EPR3: A Pediatric Asthma Diagnosis and Management Update

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Faculty

Mary Dell Railey, M.D.
Pediatric Allergy and Immunology
University of Alabama at Birmingham
Birmingham, AL

Outline
• Allergic rhinitis and its connection to asthma
• Allergens involved
• Treatment options
  – Allergen avoidance
  – Drugs
  – Immunotherapy

Definition of AR
• Inflammation of the nasal mucosa triggered by IgE-mediated cross-linking of airborne antigens
• Mast cell degranulation
  – Histamine – itching, sneezing
  – PGD2, LTC4, LTD4, LTE4 – increased vasodilation & vascular permeability (congestion, inflammation)

Objective Findings

Early-Phase Response: 5 to 15 Minutes After Allergen Exposure
Other Features of AR

- Nasal hyper-responsiveness
  - Provoked by irritant triggers similar to bronchial hyper-responsiveness
  - Induced by allergic inflammation
- Priming
  - Less allergen is needed to provoke allergic response after repeated exposures to the allergen

Associations Between Asthma and Allergic Rhinitis

- Nasal and bronchial inflammation
  - Inflammatory nasal cytokines from the nose induce bronchial inflammation

Associations Between Asthma and Allergic Rhinitis

- Nasal and bronchial inflammation
  - Nasal inflammation could contribute to T-cell homing to the lower respiratory tract where these lymphocytes foster inflammation

Associations Between Asthma and Allergic Rhinitis

- In Watson study
  - Asthmatic children treated with topical nasal steroids for perennial rhinitis have decreased nonspecific bronchial hyperreactivity and nocturnal asthma symptoms

“One Airway, One Disease”

- Asthma and AR frequent comorbidities
- 80% of patients with asthma have AR
- 50% of patients with AR have asthma
- Communication between upper and lower airways with very similar inflammatory processes
“One Airway, One Disease”
In Allergic Inflammation
- Pathologic features of AR and allergic asthma are very similar
- Exposure to allergen promotes similar inflammatory cells and mediators
  - Eosinophils, mast cells, basophils, CD4+ T cells, IgE, histamine, LTs, PGx, and cytokines, esp IL-5

Some (not all) patients with AR alone demonstrate bronchial hyperresponsiveness to methacholine
AR might be a risk factor for subsequent development of asthma

How Do We Demonstrate That Someone Has Allergies?
- Symptoms of allergies
  - Don’t look if there are no symptoms
- Skin tests and RAST
  - Both demonstrate presence of IgE to allergen in skin or blood, does not indicate sensitivity

Allergen challenge
Nasal smear for eosinophils

Treatment Options for AR
- Allergen avoidance
- Medications
  - H1 antagonists
  - Nasal corticosteroids
  - Omalizumab (Xolair)
- Allergen immunotherapy

Allergen Avoidance: It Works!
- Large home-based asthma intervention study done over one year
  - Addressed all indoor, relevant allergens and tobacco smoke
**Allergen Avoidance: It Works!**
- Environmental home intervention caused
  - Fewer days with asthma symptoms
  - Declines in allergens at home
  - Reduced asthma-associated morbidity

**Allergen Avoidance: It Works!**
- Study of 831 homes
  - 52% of homes had at least 6 detectable allergens
  - 46% had at least 3 allergens
  - Among atopic subjects, high allergen burden increased the odds of having asthma symptoms

**Major Indoor Allergens**
- Dust mites
- Cat
- Dog
- Cockroach
- Rodents

**Dust Mites in Homes**
- House dust is complex mixture of everything found in homes
  - Human protein, mites, cat, dog, mice, rat, insects, food
- Mites studied by counting or measuring major allergen

**Dust Mites in Homes**
- Major species of dust mites
  - Dermatophagoides farinae, D. pteronyssinus, Blomia tropicalis, Lepidoglyphus destructor, Tyrophagus putrescentior

**Dust Mite Allergen**
- Mites growth dependent on
  - Water content of air (relative humidity >50%)
  - Temperature (65 – 80 degrees F)
- Mite numbers peak in summer (July-August)
### Dust Mite Allergen
- Dust allergen levels peak in summer and remain elevated through fall into winter.
- Fecal particles are 10-35 um in size.
- Settle out of air quickly so airborne levels depend upon disturbance in room.

### Mite Allergen Exposure and Disease
- Sensitization at 2-10 ug/g of dust.
- Mite allergen consistently related to asthma in many countries.
- Mite allergen related to rhinitis & atopic dermatitis, anaphylaxis from ingestion.
- Actual daily “dose” of allergen unknown.

### Cat and Dog Allergens
- Easily recognized by patients.
- Major allergens, Fel d1 and Can f1.
- Primarily synthesized in skin.
- Everywhere, detected in homes without animals, in school rooms.

### Cat and Dog Allergens
- Both allergens (particularly cat) remain airborne for many hours in undisturbed home due to small size (<10um) particles.
- Eye, nose, and respiratory symptoms can occur.

### Cockroaches
- Major source of allergen, especially in inner-city homes.
- Types:
  - German and American.
- Allergens from feces, saliva, debris.

### Cockroaches
- Allergens not easily detected in undisturbed air.
  - Large particles (like dust mites).
- Highest levels usually in kitchens.
- Several studies have correlated cockroach allergy with asthma severity in inner cities.
Control Measures:
Remove the Pests

• Stop inflow of pests
  – Seal cracks, holes
• Remove pests
  – Poisons, cleaning

Control Measures:
Remove the Pests

• Remove sources of food and water for pests
  – Remove food crumbs, stop leaking pipes or faucets
• Prevent reintroduction
  – Seal cracks, holes, clean around dwelling

Dust Mite Avoidance

• Impermeable mattress and pillow covers
• Wash bedding weekly at >130 degrees Fahrenheit
  – Everything on the bed should be washable

Dust Mite Avoidance

• Remove carpets, stuffed animals and clutter from bedroom
• Vacuum weekly with high-efficiency bag or HEPA filter vacuum

Dust Mite Control

• Home furnishings
  – Hard floors
  – Vinyl or leather furniture
• Control humidity
  – Keep below 50%

Dust Mite Control

• Chemical treatments
  – Benzyl benzoate powder
  – 3% tannic acid
• Especially avoid carpets on concrete slabs (humidity)
Animal Avoidance

- Removal of cat/dog only clearly effective avoidance
- Cat washing only temporarily reduces allergen shedding from cats
  - Lasts - 1 week

Animal Avoidance

- Aggressive cleaning of homes can reduce allergen levels more rapidly
- Steam cleaning of carpets did not seem more effective than regular vacuuming

Results of Indoor Allergen Avoidance

- Strict avoidance
  - Hospital room or mountain sanatoria associated with reduced symptoms and BHR
- Elimination of animals leads to fall in allergen levels over months
  - 4 months needed to reach basal level

Results of Indoor Allergen Avoidance

- Trials of dust mite avoidance rarely reduce allergen levels to levels of hospital rooms

Outdoor Allergens

- Trees
  - March – May
- Grasses
  - April – June
- Weeds
  - August – November

Rx for Allergic Rhinitis: How Do They Measure Up?

- Antihistamines – oral or intranasal
  - Provide 30-35% symptom reduction
  - Work best for sneezing, itching, rhinorrhea (runners)
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<td><strong>• Antihistamines – oral or intranasal</strong></td>
<td><strong>• Leukotriene blockers</strong></td>
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<td>– Oral not very effective for nasal congestion (blockers)</td>
<td>– Provide 30-35% symptom reduction</td>
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<tr>
<td>– Intranasal astemizole is effective for nasal congestion</td>
<td>– Reduce all symptoms, including nasal congestion</td>
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<td><strong>• Leukotriene blockers</strong></td>
<td><strong>• Intranasal steroids</strong></td>
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<td>– Equivalent or slightly better than loratadine</td>
<td>– Provide 50-60% symptom reduction</td>
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<td>– Have additive effect with antihistamines in some but not all studies</td>
<td>– Effective for all symptoms</td>
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<td>– Superior to antihistamines in comparative trials</td>
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<td>– Also reduce ocular symptoms</td>
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<th>Indications for Allergen Immunotherapy</th>
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<tr>
<td><strong>• Allergic rhinoconjunctivitis (~60-70% effective)</strong></td>
<td><strong>• Effective for tree, grass, weed, mold, dust mite, cat</strong></td>
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<td><strong>• Allergic asthma</strong></td>
<td><strong>• Des Roches et al (JACI 1997) &amp; Polosa et. al. (Respiratory 2005) both found</strong></td>
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<td><strong>• Hymenoptera hypersensitivity (~90% effective)</strong></td>
<td>– Immunotherapy in mono-sensitized patients may prevent allergic responses to other allergens &amp; the development of allergic asthma</td>
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<td><strong>• Possible prevention of asthma in children with allergic rhinitis</strong></td>
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### Allergen Immunotherapy

- Ross meta analysis study (Clinical Therapy 2001)
  - Immunotherapy was associated with significant clinical improvement versus that observed with control groups or medication only groups

### SCIT for Asthma

#### General Considerations

- In allergic asthma, immunotherapy is indicated for patients
  - Who do not present a severe form of the disease
  - FEV1 levels should be over 70%

### SCIT for Asthma

#### General Considerations

- In allergic asthma, immunotherapy is indicated for patients
  - In whom symptoms are not adequately controlled by allergen avoidance & pharmacologic treatment
  - Who have both nasal and bronchial symptoms

### Effects of Immunotherapy

- No change in total IgE
- Decreases seasonal increase in allergen-specific IgE
- Increases allergen specific IgG1, IgG4, IgA

### Effects of Immunotherapy

- Inhibits allergen induced late phase reaction in the skin, nose, lung
- Alters the Th2/Th1 balance toward Th1
- Induces IL-10 producing Treg cells

### Monoclonal Antibody to IgE – Omalizumab (Xolair)

- How it works
  - Binds free IgE in blood, preventing it from binding to inflam cells in skin, nose, lung; thereby preventing allergic symptoms
### Monoclonal Antibody to IgE – Omalizumab (Xolair)

- **Indication**
  - Documented allergic responsiveness to at least perennial allergen and moderate to severe persistent asthma that is refractory to inhaled corticosteroids

### Conclusions
- If symptoms of allergies are present in your patients, consider
  - Allergen avoidance first
  - Dust mite control in bedroom
  - Removal of animals including cats, dogs, cockroaches, rodents

### Reference List
- Skoner et al JACI 2001;108: S2-8
- Kelly et al. JACI 2003; 111: 79-86
- Salo et al JACI 2008; 121:678-84.

### Reference List
- NIH 2007 guidelines for the diagnosis and management of asthma

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