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Disclosures

Dr. Raschal has no financial relationships to disclose.

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Developed by the ACAAI/AAAAI Specific IgE Test Task Force
(SETTaF)

Learning Objectives

- At the completion of the session attendees will be able to:
 - Describe the role of patient history, allergy testing and examination in management of a patient presenting with symptoms of allergic rhinitis.
 - Discuss the classifications of allergic rhinitis.
 - Be able to accurately use pharmaceutical therapy for symptomatic treatment of allergic rhinitis.
 - Know the allergen immunotherapy options.
 - Be able to explain the benefits of subcutaneous immunotherapy.

Common Allergic Diseases Seen in the Primary Care Office

- Allergic Rhinitis (AR)
- Allergic Asthma
- Atopic Dermatitis/Eczema
- Food Allergy

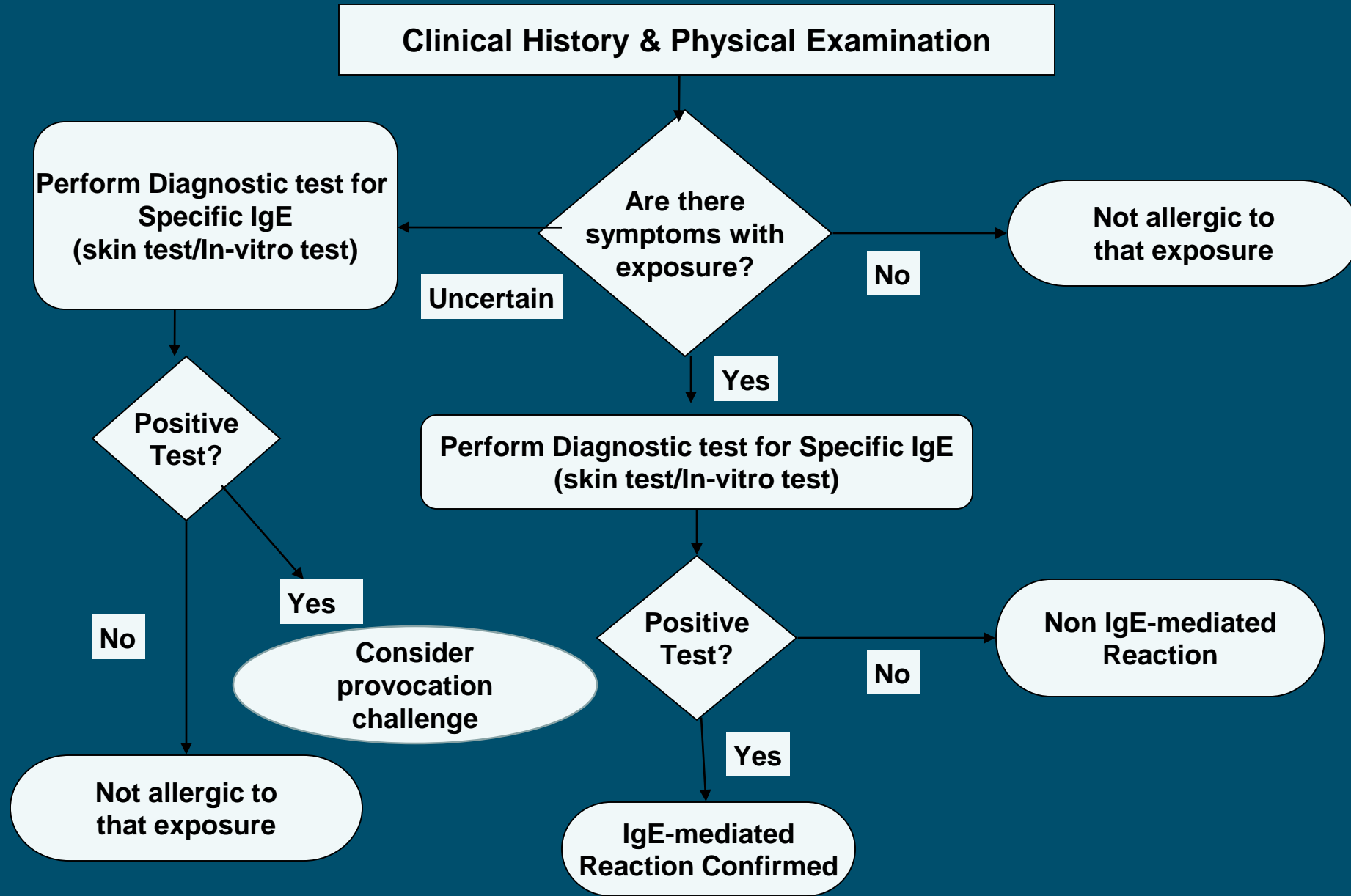
Diagnosis of allergic rhinitis

- 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

Clinical History

Diagnosis of Allergic Disease
Clinical History is Paramount

Diagnostic Algorithm for the Assessment of Human Allergic Disease



Allergy Testing



Why Test for Specific IgE? Isn't the Clinical History Good Enough?

- Although clinical history is essential for diagnosis, the history alone is insufficient to diagnose the specific allergen sensitivity(ies)
- Allergy tests help direct and optimize management
 - If non-atopic: results will allow you to focus on other etiologies
 - If atopic: will provide guidance for appropriate treatment
- Inappropriate treatment recommendations may result if allergen sensitivity is based on history alone
- This may cause unnecessary environmental controls and patient costs or failure to implement appropriate environmental controls

Allergy Skin Testing

- Skin testing remains the central test to confirm allergic sensitivity when it can be performed¹
- Skin testing is fast (15-30 minutes), safe, sensitive and a minimally invasive procedure which can be cost effective
- When performed correctly, skin testing is reproducible
- Skin testing has demonstrated good correlation with results of nasal challenge² and bronchial challenges³
- Results of skin test should always be used as an adjunct to the clinical history and physical examination when making the diagnosis of allergic disease

1. Oppenheimer et al, Ann Allergy 2006;S1:6-12

2. Bousquet et al, Clin Allergy 17:529-36, 1987

3. Cockcroft et al, Am Rev Respir Dis 135:264-7., 1987



Clinical Sensitivity & Specificity of Skin Tests

- Prick skin tests may be positive in individuals who are without respiratory symptoms
 - 42% with a positive family history for asthma or rhinitis may have + SPT and no disease
 - 29% of those with a negative family history for asthma or rhinitis may have +SPT
- Always use caution when interpreting skin tests; skin tests are a confirmatory diagnostic tool reflecting sensitization and do not make the diagnosis of clinical allergy
- Diagnosis of clinical allergy = history and confirmatory allergy diagnostic tests.

Variables that Affect Skin Test Results

Controllable

- Medications:
 - H1 Antihistamines
 - H2 Antihistamines
 - Antidepressants
 - Corticosteroids
- Immunotherapy
- Relation to adjacent positive reactions
- Extract quality
- Skin testing devices

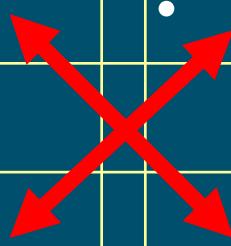
Uncontrollable

- Chronobiology:
 - Diurnal
 - Seasonal
- Menstrual Cycle
- Age:
 - Specific IgE
 - Histamine Reactivity
- Location on Body:
 - Variations on Back
 - Back vs. Forearm

Classification of Allergic Rhinitis

Allergic rhinitis classification

Intermittent	Persistent
<p>Symptoms</p> <ul style="list-style-type: none">• < 4 days / week• or < 4 weeks	<p>Symptoms</p> <ul style="list-style-type: none">• > 4 days / week• or > 4 weeks
<p>Mild</p> <ul style="list-style-type: none">• Sleep: normal• Daily activities (incl. sports): normal• Work-school activities: normal• Severe symptoms: no	<p>Moderate- severe</p> <ul style="list-style-type: none">• Sleep: disturbed• Daily activities: Restricted• Work and school activities: disrupted• Severe symptoms: yes



Allergic Rhinitis: Frequently Underdiagnosed, Undertreated and Poorly Controlled

- Underdiagnosed: 43-70% of AR patients had longstanding symptoms before the clinical diagnosis was established¹
- Undertreated and/or poorly controlled-per survey questionnaires:
 - 83% of patients with moderate to severe rhinitis were undertreated according to guideline recommendations.²
 - Diagnosed AR patients were untreated (28%) or pursued over-the-counter self-treatment (21%)³
- Associated with many comorbid illnesses and symptoms that can impair QOL and add to direct and indirect costs

1. Cox L, Current Opinion in Otolaryngology & Head and Neck Surgery 2015;23:3.

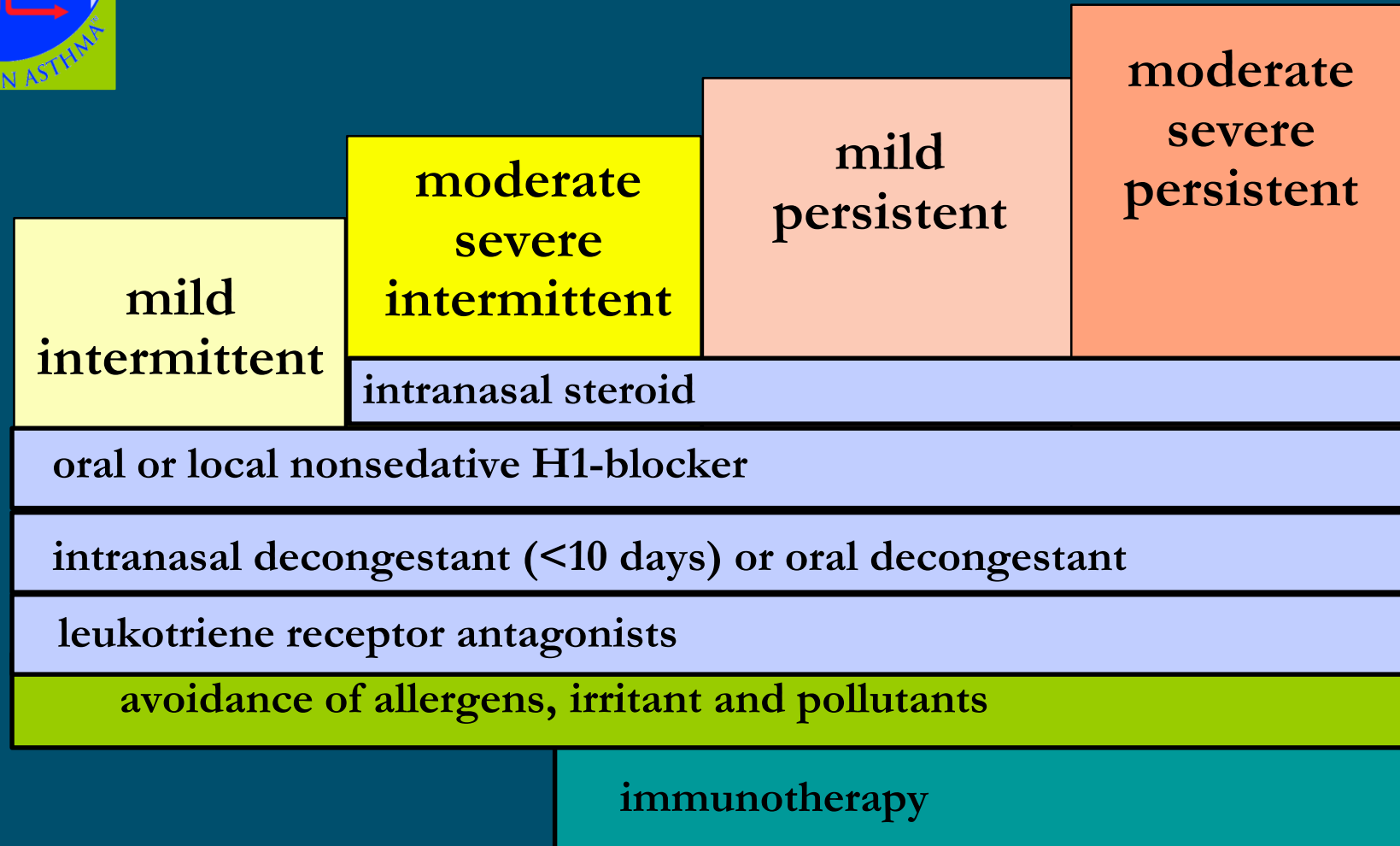
2. Nolte et al, *espir Med*. Feb 2006;100(2):354-362.

3. Mauer et al, *Allergy*. Sep 2007;62(9):1057-1063.

MANAGEMENT OF ALLERGIC RHINITIS



Management of Allergic Rhinitis: ARIA Guidelines



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

Oral antihistamines

- First generation agents

Chlorpheniramine

Brompheniramine

Diphenhydramine

Promethazine

Tripolidine

Hydroxyzine

Azatadine

- Newer agents

Acrivastine

Azelastine

Cetirizine

Desloratadine Fexofenadine

Levocetirizine Loratadine

Mizolastine

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)

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

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

CysLT1 Receptor

Antagonists

Montelukast *

Pranlukast *

Zafirlukast

5-Lipoxygenase

Inhibitors

Zileuton

* Approved for allergic rhinitis

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

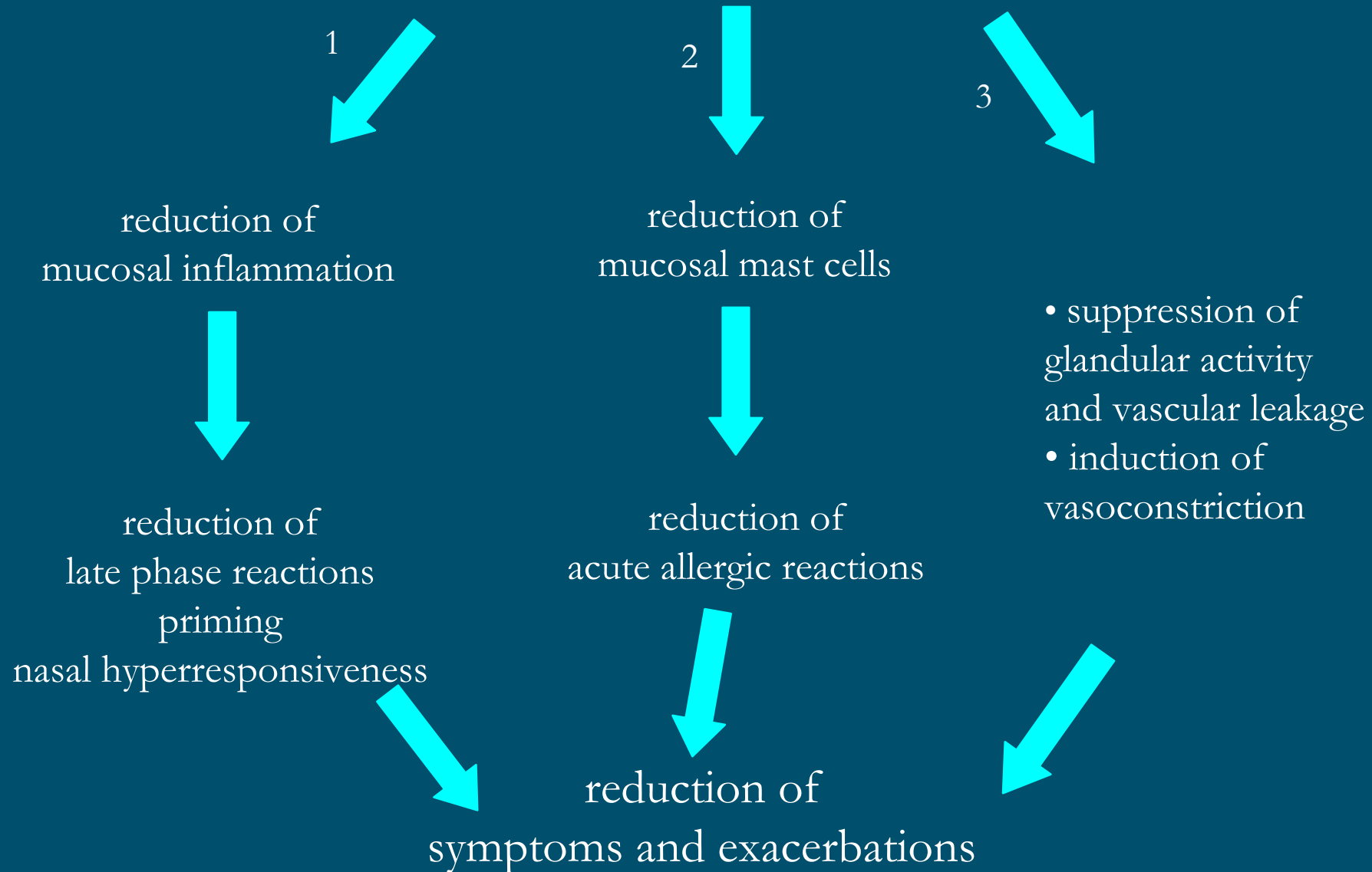
Fluticasone propionate

Mometasone furoate

Triamcinolone acetonide

* Currently only approved for asthma

Nasal corticosteroids



Allergen avoidance

- **Pets**
 - Remove pets from bedrooms and, even better, from the entire home
 - Vacuum carpets, mattresses and upholstery regularly
 - Wash pets regularly (\pm)
- **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

Sublingual Immunotherapy (SLIT)

- Indications for FDA approved sublingual tablets
 - Grass & ragweed seasonal allergic rhinitis/conjunctivitis
- Given daily at home
 - Pre-seasonal (12-16 weeks) and co-seasonal administration, first dose observed by a physician, all prescribed epinephrine
- Safe and effective in children and adults
- Insufficient studies of SLIT vs SCIT efficacy
- Common local reactions, rare systemic reactions

FDA Approved SLIT Products (Sublingual Tablets)

Product	Dose (daily)	Schedule	Age	TCS Diff	Sustained Effect	Preg
Ragwitek MSD 4/17/14	Ragweed 12 Amb a 1 Units	12wks pre/co- seasonal	18-65	-26% to -24% season -27% to -26% peak	NR	C Nursing- "caution"
Grastek MSD 4/11/14	Timothy 2800 BAU	12wks pre/co- seasonal	5-65	-27% to -23% season -29% peak	Y 3yrs -> 1yr sustained effect	B Nursing- "caution"
Oralair Stallergenes 4/1/14	Sweet Vernal, Orchard, Perennial Rye, Timothy, and Kentucky Blue 300 IR (~9000 BAU)	16wks pre/co- seasonal (10-17yo 3d build to 300IR)	10-65	-30% to -28% season (-16/-38/-38% in one 3yr study)	N	B Nursing- "caution"

PHARMACOTHERAPY OF ALLERGIC RHINITIS

Agents and actions

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

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

Nasal antihistamines

- Azelastine
- Levocabastine
- Olopatadine

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

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

Authors

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Allergen Immunotherapy

Indications

- Indicated for management of IgE mediated disorders:
 - Allergic rhinoconjunctivitis
 - Allergen-induced asthma
 - Atopic dermatitis
 - Hymenoptera and fire ant hypersensitivity



Immunotherapy

Route of Administration

- Common
 - Subcutaneous
 - Sublingual
 - Tablet
- Emerging
 - Oral (food)
 - Liquid (allergen extracts)*
- Investigational
 - Intranasal
 - Inhaled
 - Intralymphatic
 - Epicutaneous

**off-label - not FDA approved, common in Europe*

Efficacy of Allergen Injection Immunotherapy for Seasonal Allergic Rhinitis

- Meta-analysis
 - 51 studies, 2871 participants (1645 active)
- Results
 - ↓ Symptoms: SMD -0.73 (95% CI -0.97 to -0.50, $P < 0.00001$)
 - ↓ Medications: SMD -0.57 (95% CI -0.82 to -0.33, $p < 0.00001$)
- Conclusion
 - Significant reduction in symptom scores and medication use with no long term adverse effects

SLIT for Allergic Rhinoconjunctivitis Systematic Review

- Studies & participants
 - RCTs, + skin or blood test to aeroallergen
 - 63 studies, 5131 participants, age 4-74
- Findings
 - □ Symptoms & medication use by >40% in asthma & AR/ARC
 - □ Combined (symptom/med) score & □ QOL
- Conclusion
 - Moderate evidence for SLIT efficacy in asthma, AR & ARC

Summary of Safety

SCIT vs SLIT

- SCIT
 - Rare systemic reactions (3/1000 injections)
 - Rare fatalities (1/2.5M injections- declining?)
 - Frequent local reactions
 - Erythema/pruritis/swelling- injection site
- SLIT
 - Rare systemic reactions
 - No known fatalities
 - Frequent local reactions
 - Erythema/Pruritis/edema- mouth, lips, tongue, upper airway

SLIT Contraindications/Precautions

- Severe, unstable or uncontrolled asthma
- History of any severe SLIT systemic allergic reaction
- History of eosinophilic esophagitis
- Ingredient hypersensitivity (e.g. gelatin, mannitol, NaOH)
- Stop treatment to allow healing of oral inflammation or wounds

SLIT Extract Black Box Warning

- Can cause life-threatening allergic reactions
- Hold if severe, unstable or uncontrolled asthma
- Initial dose observation of 30 min
- Prescribe epinephrine & instruct on use
- May not be suitable for
 - Co-morbidity affecting survival of allergic reaction
 - Conditions/meds affecting epinephrine responsiveness (e.g. beta blockers)

Allergen Immunotherapy

Conclusions

- Allergen immunotherapy is safe and very effective in a variety of allergic disorders
- Clinics administering immunotherapy require trained personnel, proper equipment, and standardized practices to minimize risk
- New methods & patient options available
- Refer patients with allergic conditions early for immunotherapy consideration

Immunotherapy Administration Outside the Prescribing Allergist's office

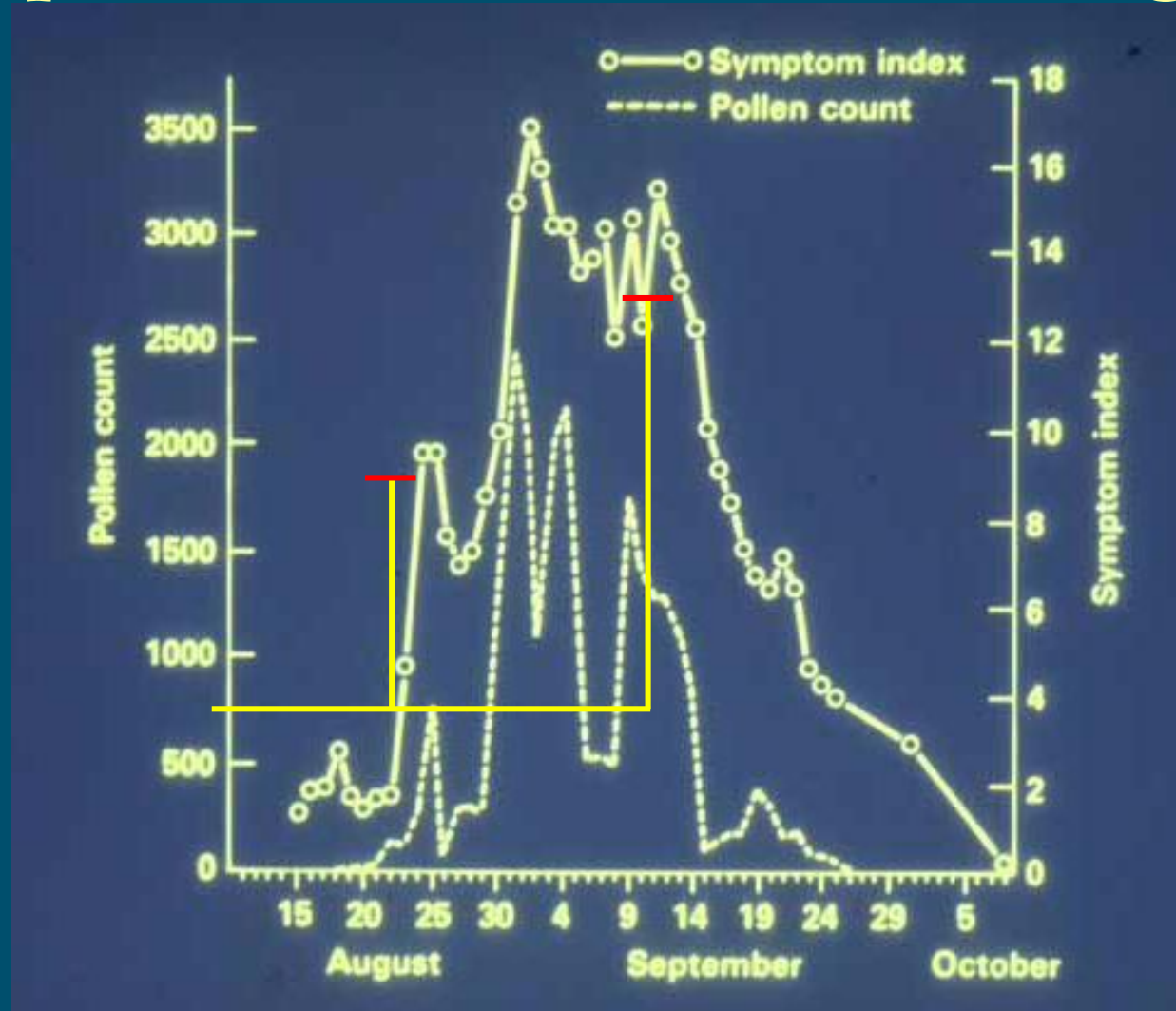
- Not at home...
- Prescribing Allergist should provide:
 - Properly prepared & labeled extract vial(s)
 - Schedule & administration instructions
 - When to postpone injection, reduce dose and call allergist
 - Risk factors for adverse reactions
- Annual follow-up with allergist is recommended



Immunotherapy Outside of the Prescribing Allergist's Office

- Administration
 - Qualified physician & staff
 - Right patient, vial, dose, schedule
 - Pre-shot screening, document, observe ≥ 30 min
- Suggested equipment
 - Epinephrine (1:1000 w/v), stethoscope, sphygmomanometer, tourniquet, syringes, needles, IV fluids & setup, airway & O2 equip., antihistamines, corticosteroids, glucagon

Nasal priming in the natural presentation of seasonal allergic rhinitis



The ratio of symptoms to pollen counts almost doubles between the beginning to the end of the pollen season

Summary

Allergic Rhinitis is a clinical diagnosis and diagnostic tests are confirmatory.

Comprehensive management plan includes avoidance measures, pharmaceuticals and allergen immunotherapy.

Appropriate use of pharmaceutical treatments are critical for optimal management of symptoms.

Early treatment with subcutaneous allergen immunotherapy may prevent asthma.

Allergic Asthma

- Allergic asthma is the most common form of asthma.
- Symptoms of allergic asthma and non-allergic asthma are similar: cough, shortness of breath, chest tightness and wheezing.
- Allergic asthma is triggered by allergen inhalation.
- An asthma specialist such as an allergist/immunologist will identify allergic triggers and develop a plan to help optimize management.
- Allergen immunotherapy has been shown to decrease the development of asthma by 50%. Allergy 2007, Niggerbaum

When to Refer Patients with Allergic Disease

- AR, AC, asthma &/or atopic dermatitis and any ONE
 - Patient preference
 - Unsatisfactory current therapy or adverse effects
 - Unsatisfactory quality of life
 - Concomitant asthma & allergic rhinitis
 - Prevention of new sensitizations?
- Insect sting allergy
 - All patients with systemic reactions
 - Possibly if extremely morbid local reactions