RHINITIS

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• **Rhinitis:** Symptomatic disorder of the nose characterized by itching, nasal discharge, sneezing and nasal airway obstruction.

• **Allergic rhinitis:** Induction of rhinitis symptoms after allergen exposure by an IgE-mediated immune reaction; accompanied by inflammation of the nasal mucosa and nasal airway hyperreactivity.
Rhinitis Phenotypes

most common forms

- Allergic
- Infectious: Viral (acute), bacterial, fungal
- Non-Allergic, Non-Infectious, Rhinitis
- Non-Allergic Rhinitis with Eosinophilia Syndrome (NARES)
- Chronic Rhinosinusitis with or without Polyps: Hypertrophic, inflammatory disorder that can affect allergic or non-allergic individuals
Non-allergic rhinitis

- Has a multifactorial etiology.

- Is a risk factor for the development of asthma.

- If eosinophilic, usually responds to treatment with corticosteroids.

- May be a presenting complaint for systemic disorders such as Wegener’s granulomatosis, Churg–Strauss and sarcoidosis.
# Infectious rhinitis

## Table 3. Infective causes of rhinitis

<table>
<thead>
<tr>
<th>Infective agent type</th>
<th>Examples of infective agent</th>
<th>Caused disease pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viruses</td>
<td>Common cold viruses, e.g. rhinovirus, coronaviruses, RSV, etc.</td>
<td>Sinus changes on CT scan remain for up to 6 weeks after the infection [214]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.5–2% become superinfected by bacteria [215]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‘Colds’ may exacerbate asthma and COPD [216, 217]</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Children average 6–8 ‘colds’ per year [218]</td>
</tr>
<tr>
<td>Bacteria</td>
<td>Streptococcus, Haemophilus, Moraxella, Staphylococcus, Mycobacteria</td>
<td>Acute infection causes nasal obstruction, facial pain, crusting, purulent discharge</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Can progress to rhinosinusitis</td>
</tr>
<tr>
<td>Fungi and other opportunistic</td>
<td>Aspergillus</td>
<td>Rarely cause symptoms; mainly affect immuno-suppressed individuals [219]</td>
</tr>
<tr>
<td>infections</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

COPD, chronic obstructive pulmonary disease; CT, computed tomography; RSV, respiratory syncytial virus.
Rhinitis Phenotypes

less common forms

• Occupational: May be allergic or non-allergic

• Drug-induced: Aspirin, some vasodilators

• Hormonal: Pregnancy, menstruation, hormonal contraceptives, thyroid disorders

• Food-induced (gustatory)

• Cold air-induced (skier’s nose)

• Atrophic (rhinitis of the elderly)
Conditions that Mimic Rhinitis

- Cystic fibrosis
- Mucociliary defects
- Cerebrospinal rhinorrhoea
- Anatomic abnormalities
- Foreign bodies
- Tumors
- Granulomas: Sarcoid, Wegener’s, Midline Granuloma
Non-Allergic, Non-Infectious Rhinitis
(a poorly-defined phenotype)

Pathophysiologic hypotheses

• Non-inflammatory (vasomotor)
  – Sensorineural hyperresponsiveness
  – Hyperesthesia
  – Dysautonomia

• Local allergic reaction
IgE can be produced in the nasal mucosa

In situ hybridization for IgE mRNA - tissue obtained from subjects with allergic rhinitis.

Cameron et al. *J Immunol* 2003;171:3816
Local Allergic Reaction
(nasal challenges with allergen in non-allergic rhinitics)

N=21

All these subjects had no response to a control challenge with diluent

Allergic Rhinitis: Impact

- High prevalence
- Impaired quality of life
- Work and school absence
- Impaired learning
- Impaired sleeping
- Associated asthma, sinusitis, otitis
Short Form Health Survey (SF-36)
Profiles of Patients with Allergic Rhinitis

Adapted from Meltzer EO et al. *J Allergy Clin Immunol.* 1997;99:S815
Allergic Rhinitis Co-Morbidities

- Conjunctivitis
- Sinusitis
- Otitis Media
- Cough
- Asthma
Presence of Sinus Disease Based on CT Findings in Patients with Allergic Rhinitis and Controls

![Bar chart showing the number of subjects with positive sinus CT in allergic rhinitis and controls. The chart indicates that 67.5% of allergic rhinitis patients and 33.4% of controls have positive sinus CT results. The p-value is 0.017.](image-url)

Allergic Rhinitis as a Risk Factor for Chronic Sinusitis

Ear Nose Throat-related flight disqualifying events that developed over a 5-year period in Naval Flight Personnel with only allergic rhinitis (N=465) versus controls (N=12,628)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Relative Risk</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Sinusitis</td>
<td>4.5</td>
<td>(1.7-11.6)</td>
</tr>
<tr>
<td>Alternobaric Disease</td>
<td>1.6</td>
<td>(0.4-6.6)</td>
</tr>
<tr>
<td>Polyposis</td>
<td>1.2</td>
<td>(0.2-8.7)</td>
</tr>
<tr>
<td>Conductive Hearing Loss</td>
<td>0.9</td>
<td>(0.1-6.6)</td>
</tr>
<tr>
<td>Requirement for ENT Surgery</td>
<td>3.4</td>
<td>(0.4-27.1)</td>
</tr>
</tbody>
</table>

Allergic rhinitis: The basis of co-morbidity with otitis media with effusion

Middle ear functions as an allergic target organ

Allergic inflammation and edema obstruct the eustachian tube

Allergic nasopharyngeal obstruction and secretions facilitate microbial middle ear inflammation

ALLERGIC RHINITIS AND ITS IMPACT ON ASTHMA

JACI 2001:56: 813-824
Allergy 2008: 63 (Suppl. 86): 8–160
Perennial Rhinitis: an Independent Risk Factor for Asthma

(European Community Respiratory Health Survey)

adapted from Leynaert B et al. J Allergy Clin Immunol 1999; 104:301
In Patients with Rhinitis:

- Routinely query for symptoms suggestive of asthma
- Perform chest examination
- Consider lung function testing
- Consider tests for bronchial hyperresponsiveness in selected cases
### Allergic Rhinitis Classification

<table>
<thead>
<tr>
<th></th>
<th><strong>Intermittent</strong></th>
<th><strong>Persistent</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td>• &lt; 4 days / week</td>
<td>• &gt; 4 days / week</td>
</tr>
<tr>
<td></td>
<td>• or &lt; 4 weeks</td>
<td>• or &gt; 4 weeks</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Mild</strong></th>
<th><strong>Moderate- severe</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptoms</strong></td>
<td></td>
</tr>
<tr>
<td>• Sleep: normal</td>
<td>• Sleep: disturbed</td>
</tr>
<tr>
<td>• Daily activities (incl. sports): normal</td>
<td>• Daily activities: Restricted</td>
</tr>
<tr>
<td>• Work-school activities: normal</td>
<td>• Work and school activities: disrupted</td>
</tr>
<tr>
<td>• Severe symptoms: no</td>
<td>• Severe symptoms: yes</td>
</tr>
</tbody>
</table>
### Seasonal Allergic Rhinitis ≠ Intermittent Perennial Allergic Rhinitis ≠ Persistent

<table>
<thead>
<tr>
<th></th>
<th>Intermittent</th>
<th>Persistent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seasonal Allergic Rhinitis (n=193)</td>
<td>133</td>
<td>60</td>
</tr>
<tr>
<td>Perennial Allergic Rhinitis (n=208)</td>
<td>151</td>
<td>57</td>
</tr>
</tbody>
</table>

Globally Important Sources of Allergens

- House dust mites
- Grass, tree and weed pollen
- Pets
- Cockroaches
- Molds
Diagnosis of Allergic Rhinitis:

- Detailed personal and family allergic history
- Intranasal examination – anterior rhinoscopy
- Symptoms of other allergic diseases
- Allergy skin tests and/or
- *In vitro* specific IgE tests
Allergy Skin Prick Testing

• Skin prick test / positive result
Concept of In Vitro IgE Assays

Substrate

Enzyme

Secondary Ab

Sample to be measured

Primary Ab
In Vitro Specific IgE Assay (standard curve)
### Immunoassay vs Skin Test for Diagnosis of Allergy

<table>
<thead>
<tr>
<th><strong>Immunoassay</strong></th>
<th><strong>Skin test</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Not influenced by medication</td>
<td>Higher sensitivity</td>
</tr>
<tr>
<td>Not influenced by skin disease</td>
<td>Immediate results</td>
</tr>
<tr>
<td>Does not require expertise</td>
<td>Requires expertise</td>
</tr>
<tr>
<td>Quality control possible</td>
<td>Cheaper</td>
</tr>
<tr>
<td>Expensive</td>
<td></td>
</tr>
</tbody>
</table>
Other Diagnostic Tests

- Nasal secretion / scraping cytology
- Nasal allergen challenge
- Nasal endoscopy
- CT scan
  - anatomic abnormalities
  - concomitant presence of sinusitis
Peak nasal inspiratory flow

- Determines nasal airway patency using a nasal inspiratory flow meter.
- The results are reproducible and correlate with rhinoscopic evidence of rhinitis but not with symptom scores.
- Most useful for comparing changes in airway patency within the same subject.

Allergy 2005; 60:795–800
Acoustic rhinometry.

- Measures changes in mucosal congestion using reflected sound.

- Sound in the nasal cavity is reflected by changes in acoustic impedance caused by changes in cavity dimensions.

- The change in acoustic impedance between the incident wave and reflected sound waves is proportional to the cross-sectional area.

- The method requires standardization and considerable experience to interpret and obtain reproducible results.

Rhinology 2000; 16 (Suppl.):3–17.
Rhinomanometry

- Estimation of nasal resistance from pressure–flow relationships.
- Considered as an accurate measure of nasal airway patency.
- Anterior RM: Pressure sensor is placed at the tip of each nostril and resistance is measured in each nostril separately.
- Posterior RM: Pressure sensor is placed in the back of the nasal cavity and total nasal airway resistance is determined.
- Expensive equipment
- Requires considerable experience in interpretation
The Nasal Allergic Response

**IMMEDIATE (early) RESPONSE**
- Sneezing
- Pruritus
- Rhinorrhea
- Nasal obstruction
- Ocular symptoms

**LATE-PHASE RESPONSES**
- Nasal obstruction
- Rhinorrhea
- Nasal hyperresponsiveness

**Endothelial cell activation**
- Leukocyte infiltration and activation (lymphocytes, eosinophils, basophils)

**Preformed & newly formed mediators/cytokines**
- Cytokines
- Chemokines

**To allergens (priming)**
- To irritants and to atmospheric changes

**IgE allergen**
- mast cell
- B-lymphocyte
- T-lymphocyte
- Dendritic cell

**Allergen**

**Immediate Response**
- Activates mast cells
- Releases mediators/cytokines

**Late-Phase Responses**
- Activates T-lymphocytes
- Activates B-lymphocytes
- Produces IgE
- Priming for future responses
The Immediate (early phase) Allergic Reaction in the Nose

- **Brain**
- **PRURITUS**
- **SNEEZING**
- **OBSTRUCTION**
- **Blood vessels**
- **Epithelium**
- **Sensory nerves**
- **Glands (mucous)**
- **Rhinorrhea**

- **Histamine**
- **Sulfidopeptide leukotrienes**
Nasal Hyperresponsiveness in Allergic Rhinitis

Sneezes induced by histamine*

Perennial Allergic Rhinitis: N = 25
Healthy: N = 18

p < 0.0001

* same dose in both groups

Sanico et al. *Int Arch Allergy Immunol* 1999;118:154
Management of Allergic Rhinitis: ARIA Guidelines

Stepwise Management of Allergic Rhinitis

Environmental control

Intermittent symptoms
- Mild
  - Oral H1-blocker or
  - Intranasal H1 blocker
  - and/or decongestant
  - or LTRA
  
  Re-evaluate patient with persistent symptoms in 2-4 weeks
  
  Responsive: Continue treatment for 1 month
  
  Unresponsive: Step-up

- Moderate
  - Oral H1 blocker or
  - Intranasal H1 blocker
  - and/or decongestant or
  - Intranasal CS
  - or anti-leukotriene

  Re-evaluate in 2-4 weeks

Responsive: Step down
Continued treatment for > 1 month

Unresponsive: Add or increase CS

Persistent symptoms
- Mild
  - Oral H1-blocker or
  - Intranasal H1 blocker
  - and/or decongestant

  Re-evaluate in 2-4 weeks

Responsive: Step down
Continued treatment for > 1 month

Unresponsive: Add or increase CS

Moderate
- Intra nasal CS ±
  - H1 blocker or
  - anti-leukotriene

  Re-evaluate in 2-4 weeks

Responsive: Step down
Continued treatment for > 1 month

Unresponsive: Add or increase CS

Severe
- Immuno therapy
  - Consider surgical approaches (?)

Modified from ARIA workshop, 2001
Environmental Control

1. **Allergens**
   - House dust mites
   - Pets
   - Cockroaches
   - Molds
   - Pollen

2. **Pollutants and Irritants**
Allergen Avoidance

• Pets
  • Remove pets from bedrooms and, even better, from the entire home
  • Vacuum carpets, mattresses and upholstery regularly
  • Wash pets regularly (±)

• Molds
  • Ensure dry indoor conditions
  • Use ammonia to remove mold from bathrooms and other wet spaces

• Cockroaches
  • Eradicate cockroaches with appropriate gel-type, non-volatile, insecticides
  • Eliminate dampness, cracks in floors, ceilings, cover food; wash surfaces, fabrics to remove allergen

• Pollen
  • Remain indoors with windows closed at peak pollen times
  • Wear sunglasses
  • Use air-conditioning, where possible
  • Install car pollen filter
House dust mite allergen avoidance

- Provide adequate ventilation to decrease humidity
- Wash bedding regularly at 60°C
- Encase pillow, mattress and quilt in allergen impermeable covers
- Use vacuum cleaner with HEPA filter
- Dispose of feather bedding
- Remove carpets
- Remove curtains, pets and stuffed toys from bedroom
Environmental Control

• The most logical strategy for disease that relates to the indoor environment

• Effectiveness requires comprehensive and multifaceted measures

• More studies are needed to also address the role of indoor pollutants (e.g. NO₂, PMs, tobacco smoke, endotoxin)
PHARMACOTHERAPY OF ALLERGIC RHINITIS
## Agents and Actions

<table>
<thead>
<tr>
<th></th>
<th>Oral antihistamines</th>
<th>Nasal antihistamines</th>
<th>Cys-LT1 receptor antagonists</th>
<th>Nasal steroids</th>
<th>Nasal decongestants</th>
<th>Oral decongestants</th>
<th>Nasal ipratropium</th>
<th>Nasal cromones</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhinorrhea</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>0</td>
<td>0</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Congestion</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+++</td>
<td>++++</td>
<td>++</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Sneezing</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Pruritus</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>+++</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Ocular symptoms</td>
<td>++</td>
<td>0</td>
<td>++</td>
<td>++</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Onset of action</td>
<td>1 hr</td>
<td>15 min</td>
<td>48 hr</td>
<td>12 hr</td>
<td>5-15 min</td>
<td>1 hr</td>
<td>15-30 min</td>
<td>-</td>
</tr>
<tr>
<td>Duration</td>
<td>12-24 hr</td>
<td>6-12 hr</td>
<td>24 hr</td>
<td>12-48 hr</td>
<td>3-6 hr</td>
<td>12-24 hr</td>
<td>4-12 hr</td>
<td>2-6 hr</td>
</tr>
</tbody>
</table>

Modified from van Cauwenberge P Allergy 2000;55:116-134
Oral Antihistamines

- First generation agents
  - Chlorpheniramine
  - Brompheniramine
  - Diphenhydramine
  - Promethazine
  - Tripolidine
  - Hydroxyzine
  - Azatadine

- Newer agents
  - Acrivastine
  - Azelastine
  - Cetirizine
  - Desloratadine
  - Fexofenadine
  - Levocetirizine
  - Loratadine
  - Mizolastine
Nasal Antihistamines

Azelastine

Levocabastine

Olopatadine
Simplified Two-State Model of the Histamine H1-Receptor

Efficacy of an Antihistamine over 6 Months in Persistent Allergic Rhinitis

Baseline total symptom score: 8.95

- Levocetirizine, 5 mg, N = 276
- Placebo, N = 271

Newer Antihistamines are Equally Effective in the Treatment of Allergic Rhinitis

Change from baseline in total symptom score (AM, instantaneous, trough)

*:* <0.05 compared to placebo

# Newer Generation Oral Antihistamines
## Somnolence/Drowsiness

<table>
<thead>
<tr>
<th>Drug</th>
<th>Active</th>
<th>Placebo</th>
<th>Data Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cetirizine 10 mg qd</td>
<td>13.7%</td>
<td>6.3%</td>
<td><a href="http://www.PDR.net">www.PDR.net</a></td>
</tr>
<tr>
<td>Desloratadine 5 mg qd</td>
<td>2.1%</td>
<td>1.8%</td>
<td><a href="http://www.PDR.net">www.PDR.net</a></td>
</tr>
<tr>
<td>Fexofenadine 60 mg bid</td>
<td>1.3%</td>
<td>0.9%</td>
<td><a href="http://www.PDR.net">www.PDR.net</a></td>
</tr>
<tr>
<td>Levocetirizine 5 mg qd</td>
<td>6.8%</td>
<td>1.8%</td>
<td>Bachert et al JACI 2004;114:838</td>
</tr>
<tr>
<td>Loratadine 10 mg qd</td>
<td>8%</td>
<td>6%</td>
<td><a href="http://www.PDR.net">www.PDR.net</a></td>
</tr>
</tbody>
</table>
Newer Generation Oral Antihistamines

• First line treatment for mild allergic rhinitis

• **Effective for**
  – Rhinorrhea
  – Nasal pruritus
  – Sneezing

• **Less effective for**
  – Nasal blockage

• Possible additional anti-allergic and anti-inflammatory effect
  • In-vitro effect > in-vivo effect

• Minimal or no sedative effects

• Once daily administration

• Rapid onset and 24 hour duration of action
Decongestants: Alpha-2 Adrenergic Agonists

- Oral
  Pseudoephedrine

- Nasal
  Phenylephrine
  Oxymetazoline
  Xylometazoline
Efficacy of Pseudoephedrine in Seasonal Allergic Rhinitis

- Pseudoephedrine 120 mg twice daily, N=211
- Placebo, N=212

Mean reduction in “nasal stuffiness” score from baseline

Adapted from Bronsky E. et al. *J Allergy Clin Immunol* 1995;96:139
Nasal Obstruction: Antihistamine vs Decongestant vs Combination in Allergic Rhinitis with Perennial Symptoms

Nasal obstruction severity score (scale: 0-3)

Cetirizine 5mg twice daily, N=70
Pseudoephedrine 120 mg twice daily, N=70
Combination, N=70

Bertrand et al. *Rhinology* 1996;34:91
Decongestants

EFFICACY:

• Oral decongestants: moderate
• Nasal decongestants: high

ADVERSE EFFECTS:

• Oral decongestants: insomnia, tachycardia, hyperkinesia, tremor, increased blood pressure, stroke (?)
• Nasal decongestants: tachyphylaxis, rebound congestion, nasal hyperresponsiveness, rhinitis medicamentosa
Mechanism of Action of Ipratropium Bromide

- Acetylcholine on muscarinic receptors
- RHINORRHEA
- submucosal glands
- vidian nerve
- brain
- sensory nerves
- epithelium

- indirect effect: cholinergic
- direct effect of mediators: not cholinergic
Efficacy of Ipratropium Bromide Against Rhinorrhea in Allergic Rhinitis with Perennial Symptoms

Ipratropium, 42 µg/nostril three times daily, N=42
Ipratropium, 21 µg/nostril three times daily, N=39
Placebo, N=42

* p<0.05 against Placebo

Adapted from Meltzer E at al. J Allergy Clin Immunol 1992;90:242
Anticholinergic Treatment: Ipratropium Bromide

- Nasal glands are activated by muscarinic, cholinergic receptors

- Ipratropium bromide is a nonselective muscarinic receptor antagonist

- Ipratropium bromide applied intranasally blocks rhinorrhea induced by cholinergic stimulation

- Ipratropium bromide has negligent systemic anticholinergic activity

- Topical adverse effects: excessive dryness, epistaxis
## Anti-Leukotriene Agents

<table>
<thead>
<tr>
<th>CysLT1 Receptor Antagonists</th>
<th>5-Lipoxygenase Inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Montelukast</td>
<td>Zileuton</td>
</tr>
<tr>
<td>Pranlukast</td>
<td></td>
</tr>
<tr>
<td>Zafirlukast</td>
<td></td>
</tr>
</tbody>
</table>

* Approved for allergic rhinitis
Cysteinyl-Leukotriene Production and the CysLT1 Receptor

- **nucleus**
- Cytosolic phospholipase A$_2$
- Arachidonic acid + 5-lipoxygenase activating protein
- 5-lipoxygenase
- Leukotriene A$_4$
- Leukotriene C$_4$ synthase
- Leukotriene C$_4$
- Leukotriene C$_4$
- Leukotriene D$_4$
- Leukotriene E$_4$
- Mast cells, basophils, eosinophils, macrophages

- CysLT1 receptor
Efficacy of a CysLT1 Receptor Antagonist in Allergic Rhinitis with Seasonal Symptoms

Daytime Nasal Symptoms Score (0-3 point scale)

Change from baseline (mean, 95% CI)

mean baseline=2.0
*p<0.01 vs placebo

Anti-Leukotriene Treatment in Allergic Rhinitis

Efficacy

- Equipotent to H1 receptor antagonists but with onset of action after 2 days
- Reduce nasal and systemic eosinophilia
- May be used for simultaneous treatment of allergic rhinitis and asthma

Safety

- Dyspepsia (approx. 2%)
Nasal Corticosteroids

- Beclomethasone dipropionate
- Budesonide
- Ciclesonide*
- Flunisolide
- Fluticasone propionate
- Mometasone furoate
- Triamcinolone acetonide

* Currently only approved for asthma
Nasal Corticosteroids

1. Reduction of mucosal inflammation
2. Reduction of mucosal mast cells
3. • Suppression of glandular activity and vascular leakage
   • Induction of vasoconstriction

- Reduction of late phase reactions
- Priming nasal hyperresponsiveness
- Reduction of acute allergic reactions
- Reduction of symptoms and exacerbations
Onset of Action of Intranasal Budesonide Against Allergen Exposure
(controlled environmental exposure - peak nasal inspiratory flow)

Comparative Efficacy of Nasal Corticosteroids

1. Shake bottle well
2. Look down
3. Using RIGHT hand for LEFT
   nostril put nozzle just inside nose
   aiming towards outside wall
4. Squirt once or twice (2 different
directions)
5. Change hands and repeat for
   other side
6. DO NOT SNIFF HARD
Wrong
Various Treatment Combinations in Seasonal Allergic Rhinitis
Nasal congestion score, Scale: 0-3

- placebo, N=20
- cetirizine + montelukast, N=20
- fluticasone + montelukast, N=20
- fluticasone + cetirizine, N=20
- fluticasone, N=20

Average congestion score over 6 weeks
[95% CI]

Adapted from Di Lorenzo et al. Clin Exp Allergy 2004;934:259
Various Treatment Combinations in Seasonal Allergic Rhinitis

total symptom score
Scale: 0-12

Average total symptom score over 6 weeks
[95% CI]

Adapted from Di Lorenzo et al. Clin Exp Allergy 2004;934:259
Nasal Corticosteroids

- Most potent anti-inflammatory agents
- Effective in treatment of all nasal symptoms including obstruction
- Superior to anti-histamines and anti-leukotienes
- First line pharmacotherapy for persistent allergic rhinitis
Nasal Corticosteroids

• Overall safe to use

• Adverse Effects
  – Nasal irritation
  – Epistaxis
  – Septal perforation (extremely rare)
  – HPA axis suppression (inconsistent and not clinically significant)
  – Suppressed growth (only in one study with beclomethasone)
Allergen Immunotherapy (Vaccines)

Subcutaneous

Sublingual

Nasal
Possible Mechanisms of Immune Response Regulation by Allergen Immunotherapy

Treg-lymphocyte

DC

Th0-lymphocyte

Th1

Th2
Possible Mechanism: Allergen Immunotherapy Induces Regulatory T-Lymphocytes

**Possible Mechanism:**

- **Treg** lymphocyte
- **TH2** lymphocyte
- Interleukin 10 (IL-10)
- TGFβ
- IgG4
Subcutaneous Immunotherapy: Effect on Serum Specific IgE

Initiation of immunotherapy

Anti-ragweed IgE (ng/ml)

August
November

Adapted from: Peng et al. J Allergy Clin Immunol 1992;89:519
Long-Term Efficacy of Subcutaneous Immunotherapy

Symptom score

May June July Aug.
1989

Placebo
Immunotherapy

May June July Aug.
1993

Symptom score

May June July Aug.
1994

Immunotherapy continued

May June July Aug.
1995

Immunotherapy discontinued

Sublingual Immunotherapy in Grass Pollen-Induced Allergic Rhinitis

SLIT, N=316
Placebo, N=318

Treatment: grass allergen tablets

Humanized Monoclonal Anti-IgE Antibody: Omalizumab

IgE

Cε3 region

Omalizumab
Efficacy of Omalizumab in Seasonal Allergic Rhinitis (ragweed pollen season)

- SQ treatments every 3-4 weeks x 3-4
- First dose prior to the pollen season

Casale T, et al. *JAMA* 2001;286:2956
Omalizumab and Subcutaneous Immunotherapy in Children: Study design

Week 0  Week 12  Week 36
SIT titration  SIT maintenance + study drug

Prescreening  Randomization

SIT (birch) + placebo  n = 54
SIT (birch) + omalizumab  n = 55
SIT (grass) + omalizumab  n = 59
SIT (grass) + placebo  n = 53

Omalizumab and Subcutaneous Immunotherapy in Children: Symptom Load
(rescue medications + symptom severity scores)
grass pollen season

![Graph showing symptom load scores for Omalizumab and Placebo with and without birch and grass SIT.](Kuehr J et al. J Allergy Clin Immunol 2002;109:274)
Anti IgE - Omalizumab

- Not licensed to treat allergic rhinitis
- Could be considered in severe cases unresponsive to conventional treatment
- Could be an adjunct to immunotherapy in severe cases