Allergen Exposure and Asthma in US Inner-cities

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May 18, 2006
Pathophysiology of Allergic Rhinitis: Sensitization

- **Allergen**
- **Macrophage** (Antigen-presenting cell)
- **Process**
- **HLA class II**
- **CD4⁺ T<sub>H2</sub> cell**
- **IL-4**
- **IL-13**
- **B cell**
- **Plasma cell**
- **IgE antibodies**
- **Primed mast cell**
Early Phase Reaction (EPR) Occurs Within Minutes of Allergen Exposure in Sensitized Subjects

- Preformed mediators
  - Histamine
  - Proteases

- Newly generated mediators
  - Cysteinyl leukotrienes
  - Prostaglandins
  - PAF
  - Bradykinin
  - Interleukins
  - TNF-α
  - GM-CSF

 Symptoms of EPR
- Blood vessels, nerves, glands
- Congestion
- Rhinorrhea
- Pruritis
- Sneezing

Allergen → Mast cell
  - Degranulation
  - Neosynthesis

11/15/00 SLIDE 9
Late Phase Reaction (LPR)

Occurs 3 to 12 Hours Post Allergen Exposure

**Mast cell**
- Allergen
- Chemotactic factors (CysLTs, PAF, IL-5)
- PGs
- Proteases
- CysLTs

**Mast cell**
- Histamine
- IL-4, IL-6

**Cellular Infiltration/Inflammation**
- Eosinophil
  - CysLTs, GM-CSF, TNF-α, IL-1, IL-3, PAF, ECP, MBP
- Basophil
  - Histamine, CysLTs, TNF-α, IL-4 to 6
- Monocyte
  - CysLTs, TNF-α, PAF, IL-1
- Lymphocyte
  - IL-4, IL-13, IL-5, IL-3, GM-CSF

**Symptoms of LPR**
- Congestion
- ± Rhinorrhea
- ± Sneezing
Allergic Rhinitis: Response to Antigen

EARLY PHASE
- Congestion
- Rhinorrhea
- Pruritis
- Sneezing

LATE PHASE
- Congestion
- ± Rhinorrhea / Sneezing

Time Postchallenge (h)

Symptom Score

Antigen Challenge

1 3-4 8-12 24
RAST

- *Radioallergosorbent test*
- Quantify IgE in serum that is specific to a particular allergen
Major Indoor Allergens

- Cat
- Cockroach ★★
- Dog
- Dust mite
- Mold
- Mouse ★★
- Rat ★★
Allergen Exposure Assessment

- Vacuum settled dust in home
- Collect airborne particles
  - Area sampling
  - Personal sampling
  - Nasal sampling
- Quantify allergen content by ELISA
Skin Test Sensitivity and Asthma

- 80% of school age children with asthma demonstrate skin test sensitivity to at least one common aeroallergen
  - NCICAS: 400/500 (80%)
  - CAMP: 873/1041 (84%)
### Sensitization as a Risk Factor for Asthma

<table>
<thead>
<tr>
<th>Site</th>
<th>Design</th>
<th>Dominant Allergen</th>
<th>OR</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>Prospective</td>
<td>Mite</td>
<td>19.7</td>
<td>Sporik</td>
</tr>
<tr>
<td>N. Zealand</td>
<td>Prospective</td>
<td>Mite</td>
<td>6.6</td>
<td>Scars</td>
</tr>
<tr>
<td>Australia</td>
<td>School</td>
<td>Mite</td>
<td>&gt;10.0</td>
<td>Peat</td>
</tr>
<tr>
<td>Virginia</td>
<td>School</td>
<td>Mite</td>
<td>6.6</td>
<td>Squillace</td>
</tr>
<tr>
<td>Atlanta</td>
<td>ER</td>
<td>Mite, CR</td>
<td>8.2</td>
<td>Call</td>
</tr>
<tr>
<td>Sweden</td>
<td>Population</td>
<td>Cat, dog</td>
<td>3.9</td>
<td>Ronmark</td>
</tr>
<tr>
<td>N. Mexico</td>
<td>School</td>
<td>Cat, dog</td>
<td>6.2</td>
<td>Sporik</td>
</tr>
</tbody>
</table>
## Prevalence of Skin Test Sensitivity to Indoor Allergens

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Inner-city (NCICAS)</th>
<th>Suburban Baltimore (HOME)</th>
<th>New Mexico (Platts-Mills)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cockroach</td>
<td>36%</td>
<td>21%</td>
<td>0%</td>
</tr>
<tr>
<td>Dust mite</td>
<td>35%</td>
<td>70%</td>
<td>5%</td>
</tr>
<tr>
<td>Cat</td>
<td>24%</td>
<td>50%</td>
<td>62%</td>
</tr>
<tr>
<td>Dog</td>
<td>16%</td>
<td>11%</td>
<td>67%</td>
</tr>
<tr>
<td>Mouse</td>
<td>15%</td>
<td>14%</td>
<td>-</td>
</tr>
</tbody>
</table>
Cockroaches

American    Oriental    German    Banded
Cockroach Allergen: Distribution

- Bla g 1/Bla g 2: major allergens of German cockroach
- Carried on heavier/larger particles
- 85% of inner-city bedrooms (NCICAS)
- 1/3 of middle-class, suburban kitchens (HOME)
- Median Bla g 1 levels
  - Inner-city homes 8U/g
  - Suburban homes BD
Cockroach Allergen and Allergic Sensitization

Sensitization and Exposure to CR Allergen and Asthma Morbidity

Rosenstreich et al NEJM336:324,1997
Cockroach Allergen Removal

• Pesticide to eliminate source
• Vacuum, wash thoroughly
• Prevent reinfestation
  – Seal cracks and holes
  – Wash dishes
  – Food in sealed containers
  – Bait stations
Summary: Cockroach

- Exposure associated with increased risk for asthma morbidity
- Extermination and cleaning result in substantial reduction in allergen
- RCTs of effect of cockroach allergen reduction on asthma are underway
IT'S ALWAYS SO NICE WHEN THE CAT'S AWAY.
Mus m 1

- 16-19kD pheromone-binding protein
- Member of the lipocalin family
- Primarily excreted in the urine
- Excreted in higher quantities by males
- Carried on small particles (< 10-20 microns) → airborne
• Airborne
• Detected in 100% of Baltimore inner-city homes and 75% of suburban bedrooms
• Long recognized as occupational health problem among lab animal workers
<table>
<thead>
<tr>
<th>Study Location</th>
<th>Sample Size</th>
<th>Location(s)</th>
<th>Percentage Detectable</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCICAS, Phipatanakul JACI 2000</td>
<td>608 children</td>
<td>kitchen, BR, or LR</td>
<td>95%</td>
</tr>
<tr>
<td>NY, NY, Chew EHP 2003</td>
<td>221 mothers</td>
<td>kitchen</td>
<td>57-66%</td>
</tr>
<tr>
<td>Baltimore, Matsui JACI 2005</td>
<td>100 children</td>
<td>kitchen</td>
<td>100%</td>
</tr>
<tr>
<td>United States, Cohn JACI 2004</td>
<td>831 housing units</td>
<td>kitchen, BR, or LR</td>
<td>82%</td>
</tr>
<tr>
<td>Suburban Maryland, Matsui JACI 2004</td>
<td>335 children</td>
<td>kitchen</td>
<td>75%</td>
</tr>
</tbody>
</table>
### Mus m 1 Levels Highest in Inner-city Homes

<table>
<thead>
<tr>
<th>Location</th>
<th>Median Kitchen Mus m 1 (µg/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suburban Maryland</td>
<td>0.007</td>
</tr>
<tr>
<td><strong>US sample</strong> (Cohn JACI 2004)</td>
<td>0.36</td>
</tr>
<tr>
<td><strong>NCICAS</strong> (Phipatanakul JACI 2000)</td>
<td>1.6</td>
</tr>
<tr>
<td><strong>Inner-city Baltimore</strong></td>
<td>14.7</td>
</tr>
</tbody>
</table>
## Predictors of Household Mouse Allergen

<table>
<thead>
<tr>
<th></th>
<th>Holes/cracks in wall/ceiling/door</th>
<th>Cat in household</th>
</tr>
</thead>
<tbody>
<tr>
<td>NY, NY Chew EHP 2003</td>
<td>4.0 (1.7-9.6)</td>
<td>0.3 (0.1-1.0)</td>
</tr>
<tr>
<td>Baltimore Matsui JACI 2005</td>
<td>1.5 (0.6-3.5)</td>
<td>0.2 (0.05-0.5)</td>
</tr>
</tbody>
</table>

High Mus m 1: > median in BR/bed
Airborne Mus m 1 in Inner-city Homes

- Detectable in air of 84% of bedrooms
- Median (IQR): 0.03 ng/m³ (0.01-0.10)
- 25% homes with levels similar to occupational levels

Matsui et al, JACI 2005

\[
\begin{align*}
\text{Settled Dust Mus m } 1 & \quad \text{(µg/g)} \\
\text{Airborne Mus m } 1 & \quad \text{(ng/m³)} \\
\end{align*}
\]

\[
r_s = 0.52 \\
p < .0001
\]
## Prevalence Rates of Skin Test Sensitivity

<table>
<thead>
<tr>
<th>Study Population</th>
<th>+ mouse SPT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Occupational</strong></td>
<td></td>
</tr>
<tr>
<td>TJL, adults</td>
<td>20</td>
</tr>
<tr>
<td><strong>NCICAS</strong></td>
<td></td>
</tr>
<tr>
<td>499 school age children</td>
<td>18</td>
</tr>
<tr>
<td>Phipatanakul JACI 2000</td>
<td></td>
</tr>
<tr>
<td><strong>Baltimore</strong></td>
<td></td>
</tr>
<tr>
<td>100 school age children</td>
<td>9</td>
</tr>
<tr>
<td>Matsui JACI 2005</td>
<td></td>
</tr>
<tr>
<td><strong>Baltimore</strong></td>
<td></td>
</tr>
<tr>
<td>150 pre-school children</td>
<td>16</td>
</tr>
<tr>
<td>Abstract, AAAAI 2005</td>
<td></td>
</tr>
<tr>
<td><strong>Suburban Maryland</strong></td>
<td></td>
</tr>
<tr>
<td>335 school age children</td>
<td>13</td>
</tr>
<tr>
<td>Matsui JACI 2004</td>
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</tbody>
</table>
Mouse Allergen Exposure and Sensitization: NCICAS

Phipatanakul, JACI 2000
Days of Rescue Medication Use

Study Visit

mean # days

- sens/low
- sens/high
+ sens/low
+ sens/high

P = .04
P = .02
P = .03
Unscheduled Doctor Visit

Study Visit

- sens/low
- sens/high
+ sens/low
+ sens/high

p = .39
p = .01
p = .005
Recent Asthma Symptoms & Rescue Medication use

* adjusted for age, sex, atopy, cockroach sensitization and exposure, public health insurance, and study visit
Asthma-related Health Care Utilization

- Hospitalization
  Adjusted OR: 69.9 (5.8-838.9)

- 9/10 hospitalizations occurred among sensitized/high exposure group

* adjusted for age, sex, atopy, cockroach sensitization and exposure, public health insurance, and study visit
RCT Environmental Intervention
Targeting Mouse Allergen

- Mus m 1 (mcg/g)

- Intervention
- Control

p < .05

Rat Allergen

- Rat n 1
- Present in rat urine
- Present in 33% of inner-city homes (NCICAS)
- Related to asthma symptoms and morbidity
Rat n 1 and Asthma Morbidity

Hospitalizations

N: 297 81 80 22

Unscheduled MD visits

N: 297 81 80 22

Perry T, JACI 2003
Conclusions: Cockroach Allergen

• Cockroach (Bla g 1, Bla g 2)
  – Extremely common in inner-city homes
  – Heavy particles, settles to surfaces
  – Exposure
    • > 1 U/g ➔ allergic sensitization
    • > 8 U/g ➔ asthma morbidity
Conclusions: Rodent Allergens

• Mouse (Mus m 1)
  – Smaller particles, airborne
  – Extremely common in inner-city homes
  – Exposure
    • > 1.6 µg/g → sensitization
    • > 0.5 µg/g → morbidity

• Rat (Rat n 1)
  – Smaller particles, airborne
  – Detectable in ~ 1/3 of inner-city homes
  – Exposure to detectable level associated with asthma morbidity