Diagnosis and Management of Inhalant Allergens

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Diagnosis and Management of Inhalant Allergens

- Anatomy
- Immunology
- Diagnosis
- Treatment
  - Environmental control
  - Pharmocotherapy
  - Immunotherapy
- Allergic Emergencies
Inhaled Allergens

- 5-22% annual prevalence of seasonal allergic rhinitis
- 9% of all visits to physicians
History

- First described by John Bostock in 1819 as “seasonal catarrah”
- 1873, Blackley observed the first reaction by applying pollen to excoriated skin
- 1911, treatment began by Leonard Noon on the assumption of “antitoxins”
History

- Cooke is said to have been the father of modern intradermal testing.
- French Hansel developed the optimal dose concept by starting at lower concentrations.
- Herbert Rinkel first identified the “endpoint for titration”
Inhaled Allergens

- Identified by their portal of entry via the respiratory tree which is richly supplied with IgE.
- Essentially all inhalant allergy is IgE mediated, producing a Type I Gell and Coomb’s reaction.
Immune System Components

- Lymphocytes, Phagocytes, Complement, and mediator cells and their products.
- Functions to distinguish self from nonself.
Gell and Coomb’s reactions

- **Type I- Immediate Hypersensitivity**
  - Immediate
  - Allergen binds 2 molecules of IgE
  - Intracellular degranulation and immediate release of products
  - Ex. Allergic rhinitis, anaphylactic shock, asthma
Gell and Coomb’s

- Type II - Cytotoxic reaction
  - Immediate
  - Binding of either IgM or IgG to cell bound antigen and activation of complement cascade.
  - Ex. Hemolytic anemia.
Gell and Coomb’s

- Type III- Immune complex reaction
  - Delayed
  - Antigen-antibody complexes deposit on tissue
Gell and Coomb’s

- Type IV - Delayed hypersensitivity
  - Delayed
  - Tissue injury involving presensitized T-Lymphocytes.
Acute Phase

- Degranulation of preformed and newly synthesized mediators, most importantly, Histamine.
- Sneezing, watery discharge, itchy eyes, nose and throat.
Transitional Phase

- Asymptomatic
- Activation and recruitment of leukocytes into nasal tissue from the blood.
Late Phase

- Local Leukocyte infiltration.
- 4-6hrs after allergen exposure.
- Nasal congestion is the most characteristic symptom.
History

- The most important method of establishing the diagnosis of inhalant allergy.
- What symptoms occur? What allergen exposure? When do they occur?
- Symptoms include sneezing, itchy eyes/nose, rhinnorhea, postnasal drip, congestion, headache, loss or diminished smell or taste.
- Itching and Sneezing are the most distinctive complaints.
History

- **PMHx:** Asthma, allergic reactions, eczema, Hypertension, Depression
- **Medications:** B-Blockers, TCA, MAOi, OTC-antihistamines/nasal sprays
- **FH:** Asthma, allergies, immune disorders
- **SH:** Geographical area, Work environment, smoker or smoker in the house, toxic/irritant exposures
Physical Exam

- Nasal mucosa tends to be pale/bluish, congested, covered by watery mucosa.
- Infraorbital edema or “allergic shiner”
- Open mouth breathing, nasal crease, infraorbital crease
- Lymphoid hyperplasia
Physical Exam

- Also rule out anatomic factors aggravating the allergic condition.
  - Septal deviation
  - Nasal Valve Collapse
  - Sinusitis
  - Choanal Stenosis
Nasal Cytology

- Anterior Inferior turbinate has shown to be the most representative.
- 5:1 Ratio of columnar to goblet cells in normal nasal epithelium.
- 1:4 Ratio in an allergic response.
- 20% or more Eosinophils suggest inhalant allergy.
Skin Endpoint Titration (SET)

- Intradermal skin test technique using 1:5 serial dilutions of allergenic extract.

- Advantages
  - Safe
  - Readable
  - Standardization
Intradermal injections of 0.01ml allergenic extract applied to the upper lateral arm.

Wheal and Flare beyond 5mm suggest positive response.

Maximal whealing occurs at 15 minutes.
The endpoint is defined as the antigen dilution which yields a wheal at least 2mm larger than the preceding negative wheal, and which is followed by a wheal at the next stronger dilution.

The confirming wheal is important for determining the true endpoint.
SET controls

- Negative Controls
  - Diluent
  - Preservative (2% Glycerin)

- Positive Controls
  - No. 3 Histamine dilution
Abnormal Whealing

- Occur in 5-15% of tests applied
- Most common include:
  - Flash Response
  - Hourglass
  - Plateau
Flash Response

- Huge whealing response to a dilution that is weaker than the true endpoint.

Day 1: 5-5-5-13-18-21
Day 2: 5-5-5-5-7-9-11
Plateau Response

- A 7mm or larger wheal that is followed by the same size wheal on progressively stronger dilutions until an additional 2mm increment is observed

7-7-7-7-9-9-11-11
Hourglass Response

- A large response of an initial weak dilution that is followed by progressively smaller reactions on stronger dilutions until a normal reaction occurs.

9-7-5-5-7-9-11
Factors influencing SET

- Volume injected
- Skin reactivity
- Increased allergen exposure
- Food Allergens
- Antihistamines
- Age
Food Ingestants

- Ragweed: Milk, Melons, Bananas
- Sage: Potato
- Grass: Beans, Peas, Soybeans
- Cedar: Beef
- Oak: Egg
Antigen Selection

- **Seasonals**
  - Pollens - short ragweed most common
  - Trees
  - Grasses
  - Weeds

- **Perennials**
  - Dust mites
  - Molds - Alternaria, Hormodendrum
  - Cockroach allergens
  - Dog and Cat dander
SET Immunotherapy

- Individualized treatment sets are developed based on weak solutions of high sensitivities and stronger solutions of low sensitivities.
- Increased strengths until the patient has relief of symptoms or serious local reactions occur.
- Length of treatment generally 3-5 years.
In Vitro Testing

- Eliminates Variables associated with skin testing.
  - non specific whealing, effects of medications, skin types.
- More specific but less sensitive.
Indications for In Vitro Testing

- Impracticality of skin testing
  - Skin disorder, drug inhibition, uncooperative patients
- Clarification of skin test results
  - Bizarre or borderline reactions
- Prevention of systemic reactions
  - Prior history of anaphylactic reaction, severe asthma, stinging hypersensitivity
- Convenience
Inappropriate Use of In Vitro Testing

- Delayed food hypersensitivity
- Penicillin hypersensitivity
- Improper Indications
  - Routine screening
  - Patients who are not candidates for immunotherapy
Radioimmunosorbant Assay (RAST)

- Allergen is coupled to a paper disc and incubated with the patient's serum.
- Disc washed and radioactive IgE added.
- Gamma counters quantify the radioactivity.
Modified RAST (MRT)

- Involves an additional washing procedure in order to reduce non immunologically bound radioactivity.
- Increased sensitivity to RAST
MRT

- MRT system is divided into 5 classes from 1-5, each representing approximately a fivefold increase in the amount of serum specific IgE antibody present in the sample.

<table>
<thead>
<tr>
<th>Class</th>
<th>Counts</th>
<th>0.1ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class 1</td>
<td>751-1600</td>
<td>1:500</td>
</tr>
<tr>
<td>Class 2</td>
<td>1601-3600</td>
<td>1:2500</td>
</tr>
<tr>
<td>Class 3</td>
<td>3601-8000</td>
<td>1:12500</td>
</tr>
<tr>
<td>Class 4</td>
<td>8001-18000</td>
<td>1:62500</td>
</tr>
<tr>
<td>Class 5</td>
<td>18001-40000</td>
<td>1:312,500</td>
</tr>
</tbody>
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MRT Immunotherapy

- Before starting immunotherapy, it is mandatory that an intradermal skin challenge of the initial vial be tested.
- After the initial doses have been administered and tolerated, the injections are increased until the dose reaches maximum level.
Specific Nasal Immunotherapy (SNIT)

- Applies the same principles as conventional immunotherapy.
- Now listed by the WHO as an alternative therapeutic option to the subcutaneous or intradermal route.
- Data is still somewhat limited.
Environmental control

- Best treatment is prevention.
- Animal dander
- Dust mites
  - High filtration air filters
  - Hot water laundry
  - Special bedding
- Pollen
  - Pollen Masks
- Avoiding irritants such as tobacco smoke.
Pharmacologic treatment

- Alpha-adrenergic agonists
- Inhaled Cromylyn
- Antihistamines
- Leukotrienes
- Inhaled Nasal Corticosteroids
- Systemic and Intraturbinal Corticosteroid injections
Alpha adrenergic agonists

- Pseudoephedrine
- Vascular constriction
- Wide variation of patient tolerance due to insomnia and irritability.
Cromolyn Sodium

- Inhibits the degranulation of sensitized mast cells.
- Inhibits both the early and late phase
- Mainly prophylactic
- OTC- 4% Nasal spray four times daily
- Very safe
Antihistamines

- Currently the primary drug for treatment of nasal allergy.
- Compete with Histamine for the H1 receptor.
- Most effective when taken prophylactically
- Anticholinergic, antiserotoninergic, and anti alpha adrenergic.
- Lipid soluble and cross the Blood Brain Barrier
- Most effective at reducing symptoms of sneezing, nasal itching, and rhinorrhea.
Second generation Antihistamines

- Loratidine, Fexofenadine, Cetrizine, and azelastine.
- Cross BBB less and have reduced CNS effects.
- Longer half lives
## Antihistamine Costs

<table>
<thead>
<tr>
<th>Antihistamine</th>
<th>Cost per month</th>
</tr>
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<tbody>
<tr>
<td>Allegra 60mg</td>
<td>$47</td>
</tr>
<tr>
<td>Allegra 180mg</td>
<td>$78</td>
</tr>
<tr>
<td>Clarinex</td>
<td>$78</td>
</tr>
<tr>
<td>Zyrtec</td>
<td>$67</td>
</tr>
</tbody>
</table>
Leukotriene inhibitors

- Act similar to antihistamines by competitive inhibition of the leukotriene receptor.
- Singular
- Very successful in Asthma
- The data available to date do not clearly support a unique role of leukotriene inhibitors in the treatment of allergic rhinitis.
Intranasal Corticosteroids

- Primarily block the late phase reaction.
- Only a small fraction is absorbed locally.
- Side effects
  - Atrophy
  - Epistaxis 5-8%
Intranasal Corticosteroids

- Bedesonide, Mometasone, fluticasone
  - Increased potency
  - Reduced systemic availability and activity
  - Quicker onset of action
- More effective than oral antihistamines at relieving all nasal symptoms as well as improving the total nasal symptom score
- May be appropriate for replacing antihistamines as first line therapy for management of nasal allergy.
<table>
<thead>
<tr>
<th>Steroid</th>
<th>Cost per month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flonase</td>
<td>$72</td>
</tr>
<tr>
<td>Nasonex</td>
<td>$87</td>
</tr>
<tr>
<td>Rhinocort AQ</td>
<td>$79</td>
</tr>
</tbody>
</table>
Systemic Corticosteroids

- The most potent agents for relieving the symptoms of allergic rhinitis.
- Because of the side effects, they are reserved for severe or chronic symptoms.
Intraturbinal injection

- Concern over vasospasm or retrograde embolization of the retinal vasculature.
- Now considered safe and effective with proper procedure.
- Side effects:
  - 2% nasal bleeding
  - Facial flushing occurs the following day due to steroid induce vasodilation.
Pregnancy and Allergic Rhinitis Therapy

- Increased levels of progesterone lead to exacerbations of nasal congestion.
- Astemizole and Cromolyn
- Intranasal steroids
Surgery

- Minor role
  - Septoplasty
  - Partial Turbinate resections
  - The effects of submucosal fibrosis on allergic rhinitis is still unproven.
Allergic Emergencies

- Immediate
- Delayed
  - Local
  - Systemic
Allergic Emergencies
Delayed

- Local reactions range on a spectrum of pain and induration
- Systemic reactions usually manifest as exacerbation of the patients symptoms
- Treatment consists of antihistamines and reassurance, with steroids for more severe symptoms.
Allergic Emergencies
Diagnosis

- **Vasovagal**
  - Most common
  - Slow pulse, normal BP, pale cool skin

- **Anaphylactic**
  - Involvement of more than one organ system, always including the cardiovascular system
  - Rapid pulse, low BP, increased secretions/nasal congestion/hoarseness or wheezing, Flushed warm skin.
Allergic Emergencies
Management

- Keep patient recumbent, loosen tight clothing
- Oxygen as needed
- Check pulse and BP
- Get Help and call ambulance
- Place tourniquet above the injection site (loosen every 20min)
- Epinephrine (1:1000) 0.3ml in the opposite arm, may repeat in 10 min intervals up to 1ml
- Assess airway- more deaths result from airway obstruction than from cardiovascular collapse
  - Oral airway
  - Inhaled albuterol
  - Intubate or surgical airway if glottic obstruction threatens
- Start IV
- Diphenhydramine 50mg IV
- Dexamethasone 4mg IV
- Transport to Hospital ASAP
Conclusion

- Allergic Rhinitis is very common.
- Thorough history and physical examination including visualization of the nasal anatomy.
- Approach to therapy
  - Environmental control
  - First line pharmacotherapy
  - Nasal Steroids, systemic steroids
  - Immunotherapy
- Adequate counseling of the patient