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.
Asthma

Normal

Asthma
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.

The Journal of Allergy and Clinical Immunology: In Practice 2014 2, 544-552.
Genetic Susceptibility
Allergy
Irritants
Infections
Medications
Comorbidities
Other Triggers &
Genetics of Asthma

Multiple genetic, epigenetic and environmental factors

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

- **Association studies**
  
  *Filaggrin* - mutations associated with asthma in the setting of eczema
  *IL4 receptor gene*
  *ORMDLR*- encodes protein linked to ER
  *Beta-2 adrenergic receptor gene* - 5q31
  *Thymic stromal lymphopoietin (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”

![Cedar Pollen Image](Pictures from Greerlabs.com)
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

- Detectable
- Sensitization (>2 U/gram)
- Asthma symptoms (>8 U/gram)

Percent of Homes

<table>
<thead>
<tr>
<th>Location</th>
<th>Detectable</th>
<th>Sensitization</th>
<th>Asthma symptoms</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 (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><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

Unscheduled Medical Visits

Change in Care Giver’s Plans

Days With Changed Plans in Past Year

No. of Visits in Past Year

- neg skin test, low allergen exposure
- neg skin test, high allergen exposure*
- pos skin test, low allergen exposure
- pos skin test, high allergen exposure*

* 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)

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.

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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\textsuperscript{1}.

- Mouse sensitization and exposure associated with asthma severity in urban children with asthma\textsuperscript{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\textsuperscript{3}.

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

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

\textsuperscript{3}Phipatanakul W, Litonjua AA, Platts-Mills TAE, et al. Sensitization to mouse allergen and asthma and asthma morbidity among women in Boston, J Allergy Clin Immunol 120 (2007), pp
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 asthma¹

- Jaakkola et al demonstrated that fungal sensitivity to Aspergillus and Cladosporium increases the risk of adult-onset asthma²

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

²Jaakkola 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
Irritants: Cigarette Smoke

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

- Exposure to second hand smoke early is 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)
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.

Interesting, a study involving adult asthmatics found that distance to the nearest road was a predictor of FEV\textsubscript{1}.\textsuperscript{1}

Physician diagnosed asthma has been reported to be more frequent among children living within 100 meters of a freeway.\textsuperscript{2}

\textsuperscript{1}Trupin L, Balmes JR, Chen H et al. An integrated model of env factors in adult asthma & lung function and disease severity: a cross-sectional study. EnvirHealth 2010.
Asthma and Air Pollution

Air pollution associated with¹:

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

¹Molfino, 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 *Chlamydophila 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!
Adkinson: Middleton's Allergy: Principles and Practice, 7th ed

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

Asthma

Resolution

Atopy

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
- Genetic Susceptibility
- Allergy
- Irritants
- Infections
- Medications
- Comorbidities
- Other Triggers &
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\(^4\)


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

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

¹Kiljander TO, Junghard O, et al. Effect of esomeprazole 40 mg once or twice daily on asthma: a randomized, placebo-controlled study. J Respir Crit Care Med. 2010;181(10):1042.)
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.

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<table>
<thead>
<tr>
<th>Assessment questions* for environmental and other factors that can make asthma worse</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inhalant allergens</strong></td>
</tr>
<tr>
<td>Does the patient have symptoms year round? (If yes, ask the following questions. If no, see next set of questions).</td>
</tr>
<tr>
<td>Does the patient keep pets indoors? What type?</td>
</tr>
<tr>
<td>Does the patient have moisture, dampness, or a moldy odor in any room of his or her home (eg, basement)? (Suggests house dust mites, molds).</td>
</tr>
<tr>
<td>Does the patient have mold visible in any part of his or her home? (Suggests molds).</td>
</tr>
<tr>
<td>Has the patient seen cockroaches or rodents in his or her home in the past month? (Suggests significant exposure).</td>
</tr>
<tr>
<td>Assume exposure to house dust mites unless patient lives in a semi-arid region. However, if a patient living in a semi-arid region uses a swamp cooler, exposure to house dust mites must still be assumed.</td>
</tr>
<tr>
<td>Do symptoms get worse at certain times of the year? (If yes, ask when symptoms occur).</td>
</tr>
<tr>
<td>Early spring? (Trees).</td>
</tr>
<tr>
<td>Late spring? (Grasses).</td>
</tr>
<tr>
<td>Late summer to autumn? (Weeds).</td>
</tr>
<tr>
<td>Summer and fall? (Alternaria, Cladosporium, mites).</td>
</tr>
<tr>
<td>Cold months in temperate climates? (Suggests indoor allergens such as animal dander).</td>
</tr>
<tr>
<td><strong>Tobacco smoke</strong></td>
</tr>
<tr>
<td>Does the patient smoke?</td>
</tr>
<tr>
<td>Does anyone smoke at home or work?</td>
</tr>
<tr>
<td>Does anyone smoke at the child’s daycare?</td>
</tr>
<tr>
<td><strong>Indoor/outdoor pollutants and irritants</strong></td>
</tr>
<tr>
<td>Is a wood-burning stove or fireplace used in the patient’s home?</td>
</tr>
<tr>
<td>Are there unvented stoves or heaters in the patient’s home?</td>
</tr>
<tr>
<td>Does the patient have contact with other smells or fumes from perfumes, cleaning agents, or sprays?</td>
</tr>
<tr>
<td>Have there been recent renovations or painting in the home?</td>
</tr>
<tr>
<td><strong>Workplace exposures</strong></td>
</tr>
<tr>
<td>Does the patient cough or wheeze during the week, but not on weekends when away from work?</td>
</tr>
<tr>
<td>Do the patient’s eyes and nasal passages get irritated soon after arriving at work?</td>
</tr>
<tr>
<td>Do coworkers have similar symptoms?</td>
</tr>
<tr>
<td>What substances are used in the patient’s workplace? (Assess for sensitizers).</td>
</tr>
<tr>
<td><strong>Rhinitis</strong></td>
</tr>
<tr>
<td>Does the patient have constant or seasonal nasal congestion, runny nose, and/or postnasal drip?</td>
</tr>
<tr>
<td><strong>Gastroesophageal reflux disease (GERD)</strong></td>
</tr>
<tr>
<td>Does the patient have heartburn?</td>
</tr>
<tr>
<td>Does food sometimes come up into the patient’s throat?</td>
</tr>
<tr>
<td>Has the patient had coughing, wheezing, or shortness of breath at night in the past four weeks?</td>
</tr>
<tr>
<td>Does the infant vomit, followed by cough, or have wheezy cough at night? Are symptoms worse after feeding?</td>
</tr>
<tr>
<td><strong>Sulfite sensitivity</strong></td>
</tr>
<tr>
<td>Does the patient have wheezing, coughing, or shortness of breath after eating shrimp, dried fruit, or processed potatoes or after drinking beer or wine?</td>
</tr>
<tr>
<td><strong>Medication sensitivities and contraindications</strong></td>
</tr>
<tr>
<td>What medications does the patient use now (prescription and nonprescription)?</td>
</tr>
<tr>
<td>Does the patient use eye drops*? What type?</td>
</tr>
<tr>
<td>Does the patient use any medications that contain beta-blockers or ACE inhibitors*?</td>
</tr>
<tr>
<td>Does the patient ever take aspirin or other nonsteroidal anti-inflammatory drugs?</td>
</tr>
<tr>
<td>Has the patient ever had symptoms of asthma after starting or taking any of these medications?</td>
</tr>
</tbody>
</table>

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ACE: angiotensin-converting enzyme.

* These questions are examples and do not represent a standardized assessment or diagnostic instrument. The validity and reliability of these questions have not been assessed.

† Rare issue in children.

Questions?