Health Effects of Air Pollution

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Learning Objectives

1. Recognize the indoor and outdoor airborne pollutants that can adversely impact respiratory health
2. Understand how airborne pollutants cause disease
3. Recognize synergistic interactions between causative agents

Definition of Air Pollutants

- Primary – pollutants directly emitted into the atmosphere (eg. SO\(_2\), some NO\(_x\) species, CO, PM)
- Secondary – pollutants that form in the air as a result of chemical reactions with other pollutants and gases (eg. Ozone, NO\(_2\), some particulates)

*PM=particulate matter; SO\(_2\)=sulfur dioxide; CO=carbon monoxide; NO\(_2\)=nitrogen dioxide; NO\(_x\)=nitrogen oxides
Gaseous Pollutants

- NO\textsubscript{x}
- SO\textsubscript{2}
- Ozone
- CO
- CO\textsubscript{2}
- SVOC (semi-volatile organic compounds include aldehydes, dioxins, benzene, 1,3-butadiene)

Particulate Matter (PM)

- Coarse PM (aerodynamic diameter 2.5-10um)
  - major sources are abraded soil, road dust from brakes and tires, construction debris, aggregation of smaller combustion particles.
- Fine PM (≤ 2.5 um) and Ultrafine PM (<0.1 um)
  - byproducts formed during the combustion of fossil fuel products
- Coarse and Fine PM have been associated with increased cardiorespiratory morbidity and mortality
- Much less is know about the adverse health effects of Ultrafine PM which is more abundant and potentially more toxic

Indoor Air Pollutants

- Sources
  - cooking
  - combustion
  - particle resuspension
  - building materials
  - air conditioning/cleaning
  - consumer products
  - tobacco smoke (active and passive)
  - heating
  - biologic agents
  - pets
- Products
  - NO\textsubscript{x}, CO, CO\textsubscript{2}, SVOCs, ozone (O\textsubscript{3}), bacteria, mold-byproducts, endotoxin
Outdoor Air Pollutants

- Sources
  - industrial
  - commercial
  - mobile
  - urban
  - regional
  - agricultural
  - natural
    - acute – volcano eruption
    - chronic – climate change
- Products
  - SO\(_2\), O\(_3\), NO\(_x\), CO, PM, SVOC

Summary

<table>
<thead>
<tr>
<th>Pollutants</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO(_2)</td>
<td>Outdoor: automobiles, burning fossil fuels&lt;br&gt;Indoor: gas appliances, kerosene heaters, wood stoves, tobacco products (side stream smoke)</td>
</tr>
<tr>
<td>SO(_2)</td>
<td>Heating fuels, coal fired plants</td>
</tr>
<tr>
<td>PM(_{2.5})</td>
<td>Diesel engines, fossil fuels</td>
</tr>
<tr>
<td>O(_3)</td>
<td>Created when sunlight reacts with VOCs, NO(_2)</td>
</tr>
</tbody>
</table>

Pollutant Health Effects - Biochemical Mechanisms

- Oxidative stress: common mechanisms involving oxidant/anti-oxidant imbalance and generation of reactive oxygen and nitrogen species
  - ozone, PM, SO\(_2\), transition metals, polyaromatic hydrocarbons, acrolein
- Activation of aryl hydrocarbon receptor
  - polyaromatic hydrocarbons
- Covalent modification of proteins/enzymes
  - acrolein, formaldehyde
- Acid formation
  - SO\(_2\) (formation of airway sulfuric acid)

Pollutant Health Effects-Biological Mechanisms

- Adjuvant effects: enhancement of allergenicity and viral susceptibility
  - DEP, nickel, O₃, NO₂
- Activation of innate immune responses through TLR, CD14, HLA-DR
  - Nickel, biorganic pollutants: glucans, endotoxin, O₃
- Suppression of macrophage function with reduced immune responses to infectious agents
  - NOₓ, O₃, LPS
- Procoagulant activity
  - ultrafine PM, NOₓ, CO
- Stimulation of the autonomic nervous system
  - SO₂, acetaldehyde

[References]

Epidemiologic Studies Of Specific Air Pollutants And Aeroallergens On Asthma Exacerbation

- Ozone and fungal spores have been demonstrated to be cofactors in increasing asthma symptoms and SABA use
- Ozone, NO₂ and SO₂ individually or in combination may enhance airway response to inhaled allergens
- Short term increases in ozone levels are associated increase in acute respiratory diseases in children.


Ozone (O₃⁻)

- O₃⁻ absorbs UV radiation and creates a warm layer of air responsible for the thermal structure of the stratosphere
- O₃⁻ present in the troposphere is mainly due to man-made pollution; higher concentrations are found in urban areas
- O₃⁻ is formed when NOX combines with volatile organics compounds (VOC, i.e. chemical vapors) in the presence of sunlight

VOC + NOx + Sunlight = Ozone

- O₃⁻ linked to causing new onset asthma and exacerbating pre-existing asthma

[Chemical and Engineering News; v72; 6-7; 1994.]
[Aviation Week and Space Technology; v140; 20-21; 1994.]

Sulfur Dioxide (SO₂)

Referred to as ‘SOX’

- Sulfur dioxide is a major primary pollutant in the atmosphere
- Originates mostly from coal fired power plants and other fossil fuel combustion
- Sulfur dioxide is usually oxidized by ozone and hydrogen peroxide to form sulfur trioxide, a secondary pollutant that is extremely soluble in water
- Sulfur oxides present in the atmosphere when condensation occurs results in droplets of sulfuric acid called “acid rain”

Science; v265; 497-9; 1994.
Nature; v366; 327-9; 1993.
**Sulfur Dioxide**

- Controlled exposure studies (5 min) to inhaled SO\(_2\) induces rapid onset bronchoconstriction in healthy and asthmatic subjects
- Asthmatic patients experience increased symptoms and a greater decrease in lung function at lower concentrations (0.25 ppm) compared to healthy volunteers that are unresponsive at concentrations less than 0.5 ppm
- Exposed asthmatic patients are refractory to the effects of SO\(_2\) for up to 4 hours after exposure
- Exposure to ozone or cold air before SO\(_2\) exposure increases BHR to SO\(_2\) in asthma patients

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**NOx (pronounced "nox") Gases**

- NO (nitric oxide) is the principal emitted NO\(_x\) gas from high temperature combustion in air.
  - Reacts with ozone and tropospheric radicals to help form NO\(_2\), ozone, and other secondary pollutants such as peroxyacetyl nitrate.
- NO\(_2\) is the lesser of the two emitted NO\(_x\) gases from high temperature combustion in air.
  - It is an important species in the atmosphere as it absorbs in the visible wavelength region
  - Manifests as the "Brown Cloud" seen over large polluted cities (e.g. Denver, LA, Mexico City, Beijing...)
  - NO\(_2\) is a precursor to photochemical smog: can be photolyzed to yield oxygen atoms that can react with molecular oxygen to create ozone (UV sunlight + hydrocarbons = ozone).

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**Nitrogen Dioxide**

- Most likely health effect as an outdoor pollutant is through the formation of ozone
- High NO\(_2\) exposure (0.02 ppb) 1 week before a respiratory URI has been associated with increased asthma exacerbations
- Healthy subjects and smokers exposed to NO\(_2\) (2-6 ppm) manifest increased PMNs in the airways and reduced lymphocyte subpopulations
- Exposure to 0.4 ppm NO\(_2\) for 4 hours enhances the immediate and late phase response to inhaled allergens

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Asthma and Air Pollution

- Air pollution has been associated with:
  - Increased bronchial hyperresponsiveness
  - Increased airway inflammation
  - Decreased lung function
  - Increased hospital admissions and ER visits
  - Enhancing airway inflammation induced by allergen exposure
  - Priming of the airways to allergic responses
  - High exposure is an independent risk factor for wheezing during infancy and early childhood.

Molfino, Lancet, 1991; Peden, AJRCCM, 1995
Bernstein DI, Traffic related pollutants and wheezing in children.

Lung Function and Air Pollutants

- Inhalation of 1 ppm of SO2 for 10 minutes during moderate exercise decreased FEV1 by 23% in adolescents with asthma.1
- An association between ambient ozone levels below EPA limits and asthma symptoms was found in children with asthma living in New England.2
- Air pollution decreases the typical increase in FEV1 in children as the level of air pollution goes up3.


Community-Specific Average Growth in FEV1 among Girls and Boys During the Eight-Year Period from 1993 to 2001 Plotted against Average Nitrogen Dioxide (NO2) Levels

ER Visits for Respiratory Complaints and Air Pollutants

- Numerous studies have found an association between PM 10 levels and ER visits for asthma.
- In Seattle, an increase of 11 µg/m³ in fine PM was associated with an 11% increase in asthma ER visits.⁴
- Ozone and SO2 have been associated with ER visits for asthma in Mexico.²
- Exposure to air pollution is an important determinant of ER visits for acute respiratory symptoms, particularly during warm season³.

Inflammatory Markers and Air Pollutants

- Exposure to ozone results in an influx of neutrophils and alveolar macrophages into the airway.¹,²
- IL-6, IL-8, LTB4, and thromboxane B2 are increased in the airways after exposure to ozone.
- mCD14 surface expression on airway macrophages is enhanced following ozone exposure.³
- PM10 exposure increases allergen specific IgE production leading to increased airway inflammation.
- Diesel exhaust particles increase production of C-C chemokines, induce a TH2 cytokine milieu in the presence of allergen, and enhance total and allergen specific IgE responses to allergen.⁴

Interactions Between Air Pollutants and Allergen

- Exposure to 0.12 ppm ozone decreased the amount of ragweed allergen required to provoke a 20% decrease in FEV1.¹
- NO2 exposure has been shown to increase airway hyperresponsiveness to tree pollen.⁷
- Exposure to PM increases total serum IgE levels.
- Nasal histamine levels are increased 3-fold when diesel exhaust particles are co-administered with allergen.
- Exposure to airborne endotoxin enhances response to inhaled allergen⁶.
- Exposure to diesel exhaust particles increases number of IgE secreting cells in the nasal mucosa.⁶
- Lowering Th-2 inflammation reduces the inflammatory response to LPS in asthmatics.²

References:

⁷ Reed M. *JACI.* 2005;115(2):221-8.
Interaction Between Air Pollutants and Allergens

- Epidemiologic studies of pollution and aeroallergens on causing asthma
- Epidemiologic studies of pollution and aeroallergens on the exacerbation of asthma
- Experimental studies on the adjuvant effects of DEPs on specific TH2 responses
- Role of pollution and global warming on natural allergen production
- Increasing levels of CO2 and temperature are associated with increased pollen levels.


Epidemiologic Studies Of Pollution And Aeroallergens On Causing Asthma

- Many studies have investigated the effects of automobile related pollutants in heavily traveled expressways on causing asthma symptoms in allergic children
- Living near highways with high vehicle traffic is associated with asthma symptoms in children with known allergen sensitization


Environmental Tobacco Smoke Exposure

- Passive smoke exposure has been demonstrated to have a direct and adjuvant effect on asthma in children and adults.
- Passive smoke exposure in early life might lead to increased vulnerability of the lungs to air pollution.1
- Passive smoke exposure is a risk factor for respiratory disease in early childhood.2

What is Smog?

- A term used to describe a mixture of smoke and fog.
- Occurs when high concentrations of moisture are combined with smoke (often containing oxides of sulfur and nitrogen) in the presence of high temperatures or thermal inversions and the absence of wind.
- These conditions cause polluted air to stagnate over industrial areas causing potential respiratory health hazards.
- Large coastal industrial centers with surrounding high ground are more prone to smog.
- There is often a diurnal variation in smog formation since a necessary component for its formation is sunlight.

Journal of Environmental Health; v56; p38; 1994.
Science News; v144; p326; 1993.

Air Quality Index

- If the AQI is below 50, the air quality is considered good.
- If the AQI value is in the 100-150 range, there may be some adverse effects in sensitive people (e.g. those with respiratory disease).
- At AQI values greater than 150, everyone may experience some adverse effects, with more severe effects in those who are more sensitive.
- An AQI value of 200 or higher may cause serious adverse effects on a large proportion of those exposed.

Air Quality Index (AQI) Values and Pollutant Concentration Equal to the Upper AQI Value

<table>
<thead>
<tr>
<th>AQI value</th>
<th>AQI Descriptor</th>
<th>O₃ ppm (8-hour avg.)</th>
<th>PM₁₀ μg/m³ (24-hr avg.)</th>
<th>PM₂.₅ μg/m³ (24-hr avg.)</th>
<th>SO₂ ppm (1-hour avg.)</th>
<th>NO₂ ppm (1-hour avg.)</th>
<th>CO ppm (8-hour avg.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤50</td>
<td>Good</td>
<td>0.059</td>
<td>12</td>
<td>54</td>
<td>35</td>
<td>63</td>
<td>4.5</td>
</tr>
<tr>
<td>51-100</td>
<td>Moderate</td>
<td>0.076</td>
<td>35</td>
<td>154</td>
<td>75</td>
<td>100</td>
<td>9.0</td>
</tr>
<tr>
<td>101-150</td>
<td>Unhealthy for Sensitive Groups</td>
<td>0.096</td>
<td>56</td>
<td>254</td>
<td>185</td>
<td>360</td>
<td>15</td>
</tr>
<tr>
<td>151-200</td>
<td>Unhealthy</td>
<td>0.115</td>
<td>150</td>
<td>354</td>
<td>304</td>
<td>844</td>
<td>30</td>
</tr>
<tr>
<td>201-300</td>
<td>Very Unhealthy</td>
<td>0.116</td>
<td>250</td>
<td>424</td>
<td>604</td>
<td>1244</td>
<td>40</td>
</tr>
<tr>
<td>&gt;300</td>
<td>Hazardous (1-hour)</td>
<td>0.405</td>
<td>&gt;250</td>
<td>&gt;424</td>
<td>&gt;605</td>
<td>&gt;1245</td>
<td>50</td>
</tr>
</tbody>
</table>

Source: http://www.epa.gov/airnow/aqi_tech_assistance.pdf
What Should We Advise Patients With Respiratory Diseases?

- Be aware of air quality health advisories and smog alerts
- Minimize outdoor activities during poor air quality days (i.e., exercise indoors)
- Advise against living in areas near high automobile traffic, power plants or chemical manufacturing plants
- Take environmental control measures (keep windows closed, run A/C, filtration, avoid passive smoke, encourage smokers in the home to stop or at least smoke outdoors)

2012 US EPA proposed revisions to the PM NAAQS

- In accordance with a court ordered deadline, on June 14, 2012 US EPA proposed revisions to the PM NAAQS:
  - Retain current 150 mcg/m³ 24-hour PM₁₀ standard
  - Retain current 35 mcg/m³ 24-hour PM₂.₅ standard
  - Strengthen the 15 mcg/m³ annual PM₂.₅ standard to a level between 12 to 13 mcg/m³
  - Require near-roadway monitoring of PM₂.₅ in cities with more than a million people
- The proposed standards will be open for public comment before a Final Rule is announced in December 2012.
  If finalized as proposed, community-oriented and near-road monitoring will be required for 3 Criteria Pollutants: PM₁₀, NO₂, and CO.

Indoor Allergens
Importance of Allergic Sensitization in Asthma

- In the US, ~56% asthma cases attributable to atopy
- Specific sensitization more important risk factor than total IgE
  - Total IgE associated with asthma, but only among atopics
- ≥80% of school age children with asthma sensitized to ≥1 common aeroallergen
- More positive skin tests → more severe asthma

Arbes S et al, JACI 2007 Nov; 119: 45

Indoor Allergen Exposure: A Therapeutic Target?

- Critical questions for assessing role of allergen avoidance in managing asthma:
  - Is exposure to the allergen associated with asthma symptoms/disease activity?
  - Is reduction of exposure feasible?
  - Does reduction of exposure result in improved asthma control?

Major Indoor Allergens

- Dust mite
- Cockroach
- Cat and dog
- Mouse and rat
- Mold
House Dust Mites

- Some important household mites:
  - Dermatophagoides pteronyssinus
  - Dermatophagoides farinae
  - Blomia tropicalis
- Live in bedding, upholstered furniture, stuffed animals and carpet.
- Feed on human skin scales.
- Grow best in relative humidity above 50-70%.


Dust Mite Antigens and the Particles on Which They Travel

- Much research has been focused on the group 1 (Der p 1 and Der f 1) and group 2 (Der p 2 and Der f 2) allergens.
- Group 1 are found in mite fecal particles.
- Airborne characteristics
  - Airborne with active disturbance (vacuum cleaning, bed making, etc...)
  - The majority of the allergens are found on 10-40 μm particles.
  - These particles settle rapidly (20 – 30 minutes).

Tovey E. et al. Nature 1981;289:592-3

Dust Mite Allergen Exposure is a Risk for Sensitization

Prevalence of sensitization to house dust mite stratified by highest and lowest quartiles of house dust mite exposure as age 6 months (n=648).


Table 2. Exposure to SDP in the House Dust Mite and Sensibility in 598 Infants.

<table>
<thead>
<tr>
<th>Score in</th>
<th>Age</th>
<th>Score in</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>&lt;6</td>
<td>0-2</td>
<td>≥6</td>
</tr>
<tr>
<td>3-9</td>
<td>&lt;6</td>
<td>3-9</td>
<td>≥6</td>
</tr>
<tr>
<td>10-49</td>
<td>&lt;6</td>
<td>10-49</td>
<td>≥6</td>
</tr>
</tbody>
</table>

Sporik et al. 1989

Dust Mites and asthma

Asthma development in children

Lung function in adult asthmatics

Custovic et al, JACI 1996;98:64-72

Reducing Dust Mite Allergen Exposure in the Home

First Line
- Mattress, pillow covers
- Wash bedding
- Remove stuffed animals
- Control humidity

Second Line
- Remove carpets
- Remove upholstered furniture
- HEPA vacuum cleaners
- Acaricides in fabrics
- Tannic acid
- Air filters unlikely to help

Dust Mite Allergen and Asthma Morbidity

• double blind, placebo-controlled RCT
• 52 school-age children
• Significant reduction in house dust mite and inhaled corticosteroid dose in active group

Halken JACI 2003; 111:169-76.
Bed Covers for Adults with Asthma

**Methods:** Randomized double blind placebo controlled study of allergen impermeable mattress covers.

**Results:**
- Mite allergen lower for the active than placebo group at 6, but not 12 months.

**Conclusion:** Mattress covers alone are not sufficient to control asthma symptoms in allergic adults.


Dust Mite Allergen - Summary

- Exposure related to development of allergic sensitization
- Sensitization associated with asthma in areas where dust mites are common
- Exposure is associated with increased asthma morbidity among sensitized individuals
- Reduction of exposure has been associated with improvements in disease activity
- Interventions that involve only mattress encasings may be ineffective

Cockroach Allergen

- *Blattella germanica* most common in U.S. inner cities
- Bla g 1 and Bla g 2 are major allergens from German cockroach
- Allergens found in cockroach feces and typically carried on larger particles (>10µM)
- Proposed cut-points for cockroach allergen exposure:
  - 1-2 U/g (allergic sensitization)
  - 2-8 U/g (asthma symptoms)

Cohn et al., Environmental Health Perspectives, 114: 522-526, 2006.
Cockroach Allergen Exposure

Risk Factors for High Bla g 1 Levels

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of dwelling</td>
<td></td>
</tr>
<tr>
<td>Detached (reference)</td>
<td>1.0</td>
</tr>
<tr>
<td>High rise apartment</td>
<td>70.0 (16.6-295.9)</td>
</tr>
<tr>
<td>No of units in building</td>
<td></td>
</tr>
<tr>
<td>Single family (reference)</td>
<td>1.0</td>
</tr>
<tr>
<td>Multifamily</td>
<td>4.89 (1.87-12.8)</td>
</tr>
<tr>
<td>Construction year</td>
<td></td>
</tr>
<tr>
<td>1978-1998 (reference)</td>
<td>1.0</td>
</tr>
<tr>
<td>pre-1940</td>
<td>3.29 (0.87-12.4)</td>
</tr>
<tr>
<td>Urbanization</td>
<td></td>
</tr>
<tr>
<td>population &lt; 1 million (reference)</td>
<td>1.0</td>
</tr>
<tr>
<td>population &gt; 1 million</td>
<td>3.15 (1.06-9.37)</td>
</tr>
<tr>
<td>Household income</td>
<td></td>
</tr>
<tr>
<td>&gt; $60,000 (reference)</td>
<td>1.0</td>
</tr>
<tr>
<td>&lt; $20,000</td>
<td>12.1 (2.05-71.7)</td>
</tr>
</tbody>
</table>

Cockroach Allergen Sensitization

- Prevalence of sensitivity to cockroach:
  - 18.1% in general U.S. population
  - 33.2% in asthmatics
- Sensitization rates vary by age, sex, race/ethnicity and poverty status

Data from NHANES 2005-2006, unpublished
Relationship between Cockroach Allergen Sensitization, Exposure, and Asthma

- The combination of cockroach sensitization and exposure is a risk factor for asthma

- Recent data from NHANES III indicates that cockroach sensitization is associated with a 2-fold increase in asthma risk in the U.S. population; however, this association is attenuated when adjusting for other allergen sensitivities
  (Arbes et al., J Allergy Clin Immunol, 2007 Nov; 120:1139-45)

Inner City Asthma Study (ICAS) Multi-component Intervention

Reductions in cockroach and dust mite allergens highly correlated with reduced asthma morbidity

Cockroach Allergen Mitigation

Principles of Integrated Pest Management (IPM)

- Targeted placement of insecticide bait to reduce exposure to potentially toxic pesticides
- Sealing of cracks and crevices to prevent re-infestation
- Removal of food and water sources
- Thorough cleaning of all surfaces including floors, cabinets, appliances
- Occupant education
Cockroach Allergen - Summary

- Bla g 1 and Bla g 2 are the major cockroach allergens
- Elevated cockroach allergen levels occur in high rise apartments, older homes and low income homes
- Cockroach sensitization is common in the US
- Exposure to high levels of cockroach allergen is associated with excess asthma morbidity in inner city children
- Effective cockroach allergen mitigation involves basic principles of integrated pest management (IPM)
- Reductions in cockroach allergen in inner city asthmatic children leads to improved asthma symptoms

Cat and Dog Allergens

- The major allergens are
  - Cat - Fel d 1: produced in sebaceous and salivary glands
  - Dog - Can f 1: found in dander and saliva
- Particles that carry cat and dog allergens can be small (2-10 μm), become airborne with minimal disturbance and remain airborne for hours.
- Travel on particles that are passively transferred.
- Are ubiquitous in public buildings and moderate exposure in communities with domestic cat ownership is unavoidable.
- Homes with pets have allergen levels ~100x higher than homes without

Asthma Symptoms Associated with Passive Transfer of Cat Allergen

- Change in morning PEFR
- Change in symptoms
  - Week 2: P=0.01
  - Week 3: P=0.06

Study Population: Swedish school children with asthma and cat sensitization

Recommendations for Allergen Avoidance for Pet Allergic Patients

• First Line
  • Do not have pets
  • Find existing pet a new home

• Second line
  • Keep the pet outside at all times
  • Isolate the pet from the bedroom
  • Air cleaners
  • Wash pet regularly

Cat Allergen in Home Declines Slowly After Pet Removal

Effect of Air Filters and Pet Washing

Air filters
• The clinical effects of home air filtration in homes where the cat remains has been mixed
  • Wood et al. found no clinical effect on symptoms or peak flow for young adult asthmatics
  • Van der Heide et al. found a reduction in bronchial hyper-reactivity for asthmatic children when air filters were placed in the living and bed rooms.

Washing cats and dogs
• Washing cats and dogs can significantly reduce airborne cat allergen, but the decrease is not maintained for more than a few days.

Wood et al., AJRCCM 1996;158:115-20
Van der Heide et al., JACI 1999;104:447-51
Cat and Dog Allergens - Summary

- Direct and indirect cat exposure associated with asthma symptoms and morbidity
- The association between pet ownership and the development of sensitization and asthma is mixed in the literature, with increased, decreased and no risk reported.
- Cat removal is effective in lowering cat allergen levels over months and improving asthma outcomes
- Results of studies of air filters are mixed
- Pet washing only reduces allergen temporarily


Mouse Allergen: Characteristics

- **Mus m 1**
  - Molecular weight 19 kD
  - Found in hair follicles, dander and urine
  - 4 times higher in male mice than in females
- **Mus m 2**
  - Molecular weight 16 kD
  - Found in hair, dander, but not urine
  - Albumin is allergenic in about 30% of mice-sensitive individuals.
- ~90% of Mus m 1 found on particles ≤10 microns


Prevalence of Mouse Allergen

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Popul'n</th>
<th>Room</th>
<th>% detectable</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCICAS</td>
<td>608 children</td>
<td>kitchen, BR, or LR</td>
<td>95%</td>
</tr>
<tr>
<td>NY-Ni</td>
<td>221 mothers</td>
<td>kitchen</td>
<td>57-66%</td>
</tr>
<tr>
<td>Baltimore</td>
<td>100 children</td>
<td>kitchen</td>
<td>100%</td>
</tr>
<tr>
<td>United States</td>
<td>831 housing units</td>
<td>kitchen, BR, or LR</td>
<td>82%</td>
</tr>
<tr>
<td>Suburban Maryland</td>
<td>335 children</td>
<td>kitchen</td>
<td>75%</td>
</tr>
</tbody>
</table>

Chew et al., EHP, 2003; 111:1348–1351
Matsui et al., JACI, 2004; 113:910-5
### Sensitization to Mouse

**Prevalence Rates of Skin Test Sensitivity**

<table>
<thead>
<tr>
<th>Study Population</th>
<th>Study</th>
<th>+ mouse SPT/IgE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occupational Matsui Annals 2004</td>
<td></td>
<td>151 adults 20</td>
</tr>
<tr>
<td>NCICAS Phitpanakul JACI 2000</td>
<td></td>
<td>499 children 18</td>
</tr>
<tr>
<td>JACI Guachal JACI 2005, Pongracic Annals 2008</td>
<td></td>
<td>937 children 22</td>
</tr>
<tr>
<td>Baltimore Matsui Annals 2006</td>
<td></td>
<td>150 children 26</td>
</tr>
<tr>
<td>West Virginia Welch Annals 2003</td>
<td></td>
<td>209 children 12</td>
</tr>
<tr>
<td>Suburban Maryland Matsui JACI 2004</td>
<td></td>
<td>335 children 13</td>
</tr>
</tbody>
</table>

Gergen et al., JACI, 2009, 123: 447-452

### Mouse Sensitization/Exposure and Morbidity

Mouse sensitized and exposed urban children with asthma are at greater risk for asthma morbidity than non-sensitized or non-exposed children.

- Odds for unscheduled doctor visit (UD) and ED visit for mouse sensitized and exposed children compared to non-sensitized or non-exposed children
- Adjusted for age, sex, atopy, cockroach sensitization and exposure, public health insurance, and study visit
- Hospitalization, adjusted OR: 69.9 (5.8-838.9)

### Rat Allergen

- Urine, saliva, hair, and dander
  - Rat n 1A MW = 20 to 21 kD
  - Rat n 1B MW = 16 to 17 kD
- Rat fur contains 5 allergens
- Salivary glands demonstrate at least five other allergens
- Rat-specific IgE found in 1.2% US population
- 24% of rat allergic individuals show sensitivity to rat albumin
- Remains airborne ≥60 minutes after disturbance

Gordon et al. Allergy 2001, 56: 583-596
### Rat Allergen and Asthma Morbidity

**National Cooperative Inner-city Asthma Study**

<table>
<thead>
<tr>
<th></th>
<th>Negative Skin Test</th>
<th>Positive Skin Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not Exposed</td>
<td>Exposed</td>
</tr>
<tr>
<td>Hosp. (mean number)</td>
<td>0.03</td>
<td>0.04</td>
</tr>
<tr>
<td>Unsch. Visits (mean number)</td>
<td>0.41</td>
<td>0.44</td>
</tr>
<tr>
<td>↓ Activity (mean days)</td>
<td>1.86</td>
<td>2.02</td>
</tr>
</tbody>
</table>

School age inner-city children with asthma

Perry, et al. JACI 2003;112:346-52

### Mouse & Rat Allergens - Summary

- Mouse allergen is widespread in occupation and home settings, with higher levels occurring in urban areas and low income, multi-family dwellings.
- Mouse sensitization is more common in minority race/ethnicity and lower socioeconomic groups.
- Exposure to high levels of mouse/rat allergen is associated with excess asthma morbidity in inner city children who are sensitive to mouse/rat allergen.
- Effective mouse allergen mitigation involves basic principles of integrated pest management (IPM).
- Reductions in mouse allergen in inner city asthmatic children may improve asthma symptoms.


### Definition of Mold

- Mold is not a scientific term. It stems from old English for earth. The term, also often called "mildew," refers to the fuzzy growth found indoors and outdoors composed of bundles of hyphae which form a mycelium (pleural = mycelia).
- The kingdom of Fungi encompasses both the single celled yeasts and the multi-celled molds.
- The fungi are eukaryotes like animals and plants, but are a separate kingdom. Most exist as masses of filaments, living off of dead or decaying organic matter, and reproducing sexually and/or asexually by spores.

Fungi grown from house dust

Alternaria
Fungi and Allergy/Asthma are Linked by Much Anecdotal Evidence

- The association of fungal spore exposure and respiratory disease is historically appreciated.
- Charles Blackley (1820–1900) recorded that he suffered for days from “aphonia and bronchael distress” after inhaling Penicillium spores.
- Bouts of asthma have been associated with cool mist humidifiers when they emit high levels of fungal propagules.
- Solomon linked asthma attacks with spore release from cool mist humidifiers.

Association Between Spore Peaks and Asthma Hospitalizations

- First documented by Salvaggio 1971

Sensitization and Exposure to Common Fungi is Associated with Asthma

- A case report of a patient with IgE-mediated sensitivity to Alternaria describes a life-threatening asthma attack during peak Alternaria season.
- Exposure to Alternaria is a risk factor for respiratory arrest. 10 of 11 asthma patients with RA were skin test positive for Alternaria, compared to 31% of controls (p < 0.001)
- In the NHANES, asthma was associated with skin prick test reactivity to Alternaria (OR, 5.1; 95% CI: 2.9-8.9)
- Sensitization to Alternaria, Aspergillus, Penicillium, or Cladosporium is associated with a higher number of symptom days among inner-city children with asthma.

Exposure to *A alternata* in US Homes is Associated with Active Asthma

The National Survey of Lead and Allergens in Housing (831 units from 75 locations) found increasing *Alternaria* levels correlated with asthma.


There is an Association Between Damp Indoor Environments and Poor Respiratory Health

- An IOM expert panel reviewed the relationship between damp or moldy environments and adverse health effects.
- They reported an epidemiologic association between damp indoor environments or indoor mold or other agents and:
  - upper respiratory tract symptoms
  - cough
  - wheeze
  - hypersensitivity pneumonitis
  - asthma sx in sensitized asthmatic persons


2007 NAEPP Guidelines Recommend Controlling Dampness and Mold

- Mold growth indoors can be inhibited by reducing moisture and humidity.
- Proper building maintenance, dehumidification, air conditioning, and increased ventilation are all helpful.
- Humidifiers and vaporizers increase indoor humidity and can become contaminated with mold and should not be used in homes of asthmatics.
Indoor Allergens and Patient Care: NAEPP Guidelines

- Assess exposures
  - Patient’s history may help identify relevant allergen exposures
- Assess sensitization
  - Use skin testing or in vitro testing to determine sensitivity to perennial indoor inhalant allergens, including common molds
  - Consider testing for seasonal allergens if suggested by patient history
  - Assess the significance of positive tests in the context of the patient’s medical history.

Expert Panel Report 3 (EPR3):
Guidelines for the Diagnosis and Management of Asthma

Indoor Allergens and Patient Care: NAEPP Guidelines (cont)

- Patients who have asthma at any level of severity should:
  - Reduce, if possible, exposure to allergens to which the patient is sensitized
  - Effective allergen avoidance requires a multifaceted, comprehensive approach

Resources

- www.epa.gov
- www.aaaai.org
- www.acaai.org
- Health Effects of Air Pollution Rostrum.  J Allergy Clinical Immunology 2004;114:1116-23.