

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

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Key Personnel

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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**
(1998, Ann Allergy Asthma Immunol 81:203)
 - **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 ($r = 0.90$, $p < 0.001$)

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

Asthma Panel Studies Cont'd

- **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

Allergen	AR ¹ or Asthma N=566	AR only N=288	Asthma only N=72	AR AND Asthma N=206
Bermuda	60%	65%	18%	68%
Kentucky	65%	72%	21%	72%
Perennial Rye	60%	67%	19%	66%
Timothy	60%	65%	19%	68%

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¹AR = Allergic rhinitis

Summary of positive skin tests: Weeds

Allergen	AR or Asthma N=566	AR only N=288	Asthma only N=72	AR AND Asthma N=206
English Plantain	41%	42%	6.9	50%
Western Ragweed	35%	34%	10%	46%
Pigweed	38%	38%	11%	46%
Lamb's Quarters	26%	29%	8.3%	28%
Russian Thistle	25%	25%	6%	32%

Summary of positive skin tests: Trees

Allergen	AR or Asthma N=566	AR only N=288	Asthma only N=72	AR AND Asthma N=206
Olive	57%	62%	15%	65%
Oak	39%	41%	7%	49%
Acacia	39%	39%	11%	50%
Chinese Elm	39%	41%	6%	47%
Mulberry	37%	40%	7%	45%

Summary of positive skin tests: Molds

Allergen	AR or Asthma N=566	AR only N=288	Asthma only N=72	AR AND Asthma N=206
Alternaria	24%	24%	10%	28%
Cladosporium	7%	6%	3%	10%
Penicillium	8%	9%	6%	8%
Aspergillus	4%	3%	4%	5%

Summary of positive skin tests: Danders and Mites

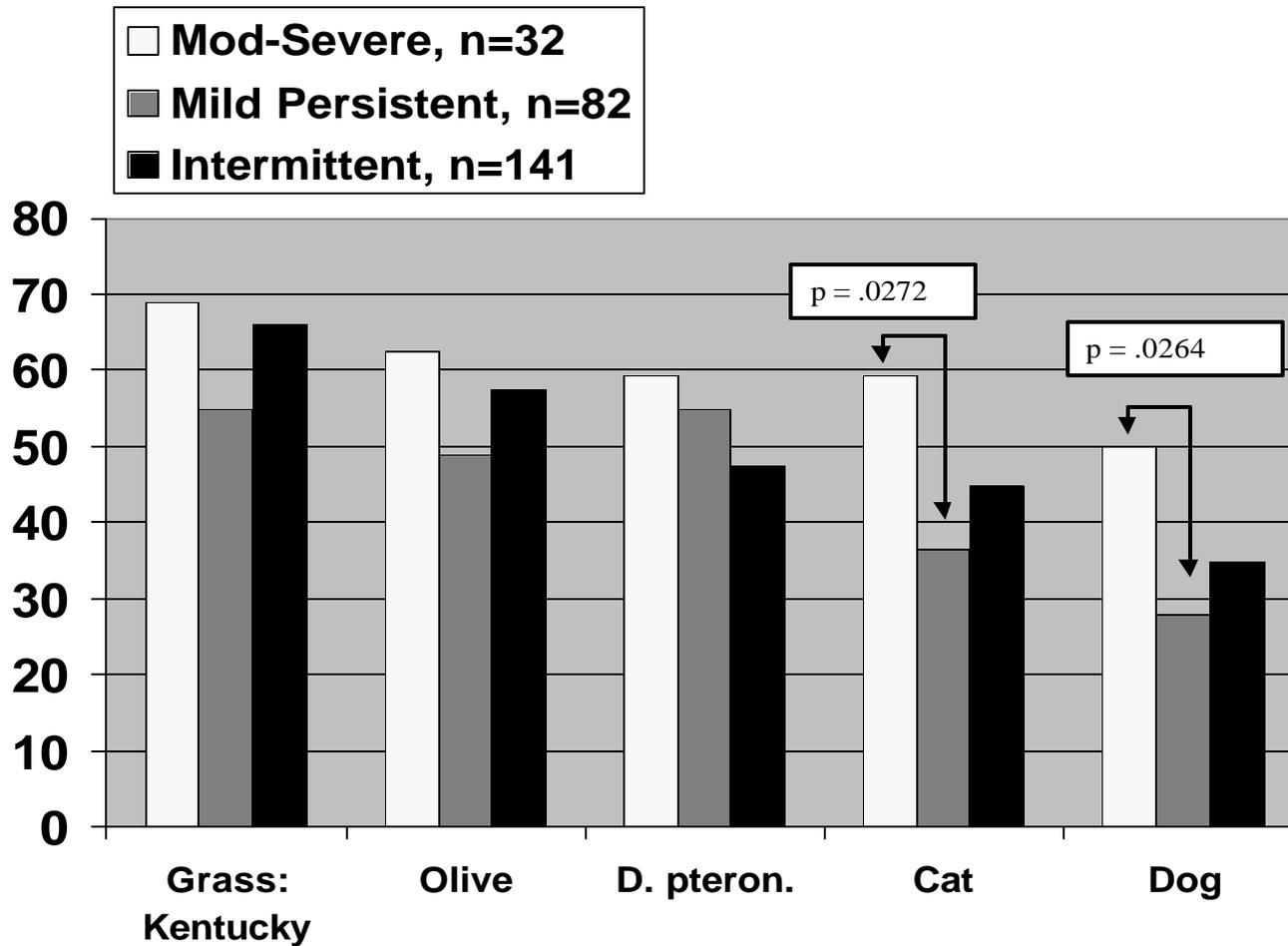
Allergen	AR or Asthma N=566	AR only N=288	Asthma only N=72	AR AND Asthma N=206
Cat	41%	39%	24%	49%
Dog	29%	25%	17%	38%
D. farinae	37%	35%	15%	46%
D. pteron.	49%	48%	31%	56%

Associations with asthma?

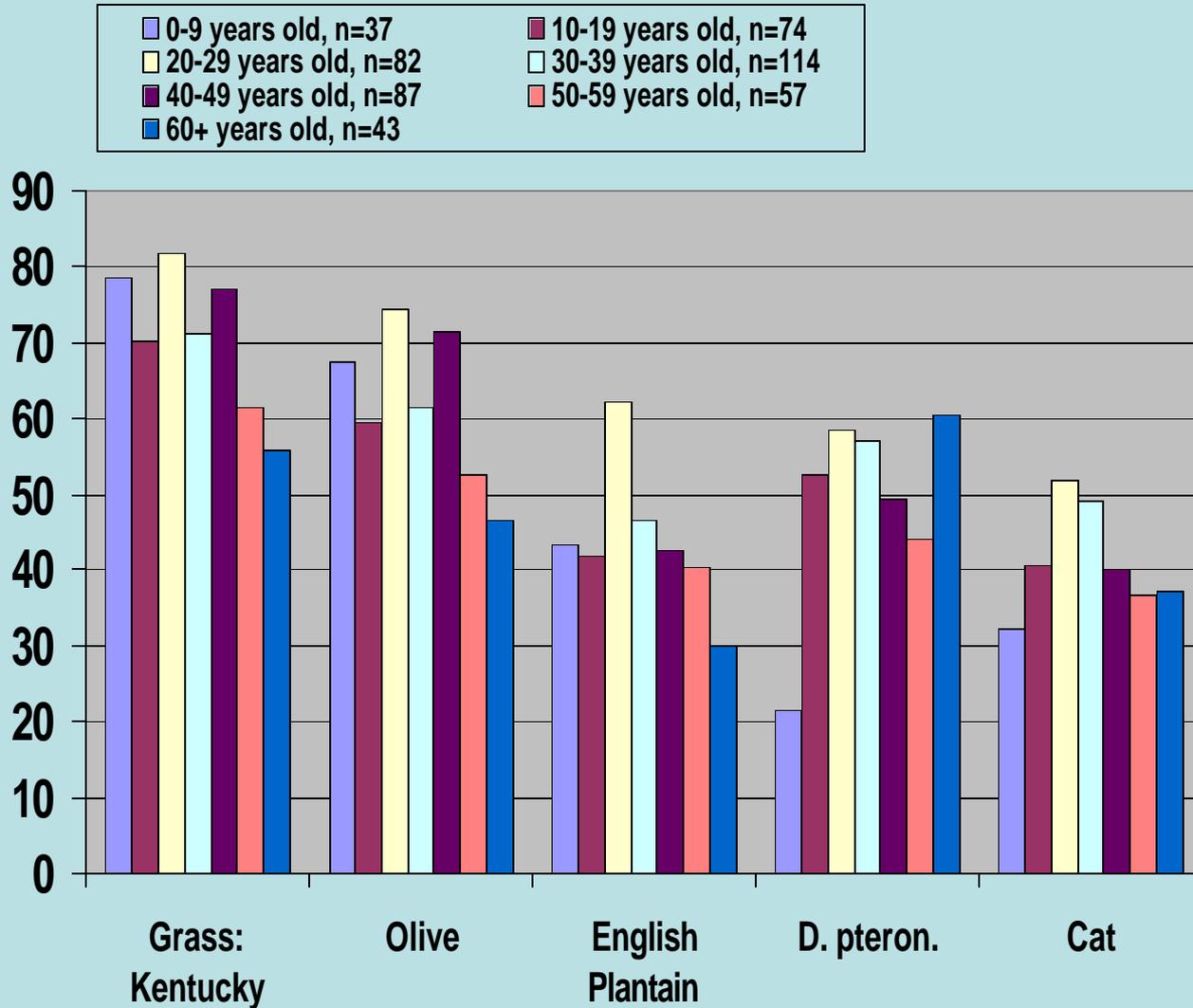
- Principal components analysis: first component largest: positive weights on all tests except controls. This showed that the major way subjects vary is that some have multiple positive results, while others fewer.
- Logistic regression: first principal component + x , predictive of AR or asthma

- **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)

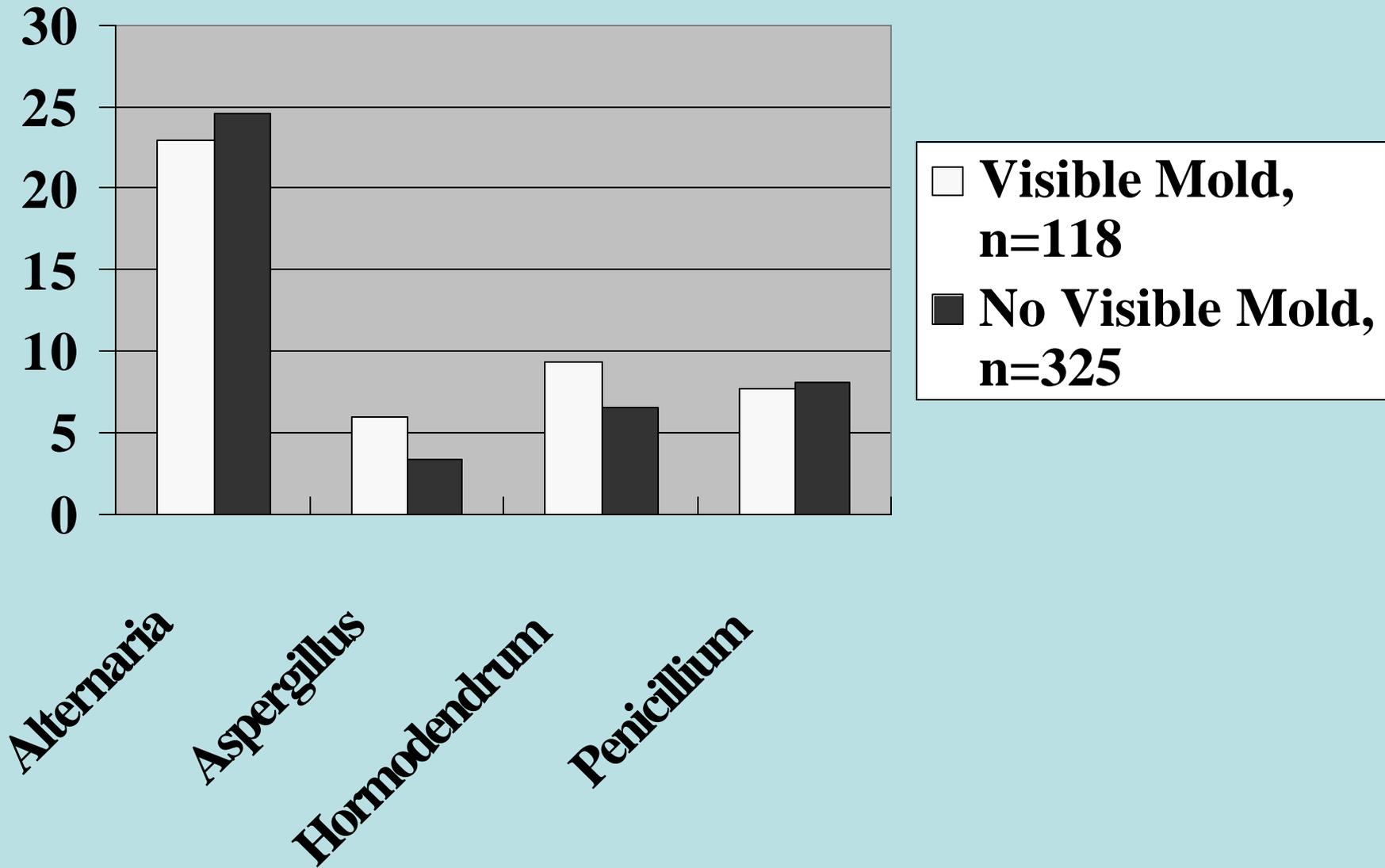
Severity of asthma and sensitizations



Effects of age on skin test results



Visible mold and positive skin tests to molds



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, cockroach, rodents also very important. Mold exposure in inner-city areas 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