

Allergic Rhinitis

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Disclosures

- None

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Learning objectives

- Discuss clinical history that suggests an underlying allergic disorder
- Review clinical exam findings and other diagnostic considerations for allergic rhinitis
- Discuss management options for allergic rhinitis, with emphasis on pharmacologic therapies

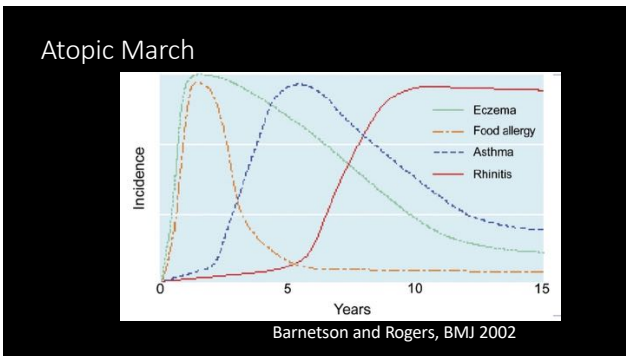
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- Allergic Rhinitis
 - Prevalence: 10-30% of the population
- Risk Factors for AR:
 - Cigarette Exposure
 - Family history of atopy
 - Higher socioeconomic class
 - First-born or only child
 - Elevated total IgE (>100 IU/L) before age 6

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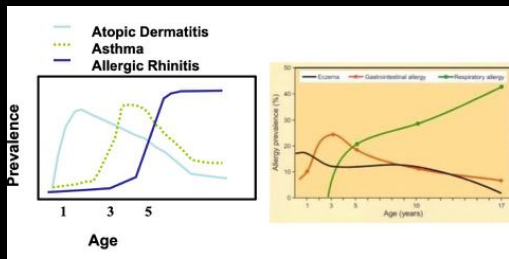
- 50-100% of patients with asthma have allergic rhinitis
 - 20-40% of patients with allergic rhinitis have asthma
- Gaurgis, et al. J Asthma 2006; 43:1-7
Pineda JL, Clin Exp Allergy 1996;26(1):15-8
Meltzer EO Allergy Asthma Proc 2005;26:336-340

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Atopic dermatitis → 30% develop asthma & 35% AR



Spierger J, Paller A. JACI. 2003; 112:5118-5127.

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Atopic March

- Infant/Toddler- atopic dermatitis
 - Proposed defects in epidermal barrier
 - Skin as primary sensitization site
- Later Childhood
 - Asthma
 - Allergic rhinitis

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Diagnosis of Allergic Rhinitis

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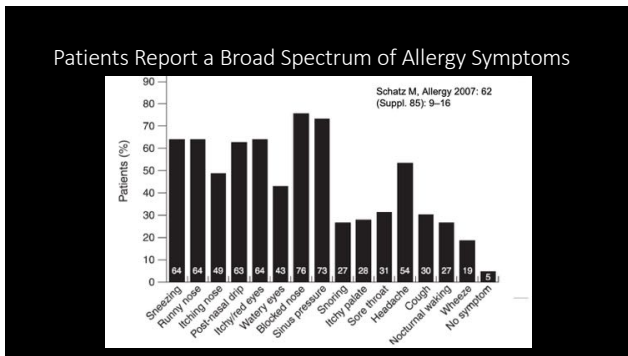
Diagnosis of Allergic Rhinitis

- Based on :
 - History
 - Physical Examination
 - Skin Testing &/- Blood Testing

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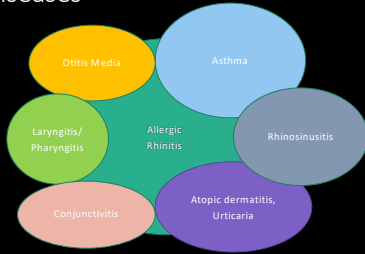
What are the symptoms of allergic rhinitis?

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Allergic Rhinitis is associated with a variety of other diseases



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Clinical History

- Establish main symptoms: itchy, sneezy, runny, etc
- Total duration
- Frequency: intermittent, persistent, acute exacerbations
- Alleviating and exacerbating factors
 - Non-allergic irritants: fragrances, smoke, chemicals, change in temp/humidity
- Associated symptoms : sinuses, eyes, throat, snoring
- History of asthma, eczema, food allergy
- Allergen exposure: home, hobbies, sports, occupational
- Family History
- Medication use: type, duration, compliance, efficacy
- Impact on QOL

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Symptom profile can point to relevant aeroallergens

Seasonal symptoms: Outdoor

Trees

Grasses

Weeds

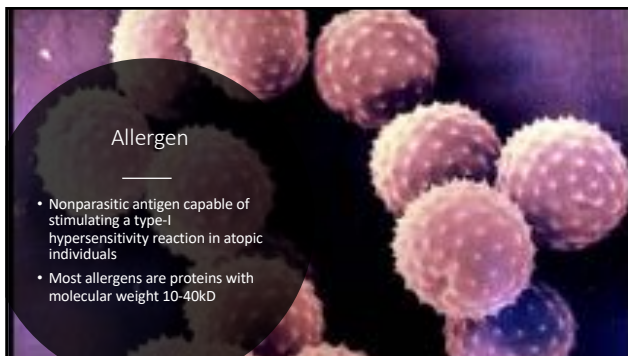
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Symptom profile can point to relevant aeroallergens

Non-seasonal Symptoms: Indoor

Mites Cockroaches Molds Animal Danders

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Allergen

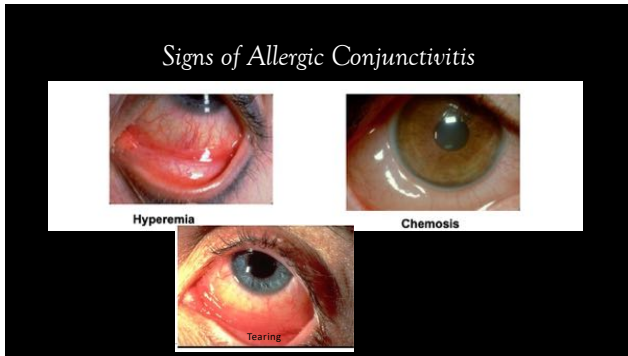
- Nonparasitic antigen capable of stimulating a type-I hypersensitivity reaction in atopic individuals
- Most allergens are proteins with molecular weight 10-40kD

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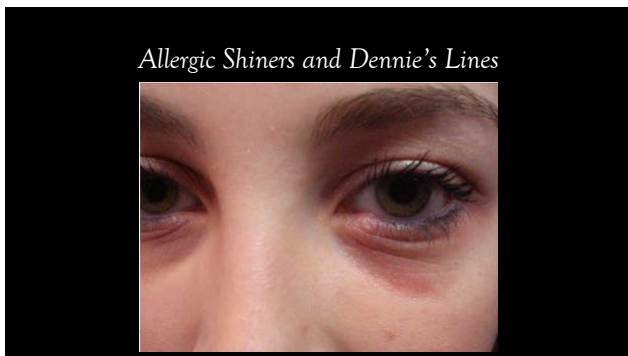
Physical Signs of Allergy

- Nose
- Throat
- Mouth
- Ears
- Eyes
- Skin
- Bronchial Tree
- GI Tract

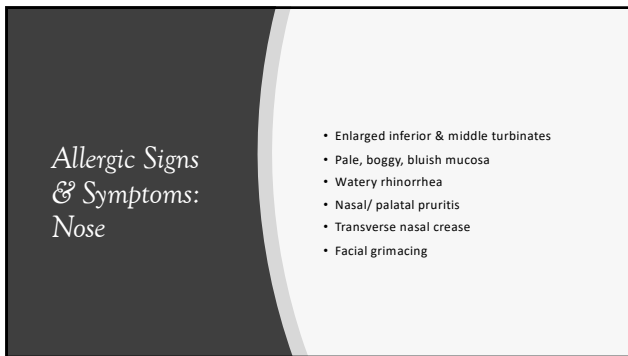
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Facial grimacing from nasal pruritis



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Allergic Salute



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Edematous ("boggy"), pale or bluish, & "wet" turbinate



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Posterior pharyngeal cobblestoning



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Diagnosis of Allergic Rhinitis

****History****

Exam

Testing

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Diagnosis

History

Exam

Testing

- 1) Confirm the diagnosis
Test results must be interpreted in the context of the patient's history
- 2) Identify clinically significant allergens
- 3) Determine the degree of sensitivity
- 4) Offer more treatment options

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Skin testing

- Why the skin? Mast cells reside in the subepithelial layer of the skin
- Allergen + Sensitized mast cell = Allergic reaction which leads to release of chemical mediators
- Classic wheal (edema) and flare (erythema) is easily seen on the skin
- Skin testing is an indirect measure of cutaneous mast cell reactivity due to the presence of IgE

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Skin testing

- Positive and negative controls to determine that the skin:
 - Responds normally to histamine
 - Does not exhibit whealing responses to non-antigenic stimuli

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Medications to avoid before skin testing

Suppressant Effects of Drugs on Immediate Skin Tests*		
MEDICATIONS	MEAN DAYS SUPPRESSED	MAX DAYS SUPPRESSED
First Generation Antihistamines†	2	5
Second Generation Antihistamines	2	7
Antihistamine Nasal Sprays	0	1
Antihistamine Eye Drops	0	1
Tricyclic Antidepressants and Tranquilizers		14
Histamine2 Antihistamines (H2 Blocker)	0	2
Topical Corticosteroids		Up to 21


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The most important skin tests for allergy: prick and intradermal testing

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Prick testing


- Delivers reproducible amount of antigen to a precise depth in the epidermis or superficial dermis
- Several allergens can be placed on the skin simultaneously



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Prick testing

- Interpretation:
 - Wheal diameter > 3mm (larger than negative control) in 20 minutes is considered positive
 - Erythema (flare) and itching are part of the positive response



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Intradermal testing

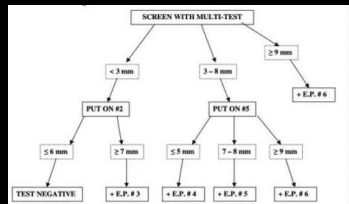
- Injection of diluted allergen into the dermal layer of skin
 - 0.01-0.05mL of allergen dilution injected intradermally to create a 4mm wheal
 - Wheal diameter measured at 10 min
- Negative:
 - Grows less than 2mm larger than the 4mm wheal initially created
 - i.e. wheal of 6 mm diameter or less
- Positive wheal: 7mm or greater



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Principles of Intradermal Dilutional Testing

- Consecutive dilutions of antigenic concentrates are applied in a sequential manner
- Quantitates the degree of sensitivity
- Determines a safe initial starting dose for desensitization immunotherapy



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- Modified quantitative testing (MQT) and Intradermal testing (IDT) yield 10% more positive tests than skin prick testing alone
- Intradermal dilution testing is the gold standard for 'quantitative' skin testing

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Specific IgE Testing/ In Vitro Testing

- Reasons:
 - Dermatographia
 - Chronic dermatitis
 - Unable to come off antihistamines
 - Children
 - Beta-blocker therapy
 - Patient preference

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Treatment

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Treatment

- Environmental control/ Avoidance
- Pharmacotherapy
- Immunotherapy

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Environmental Control

Intent: Decreasing allergen load to which the patient is exposed to

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Environmental control

Dust/dust mites

- Use of synthetic carpets or elimination of carpets
- Regular and frequent vacuuming
 - HEPA vacuums distribute lesser levels of dust into the air
- Regular changing of filters in the heating and air-conditioning systems
- Use of impervious pillow and mattress covers on bedding
- Regular washing of bedding in hot (>140°F) water
- Freezing
- HEPA filters in the bedroom and other frequently occupied areas of home
- Dehumidification
- Acaricides (kill mites)- benzyl benzonate for carpets

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Dust Mites



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Environmental control

Pets

- 60-70% of households in western world own 1 or more pet
- Cat (Fel d1) produced in salivary and sebaceous glands; flakes off with old skin (dander)
- Fish: mold around aquarium

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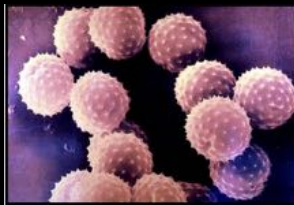
Environmental control

Pollens

- Difficult due to wide airborne distribution
- Avoidance of outdoor activities in the morning
 - Pollen released in greater amounts in the AM
- Use of air-conditioners in the home
 - Keep windows closed
- Limit presence of offending plants in immediate vicinity

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Ragweed pollen



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Environmental control

Molds

- Avoid damp environments
- Avoid dense landscaping with decaying organic material near the house
- Prevent moisture accumulation indoors around pipes, air conditioners, refrigerators, bathroom fixtures

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Pharmacotherapy

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Pharmacotherapy

- Corticosteroids
- Antihistamines
- Decongestants
- Leukotriene receptor antagonists
- Anticholinergics
- Mucolytics

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Steroids- mechanism

Mechanism of action:
downregulate inflammatory responses by binding to intracellular glucocorticoid receptors
suppress transcription of cytokine and chemokine genes

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Steroids-mechanism

- | | |
|---|--|
| <ul style="list-style-type: none">• Effector Cells<ul style="list-style-type: none">- Eosinophils<ul style="list-style-type: none">• Decreased recruitment• Decreased immigration• Increased apoptosis- Basophils & Masts<ul style="list-style-type: none">• Decreased<ul style="list-style-type: none">- Less histamine | <ul style="list-style-type: none">• Director Cells<ul style="list-style-type: none">- APCs - decreased- T-lymphocytes<ul style="list-style-type: none">• CD₄, CD₂₅, CD₂₈• IL-4, IL-5<ul style="list-style-type: none">- Down-regulation of VCAM-1- B-lymphocytes- Cytokine expression |
|---|--|

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Intranasal Corticosteroids

- Budesonide
- Fluticasone
- Mometasone
- Triamcinolone
- Beclomethasone

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Topical Nasal Steroids -Safety

- Potential adverse effects
 - Intranasal effects
 - Burning
 - Dryness
 - Nosebleeds
 - Possible mechanical complication
 - Septal perforation- rare
 - Systemic risks
 - Glaucoma or cataracts
 - Bone loss, growth retardation
 - Other systemic corticosteroid risks
- Insufficient data to base estimate of risk. Reasonable to inform risks likely small and impact over lifetime not yet understood

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Intranasal Corticosteroids

- Very effective medication for AR
- Effective for all symptoms of AR
- Clinical response about equal for all currently available intranasal steroids
- Onset of action b/w 3-12 hrs.
- More effective with continuous use
- Not generally assoc w systemic s/e

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Systemic Corticosteroids

- Short course may be appropriate for severe symptoms, especially if nasal polyposis present
- Recurrent administration potential for long term corticosteroid side effects

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Antihistamines

- First generation
 - Diphenhydramine, chlorpheniramine, hydroxyzine, promethazine, triprolidine, azatadine,
 - Highly lipophilic
 - Cross blood brain barrier
 - Result in high incidence of sedation and CNS suppressive effects
 - Patients can exhibit cognitive and psychomotor impairment without subjective sense of sedation
 - Use judiciously due to significant adverse impact on performance and quality of life.
 - Highly anticholinergic
 - Drying of mucous membranes
 - Increase in mucus tenacity
 - Blurring of vision
 - Constipation
 - Urinary retention
 - May be accompanied w tachyphylaxis

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Antihistamines

- Second-generation oral antihistamines
 - Loratadine, fexofenadine, cetirizine, desloratadine, levocetirizine
 - Effective for rhinorrhea, sneeze, itch
 - Among the 2nd gen agents, no one agent has conclusively demonstrated superior efficacy
 - 2nd gen preferred over 1st generation bc less:
 - Sedation, performance impairment, anticholinergic effects

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Topical Intranasal Antihistamines

- Azelastine
 - Age 5 and older
- Olopatadine
 - Age 6 and older

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Anticholinergics

- Ipratropium bromide
 - Decreases parasympathetic tone
 - Decreases watery rhinorrhea
 - Does not reduce
 - Congestion, irritation, itching, sneezing
 - Age 5 and older

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Leukotrienes- effects of leukotrienes in rhinitis

- Promote inflammatory cell recruitment and activation
- Enhance production of cytokines
- Induce vascular leakage and vasodilation
- Stimulate mucus secretion
- Decrease mucociliary clearance
- Increases mucosal blood flow and nasal airway resistance
- Increases nasal secretions
- LTD4 is 5000 times more potent than histamine at inducing nasal congestion and longer duration of action

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Leukotriene Modifiers

- Synthesis inhibitors (5-lipoxygenase)
 - Zileuton
- Receptor Antagonists (CysLT1 receptor)
 - Montelukast
 - Zafirlukast

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Topical Decongestants

- Oxymetazoline, phenylephrine

- Prolonged use NOT recommended
 - Tachyphylaxis
 - Rhinitis medicamentosa

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Oral Decongestants

- Pseudoephedrine, Phenylephrine
- Risks:
Insomnia, irritability, palpitations
caution esp w HTN, CAD, glaucoma, hyperthyroidism, urinary retention, stroke...
- Prolonged use not recommended

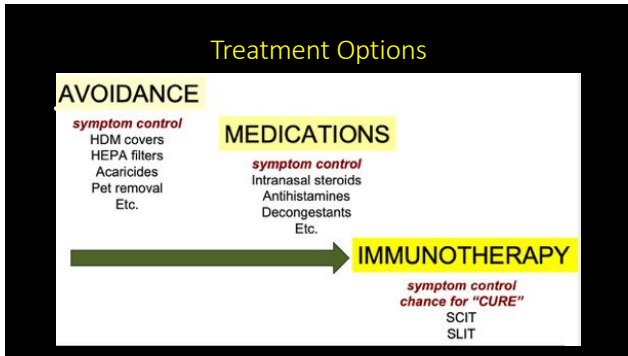
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Mucolytics

- Increases parasympathetic tone
 - Decreases viscosity

- Guaifenesin

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Aeroallergen Immunotherapy: Intent

- Produce a host immunologic response to a specific antigen
- Accomplished via
 - Intentional exposure to specific antigens
 - Regular dosing
 - Progressive escalation

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Immunotherapy

- Potential Routes:
 - Subcutaneous
 - Sublingual
- Goals:
 - Control symptoms
 - Reduce medication use
 - Avoid local (or systemic) reactions
- Success depends on:
 - Symptom-direct Ag dose
 - Continuous treatment
 - Generally 3-5 years

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Immunotherapy Mechanism

- “allergy” involves activation of Th2 cells in predisposed individuals
- Th2 cells produce IL-4, IL-5, IL-13
 - These activate:
 - Mast cells
 - B-cells (to produce IgE)
 - Eosinophils

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Immunotherapy Mechanisms

- Shift in Th2/Th1 balance
 - Increase Th1/Th2 ratio
- Antibody changes (IgG4 blocking antibodies)
 - Induction of specific IgG4 suppresses IgE-mediated degranulation, antigen presentation, memory B-cells
- T-reg induction

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Immunotherapy Indications

- Aero-allergy
 - Allergic rhinitis/conjunctivitis
 - Allergic Asthma
 - Atopic dermatitis with aeroallergen sensitivity (potential indication)

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Immunotherapy Pre-requisites

- 1) IgE- mediated hypersensitivity
 - Allergic rhinoconjunctivitis
 - Allergic asthma
- 2) Symptoms and sensitivity should be plausibly related
- 3) Pharmacotherapy and environmental avoidance should be insufficient

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IgE mediated conditions not proven to respond to IT

- Urticaria
- Angioedema
- Food allergy
- Allergic fungal sinusitis

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Immunotherapy efficacy has been shown in:

- Allergic rhinitis
- Allergic conjunctivitis
- Asthma
- Prevention:
 - Asthma
 - Development of new sensitivities
- Adults
- Children

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Aeroallergen specific immunotherapy

- Reduces medication use
- Reduces symptoms
- Reduces new sensitizations and new onset asthma

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Treatment Options

AVOIDANCE

symptom control
HDM covers
HEPA filters
Acaricides
Pet removal
Etc.

MEDICATIONS

symptom control
Intranasal steroids
Antihistamines
Decongestants
Etc.

IMMUNOTHERAPY

symptom control
chance for "CURE"
SCIT
SLIT



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Questions?

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