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# What are the Effects of Indoor Bioaerosols on Asthma? How Do We Measure Exposure and Manage Risk?

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B · O · S · C HUMAN HEALTH PROGRAM REVIEW

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RESEARCH & DEVELOPMENT

## LTG 3 Poster 12

### Science Questions

- What is the role of dampness and/or mold exposure in the induction/exacerbation of asthma?
- How can we best assess mold exposure?
- How can interventions be used to reduce the burden of asthma by reducing exposure to bioaerosols particularly molds?
- Does epidemiology identify other important (and understudied) bioaerosols associated with asthma?

### Research Goals

- To develop a method to identify and quantify indoor mold exposure and risk
- To assess the allergic potential of various indoor molds using a mouse model of allergy/asthma
  - Determine dose-response
  - Comparison to well characterized indoor allergen (house dust mite)
  - Characterized potential mold allergens
  - Extrapolate data from mouse to man
- To develop testing and verification methods to assess indoor building materials marketed as microbial resistant products for microbial resistance, moisture resistance, and VOC production properties
- To determine the impact of endotoxin on asthma and gain insight into the mechanism for this impact
- To determine the distribution of mouse allergen, its relationship to mouse skin test sensitivity, and the relationship between exposure and allergen-specific IgE and IgG responses

### Researchers Involved

- NHEERL:** MaryJane Selgrade, Lucas Neas, Jane Gallagher
- NERL:** Richard Haugland, Karen Bradham
- NRML:** Marc Menetrez, Doris Betancourt
- University of North Carolina:** David Peden, Neil Alexis
- Johns Hopkins University:** Elizabeth Matsui, Pat Breyse
- Case Western Reserve University:** Dorr Dearborn, Carolyn Kercsmar
- HUD:** Peter Ashley
- Research Triangle Institute:** Karin Forade

- Developed PCR based method of mold identification and quantification (MSQPCR)
- ~1100 homes surveyed in the National American Healthy Home Survey (partnered with HUD).
- Developed the Environmental Relative Moldiness Index (ERMI)
- Molds have varying potential to induce allergic or asthma-like responses in the mouse model
- Allergic responses to mold extracts occur in a dose-response manner (threshold dose)

### Findings and Conclusions

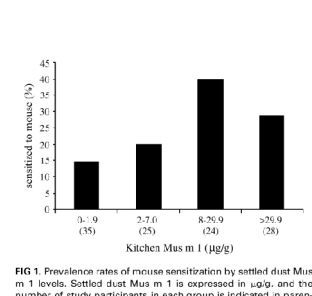
- Endotoxin, identified in both coarse and fine ambient air PM, enhanced responses to allergen in allergic asthmatic volunteers
- Endotoxin at agricultural exposure levels increased cell surface markers engaged in allergen presentation and increased cells bearing IgE after allergen challenge
- Mouse allergen exposure is common among suburban, middle-class asthmatic children as well as inner city asthmatic children
- High levels of mouse allergen exposure in children may be associated with attenuated humoral responses of all isotypes.
- Cross-species fungal protein allergens may provide environmental assessment biomarkers
- Similar IgE-reactive protein profiles are detected by human and mouse sera.
- Methods have been developed for testing the efficacy of microbial resistant building products.

### Methods/Approach

#### BIOAEROSOLS HAZARD CHARACTERIZATION

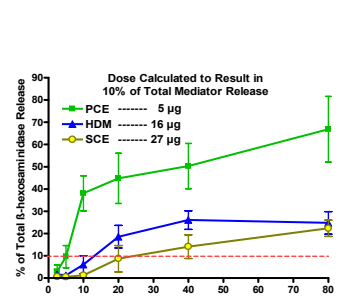
#### MOUSE ALLERGENS

- Sensitization prevalence rates for mouse allergens was lowest with exposure to <2 µg/g settled dust
- Children exposed to >8 µg/g were more likely to be sensitized to mouse allergen
- Mouse allergen-specific IgG and IgG<sub>4</sub> were associated with IgE sensitization



#### MOLDS

- Different molds induce various responses:
  - Allergic asthma-like endpoints in a dose-response manner with a threshold dose
  - Airway reactivity without significant allergic responses
  - Neither allergy nor airway responses



#### Extrapolation from Mouse to Man

Human sera IgE reacts with molds not commonly assessed.

Human and mouse sera IgE react with similar protein profiles identified as a fungal catalase

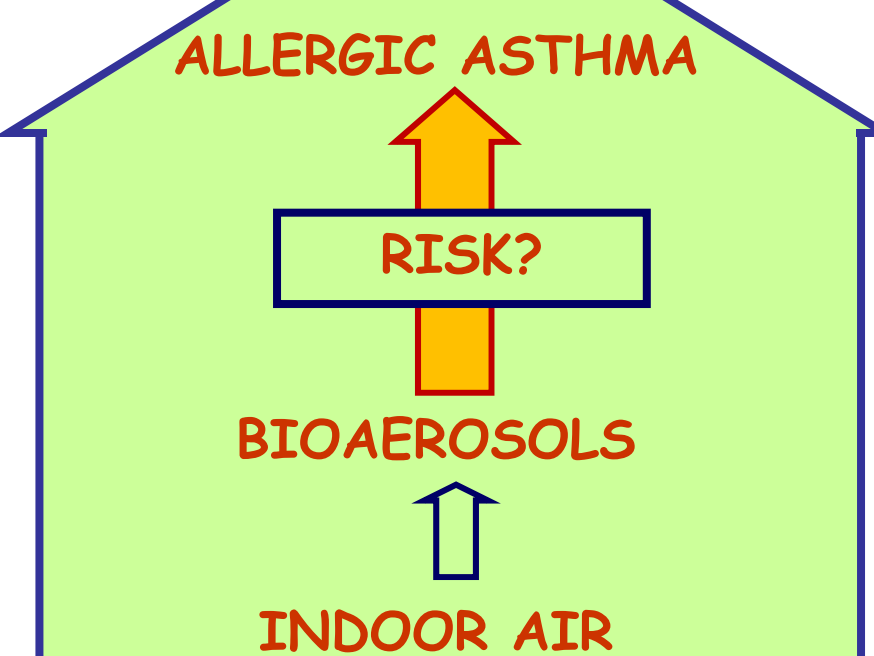
#### ENDOTOXIN

Effect of endotoxin on response to inhaled allergen

Potential Mechanism of Enhanced Response

Endotoxin exposure significantly enhances response of allergic asthmatic volunteers to inhaled allergen

- ↑ levels of CD80, CD86 and HLA-DR (involved allergen presentation to airway lymphocytes) on macrophages and monocytes
- ↑ eosinophilic airway inflammation
- ↑ in IgE bearing cells after allergen challenge



#### EXPOSURE ASSESSMENT

The Environmental Relative Moldiness Index (ERMI) is a method to quantitate mold exposure  
 The ERMI Calculation: Σ concentration logs of Grp 1 Molds (water-damaged environments) - Σ concentration logs of Grp 2 Molds (common)  
 Cincinnati - Prospective study predictive of development of wheeze  
 Detroit - Significantly higher ERMI values in homes of severely asthmatic children

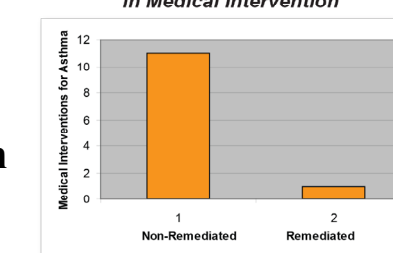
#### RISK MANAGEMENT

#### Microbial Resistant Product

- Use of Microbial resistant products may have unintended consequences (e.g. produce unhealthy levels of VOCs)
- EPA Environmental and Sustainable Technology Evaluation (ESTE) system
  - Test method developed to verify materials performance according ASTM test guidelines
  - Moisture resistance (ASTM D6329)
  - Fungi/mold resistance (ASTM 6329-98)
  - VOC emissions (ASTM D 5116)
  - Broad based technical stakeholder group determine the optimum testing procedures

#### Remediation

- ERMI APPLICATIONS:
  - Cuyahoga County -
    - Higher ERMI values in asthmatic's homes
    - Remediation of mold and moisture = less asthma symptoms
  - Stakeholders:
    - EPA Regional Offices
    - Office of Indoor Air
    - Office of Children's Health Protection



### Impact and Outcomes

- Ongoing research addresses indoor environment research needs identified in the Indoor Environments Division document *Program Needs for Indoor Environments Research* (PNIER).
- ERMI scale describing household mold burden used in epidemiological studies (Cleveland, Cincinnati, Chapel Hill, Detroit, Baltimore and New Orleans) and an association of higher ERMI values with increased asthma related symptoms reported.
- UV/HVAC studies led to GAO requiring that all new GAO buildings be equipped with UV capabilities in their HVAC systems.
- The ESTE product verification system can be used by building professionals and consumers to make informed decisions regarding the use of building products.
- The mold research has provided Congress (GAO Review on Indoor Mold) with insight into the current state of the science regarding indoor mold. GAO identified a need for more mold research.
- Identification of mouse allergen as an important risk factor for asthma is the basis of a NIH funded clinical trial targeted on mouse contamination in inner city homes.

### Future Directions

- Epidemiological studies are needed to help understand the relationship between mold exposure and potential health problems.
- Determine the impact of gestational allergen exposure on adult allergen responses.
- Determine if there are common physico-chemical properties of mold allergens.
- Identify a panel of differentially expressed genes following an acute exposure that are indicative of allergic sensitization.
- Utilize the testing and verification data to generate a product labeling system that can be used by consumers to make informed decisions when purchasing a microbial resistant building products, thus reducing potential bioaerosol exposure. Test products will include: microbial resistant gypsum wallboard, laminant flooring product, board insulation, and spray insulation.

### Key Products

- Chung *et al.* Dose-dependent allergic responses to an extract of *Penicillium chrysogenum* in BALB/c mice. *Toxicology*, 2005, 209(1):77-89.
- Kercsmar *et al.* Reduction in asthma morbidity in children as a result of home remediation aimed at moisture sources. *Environ Health Perspect.*, 2006, 114(10):1574-80.
- Matsui *et al.* Mouse allergen-specific antibody responses in inner-city children with asthma. *J Allergy Clin Immunol.*, 2007, 119(4):910-5.
- Vesper *et al.* Development of an Environmental Relative Moldiness index for US homes. *J Occup Environ Med.*, 2007, 49(8):829-33.
- Ward *et al.* Human sera IgE reacts with a *Metarhizium anisopliae* fungal catalase. (Submitted)
- Zeldin *et al.* How exposures to biologics influence the induction and incidence of asthma. *Environ Health Perspect.*, 2006, 114(4):620-6.

## Susceptible Populations

This poster does not necessarily reflect EPA policy. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.

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