EPR3: A Pediatric Asthma Diagnosis and Management Update

Produced by the Alabama Department of Public Health
Video Communications and Distance Learning Division

Faculty

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Outline

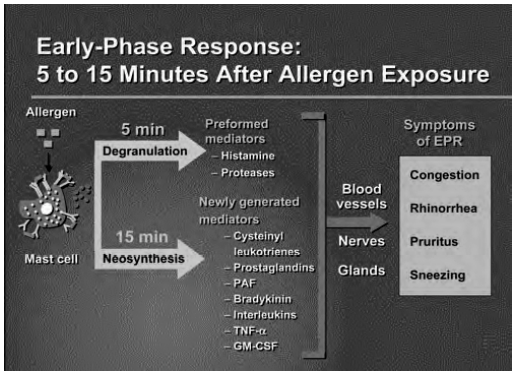
- Allergic rhinitis and its connection to asthma
- Allergens involved
- Treatment options
  - Allergen avoidance
  - Drugs
  - Immunotherapy

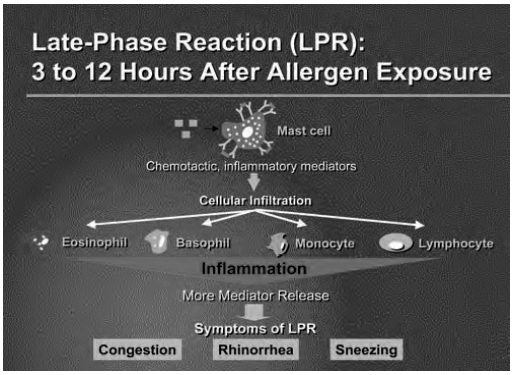
Definition of AR

- 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





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

"One Airway, One Disease" In Allergic Inflammation

- 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

How Do We Demonstrate That Someone Has Allergies?

- 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)

Rx for Allergic Rhinitis: How Do They Measure Up?

- Antihistamines – oral or intranasal
  - Oral not very effective for nasal congestion (blockers)
  - Intranasal astemizole is effective for nasal congestion

Rx for Allergic Rhinitis: How Do They Measure Up?

- Leukotriene blockers
  - Provide 30-35% symptom reduction
  - Reduce all symptoms, including nasal congestion

Rx for Allergic Rhinitis: How Do They Measure Up?

- Leukotriene blockers
  - Equivalent or slightly better than loratadine
  - Have additive effect with antihistamines in some but not all studies

Rx for Allergic Rhinitis: How Do They Measure Up?

- Intranasal steroids
  - Provide 50-60% symptom reduction
  - Effective for all symptoms
  - Superior to antihistamines in comparative trials
  - Also reduce ocular symptoms

Indications for Allergen Immunotherapy

- Allergic rhinoconjunctivitis (~60-70% effective)
- Allergic asthma
- Hymenoptera hypersensitivity (~90% effective)
- Possible prevention of asthma in children with allergic rhinitis

Allergen Immunotherapy

- Effective for tree, grass, weed, mold, dust mite, cat
- Des Roches et al (JACI 1997) & Polosa et. al. (Respiratory 2005) both found
  - Immunotherapy in mono-sensitized patients may prevent allergic responses to other allergens & the development of allergic asthma

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

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