Rhinitis – Part 2

Pharmacotherapy II
728-556
2021

Valerie Schend RPh

Epidemiology

- Affects 40-60 million Americans
  - 10-40% of adults, and up to 40% of children
  - 80% develop before age 20
  - 80-89% of children with AR continue into adulthood
  - Increased risk with parental history of AR
  - Decreased risk if a younger sib or farm environment
- Direct and indirect / total costs up to $12 billion per year
  - $3.4 billion direct with ½ of costs due to meds

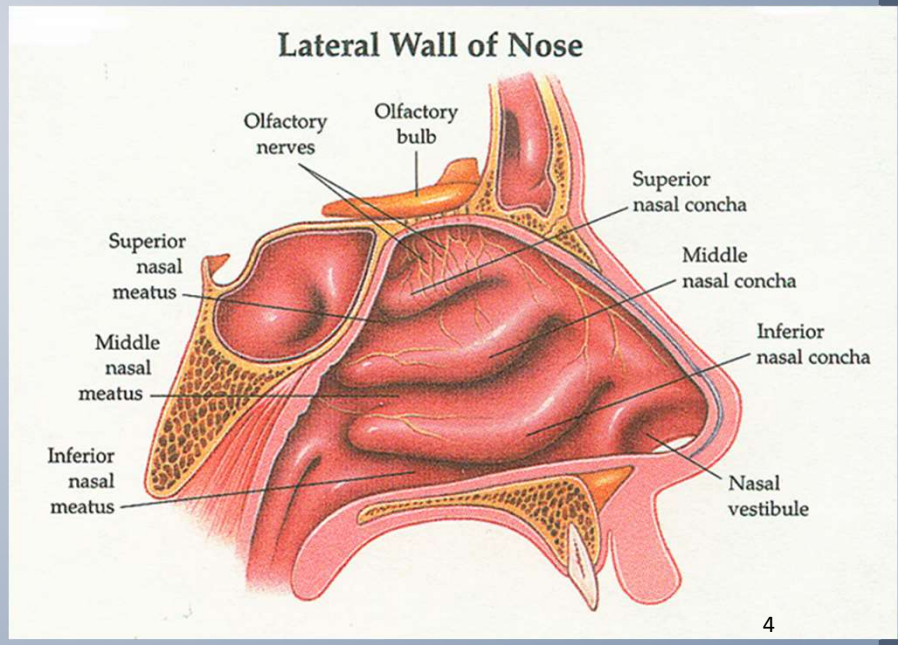
Meltzer EO. *Ann Allergy Asthma Immunol* 2011 Feb;106(2 Suppl):S12-6

Co-Morbidities

- Asthma
- Sinus involvement
- Atopic dermatitis/eczema
- Psychomotor and/or performance deficits
- Otitis media
- Impaired sense of taste or smell
- Conjunctivitis
- Snoring ± sleep apnea
- Nasal polyps
- GERD
- Mouth breathing

Nasal Physiology

- Three tubinates on lateral nasal wall
  - Increase surface area
  - Warm, cleanse and humidify inspired air
  - Regulate airflow
    - Airflow partially obstructed (modify resistance) to aid nasal function



History

- When and how long do symptoms occur
  - Onset, duration, frequency
- What are the symptoms
  - Severity
- Exposures/triggers
  - Patterns
- Other medical issues, surgeries, trauma

History

- Personal
  - Symptoms: onset, duration, frequency, triggers, severity
- Family
  - History of allergy or asthma
- Environmental
- Medication Use
  - Treatment: response to previous interventions
  - Causation
- QoL

Symptoms	Seasonal Allergies	Asthma**	Common Cold	Coronavirus	Influenza
Duration	varies	varies	< 14 days	7-25 days	7-14 days sudden onset
Cough	rare	common	common (mild)	common (usually dry)	common (usually dry)
Wheezing	no	common	no	no	no
SOB	no	common	no	sometimes	no
Chest pain/ tightness	no	common	no	sometimes	no
Rapid breathing	no	common	no	sometimes	no
Sneezing	common	no	common	no	no
Nasal symptoms	common	no	common	rare	sometimes
Sore throat	sometimes	no	common	sometimes	sometimes
Fever	no	no	short period	common	common

** Allergic asthma may have the same signs and symptoms of seasonal allergies

Symptoms	Seasonal Allergies	Asthma**	Common Cold	Coronavirus	Influenza
Feeling tired and/or weak	sometimes	sometimes	sometimes	sometimes	common
Headaches	sometimes	rare	rare	sometimes	common
Body aches / pain	no	no	Common	sometimes	common
D/N/V	no	no	rare	sometimes	sometimes
Chills	no	no	no	sometimes	sometimes
Loss of taste and/or smell	rare	no	rare	sometimes	rare
Possible complications	asthma exacerbation sinusitis		otitis pneumonia sinusitis	pneumonia ARDS respiratory failure septic shock	pneumonia encephalitis meningitis seizures

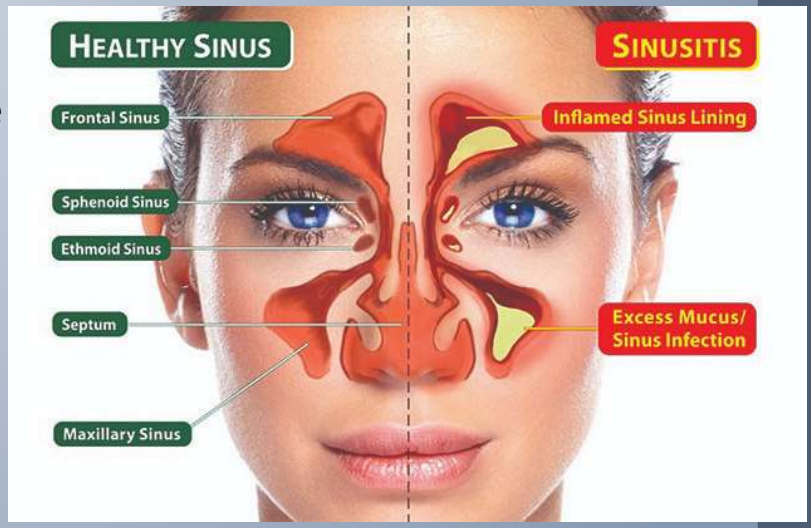
https://www.aafa.org/media/2631respiratory-illness-symptoms-shart-coronavirus-flu-cold-allergies.png
https://www.empr.com/home/clinical-charts-upper-respiratory-tract-infection-symtoms-comparison

Subgroups

- Infectious
  - Viral – common cold
  - Bacterial - rhinosinusitis
- Autonomic (Non-allergic, non-infectious)
  - Drug-induced
  - Rhinitis of the elderly
  - Hormonal
  - Non-allergic occupational
  - Gustatory
  - Atrophic
  - NARES/AER
  - Idiopathic / Vasomotor
- Allergic (IgE-mediated)
- Mixed

Rhinosinusitis / Infectious Rhinitis

- Inflammation of the nasal and paranasal passages
  - Chronic: Persisting ≥ 12 weeks
    - Dysfunctional immune system
    - With 2 or more of the following symptoms
      - Nasal obstruction/discharge
        - Discolored, thick, foul smell/taste
      - Facial pressure/pain/fullness
      - Impaired sense of smell
      - May also have complaints of lethargy, fatigue
  - Acute
    - Most often viral
    - Symptoms present for a minimum of 10 days (worsening after 5 days)



Rhinosinusitis

- Consider bacterial if any of the 3 following are present
  - Symptoms ≥ 10 days without signs of clinical improvement
  - Symptoms are severe
    - Fever ≥ 102° F
    - Nasal discharge and facial pain ≥ 3 consecutive days at onset
  - Symptoms worsen
- Treatment
  - Antibiotics for 5-7 days (peds 10 days)
  - Hydration, analgesics, antipyretics, saline irrigation, INCS
  - Chronic rhinosinusitis
    - **INCS, saline irrigation**
    - Acutely: antibiotics AND systemic corticosteroids
    - Montelukast, allergen immunotherapy, pseudoephedrine, oxymetazoline
    - Omalizumab, mepolizumab (w/polyps)

Clin Infect Dis. (2012) 54(8):1041-45 – Allergy Asthma Proc 34:132-37
JAMA Otolaryngol Head Neck Surg. 2018 Jun 7. doi: 10.1001/jamaoto.2018.0667

Rhinosinusitis

- Bacterial:
  - *Streptococcus pneumoniae, Hemophilus influenzae, Moraxella catarrhalis,* group-A beta-hemolytic *Streptococci, . . .*
  - Possible alterations in the microbiome
- Viral: initially clear, watery rhinorrhea accompanied by sneezing and nasal obstruction
  - Majority of infections
  - *Rhinovirus, para-influenza A & B, adenovirus*, RSV
  - Generally self-limited
- Fungal:
  - *Aspergillis, Mucor, Cladosporium, Candida, Alternaria, Curvularia*
  - Colonization vs. active infection
  - Constant nasal congestion with thick (peanut butter-like secretions)
  - Gradual worsening of symptoms
    - Congestion; sense of smell; mucus production (thick, brownish); facial pain/pressure; loss of visual acuity (encroachment on optic canal)

Drug-Induced Rhinitis

- Aspirin/NSAID's
- α-receptor antagonists (terazosin, doxazosin)
- ACE inhibitors (lisinopril, captopril)
- β-blockers (carvedilol, ophthalmic agents)
- Diuretics
- Oxymetazoline
- Calcium channel blockers (nifedipine)
- Oral contraceptives
- Phosphodiesterase-5 inhibitors (sildenafil, tadafanil)
- Psychotropics (amitriptyline, risperidone)
- Phentolamine
- Cocaine

Drug-Induced Rhinitis

- Adverse effect
  - Resolves readily with discontinuation of medication
- Rhinitis Medicamentosa
  - Prolonged use of decongestant nasal sprays
  - Vasodilation, intravascular edema, hyperreactivity, mucosal hypertrophy, rebound congestion
  - Taper or abrupt withdrawal
- Treatment – avoidance

Rhinitis in the elderly (Senile rhinitis)

- Patients > 65 yo
- Affects up to 30%, some may also have AR
- Due to neurogenic dysregulation/inflammation?
  - Structural changes, changes in airflow
  - Mucosal hypertrophy
- Symptoms
  - Bilateral watery secretions
  - Clear anterior rhinorrhea
    - Increased drip quantity and frequency
  - Treatment
    - Ipratropium

Hormonal Rhinitis

- Due to hormonal imbalances
  - Menses, puberty, pregnancy, menopause,
  - Hypothyroidism, acromegaly
- Estrogen
  - Vascular engorgement → nasal obstruction and/or hypersecretion
- Beta-estradiol, progesterone
  - Increase the expression of H1-receptors and induce eosinophil migration and/or degranulation
- Testosterone
  - Decreases eosinophil activation
- Treatment – INCS, cromolyn

Occupational Rhinitis

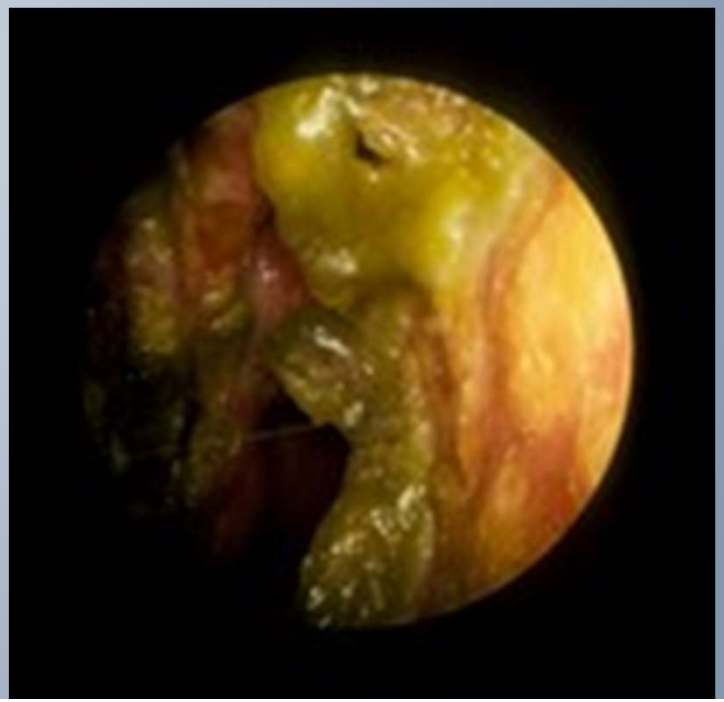
- Rule out allergic causes
  - Lab animals, dust mites, grain dust, plants, food proteins, . . .
- Inflammatory disease of the nose
  - Intermittent or persistent
  - Nonspecific nasal hyperreactivity
  - Congestion, rhinorrhea, sneezing, itching
- Occupational or environmental airborne agents
  - Chemicals, irritants
- Treatment – avoidance if possible
  - Symptom based

Gustatory Rhinitis

- Associated with hyperactive neural system
  - After ingestion of hot, spicy food
  - Non-adrenergic, non-cholinergic
  - Vagally mediated – direct nasal vasodilation
- Watery rhinorrhea
- Treatment – avoidance, ipratropium

Atrophic

- Progressive atrophy of nasal mucosa
  - Hardened nasal crusts, anosmia, foul odor
  - Dryness, obstruction, epistaxis, septal perforation
- Saline irrigation
  - ± antibiotics
  - ± corticosteroids



NARES

- **N**on**A**llergic **R**hinitis with **E**osinophilic **S**yndrome
- >20% eosinophils in nasal smear
- Perennial symptoms
  - Paroxysmal sneezing; profuse, clear rhinorrhea, nasal itching, congestion, reduced sense of smell
- May develop aspirin sensitivity, nasal polyps, asthma
- At increased risk for development of obstructive sleep apnea

Aspirin (NSAID) Exacerbated Rhinosinusitis

- Persistent rhinorrhea and nasal congestion
  - Increased severity and worsening with exposure to ASA/NSAID
  - Symptoms generally refractory to pharmacotherapy
    - Avoidance, desensitization
  - Conjunctival edema/watering
  - Decrease or loss of sense of smell
  - Symptoms exacerbate ½ to 3 hours after ingestion
- Eosinophilic inflammation
  - Increase in leukotrienes, decrease in prostaglandins
- Comorbidities
  - Often asthma and nasal polyps

Idiophathic/Vasomotor (NAR)

- No uniform definition or diagnostic criteria
- Diagnosis of exclusion
- Nasal hyperreactivity to unspecific environmental stimuli
  - Unrelated to allergy, infection, structural lesions, systemic disease, drug abuse
  - Variety of stimuli: (chemical) irritants, strong odors, emotional stress, cold dry air, environmental/atmospheric changes, exercise
- Treatment
  - INCS, INAH, ipratropium

Table 1
Rhinitis Control Assessment Test: questionnaire

During the past week, how often did you have nasal congestion?				
Never 5	Rarely 4	Sometimes 3	Often 2	Extremely Often 1
During the past week, how often did you sneeze?				
Never 5	Rarely 4	Sometimes 3	Often 2	Extremely Often 1
During the past week, how often do you have watery eyes?				
Never 5	Rarely 4	Sometimes 3	Often 2	Extremely Often 1
During the past week, to what extent did your nasal or other allergy symptoms interfere with your sleep?				
Never 5	Rarely 4	Sometimes 3	Often 2	Extremely Often 1
During the past week, how often did avoid activities (for example, visiting a house with a dog or cat, gardening) because of your nasal or other allergy symptoms?				
Never 5	Rarely 4	Sometimes 3	Often 2	Extremely Often 1
During the past week, how well were your nasal or other allergy symptoms controlled?				
Completely (5)	Very (4)	Somewhat (3)	A little (2)	Not at all (1)

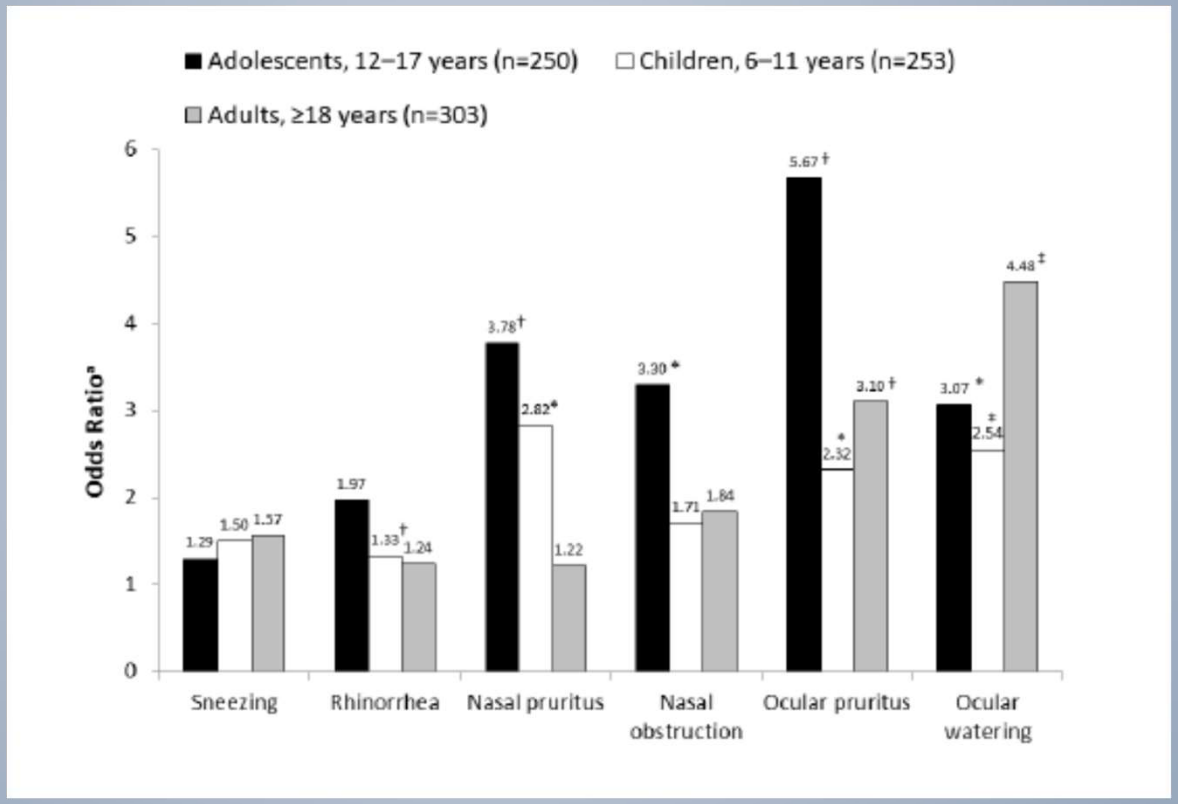
From Meltzer EO, Schatz M, Nathan R, et al. Reliability, validity and responsiveness of the Rhinitis Control Assessment Test in patients with rhinitis. J Allergy Clin Immunol 2013;131:381; with


POLLEN
SEASON
AHEAD

Allergic Rhinitis (AR)

- Symptoms: nasal congestion (*stuffy nose*), rhinorrhea (*runny nose*), sneezing, nasal/ocular itching (*itchy nose, throat or eyes*)
- Inflammation of the nasal mucosa
- Most prevalent
- Exposures may be seasonal (SAR), perennial (PAR), episodic
- Symptom frequency
  - Intermittent < 4 days/week or 4 weeks/year
  - Persistent > 4 days/week or 4 weeks/year
- Severity
  - Mild – no interference in QoL
  - More Severe – symptoms interfere with QoL
    - Exacerbations of coexisting asthma; sleep disturbances; impairment of daily activities, leisure, sports, school or work performance

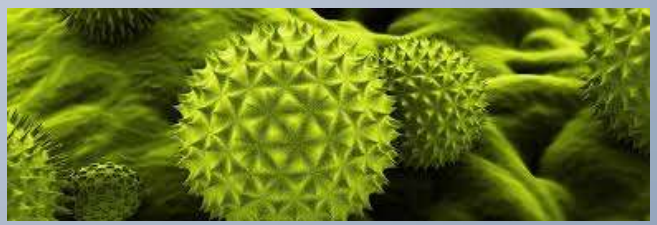
Symptom Burden

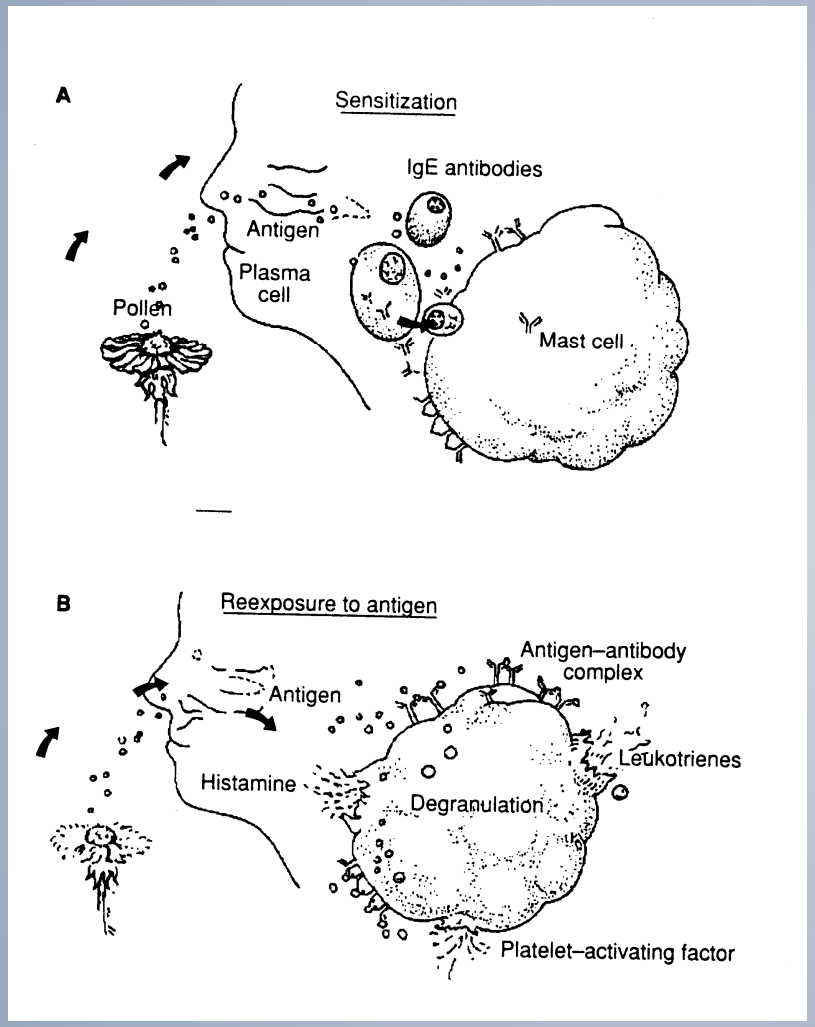


Blais MS, et al. *Annals of Allergy, Asthma and Immunology* (2018), https://doi.org/10.1016/j.anai.2018.03.028.[26]

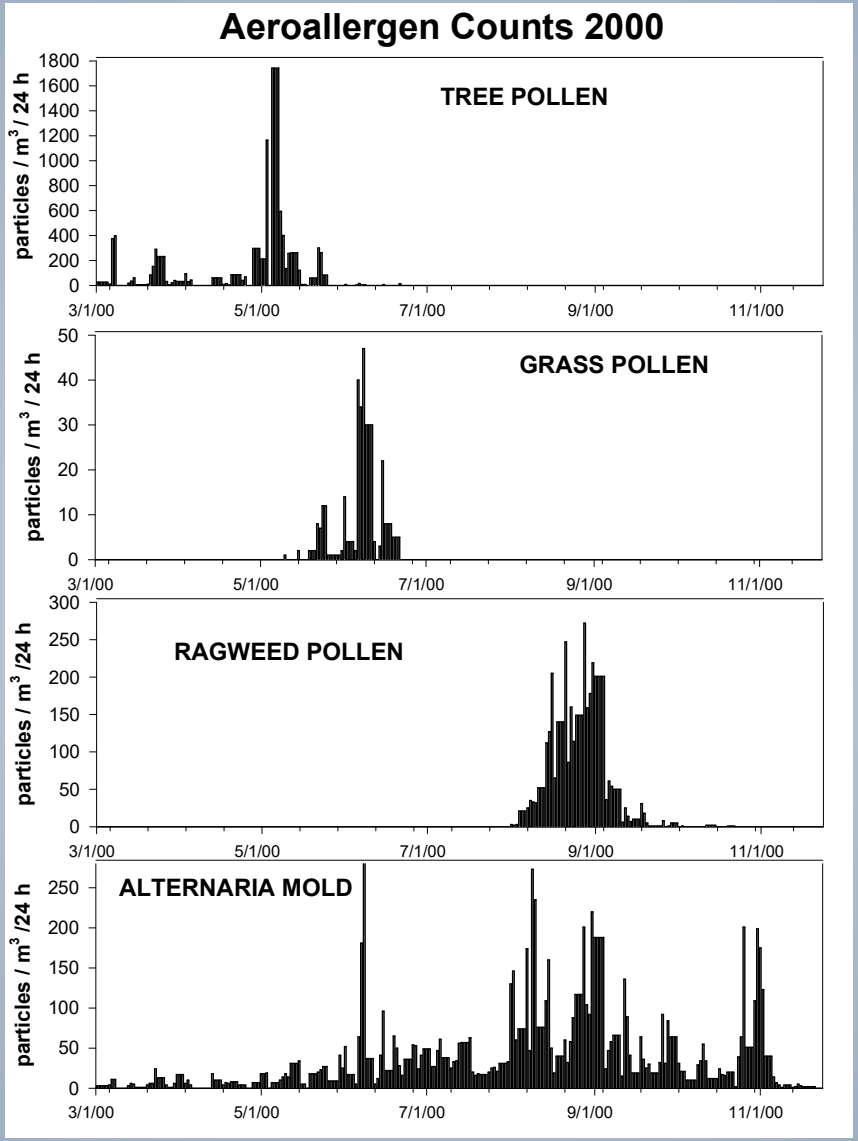
Allergic Rhinitis

- IgE mediated
- Seasonal = intermittent
- Perennial = persistent
  - PARSE: perennial allergic asthma w/seasonal exacerbations
- LAR = local allergic rhinitis
  - Absence of atopy
- Risk factors
  - Family history
  - Increased serum IgE, positive allergen skin prick tests
  - Higher socioeconomic status
  - Exposures to allergens/irritants
  - No older siblings
  - Gender

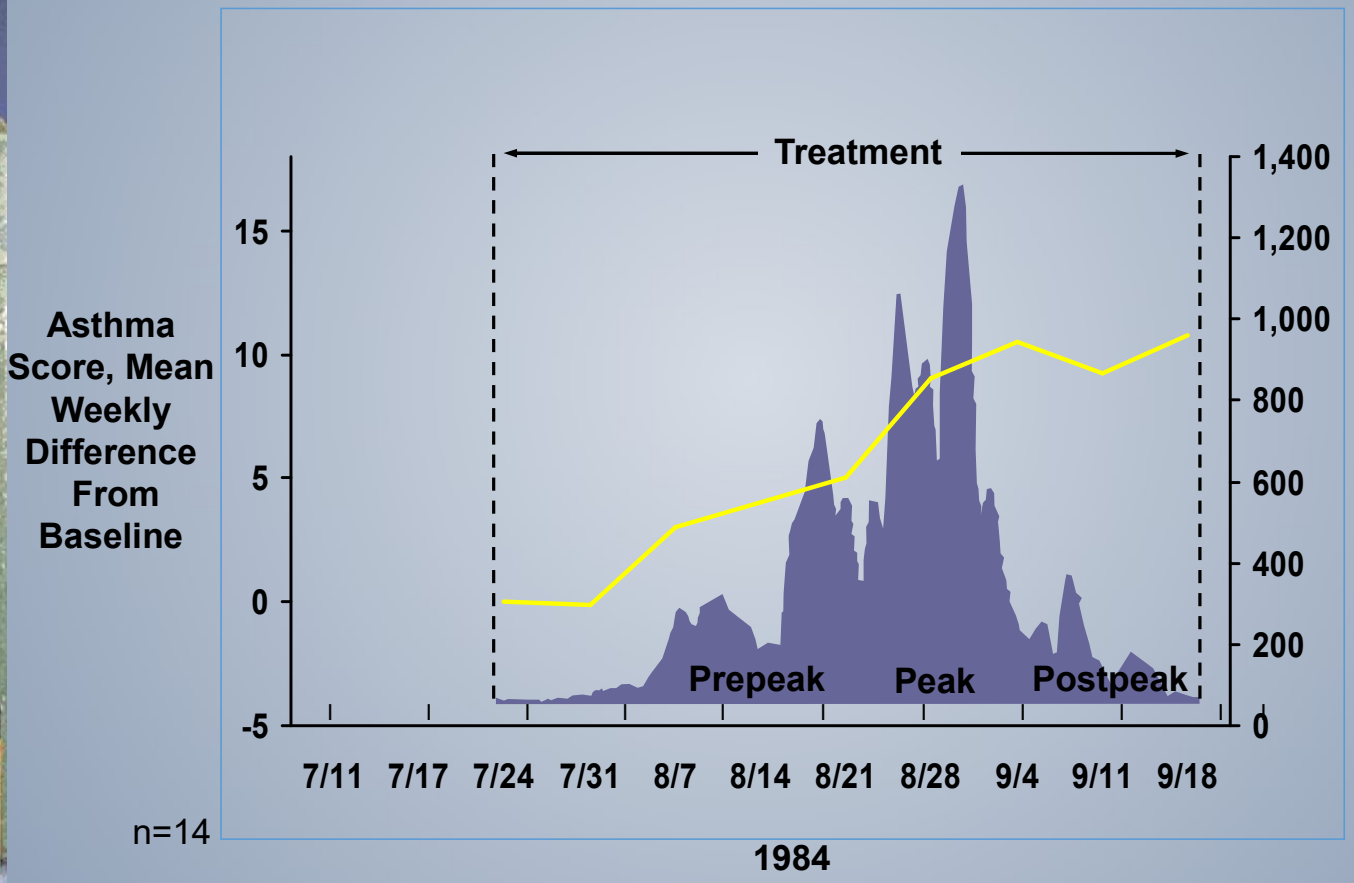




Repeated exposures have a priming effect resulting in hypersensitivity

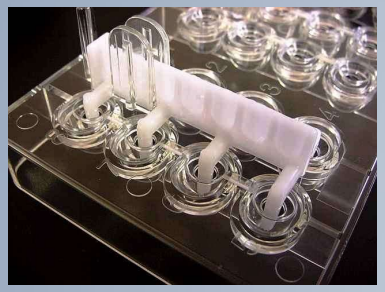

Aeroallergen Counts 2000
TREE POLLEN
GRASS POLLEN
RAGWEED POLLEN
ALTERNARIA MOLD
particles / m3 / 24 h
3/1/00
5/1/00
7/1/00
9/1/00
11/1/00

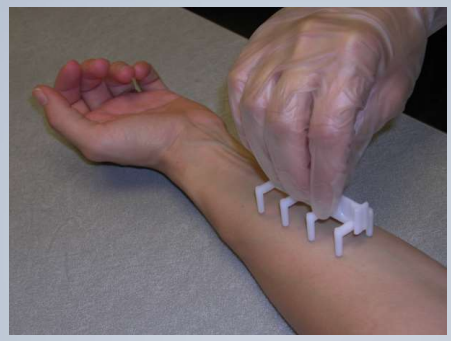
Relationship Between Ragweed Pollen Count and Asthma Symptoms in Patients With Seasonal Allergic Rhinitis and Asthma



Adapted from Welsh PW et al. *Mayo Clin Proc*. 1987;62:125-134.

Allergy Skin Testing





Atopy: abnormal tendency to produce specific IgE in response to low doses of allergens (proteins) with subsequent development of symptoms

in vitro blood tests:
RAST, ImmunoCAP, Immulite, HYTEC-288

Allergy 2001; 56:813-824
JACI 2010; 126:33-38

ARIA Classification of Allergic Rhinitis

Intermittent symptoms
- < 4 days per week, or
  < 4 consecutive weeks

Persistent symptoms
- ≥ 4 days per week or
  ≥ 4 consecutive weeks

Mild
- Normal sleep
- Normal daily activities
- Normal work and school
- No troublesome symptoms

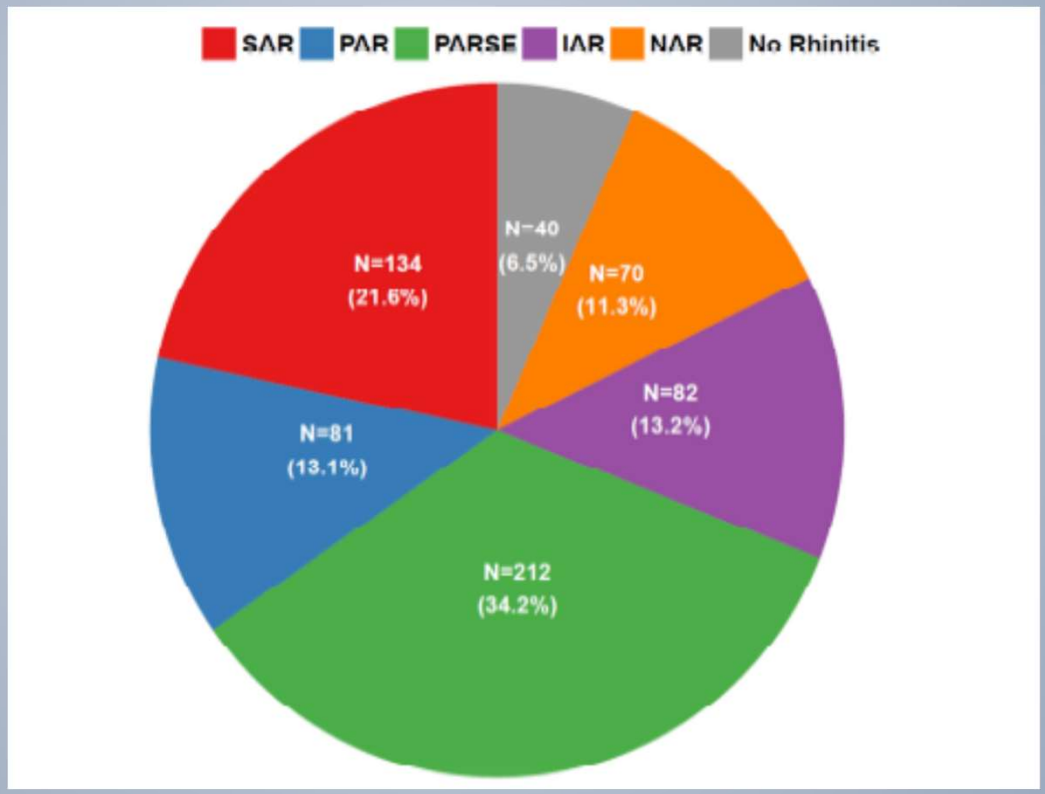
Moderate–severe
(one or more)
- Abnormal sleep
- Impairment of daily activities, sport, leisure
- Difficulties caused at work or school
- Troublesome symptoms

Dykewicz MS. et al. Practice Guideline Treatment of Seasonal Allergic Rhinitis
Ann Allergy Asthma Immunol. 2017;119:489-511

Pathophysiology

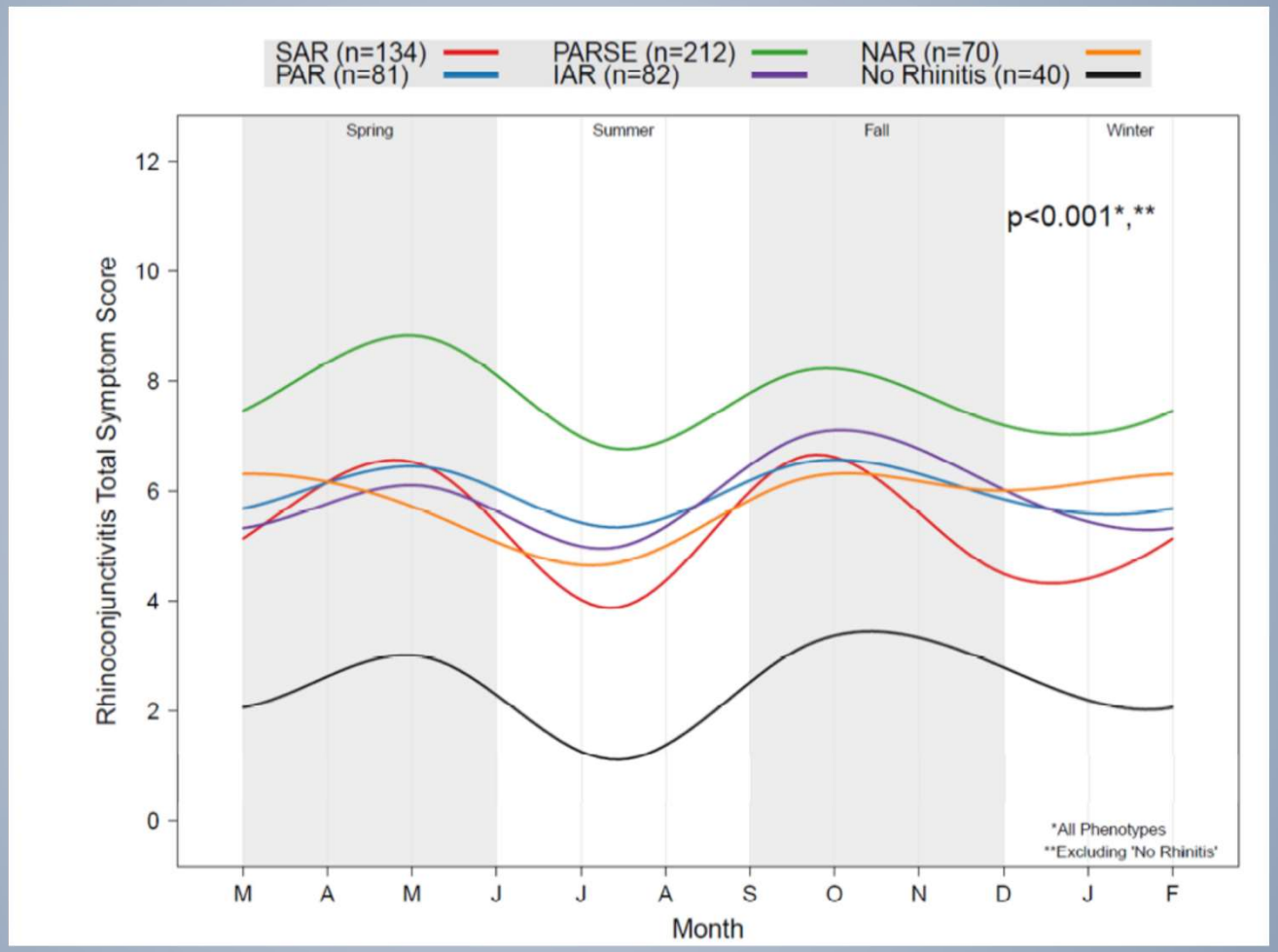
- Inflammatory Cells
  - Mast cells, CD4-+ T cells, B cells, macrophages, eosinophils, neutrophils
- Cytokines
  - Interleukins (IL-3, IL-4, IL-5, IL-13)
  - Promote the production of IgE
- Mediators
  - Histamine: stimulation of irritant receptors, pruritus, increased vascular permeability, increased mucosal permeability
  - Leukotrienes: Smooth muscle contraction, increased vascular and mucosal permeability, chemotaxis

Rhinitis Phenotypes



Togias A, et al. *Journal of Allergy and Clinical Immunology* (2018), doi: 10.1016/j.jaci.2018.07.041

Seasonal Variation in Symptom Scores



Pharmacist Management of AR

- Recognize and identify AR
- Risk assessment
- Medication therapy
- Patient Education
- Referral to PCP
- Treatment technique/adherence

Bosnic-Anticevich S. et al. *ARIA Pharmacy 2018* doi: 10.1111/all.13701

Symptoms of Rhinitis	
Suggestive of Allergic Rhinitis	**Usually NOT associated with allergic rhinitis**
Two or more of the following on most days:	Unilateral symptoms
•Profuse watery rhinorrhea	Mucopurulent rhinorrhea Post nasal drip with thick mucus
•Sneezing – episodic, paroxysmal	Decreased sense of smell
•Nasal obstruction	Nasal obstruction (with no other symptoms)
•Nasal pruritus	Pain
• Eye symptoms can be +/-	Recurrent epistaxis

Bousquet J. *Allergy*. 2008;63:990

Symptoms	Allergic Rhinitis	URI (Common cold)
Duration	Variable	5-10 days
Season	Any time of year	Mostly winter
Disease course	Severe within minutes	Increase in severity over course
Nasal/Ocular	Profuse watery rhinorrhea Sneezing –episodic Pruritus Nasal congestion Ocular – redness, itching, tearing Loss of smell	Severe nasal congestion Rhinorrhea Sneezing Frequent loss of smell
Sore throat	Occasional	Common
Cough	Occasional	Common
Chest discomfort	Rare (except allergic asthma)	Mild – moderate Asthma exacerbation?

Benefits of Treatment

- Impact of untreated/undertreated symptoms
  - Adults: HA, fatigue, impaired physical functioning, reduced ability to concentrate, slower cognition, lower positive affect, absenteeism, loss of productivity (presenteeism)
  - Children: learning impairment, fatigue, decreased appetite, poor sleep, irritability, allergic shiner/crease, school absences
- Treatment will:
  - Relieve symptoms
  - Improve QOL
  - Prevent future morbidities

Allergy: effects on Asthma

- Associated with worsening asthma
- Increased allergen exposure – increased risk of asthma exacerbations
- More severe asthma

- Poorer asthma control
- Decreased QoL
- Increased risk
  - ED visits
  - Hospitalizations
- Increased health care costs

Allergic Asthma: asthma that becomes symptomatic after acute exposure to something to which the individual is allergic (eg. a pet) or during a specific season

ERJ Express. Published 3/5/15 as doi: 10.01183/09093136.00088814

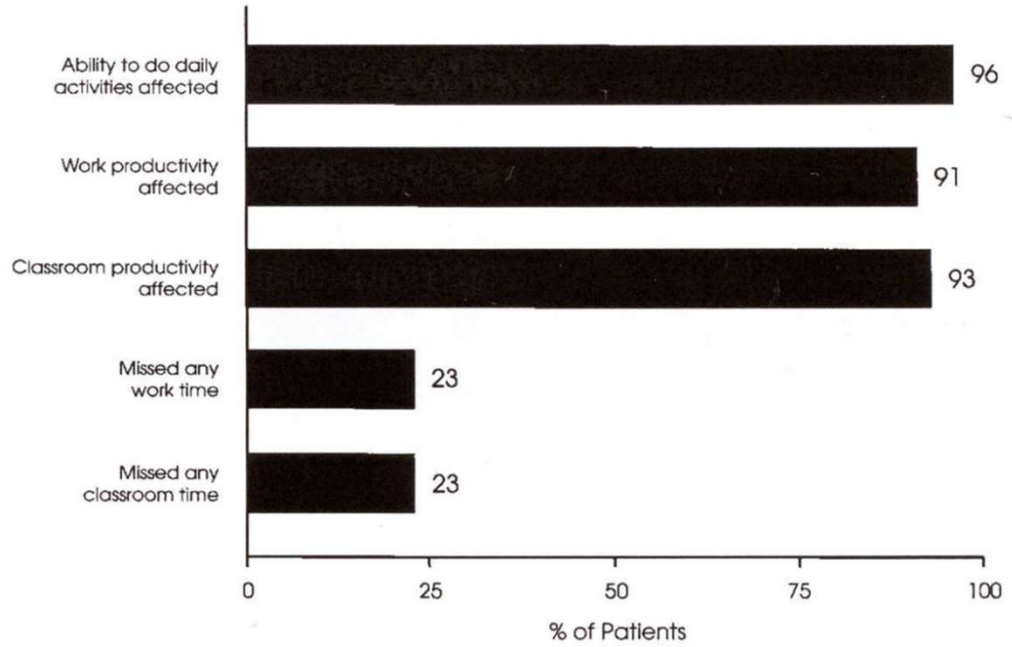


Fig. 3. Percent of patients who report impairment due to allergies as measured by the Work Productivity and Activity Impairment (WPAI) questionnaire. *Percent of patients reporting any work or classroom time missed, or any impairment in daily activities at work, or in the classroom, secondary to allergies (WPAI-AS).

Thompson AK, et al, *Annals of Allergy, Asthma & Immunology*, 2000;85:338-334

Allergic Conjunctivitis

- Symptoms
  - Associated with rhinitis
  - Bilateral
  - Itchy, watery eyes
  - NO photophobia

- Treatment
  - Sunglasses
  - Cold compresses
  - Lubricants
  - Topical/oral antihistamines
  - Topical mast cell stabilizer
  - 7-15 day trial
- Seek medical help
  - Pain +/- photophobia
  - Copious, thick mucus production
  - Blurring or loss of vision
  - Red eyes for contact lens wearers
  - Recent eye surgery
  - Unilateral

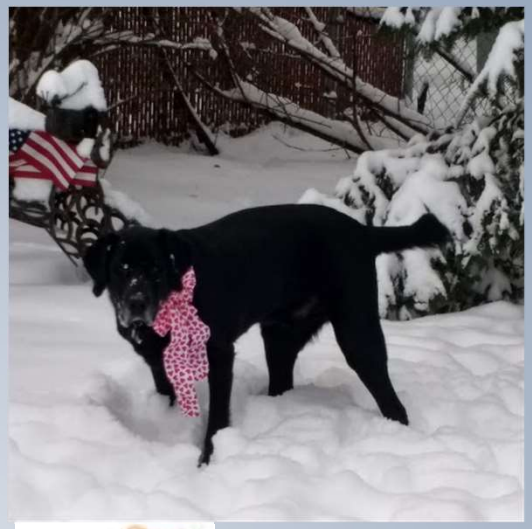
Medications

- Topical Antihistamines
  - Emedastine
  - Epinastine*
  - Azelastine*
  - Ketotifin*
  - Olopatadine
  - Cetirizine
  - Alcaftadine
  - Bepotastine*
- Topical Corticosteroids
  - Loteprednol
  - Fluormetholone
- Mast cell stabilizers
  - Cromolyn
  - Nedocromil
  - Lodoxamide
- Decongestants
  - Naphazoline
    - Short acting
    - Rebound redness

*antihistaminic and mast cell stabilizing activity

Environmental Exposures

- Aeroallergens
- Ambient air pollution
- Climate



House Dust Mites

- Cover mattress, box spring, pillows
- Wash linens, blankets every week (1-2 weeks) in hot* water
- Remove carpets, especially on concrete slabs (curtains, upholstered furniture, stuffed animals)
- HEPA filter room cleaner on polished floor*
- Decrease relative humidity 35-50%
- Ventilate
- Vacuum 2x/week*
- Interventions should be multicomponent

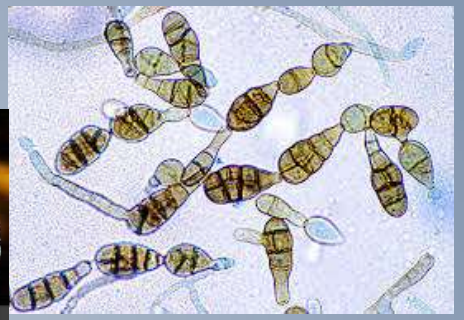
Furry Pets

- Allergenic protein found in saliva, skin, hair follicles
  - Easily airborne, cling to clothing
- Remove pet from home
- Wash regularly
- HEPA filter AND regular vacuuming
- Remove carpets, upholstered furniture
- Rodents
  - Protein in urine, dander, fur
  - Increase asthma morbidity/rhinitis
  - IPM (Integrated Pest Management)

Cockroach

- Allergen found in saliva, fecal debris, other secretions
- Increased asthma health care utilization
- Gel bait insecticides
  - ⃠ insecticide sprays
- Meticulous cleaning
  - Remove trash
  - Seal food
  - Remove water sources
- IPM
  - Suppression of population
  - Removal of allergen

Molds



- Indoor/Outdoor
  - Excessive moisture
    - Water leaks
    - Reduce humidity
    - Ventilate
  - Central heating/air conditioning - HEPA
  - 5% bleach solution
  - Professional mold removal – single component (cleaning sanitizing, removal)

- Pollen
  - Keep windows and doors closed – use AC
  - Eliminate outdoor activities when counts are high
  - Shower, wash hair, change clothing before going to bed
  - Do not hang clothes on clothesline

IPM – Integrated Pest Management

- Fix all gaps and holes
- Remove all food sources/disposal
- Remove easy access to water
- Remove clutter
- Thorough cleaning after pest removal
- Barriers
  - Cost
  - Home ownership
  - Behavioral practices
  - Preferences

Irritants

- Irritants
  - Non-IgE mediated
  - Dose dependent
  - Dose threshold effect
  - Examples
    - Tobacco smoke, ozone, exhaust/diesel fumes, sulfur dioxide, perfumes, VOC's, . . .

Interventions

- Multifaceted – optimize
  - IPM
  - HEPA – vacuum and air filters
  - Allergen impermeable covers (mattress, pillows)
  - Food storage
- Specific to allergen sensitivities
- Use along with
  - Optimal health care access
  - Optimal access to medications
  - Appropriate management – allergies and asthma

Allergen Mitigation

- Only for patients with allergic sensitization to specific indoor allergens or allergen-induced symptoms
- Allergen mitigation should be multi-modal
- Integrated pest management and/or mold remediation may be used alone or as part of a multi-modal approach

J Allergy Clin Immunol 2020:146;1217-70

Efficacy of Environmental Control Measures

Environmental Control	Reduces Allergen Levels	Reduces Symptoms
Pet removal	X	X
Washing pets 2x/week	X	
Acaricides	X	X
Impermeable covers	X	
Air filtration	X	
Combined measures	X	X

Seidman MD, et al. Otolaryngology-Head and Neck Surgery 2015, 152(1S)

Mitigation Interventions

TABLE IIIA. Examples of allergen mitigation interventions and their targeted allergens

Intervention assessed in studies in the SR	Allergen			
	Animal dander	Dust mites	Cockroaches	Mold
Acaricide		++		
Air filtration systems and air purifiers	++	+	+	++
Carpet removal	++	++		+
Cleaning products (eg, bleach)				++
HEPA vacuum cleaners	++	+	+	++
Impermeable pillow and mattress covers		++		
Integrated pest management	+*		++	
Mold mitigation				++
Pet removal	++			

SR, Systematic review.
++Primary target allergen(s) for the intervention.
+Secondary target allergen(s) for the intervention.
*Dander from rodents.

J Allergy Clin Immunol 2020;146:1217-70

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