Allergic Disorders

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Allergic Disorders

- IgE-mediated immune reactions
- Clinical entities include:
  - asthma
  - allergic rhinitis
  - atopic dermatitis
  - urticaria and angioedema
  - anaphylaxis (foods, drugs, venom, idiopathic)

Development of Immediate Hypersensitivity

IgE production ➔ mast cells & basophils ➔ trigger mediator release ➔ clinical effects

Anaphylaxis
Hives
Asthma
Rhinitis
Conjunctivitis

IgE-dependent Release of Inflammatory Mediators

Immediate Reactions
- Granule contents: Histamine, TNF-α, Protases, Heparin
- Sneezing, Nasal congestion, Itchy, runny nose, Watery eyes

Late Reactions
- Cytokine production: Specifically IL-4, IL-13
- Mucus production
- Eosinophil recruitment

Immediate and Late Reactions in IgE-mediated Hypersensitivity

Time ➔ Immediate Reactions ➔ Late Reactions

TH1/TH2 Paradigm

IL-2
INF-γ
IL-3
GM-CSF
TNF-α

IL-4 (IL-13)

Delayed Hypersensitivity
Allergic Inflammation
Why is the Prevalence of Asthma and Allergic Disorders Increasing Worldwide?

Developmental Component

The Hygiene Hypothesis

Diagnostic Testing: Allergen-specific IgE

- Total IgE level not diagnostic
- Immediate Hypersensitivity Skin Tests
  - epicutaneous (prick)/intradermal
  - results read within 15-20 minutes
  - more sensitive, less specific
- Serum Specific IgE Tests
  - less sensitive, more specific
  - RAST: radioallergosorbent test; qualitative
  - immunocap: quantitative

Allergy Skin Testing
Epidemiology, Diagnosis, and Pharmacologic Management of Allergic Rhinitis

AR and Comorbid Airway Disease

Allergic Rhinitis and Asthma: One Airway, One Disease

Allergic Rhinitis: Clues

Normal Nasal Cytology
**Pharmacotherapy for Rhinitis**

- **Oral**
  - antihistamines
  - decongestants
  - combination drugs
  - leukotriene modifiers
  - corticosteroids
- **Subcutaneous**
  - anti-IgE antibody
- **Intranasal**
  - corticosteroids
  - antihistamines
  - anticholinergics
  - decongestants
  - saline
  - cromolyn sodium

**Medications: Targeting Symptoms**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Sneezing</th>
<th>Congestion</th>
<th>Rhinorrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intranasal corticosteroids</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Oral antihistamines</td>
<td>++</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td>Nasal antihistamines</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Oral decongestants</td>
<td>–</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Intranasal decongestants</td>
<td>–</td>
<td>++</td>
<td>–</td>
</tr>
<tr>
<td>Intranasal mast cell stabilizers</td>
<td>–</td>
<td>–</td>
<td>++</td>
</tr>
<tr>
<td>Topical anticholinergics</td>
<td>–</td>
<td>–</td>
<td>++</td>
</tr>
</tbody>
</table>

- ++ = provides substantial benefit
- +/– = provides little or minimal benefit
- + = provides modest benefit
- – = provides no benefit

Adapted from Pedersen S, et al. *Allergy*. 1997;52(suppl 39):1-34.

**Intranasal Corticosteroids in Allergic Rhinitis: An Overview**

- **Benefits**
  - Most effective medication class for controlling symptoms of allergic rhinitis
  - Relieve sneezing, rhinorrhea, and mucosal edema leading to nasal congestion
  - Associated with minimal side effects
- **Drawbacks**
  - Require careful patient instruction to ensure proper use
  - May cause nasal dryness, irritation, and/or bleeding
  - Reports of nasal septal perforation and limited suppression of bone growth

**Total Systemic Exposure**

Adapted from Pedersen S, et al. *Allergy*. 1997;52(suppl 39):1-34.

**First and Second generation H1 Histamine Receptor Antagonists**

<table>
<thead>
<tr>
<th>Generation</th>
<th>Benefits</th>
<th>Drawbacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>First</td>
<td>Reduce itching, sneezing, rhinorrhea</td>
<td>Have little effect on nasal congestion</td>
</tr>
<tr>
<td></td>
<td>Lower costs</td>
<td>Can cause sedation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anticholinergic activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Short duration of action</td>
</tr>
<tr>
<td>Second</td>
<td>Reduce itching, sneezing, rhinorrhea Some effect on nasal congestion</td>
<td>Minimal effect on rhinorrhea</td>
</tr>
<tr>
<td></td>
<td>Non-sedating</td>
<td>Higher costs</td>
</tr>
<tr>
<td></td>
<td>Minimal anticholinergic activity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Once daily dose</td>
<td></td>
</tr>
</tbody>
</table>
Immunotherapy for Allergic Rhinitis: An Overview

**Benefits**
- Especially effective for grass pollen, ragweed pollen, and house-dust mites.
- Improvement of childhood allergies in children.
- May prevent progression of rhinitis to asthma.
- May reduce need for symptomatic pharmacotherapy.

**Drawbacks**
- Must be administered in facilities equipped to handle adverse reactions (urticaria, laryngeal edema, bronchospasm, and anaphylaxis).
- Requires high level of patient compliance.
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Atopic Dermatitis

“Chronic relapsing, highly pruritic, inflammatory skin disease.”

**Diagnostic Features of AD Clinical**

**Essential**
- Atopy
  - personal Hx / FHx of eczema, hay fever, asthma.
- Pruritus
- Eczema (Spongiosis)
  - acute
  - subacute
  - chronic
- (Vascular instability)

**Nonessential**
- Xerosis
- Keratosis pilaris
- Pityriasis alba
- Allergic shiners
- Morgan-Dennie lines
- Palmar/Dennie lines
- Chronic hyperlinearity
- Anterior Capsular Cataracts
- Keratoconus

**Food Allergy and Atopic Dermatitis**

- Children:
  - moderate - Severe AD (33%) have food allergy
  - increasing severity of AD ~ increasing risk of FA
- Adults:
  - low incidence (< 2%)
- Foods responsible (~ 85% of cases):
  - outgrown: milk, egg, soy, wheat
  - persistent: peanut, nuts, fish, shellfish

**Evaluation of Food Allergy in AD**

- Allergy prick skin tests:
  Negative is very reliable
  Positive carries 50-80% false positive rate
- Laboratory studies:
  - specific IgE (pharmacia immunoCAP-RAST system)
    - predictive value (> 95% reaction rate) in children
      - egg, milk, peanut, codfish
Evaluation of Food Allergy in AD

- Clinical evaluation:
  - elimination diets
  - oral food challenges
    - physician supervised
    - open, single blind, double-blind, placebo-controlled

Treatment

- Skin hydration & moisturizers
- Avoidance of irritants
- Avoidance of allergens
- Topical corticosteroids
- Topical calcineurin inhibitors

Incidence of different types of atopy. AD peaks in the first years of life and declines after that time. Asthma and allergic rhinitis increase over time as sensitization develops.