**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)

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**Development of Immediate Hypersensitivity**

**IgE-dependent Release of Inflammatory Mediators**

- Immediate Release
  - Granule contents: Histamine, TNF-α, Proteases, Heparin
  - Mucosal edema, sneezing, nasal congestion, itchy, runny nose, watery eyes

- Over Minutes
  - Lipid mediators: Prostaglandins, Leukotrienes
  - Wheezing, bronchoconstriction

- Over Hours
  - Cytokine production: Specifically IL-4, IL-13
  - Mucus production, Eosinophil recruitment

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**Immediate and Late Reactions in IgE-mediated Hypersensitivity**

- **Immediate Reactions**
  - Time: Minutes (A)
  - Symptoms: Nasal congestion, sneezing, itchy, runny nose, watery eyes

- **Late Reactions**
  - Time: Hours (B)
  - Symptoms: Wheezing, bronchoconstriction

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**TH1/TH2 Paradigm**

- IL-2 → INF-γ → IL-3 → GM-CSF → TNF-α
  - **Delayed Hypersensitivity**
  - Allergic Inflammation

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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
Eosinophilic Rhinitis

Pharmacotherapy for Rhinitis

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

Medications: Targeting Symptoms

<table>
<thead>
<tr>
<th>Agent</th>
<th>Rhinorrhea</th>
<th>Congestion</th>
<th>Sneezing</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>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>
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</tbody>
</table>

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


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, itching, and/or bleeding
- Reports of nasal septal perforation and limited suppression of bone growth

Physicians should routinely monitor the growth of children taking nasal corticosteroids and weigh the benefits of corticosteroid therapy against the possibility of effects on growth velocity.

First and Second generation H1 Histamine Receptor Antagonists

**Benefits**
- First Generation
  - Reduce itching, sneezing, rhinorrhea
  - Lower costs
- Second Generation
  - Reduce itching, sneezing, rhinorrhea
  - Some effect on nasal congestion
  - Non-sedating
  - Minimal anticholinergic activity
  - Once daily dose

**Drawbacks**
- First Generation
  - Have little effect on nasal congestion
  - Can cause sedation
  - Anticholinergic activity
  - Short duration of action
- Second Generation
  - Minimal effect on rhinorrhea
  - Higher costs

Immunotherapy for Allergic Rhinitis: An Overview

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Drawbacks</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Especially effective for grass pollen, ragweed pollen, and house-dust mites</td>
<td>• Must be administered in facilities equipped to handle adverse reactions (urticaria, laryngeal edema, bronchospasm, and anaphylaxis)</td>
</tr>
<tr>
<td>• Improvement of childhood allergies in children</td>
<td>• Requires high level of patient compliance</td>
</tr>
<tr>
<td>• May prevent progression of rhinitis to asthma</td>
<td>• May reduce need for symptomatic pharmacotherapy</td>
</tr>
</tbody>
</table>

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 / plantar hyperlinearity
- Anterior Capsular Cataracts
- Keratoconus

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

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

- 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.