Introduction on Allergy and Allergic Diseases

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Allergic disease: A major global public health issue

- Asthma
- Allergic rhinitis
- Allergic dermatitis (eczema)
- Allergic conjunctivitis
- Allergic enteroctitis
- Food allergy
- Anaphylaxis
- Angioedma and urticara
- Eosinophilic disorder
**Asthma prevalence in children**

- Asthma is the most common disease among children\(^1,2\)
- Children living in poverty: \(^2\)
  - Suffer the largest burden of childhood asthma morbidity
  - Are more likely to receive inadequate therapy

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**Asthma and Allergy: Diseases of the West?**

Global burden of asthma (WHO 2004)

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Pediatric Allergy in Asia (APAPARI)

Starting 1998

About the APAPARI

<table>
<thead>
<tr>
<th>Period</th>
<th>President</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>The 1st</td>
<td>Pakit Vichyanond</td>
<td>Thailand</td>
</tr>
<tr>
<td>The 2nd</td>
<td>Yoji Ikura</td>
<td>Japan</td>
</tr>
<tr>
<td>The 3rd</td>
<td>Sang-il Lee</td>
<td>Korea</td>
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<td>The 4th</td>
<td>Bee Wah Lee</td>
<td>Singapore</td>
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<tr>
<td>The 5th</td>
<td>Akihiro Morikawa</td>
<td>Japan</td>
</tr>
<tr>
<td>The 6th</td>
<td>Gary Wong</td>
<td>Hong Kong</td>
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</tbody>
</table>
ISAAC-based asthma and atopic symptoms among Hanoi school children

- Hanoi
- Cross-sectional study
- 5 - 11 year-old
- Response rate 66.4%
- 969 responders

The prevalence of allergic diseases in Taipei

<table>
<thead>
<tr>
<th></th>
<th>Primary school 1994</th>
<th>Primary school 2002</th>
<th>Junior High school 1994</th>
<th>Junior High school 2002</th>
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</thead>
<tbody>
<tr>
<td><strong>Allergic diseases</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wheezing ever</td>
<td>16.1%</td>
<td>19.8%</td>
<td>10.6%</td>
<td>14.3%</td>
</tr>
<tr>
<td>Wheezing within one year</td>
<td>9.6%</td>
<td>10.1%</td>
<td>5.2%</td>
<td>7.0%</td>
</tr>
<tr>
<td><strong>AR symptoms ever</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AR within one year</td>
<td>36.5%</td>
<td>47.8%</td>
<td>35.1%</td>
<td>53.1%</td>
</tr>
<tr>
<td><strong>Eczema ever</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eczema within one year</td>
<td>5.2%</td>
<td>10.7%</td>
<td>2.9%</td>
<td>7.4%</td>
</tr>
<tr>
<td></td>
<td>3.5%</td>
<td>6.8%</td>
<td>1.4%</td>
<td>4.1%</td>
</tr>
</tbody>
</table>
Asthma prevalence

7 years old Schoolchildren

Tainan


Asthma prevalence [%]

4 5 6 7 8 9

~6.3 million <18 years of age
~3.5 million physician visits*
~203,000 Hospitalizations*
~14 million missed school days annually
~658,000 emergency department visits*
~1/3 of pediatric asthma deaths in those classified with mild asthma

*Includes 1999 or 2000 annual estimates for children <15 years of age.

The Allergy March: One disease with many faces
Environmental Exposures Constituting Prenatal Epigenetic Changes to Immunity

Pollution
- Tobacco
- Pollution

Food
- Folate
- n-3 Polyunsaturated Fatty Acids
- Anti-oxidants

Farming
- Bacteria
- Viruses

Pets
- Probiotics

Agriculture

Microbiota

Factors favoring the Th1 phenotype
- Presence of older siblings
- Early exposure to day care
- Tuberculosis, measles, or hepatitis A infection
- Rural environment

Factors favoring the Th2 phenotype
- Widespread use of antibiotics
- Western lifestyle
- Urban environment
- Diet
- Sensitization to house-dust mites and cockroaches

Th1
Protective immunity

Th2

Cytokine balance

Allergic diseases including asthma

Figure 3: Environmental exposures, including pollution, food, agriculture, and microbiota, have been shown to alter early immune development. Prenatal elements influence changes to gene expression, affecting fetal immunity.

Table 4. Relationship between acetaminophen/antibiotic exposure during the first year of life and the subsequent development of atopic dermatitis, asthma and allergic rhinitis, individually in two birth cohorts (1998 and 2003).

<table>
<thead>
<tr>
<th>Drug exposure</th>
<th>1998 birth cohort</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Atopic dermatitis</td>
</tr>
<tr>
<td></td>
<td>Adj. HR ± (95% CI)</td>
</tr>
<tr>
<td>Non exposure</td>
<td>ref</td>
</tr>
<tr>
<td>Only exposure to antibiotics</td>
<td>1.61 (1.53-1.70)</td>
</tr>
<tr>
<td>Only exposure to acetaminophen</td>
<td>2.02 (1.92-2.13)</td>
</tr>
<tr>
<td>Exposure to both drugs</td>
<td>1.98 (1.89-2.07)</td>
</tr>
</tbody>
</table>
**Airway Inflammation and Remodeling**

- **Allergen** interacts with mast cells to release cytokines like IL-4, TNF, IL-5, GM-CSF, ICAM, and VCAM.
- **Th2** cells are activated, promoting the release of eosinophils and neutrophils.
- **Macrophages** release LT PE TxA2, histamine MBP, ECP, and EPO.
- **Eosinophils** and **neutrophils** contribute to the inflammation process.
- **Vascular permeability** increases, leading to edema and epithelial fibrogenesis.
- **Airway wall remodeling** involves fibroblast activation, epithelial fibrogenesis, hypertrophy and hyperplasia of smooth muscle and mucous gland.

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**Interaction of Mite Allergens and Lung Epithelial Cells**

- **Dectin** recognizes **Der p1**, a cysteine protease.
- **CD14**, **TLR2/4**, and **MD2** are involved in the recognition process.
- **CCL20**, **TSLP**, **IL-25**, and **IL-33** are released, activating **Type 2 innate helper cells**.
- **CD161** and **CRTH2** further enhance the response.
- **NF-κB activation** results in **GM-CSF**, **RANTES protein**, and **eotaxin**.
- **Airway hyperresponsiveness and inflammation** are observed.

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**Phosphoinositide hydrolysis** and **Cytosolic Ca2+ mobilization** contribute to the inflammatory response.
Allergy skin prick testing

• Skin prick test / positive result

Inhalant Allergens in 196 Asthmatic Children in Tainan Area

Inspiratory nasal peak-flow

Bronchial challenge tests

There are different methods of doing it: dosimeter, nebulizers like De Vilbiss, Hudson, etc., chamber exposure for occupational asthma.
IN VITRO ALLERGY DIAGNOSIS – ALLERGEN-SPECIFIC IgE

Steps involved in the development of allergic diseases. A switch to the production of allergen-specific IgE detectable in serum leads to the sensitization of a patient, reflecting its atopic status. However, not all sensitized individuals suffer from allergic symptoms highlighting the limitation of in vitro allergy diagnoses. Allergen challenge tests are needed to confirm the clinical relevance of an allergy suspected from the clinical history and from the presence of allergen-specific IgE in serum.

Diagnosis of allergy

1. History
2. Clinical examination
3. SPT = golden standard!
4. Specific IgE in sera
5. Other lab tests: ECP, cytokines, etc...
6. FeNO
7. Allergen provocation test (nasal, bronchial, etc...)