Identification of Target Bioallergens: Frequency of Specific Aeroallergen Sensitization in an Atopic Population in the Sacramento Region

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March 1, 2005
Key Personnel

- Arif Seyal, M.D., co-PI
- Suzanne Teuber, M.D., co-PI
- Rosemary Hallett, M.D., UCD allergy fellow
- Neil Willitts, Ph.D., UCD statistical consulting
- John Moore, Ph.D., ARB statistical consulting

March 1, 2005
Why this study?

• If bioaerosols are important factors in asthma exacerbations, should the ARB be involved in monitoring aeroallergens, or in examining the interactions with air pollution in California?
• If the ARB moves in this direction, what are the relevant aeroallergens to study?
• Indoor vs. outdoor
ARB Proposals

- Kaiser contacted by ARB
- We suggested a study looking at asthma emergency room admissions throughout Kaiser correlated with specific pollen/spore counts (NOT total), viral cultures, quantitative specific IgE to key allergens, measures of air pollutants at that time – Inland Northern California could be a site, should be coordinated by others experienced in this type of study
- Expensive, would require multi-site study
Could we at least help narrow down what aeroallergens should be looked at in a future study by others?

- California may not have as much indoor mold growth as other states (e.g., the Southeast) – indoor molds are the target bioaerosol in the Asthma Research Strategy report of the EPA (EPA 600/R-01/061 September 2002)

- Informal beliefs of area MDs: *anecdotally*, grass and olive pollen associated with seasonal asthma April-June. *Alternaria* with fall asthma (also blamed at this time: air pollution, and in school kids, viruses)
Previous California Studies

- **Prevalence of sensitization to aeroallergens in California patients with respiratory allergy**

  - Mainly Southern California. Only 18% of 141 patients were from Northern California.
    - Olive pollen: 42%
    - Grasses: 54%
    - Dust mites: 53%
    - Cat: 37%
    - Dog: 19%
    - Cockroach 23%
    - *Alternaria* 18%
Grass Season Asthma

- Epidemiology of emergency room asthma in northern California: association with IgE antibody to ryegrass pollen (JACI 1988;82:224 also see JACI 1986;78:590)
  - 59 patients with current ED visit for asthma, 59 controls without asthma
  - 92% of patients had >200 units IgE to grasses, 14% of controls
  - No difference in the prevalence of IgE Ab to mite, cockroach or cat
  - Previously showed that grass pollen counts correlated with asthma ED visits ($r = 0.90$, $p<0.001$)

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Asthma Panel Studies

- **Air pollution and exacerbation of asthma in African-American children in Los Angeles.**
  
  (Epidemiol 2001;12:200) (ARB study)
  
  - 138 children
  - August to November: grasses extremely low or absent, olive pollen absent
  - Examined: Total pollens; grasses, total tree, total weeds, *Alternaria, Cladosporium*
  - No allergy information on subjects is given
  - PM10, PM25, NO2, *Cladosporium* and *Alternaria* had effects that may be clinically significant
• Association of asthma symptoms with peak particulate air pollution and effect modification by anti-inflammatory medication use. (Delfino et al. Env Health Persp 2002;110:A607-617)
  – 10 children on anti-inflammatory med, 12 children not
  – Allergic status known by skin tests
  – March – April, peak pollen season in Alpine, CA (chaparral canyon area near San Diego)
  – Episodes of asthma symptoms: no allergen/pollutant interaction. In those not on anti-inflammatories strongest effects seen: PM10, O3, NO2, and pollens/spores
Design

- Retrospective, cross-sectional observational study using existing data de-identified. IRB approved.
- Year 2000 data from 4 Kaiser clinic sites in the greater Sacramento region
- Patient questionnaire data, prescription medications in Kaiser system, skin test results and physician diagnosis
Analysis

- What were the most frequently seen positive skin tests?
- Were there associations with a diagnosis of asthma?
- ARB staff also requested the following if possible: effect of years in California, years in Sacramento area, or city of residence/zone of residence
Results

- 790 charts
- 51 incomplete, 3 duplicates
- 736 complete charts
- Only 566 had a physician diagnosis of asthma or allergic rhinitis
Subject Summary

- Mean age 34, range 2-79
- Male 46%, Female 54%
- Current smoker: 6.4%, not stated 3.0%
- Dog owner: 42%; cat owner: 40%
- Visible mold in home: 21%
- State of residence at onset of symptoms: California 81%
Summary of positive skin tests: Grasses

<table>
<thead>
<tr>
<th>Allergen</th>
<th>AR¹ or Asthma N=566</th>
<th>AR only N=288</th>
<th>Asthma only N=72</th>
<th>AR AND Asthma N=206</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bermuda</td>
<td>60%</td>
<td>65%</td>
<td>18%</td>
<td>68%</td>
</tr>
<tr>
<td>Kentucky</td>
<td>65%</td>
<td>72%</td>
<td>21%</td>
<td>72%</td>
</tr>
<tr>
<td>Perennial</td>
<td>60%</td>
<td>67%</td>
<td>19%</td>
<td>66%</td>
</tr>
<tr>
<td>Rye</td>
<td>60%</td>
<td>65%</td>
<td>19%</td>
<td>68%</td>
</tr>
<tr>
<td>Timothy</td>
<td>60%</td>
<td>65%</td>
<td>19%</td>
<td>68%</td>
</tr>
</tbody>
</table>

¹AR = Allergic rhinitis
# Summary of positive skin tests: Weeds

<table>
<thead>
<tr>
<th>Allergen</th>
<th>AR or Asthma N=566</th>
<th>AR only N=288</th>
<th>Asthma only N=72</th>
<th>AR AND Asthma N=206</th>
</tr>
</thead>
<tbody>
<tr>
<td>English Plantain</td>
<td>41%</td>
<td>42%</td>
<td>6.9</td>
<td>50%</td>
</tr>
<tr>
<td>Western Ragweed</td>
<td>35%</td>
<td>34%</td>
<td>10%</td>
<td>46%</td>
</tr>
<tr>
<td>Pigweed</td>
<td>38%</td>
<td>38%</td>
<td>11%</td>
<td>46%</td>
</tr>
<tr>
<td>Lamb’s Quarters</td>
<td>26%</td>
<td>29%</td>
<td>8.3%</td>
<td>28%</td>
</tr>
<tr>
<td>Russian Thistle</td>
<td>25%</td>
<td>25%</td>
<td>6%</td>
<td>32%</td>
</tr>
</tbody>
</table>
## Summary of positive skin tests: Trees

<table>
<thead>
<tr>
<th>Allergen</th>
<th>AR or Asthma N=566</th>
<th>AR only N=288</th>
<th>Asthma only N=72</th>
<th>AR AND Asthma N=206</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olive</td>
<td>57%</td>
<td>62%</td>
<td>15%</td>
<td>65%</td>
</tr>
<tr>
<td>Oak</td>
<td>39%</td>
<td>41%</td>
<td>7%</td>
<td>49%</td>
</tr>
<tr>
<td>Acacia</td>
<td>39%</td>
<td>39%</td>
<td>11%</td>
<td>50%</td>
</tr>
<tr>
<td>Chinese Elm</td>
<td>39%</td>
<td>41%</td>
<td>6%</td>
<td>47%</td>
</tr>
<tr>
<td>Mulberry</td>
<td>37%</td>
<td>40%</td>
<td>7%</td>
<td>45%</td>
</tr>
</tbody>
</table>
### Summary of positive skin tests: Molds

<table>
<thead>
<tr>
<th>Allergen</th>
<th>AR or Asthma N=566</th>
<th>AR only N=288</th>
<th>Asthma only N=72</th>
<th>AR AND Asthma N=206</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alternaria</td>
<td>24%</td>
<td>24%</td>
<td>10%</td>
<td>28%</td>
</tr>
<tr>
<td>Cladosporium</td>
<td>7%</td>
<td>6%</td>
<td>3%</td>
<td>10%</td>
</tr>
<tr>
<td>Penicillium</td>
<td>8%</td>
<td>9%</td>
<td>6%</td>
<td>8%</td>
</tr>
<tr>
<td>Aspergillus</td>
<td>4%</td>
<td>3%</td>
<td>4%</td>
<td>5%</td>
</tr>
</tbody>
</table>

March 1, 2005
Summary of positive skin tests: Danders and Mites

<table>
<thead>
<tr>
<th>Allergen</th>
<th>AR or Asthma N=566</th>
<th>AR only N=288</th>
<th>Asthma only N=72</th>
<th>AR AND Asthma N=206</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat</td>
<td>41%</td>
<td>39%</td>
<td>24%</td>
<td>49%</td>
</tr>
<tr>
<td>Dog</td>
<td>29%</td>
<td>25%</td>
<td>17%</td>
<td>38%</td>
</tr>
<tr>
<td>D. farinae</td>
<td>37%</td>
<td>35%</td>
<td>15%</td>
<td>46%</td>
</tr>
<tr>
<td>D. pteron.</td>
<td>49%</td>
<td>48%</td>
<td>31%</td>
<td>56%</td>
</tr>
</tbody>
</table>

March 1, 2005
Associations with asthma?

- Principal components analysis: first component largest: positive weights on all tests except controls. This showed that the major way subjects vary is that some have multiple positive results, while others fewer.

- Logistic regression: first principal component + x, predictive of AR or asthma
• **Allergic rhinitis**: no allergens predictive beyond the first principal component

• **Asthma**: Grass pollen, e.g., Ryegrass pollen associated with asthma, $p = 0.001$, OR = 2.15

• **Of those with allergic rhinitis AND asthma**, there were trends that did not reach significance to predict asthma beyond allergic rhinitis alone (dust mites, dog, cat, ragweed, acacia)
Severity of asthma and sensitizations

- Grass: Kentucky
- Olive
- D. pteron.
- Cat
- Dog

- Mod-Severe, n=32
- Mild Persistent, n=82
- Intermittent, n=141

- p = .0272
- p = .0264
Effects of age on skin test results

- Grass: Kentucky
- Olive
- English Plantain
- D. pteron.
- Cat

Legend:
- 0-9 years old, n=37
- 10-19 years old, n=74
- 20-29 years old, n=82
- 30-39 years old, n=114
- 40-49 years old, n=87
- 50-59 years old, n=57
- 60+ years old, n=43
Visible mold and positive skin tests to molds

- Alternaria
- Aspergillus
- Hormodendrum
- Penicillium

Visible Mold, n=118
No Visible Mold, n=325
Other Effects

- **Gender**: No association for asthma or allergic rhinitis
- **Clinical site of skin testing**: no associations
- **Effect of cigarette smoking** *(current or ever)*: no associations
- **Effect of pet ownership**: no associations with AR or asthma or on current sensitization
Other Effects Cont’d

- **Years in California**: no association with AR or asthma, or specific allergen sensitization.
- **Years in Sacramento region** – incomplete data.
- **Zone of current residence**: Gold Country, North Sacramento, and Other – discarded, incomplete, and workplace differs from residence – no way to gauge exposures.
Conclusions

- Aeroallergens with greatest frequency of positive skin tests in this population with physician-diagnosed AR or Asthma
  
  **Outdoor:**
  - Grasses: 60-65% (April-June, see NAB counts)
    - E.g., Bermuda and perennial rye
  - Olive 57% (May)
  - Of the molds: *Alternaria* 24% (see NAB counts for high variability across California)

  **Indoor:**
  - D. pteron: 49%
  - Cat: 41%
Conclusions continued

- In this population, grass pollen sensitization was positively associated with a diagnosis of asthma.
Problem with Generalizing

- **Kaiser population is not inner-city.** In inner-city populations elsewhere, cockroaches and rodents are also very important. Mold exposure in inner-city areas is also likely different.

- **Many microenvironments in California**

- Reassuring that results are very close to the small study looking at mainly Southern California patients
How this data could be used

• A large, prospective ED study of asthmatics presenting to the ED as mentioned earlier – i.e., clinically and economically relevant morbidity. (Fundamental difference from panel studies generalizing from lesser morbidity)

  – Need allergy testing with **no risk** to patient that can be done on sample from ED: In vitro specific IgE assays can be restricted in number to save $ (but include *Alternaria* and *Cladosporium*)
• Or, in panel studies, perform in vitro assays for quantitative measure of IgE to selected aeroallergens – may have new findings and/or correlate better to use specific pollen/spores and the individual titers than totals

• Bioaerosol studies: interactions of PM, O3, NO2 with the key pollens and Alternaria spores…e.g., effects on basophil activation in human PBMCs, effects on IgE sensitization in murine models, effects on IgE epitopes