**CD63 (%)**

**Actual GOS concentration in the samples (µg/ml)**

scGOS = short chain Galacto-oligosaccharides
lcFOS = long chain Fructo-oligosaccharides

Chiang et al J Allergy Clin Immunol 2012
GOS GRAS dossier 2007

Structure of GOS

GOS is produced by enzymatic transgalactosylation of lactose by β-galactosidase

Variable chains of galactose with one molecule of glucose

Fractions of GOS mixture
High-Performance Anion-Exchange Chromatography with Pulsed Amperometric Detection (HPAEC-PAD)

Table 1. Intended Uses of GOS

<table>
<thead>
<tr>
<th>Food Group</th>
<th>Food Group Category</th>
<th>Approximate serving size (a)</th>
<th>Maximum g GOS per serving</th>
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<tbody>
<tr>
<td>Dairy</td>
<td>ice cream</td>
<td>50</td>
<td>5.0</td>
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<tr>
<td>Dairy products</td>
<td>yogurt</td>
<td>27</td>
<td>7.5</td>
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<tr>
<td>Beverages</td>
<td>brown ale, kolsch</td>
<td>15 (% rel.)</td>
<td>2.0</td>
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(a) In some food categories, not all type of foods are intended for addition of GOS (e.g., addition of GOS is intended in emulsions and low fat milk only not whole and reduced fat milk). The specific type of products intended for addition of GOS are detailed in Table 1.

Inhibition of scGOS-induced basophil degranulation by the phosphatidylinositol 3-kinase inhibitor wortmannin

Dose-dependent effect of scGOS fractions on activation of in vitro-sensitized control basophils


Chiang et al J Allergy Clin Immunol 2012
Development of hypoallergenic galacto-oligosaccharides on the basis of allergen analysis

Kimiuki Kaneko1, Yoko Watanabe1, Kazumasa Kimura2, Keisuke Matsumoto3, Takahiro Mizobuchi4 & Masaharu Onoue5

1 Yokult Central Institute for Microbiological Research, Tokyo, Japan
2 Yokult Pharmaceuticals Industry Co., Ltd., Tokyo, Japan
3 Development Department, Yokult Honsha Co., Ltd., Tokyo, Japan

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Acute Allergic Reactions in Vietnamese Children

After Drinking a New Milk Product

- Milk product with GOS introduced in Sept 2009
- 3 million cartons sold a day in Vietnam

- 15/16 cases aged 2-15 years old consumed milk with GOS
- 12/15 within 3 to 20 mins of milk consumption.
- 3/15 with acute respiratory problems

FIG. 1. Number of children (n=17) with allergic reactions by date of onset, October 2009, Ho Chi Minh City, Vietnam.
What is the Primary Sensitizer?

Hoya Antigen Asthma in Japan

- Sea squirt antigen – H or Hoya antigen
- It is a hexosamine rich glycoprotein
- Causes occupational asthma in oyster shucklers

Alpha-Galactose IgE Epitopes (mammalian CCD)

- Cetuximab: N-linked oligosaccharides contains the α-gal epitopes
  - Immediate onset anaphylaxis
- Mammalian meat - Pork and Beef: gal-α-1,3-gal-β-1,4-GlcNAc
  - Delayed anaphylaxis reaction (3-6 hours)

Cabohydrate Allergen Epitopes
- cross-reactive carbohydrate determinants (CCD) of N-linked glycans

- Clinically insignificant
  - Low titre anti-glycan IgE antibodies
  - High affinity ‘blocking’ IgG antibodies
- ‘False positive’ specific IgE tests

Conclusions

• It does not appear that Asia is facing a food allergy epidemic
  – Better oral tolerance?

• Pattern of food allergy is different and may be related to environmental allergens
  – Inhalant/environmental and food allergens