Recognizing Asthma Triggers

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Objectives

- Discuss environmental factors that contribute to asthma
- Highlight the role of infections with asthma exacerbations
- Explore comorbid conditions that influence asthma
Disclosures

- None
Asthma: Overview

- Patients with asthma experience recurrent cough, shortness of breath and wheezing.

- Asthma is characterized by inflammation, variable airflow obstruction and airway hyper-responsiveness.

- Susceptibility to asthma involves a complex interplay between genetic factors and environmental exposures.
Impact of Asthma Triggers

- Association between increased number of asthma triggers and reduced asthma-related quality of life
- Association with increased number of asthma triggers and number (and severity) of asthma exacerbations
Genetic Susceptibility

Allergy

Irritants

Medications

Infections

Other Triggers & Comorbidities

ASTHMA
Genetics of Asthma

Multiple genetic, epigenetic and environmental factors

- **Linkage studies**

  - *Dipeptidyl peptidase X (DPP10)* - 2q14, SNPs associated with asthma in Northern European Cohorts
  - *ADAM33* - 20p13, A disintegrin and metallopeptidase domain 33
  - *Protocadherin 1* - 5q31-33, encodes adhesion molecule in alveolar macrophages
  - *GPRA* (G protein-coupled receptor for asthma susceptibility) - 7p

- **Association studies**

  - *Filaggrin* - mutations associated with asthma in the setting of eczema
  - *IL4 receptor gene*
  - *ORMDLE* - encodes protein linked to ER
  - *Beta-2 adrenergic receptor gene* - 5q31
  - *Thymic stromal lymphopoitin (TSLP) gene*

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Asthma Triggers: Allergy

Most children with asthma (>75%) are sensitized to environmental allergens.

When sensitized asthmatics are exposed to allergens:
- Increase in asthma symptoms
- Precipitate asthma exacerbations

Important questions include:
- Is exposure to the allergen associated with asthma symptoms?
- Is reduction of exposure possible?

1 Middleton’s Allergy Principles and Practice, 6th edition, volume 2, 1184.
Allergies and Asthma

Seasonal variation in allergen exposure is regional and can influence the degree of asthma symptoms

Late winter  Cedar Pollen (Texas, Oklahoma)
Spring      Tree pollens such as Oak, Pecan, Cottonwood, Elm
Summer     Grass pollens such as Timothy, Bermuda
Fall        Weeds such as Ragweed

Perennial  Indoor allergens, molds, roach, mouse
Common Allergens

Mountain Cedar (Ashe Juniper)

- Common in Texas and Oklahoma
- Pollinate in late winter, early spring
- Small, gnarled tree
- Spreading aggressively
- Can trigger “cedar fever” or “cedar asthma”
Common Allergens

Ragweed

- Pollen occurs in late summer, fall
- Produces copious amounts of pollen
- Pollen is highly allergenic

Pictures from Greerlabs.com
Allergy: Treatment

- Identify and reduce exposure to allergic triggers
- Pharmacologic management

Consider allergen immunotherapy if:

- There is clear evidence that exposure to the unavoidable allergens results in asthma symptoms
- There is difficulty controlling symptoms with medications
Dust Mites

- Microscopic mites that consume flakes of human skin
- Accumulate in pillows, mattresses, stuffed animals, carpet
- Emit tiny particles that when respired can trigger allergy symptoms
- Can affect both nose (nasal allergy) and lung (asthma)

Increasing exposure to dust mite allergen is associated with early wheezing in children.

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

Dust Mite Avoidance

- Wash sheets in hot water
- Keep carpet vacuumed
- Avoidance of feather-stuffed (down) bedding
- Washing stuffed animals in hot water routinely
- Air filters do not significantly reduce exposure
- Dust mite encasements for pillow, box spring and mattress
Cockroach Allergy

Exposure to cockroach allergen is a risk factor for:
- Development of asthma
- Morbidity of asthma

Cockroach allergens are found in droppings:
- 1-2U/g can lead to sensitization
- 2-8U/g can trigger asthma symptoms

## Cockroach Allergen Exposure

### Bla g 1 level

<table>
<thead>
<tr>
<th>Location</th>
<th>Detectable</th>
<th>Sensitization (&gt;2 U/gram)</th>
<th>Asthma symptoms (&gt;8 U/gram)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bedroom Bed</td>
<td>6.1%</td>
<td>1.3%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Bedroom Floor</td>
<td>17.6%</td>
<td>6.7%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Kitchen Floor</td>
<td>28.5%</td>
<td>13.4%</td>
<td>9.5%</td>
</tr>
<tr>
<td>Living Room Floor</td>
<td>44.4%</td>
<td>10.7%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Living Room Sofa</td>
<td>38.4%</td>
<td>8.8%</td>
<td>1.1%</td>
</tr>
</tbody>
</table>

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><strong>Type of dwelling</strong></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><strong>No of units in building</strong></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><strong>Construction year</strong></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><strong>Urbanization</strong></td>
<td></td>
</tr>
<tr>
<td>population &lt; 1 million</td>
<td>1.0</td>
</tr>
<tr>
<td>population &gt; 1 million</td>
<td>3.15 (1.06-9.37)</td>
</tr>
<tr>
<td><strong>Household income</strong></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 Exposure and Asthma Morbidity in Inner City Children

- Hospitalizations: \( p=0.001 \)
- Unscheduled Medical Visits: \( p<0.001 \)
- Change in Care Giver’s Plans: \( p=0.006 \)

<table>
<thead>
<tr>
<th>Skin Test</th>
<th>Allergen Exposure</th>
<th>Hospitalizations</th>
<th>Unscheduled Medical Visits</th>
<th>Change in Care Giver’s Plans</th>
</tr>
</thead>
<tbody>
<tr>
<td>neg</td>
<td>low</td>
<td>0.1</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>neg</td>
<td>high</td>
<td>0.3</td>
<td>2</td>
<td>20</td>
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<tr>
<td>pos</td>
<td>low</td>
<td>0.2</td>
<td>2</td>
<td>15</td>
</tr>
<tr>
<td>pos</td>
<td>high</td>
<td>0.4</td>
<td>3</td>
<td>20</td>
</tr>
</tbody>
</table>

* Bla g 1 > 8 U/gram
### Avoidance Measures

**Environmental assessment and exposure reduction of cockroaches: A practice parameter**

- Factors that facilitate the growth and persistence of cockroach populations, such as food and water, paths of ingress, and microenvironments that can provide shelter, should be mitigated to reduce the cockroach carrying capacity of the environment. (D Evidence)

- The extent and duration of a cockroach infestation should be monitored by using strategically placed sticky traps. (D Evidence)

- Pesticides should be used judiciously and ideally should be applied by a professional exterminator as part of an integrated pest management program. (C Evidence)

- Reservoirs of cockroach contaminants should be cleaned or removed to prevent additional exposure to occupants. (A Evidence)

- Integrated pest management with a combination of interventions appears to be the most effective method for preventing and eliminating cockroach infestations. (B Evidence)

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Animal Allergy

- Direct and indirect exposure to cat allergen associated with asthma
- Dog allergen occurs with all species (no hypoallergenic dog)
- Also consider exposure to Guinea pig, hamsters, etc in the classroom
- Exposure can trigger asthma symptoms

First line: complete avoidance
Second line: Keep pet outdoors, out of bedroom
  (washing animal and purifiers only partially beneficial)
Cat Allergen in Home Declines Slowly After Pet Removal

Fel d 1 content in the dust from homes after removal of a cat

Wood et al JACI 83:730,1989
Mouse Allergy: Occupational Exposure

- ~100,000 in the US are exposed to laboratory animals in the workplace.

- Laboratory animal allergy affects 15-27%\(^1\) of laboratory workers.

- Rats and mice are frequent sources of occupational allergen given their widespread use and large numbers in the laboratory environment.

- Sensitization typically occurs within the first 3 years of exposure but can occur at any time, leading to symptoms such as rhinitis, conjunctivitis, cutaneous reactions and asthma.

- The primary risk factor for development of laboratory animal allergy is the level of exposure to the allergen, but some studies also suggest that an atopic history or cigarette use poses additional risk.

Mouse Allergy: Domestic Exposure

Mouse allergen exposure in the home is both common and clinically significant.

A subset of homes from the National Cooperative Inner-City Asthma Study (NCICAS) was analyzed for the presence of mouse allergen (Mus m 1), revealing that over 95% of these urban homes had detectable levels\(^1\).

Matsui et al then demonstrated that mouse allergen is also common in suburban homes. Mus m 1 was detected in 69.3% of suburban bedrooms vs. 93.6% of city bedrooms although the level of Mus m 1 in the urban bedrooms was much higher (757ng/g vs. 12ng/g)\(^2\).

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Mouse Allergy: Clinical Significance

- Mouse allergen sensitization has been shown to be an independent risk factor for asthma morbidity in inner-city children with asthma\(^1\).

- Mouse sensitization and exposure associated with asthma severity in urban children with asthma\(^2\).

- A birth cohort study of asthma involving adult women of Boston revealed that mouse sensitization was associated with an increased risk of physician-diagnosed asthma and overall asthma morbidity in the prior year\(^3\).

Adjusted Odds Ratio for asthma-related ER visits in the past year

- mouse allergy negative: 1
- mouse allergy positive: 3.3


Avoidance Measures

- Keep food in containers
- Keep trash covered, in sealed containers
- Seal areas that allow entry in walls, doors, windows, etc.
- Professional extermination
- Often requires integrated pest management
Mold

- Exposure to various molds including alternaria has been associated with active asthma\textsuperscript{1}

- Jaakkola et al demonstrated that fungal sensitivity to Aspergillus and Cladosporium increases the risk of adult-onset asthma\textsuperscript{2}

- Mold can trigger asthma in both mold allergic and non-allergic individuals

\textsuperscript{1}Salo PM et al. JACI 2006:118:892-898.
\textsuperscript{2}Jaakkola MS, et al. Are atopy and specific Ige to mites and molds important for adult asthma? JACI 2006; 117:642-8.
Mold Remediation

- Reduce humidity
- Prevent and repair water leaks
- Treat small surfaces with detergent and water and dry
- Larger areas should be removed and replaced
Occupational Allergens

- Low molecular weight chemicals
  - Isocyanates
  - Metals
  - Wood dusts
  - Glues/resins

- High molecular weight organic chemicals
  - Animal proteins
  - Flours
  - Grain dust
Genetic Susceptibility

Irritants

Medications

Other Triggers & Comorbidities

Allergy

Infections

ASTHMA
Irritants: Cigarette Smoke

- Numerous studies show that active smoking increases risk for developing asthma\(^1\)

- Exposure to second hand smoke early in life is also associated with the development of asthma\(^2\)

- Children exposed to tobacco smoke have more severe asthma symptoms and more frequent exacerbations\(^3\)

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Irritant Triggers for Asthma

- Strong odors
- Perfumes
- Chlorine based cleaning supplies
- Fumes from gas stoves
- Fumes from wood-burning fireplaces/stoves
- Occupational irritants
- Air pollution (indoor and outdoor)
AIR POLLUTION

- Numerous studies have evaluated the effects of biomass fuel and traffic-related air pollution on the development and severity of pulmonary disease such as asthma.

- Interestingly, a study involving adult asthmatics found that distance to the nearest road was a predictor of FEV$ _1 ^1$

- Physician diagnosed asthma has been reported to be more frequent among children living within 100 meters of a freeway$ ^2$

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Asthma and Air Pollution

Air pollution associated with:\(^1\):

- Increased bronchial hyperreactivity
- Increased airway inflammation
- Decreased lung function
- Increased hospital admissions and ER visits
- Enhancing airway inflammation induced by allergen exposure

\(^1\)Molfino, Lancet, 1991; Peden, AJRCCM, 1995)
Infections and Asthma

- Respiratory infections are one of the most common triggers for exacerbations (URI viruses, RSV, influenza)

- Atypical bacterial infections such as *Mycoplasma pneumoniae* and *Chylamydophila pneumonia* may also play a role in inducing and exacerbating asthma, but the data is not entirely clear

- Viral pathogens such as RSV and human rhinovirus may also participate in asthma development.

- Recommend hand washing, avoidance of sick contacts, vaccination!
Increased viral replication and cytopathic cell death instead of cell apoptosis (without further replication)
Adkinson: Middleton's Allergy: Principles and Practice, 7th ed

**INCEPTION**
- Healthy infant
  - RSV
  - Parainfluenza
  - Rhinovirus
- Wheezing illness
  - Atopy
  - Resolution
  - Asthma

**EXACERBATION**
- Child or adult with asthma
  - Rhinovirus
- Exacerbation of asthma
  - Emergency room visits
  - Hospitalization

**PERSISTENCE**
- Adult (pre-existing asthma)
  - Mycoplasma
  - Chlamydia
  - Persistent asthma
Chronic Sinusitis

- Chronic sinusitis can be an exacerbant of asthma
- Chronic cough, post nasal drip
- Occur with or without underlying nasal polyps
Normal Sinus CT Scan through the OMU

- Eyeball
- Ethmoid sinus
- Maxillary sinus
- Nasal cavity
Obstruction of the OMU with Associated Sinusitis

Sinusitis in the ethmoid sinus

Sinusitis in the maxillary sinus
Medications

- Non selective beta blockers can trigger asthma
- Topical beta blockers (glaucoma)
- Aspirin and NSAIDs can trigger asthma in 3-5% of adult asthmatics (but much less common in children)
ASTHMA: OTHER TRIGGERS

- Temperature extremes (cold/dry air AND hot/humid air)
- Weather (thunderstorm induced asthma)
- Emotional stimuli (laughing, crying, etc)
- Hormonal (peri-menstrual asthma)
- Exercise
  - Typically physical activity is a trigger (one of many) of poorly controlled asthma
  - Isolated exercise induced asthma is rare especially in children
OBESITY AND ASTHMA

- 26% of preschool children are overweight or obese (BMI >85 percentile)\(^1\)

- 34% of adults are overweight or obese\(^2\)

- Some studies suggest that obesity is associated with systemic inflammatory state AND possible steroid resistance

- Increased BMI is associated with increased asthma symptoms, increased exacerbations and higher ER visits\(^3\)

- In adults, increased is BMI associated with increased asthma severity\(^4\)

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OBSTRUCTIVE SLEEP APNEA

- Comorbid obstructive sleep apnea can lead to pulmonary symptoms (Nocturnal dyspnea, snoring, mouth breathing, headaches, fatigue, sleepy)

- Obstructive sleep apnea contributes to poor asthma control\(^1\)

GE Reflux

- GERD can lead to respiratory symptoms such as cough and dyspnea

- In patients with symptomatic GERD and asthma, there is evidence that anti-reflux therapy improves asthma\(^1\)

- However, minimal evidence for treating asymptomatic GERD with PPI in asthma\(^2\)

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Conclusions

- A basic tenet of asthma management is controlling environmental factors and comorbid conditions that contribute to asthma.

- A thorough history and evaluation can help identify an individual’s asthma triggers allowing for targeted interventions.
Questions?