# Therapy in Allergic Rhinitis and the Pharmacist's Role

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## Objectives – Pharmacists

1. Describe the basic pathophysiology of allergic rhinitis.
2. Identify signs and symptoms of allergic rhinitis.
3. Distinguish the appropriateness of self-treatment versus physician referral.
4. List and recommend non-pharmacologic treatment options for allergic rhinitis.
5. Differentiate between and evaluate common pharmacologic treatment options used in allergic rhinitis.
6. Apply treatment recommendations to formulate a treatment plan when presented a clinical scenario.

## Objectives – Pharmacy Technicians

1. List and identify common symptoms of allergic rhinitis
2. Evaluate the appropriateness of self-treatment versus physician referral.
3. Recall and understand the role of non-pharmacologic treatment in allergic rhinitis.
4. Compare and contrast pharmacologic agents used for allergic rhinitis.

## What is Rhinitis?

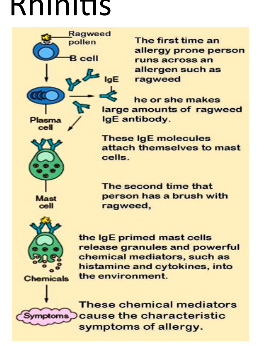
- According to AAAAI and ACAAI:
  - Characterized by 1 or more of the following:
    - Nasal congestion
    - Rhinorrhea (anterior and posterior)
    - Sneezing
    - Itching

## The Many Types of Rhinitis

- **Allergic rhinitis**
  - Seasonal
  - Perennial
  - Episodic
- **Conditions that mimic rhinitis**
  - Nasal polyps
  - Anatomic abnormalities
  - Cerebral spinal fluid rhinorrhea
  - Ciliary dysfunction
- **Non-Allergic rhinitis**
  - Vasomotor rhinitis
  - Rhinitis from foods and alcohol
  - Infectious rhinitis
  - Non-allergic rhinitis with eosinophilia syndrome (NARES)
  - Occupational rhinitis
  - Hormonal rhinitis
  - Drug-induced rhinitis
  - Atrophic rhinitis
- **Mixed rhinitis** (allergic & nonallergic rhinitis)

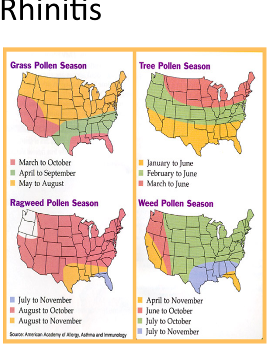
## Allergic Rhinitis

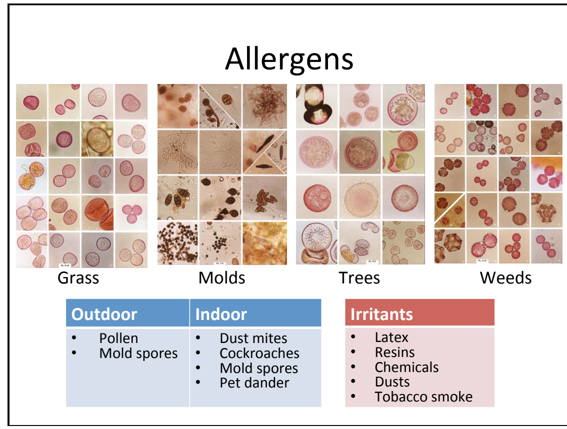
- **IgE**-mediated
  - Mast cells
  - Granulocytes
  - Histamine
  - Kinins
  - Prostaglandins
  - Leukotrienes



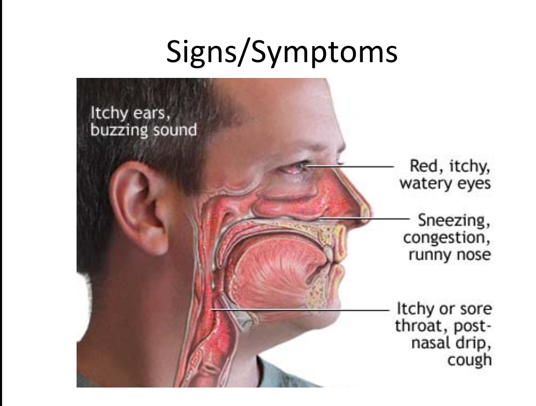

http://www.health-choices-for-life.com/allergic_reaction.html

- Seasonal
  - Seasonal aeroallergens
  - Dependent on geography and climate
- Perennial
  - Environmental aeroallergens
  - Areas where pollen is prevalent perennially
- Episodic
  - Sporadic exposures to inhalant aeroallergens

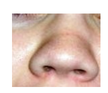


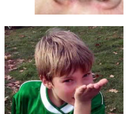

## Signs/Symptoms




## Signs/Symptoms

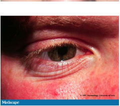


- “Allergic salute”
  - Upward stroking of nose with palm
- “Allergic crease”
  - Creases on nose secondary to the “allergic salute”



- "Dennie's lines”
  - wrinkles beneath lower eyelids)
- “Allergic shiner”
  - Suborbital edema secondary to venous congestion

- “Allergic gape”
  - Open-mouth breathing secondary to nasal obstruction
- Engorged nasal mucosa
  - Nonexudative cobblestone appearance of posterior oropharynx



- Nasal voice

## Case

It is August, and AB is a 65 year old female presenting to your pharmacy for a recommendation for self-treatment of sore joints, a runny nose, nasal congestion, and uncontrollable sneezing. She is breathing mostly through her mouth.

She notices her symptoms worsen when she goes outside, but don’t keep her up at night.

Current medications:

- Simvastatin 20mg HS
- Lisinopril 10mg daily
- ASA 81mg once daily
- MVI once daily

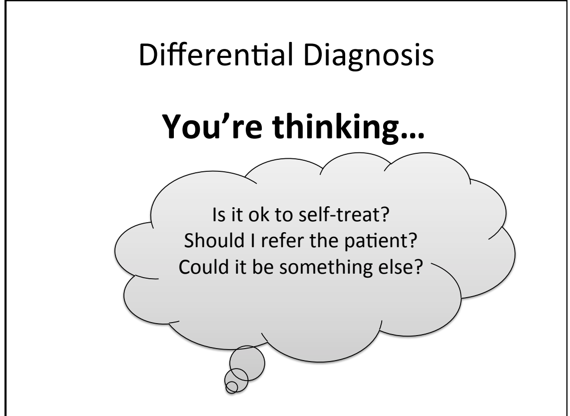
## Case

What symptoms of rhinitis does AB exhibit?

1. Rhinorrhea
2. Sneezing
3. Cough
4. Difficulty breathing properly
5. Itchy eyes

## Differential Diagnosis

**You're thinking…**




## Case

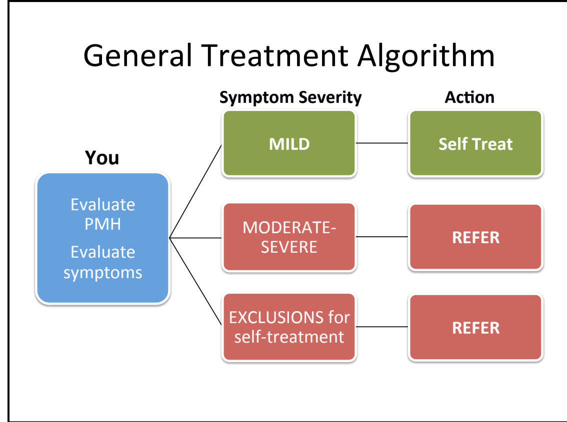
What complications and/or other disease processes should we include in our differential diagnosis?

1. Cold / Respiratory infection
2. Asthma exacerbation
3. COPD exacerbation
4. All of the above

## Differential Diagnosis

- Detailed description of symptoms
- Medication use (previous and current)
- History
  - Respiratory illnesses which may complicate treatment of allergic rhinitis
    - Asthma, cold, infection, non-allergic rhinitis?
  - Had an attack or recurrent attacks of wheezing?
  - Troublesome cough, especially at night?
  - Cough or wheeze after exercise?
  - Chest tightness?

## General Treatment Algorithm




## Self Treat or Refer?

- **MILD** → can **SELF-TREAT**
  - Symptoms **not troublesome**
    - No sleep disturbance
    - No impairment of daily activities/leisure/sport
    - No impairment of school/work
- **MODERATE-SEVERE** → **REFER**
  - **Interference** w/ quality of life (QOL)
    - No improvement / worsening symptoms
    - Signs/symptoms of infection (sinus, respiratory)
- **Exclusions** → **REFER**
  - Elderly
  - Pregnancy

Bernstein et al. ARIA Classification: Allergic Rhinitis and It's Impact on Asthma. Ann Allergy 2008;100:S1-148.

## Self Treat or Refer?

- Allergist/Immunologist Referral
  - Inadequately controlled Sx
  - Reduced QOL and/or ability to function
  - Drug-related adverse reactions
  - Desire to identify allergens sensitized
  - To receive advice on environmental control
  - Comorbid conditions
  - Consideration of immunotherapy

Wallace et al. J Allergy Clin Immunol 2008;122:S1-84.

## Case

You ask AB more about her PMH.

- She smoked cigarettes for 4-5 years while in her 20s, but quit then.
- Her symptoms start "like clockwork" in August. She has never used any allergy medicines.

She prefers something low-cost since she does not have any prescription insurance.

## Case

Based on AB's complaints, what would be a reasonable first approach to treatment?

1. Recommend self-treatment
2. Recommend referral to her primary care provider

## Therapy

Treatment
(Self-treatment or Referral)

Non-pharmacologic

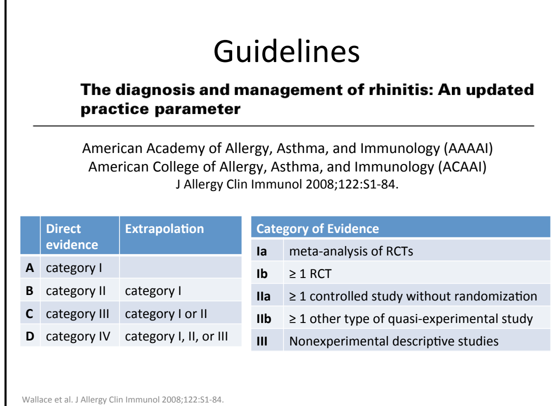
Pharmacologic

## Case

Based on what you know about AB so far, what type of treatment do you think would be reasonable as a first recommendation/attempt?

1. Non-pharmacologic
2. Pharmacologic
3. Non-pharmacologic + Pharmacologic

## Guidelines



**The diagnosis and management of rhinitis: An updated practice parameter**

American Academy of Allergy, Asthma, and Immunology (AAAAI)
American College of Allergy, Asthma, and Immunology (ACAAI)
J Allergy Clin Immunol 2008;122:S1-84.

| | Direct evidence | Extrapolation |
|---|---|---|
| A | category I | |
| B | category II | category I |
| C | category III | category I or II |
| D | category IV | category I, II, or III |

| Category of Evidence | |
|---|---|
| Ia | meta-analysis of RCTs |
| Ib | ≥ 1 RCT |
| IIa | ≥ 1 controlled study without randomization |
| IIb | ≥ 1 other type of quasi-experimental study |
| III | Nonexperimental descriptive studies |

Wallace et al. J Allergy Clin Immunol 2008;122:S1-84.

## Non-Pharmacologic Treatment

- ↓ **sensitization / IgE production**
- Usually **first step**
- Strategies **allergen-specific**

- Guideline Recommendations (B, D)
  - **Environmental Controls**
    - Avoidance
    - Limiting Exposure
  - **Nasal saline irrigation (NSI)**

Wallace et al. J Allergy Clin Immunol 2008;122:S1-84.

# Environmental Controls

Today's Local & National Allergy Forecast

Click on your state to see the 4 Day Allergy Forecast in your area.

- Reducing pollen exposure (B)
  - Avoid/limiting activities increasing exposure
  - Avoid outdoor activities on days with high allergen counts
    - **Air Quality Index (AQI)**: LOWER number better
    - **Local daily allergy forecast** → www.pollen.com
- Reducing animal exposure (cats > dogs)
  - Avoidance most effective (D)
  - ~20 weeks until allergen levels at "animal-free" levels
  - Washing animal 1-2x/week

Wood et al. J Allergy Clin Immunol 1989;83:730-4.
De Blay et al. Am Rev Respir Dis 1991;143: 1334-9.
Moira et al. Ann Allergy Asthma Immunol 2002;88:52-8.

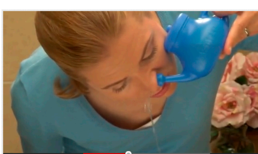
# Environmental Controls

- Reduce dust mite exposure
  - Mattress/pillow covers; Synthetic pillows
  - Remove dust-collecting furniture/materials
    - Bulky, upholstered furniture, drapery, books, stuffed toys, carpet
    - Replace w/ vinyl, leather, wooden furniture
  - Wash sheets, mattress pads, bedspreads, stuffed toys **every 7 DAYS** in **HOT** water (130 °F)
  - Humidity <50%
  - Air conditioner/heater <70 °F
  - Acaracides
  - Filtration systems, HEPA filters, air purifiers (???)
- Reduce fungal/mold exposure
  - Eliminate moisture source
  - Wash non-porous surfaces with dilute beach solutions (D)

Wallace et al. J Allergy Clin Immunol 2008;122:S1-84.

# Nasal Saline Irrigation (NSI)

- **Beneficial** for treating chronic Sx as a **sole** modality or **adjunctive** treatment (A)
- ↓ nasal mucosal irritation, dryness, clearance
- No evidence for superior delivery device, volume, solution concentration
  - Neti pot
  - Sinus **flush** (NOT spray)
  - Homemade vs manufacturer **saline** solution
- At least **BID**
- No major side effects
- Avoid irrigating…
  - After intranasal medications
  - Before bedtime



Wallace et al. J Allergy Clin Immunol 2008;122:S1-84.

# Nasal Saline Irrigation

Process

1. Fill irrigation tool with saline solution
2. Lean over sink, bathtub (can also be done in the shower
3. Position head
   - Med syringe/bottle → Chin to chest
   - Neti pot → Tilt head laterally
4. Place tool in nostril and administer full amount
5. Once dripping stops, gently blow nose
   - Dripping may continue for up to 10 minutes
   - Avoid pinching nose

Online media

- Demo video: www.neilmed.com/usa/nmvideos.php
- NSI solution recipe: www.aaaai.org/conditions-and-treatments/treatments/saline-sinus-rinse-recipe.aspx

# Case

What of the following non-pharmacologic therapy(ies) would you consider recommending to AB?

1. Regular use of NSI
2. As needed use of NSI
3. Limiting outdoor activities during her season. It's cold!
4. Checking the daily pollen forecast
5. Pillow/mattress covers
6. Turn up the heater! It's cold!

# Pharmacologic Treatment

- Antihistamines (oral, intranasal)
- Corticosteroids (systemic, intranasal)
- Anticholinergics (intranasal)

- Decongestants (oral, topical)
- Anti-leukotriene agents
- Cromolyn sodium
- Omalizumab
- Immunotherapy

## Oral Antihistamines

- Guideline Recommendations (B)
  - **2nd-generation preferred** due to poor adverse effect profile of 1st-generation antihistamines
- Symptoms targeted:
  - **Itchiness**
  - **Nasal congestion** when combined w/ oral decongestant
- Evidence
  - Superiority of 1st- vs 2nd generation not well studied
  - Limited data elsewhere: Less effective than intranasal corticosteroids, but similar effectiveness in treating ocular symptoms

Wallace et al. J Allergy Clin Immunol 2008;122:S1-84.

## Oral Antihistamines

| | SEDATING | POTENTIAL for Sedation | NO sedation |
|---|---|---|---|
| 1st Gen OTC | Brompheniramine (Dimetapp®)<br>Chlorpheniramine<br>Diphenhydramine (Benadryl®)<br>Doxylamine (in Nyquil®) | -------- | -------- |
| 1st Gen Rx | Hydroxyzine<br>Promethazine | -------- | -------- |
| 2nd Gen OTC | -------- | Cetirizine | Loratadine<br>Fexofenadine |
| 2nd Gen Rx | -------- | Levocetirizine (Xyzal®) | Desloratadine (Clarinex®) |

## Oral Antihistamines – 1st generation

- **SEDATING**
  - Lipophilicity → crosses **blood-brain barrier**
    - Activates serotonin (5-HT) and alpha-adrenergic receptors
    - Cholinergic receptor blockade
  - Individual variation

| CNS | Anticholinergic |
|---|---|
| • Drowsiness/sedation<br>• Appetite stimulation<br>• Impaired activity<br>• Anxiety | • Dry eyes, mucous membranes<br>• Urinary retention/hesitancy<br>• Constipation<br>• Blurred vision<br>• Tachycardia |

- Potentially harmful in select populations
  - i.e. elderly, comorbid conditions
  - Performance impairment

## Oral Antihistamines – 2nd generation

- **"Non-sedating"** → improved adverse effect profile
  - Peripherally selective
  - Highly protein-bound/lipo**phobic** → does NOT easily cross blood brain barrier
- **No** single agent superior to other same-class agents (C)

## Intranasal Corticosteroids

- Guideline Recommendations (A)
  - **Most effective** class
- Symptoms targeted:
  - Nasal congestion
  - Similar efficacy as PO antihistamines for ocular symptoms
- Evidence
  - More effective vs. antihistamine + montelukast (A)
  - Growth suppression in children not demonstrated to be significant

Wallace et al. J Allergy Clin Immunol 2008;122:S1-84.

## Intranasal Corticosteroids

| (All Rx) | Starting Dose | Age Limit | Preservative Contents |
|---|---|---|---|
| **Beclamethasone** (Beconase AQ) | **BID** | 6 | Alcohol, BKC |
| **Budesonide** (Rhinocort AQ) | Daily | 6 | **None** |
| **Ciclosonide** (Omnaris) | Daily | **12** | **None** |
| **Flunisolide** (Nasarel) | **BID** | 6 | BKC, Propylene glycol |
| ***Fluticasone proprionate** (Flonase) | Daily | 4 | Alcohol, BKC |
| **Fluticasone furoate** (Veramyst) | Daily | 2 | BKC |
| **Mometasone** (Nasonex) | Daily | 2 | BKC |
| ***Triamcinolone** (Nasocort AQ) | Daily | 6 | BKC |

- **No** significant **clinical** superiority **between products**. (C)
- **Cost** → biggest factor in selection (few generics*)
- Preservatives, scents

Wallace et al. J Allergy Clin Immunol 2008;122:S1-84.
Nielsen et al. Am J Respir Med 2003;2:55-65.

## Intranasal Steroids

- **How do you counsel your patients to administer?**

- Not generally associated w/ clinically significant systemic adverse effects (A)
  - Nasal irritation, bleeding minimal
  - Nasal septal perforation rarely reported

## Intranasal Steroids

- **Education** key!
  - Tilt head forward and avoid administering towards septum
    - **RIGHT** hand – **LEFT** nostril
    - **LEFT** hand – **RIGHT** nostril
  - Effective when used on **scheduled** or **as-needed** (**B**)
    - **2-4 weeks** before full effect
    - **As-needed** use **may not** be as effective. (**D** )
- Not generally associated w/ clinically significant systemic adverse effects (A)
  - Nasal irritation, bleeding minimal
  - Nasal septal perforation rarely reported

## Systemic Steroids

- Guideline Recommendations & Evidence (D)
  - Oral route
    - **Short course** (5-7 days) may be appropriate for **very severe** or **intractable nasal** symptoms
  - Parenteral route
    - Single administration **discouraged**
    - Recurrent administration **contraindicated**
    - Greater potential for **long-term side effects** reported in case studies
      - Cushing's syndrome, **atrophy**, visual loss

Wallace et al. J Allergy Clin Immunol 2008;122:S1-84.

## Intranasal Antihistamines

- Guideline recommendations (A)
  - A **first-line** treatment
- Symptoms targeted
  - Nasal **congestion** (A)
- Evidence (A)
  - **Equal** or **superior** to **2nd-generation antihistamines**
  - Less effective than intranasal corticosteroids, but combined use may provide added benefit
  - Associated w/**sedation**
  - Can theoretically inhibit skin test reactions

Wallace et al. J Allergy Clin Immunol 2008;122:S1-84.

## Intranasal Antihistamines

Azelastine (Astelin®, Astepro®)
Olopatadine (Patanase®)

- Rx only
- Rapid onset; systemically absorbed
- Tolerability
  - Astelin®
    - High incidence of bitter taste
    - Now generic
  - Astepro® → new formulation
    - Similar efficacy as Astelin®
    - Significantly less bitter taste than Astelin®

Astepro prescribing information. Meda Pharmaceuticals. Nov 2010.

## Case

Which of the following medications would probably NOT be a good 1st-line pharmacologic treatment option for AB?

1. Cetirizine
2. Diphenhydramine
3. Fluticasone proprionate
4. Azelastine

## Montelukast (Singulair®)

Leukotriene receptor antagonist (LTRA)

- Symptoms Targeted
  - Mucosal inflammation
- ~40% with allergic rhinitis have coexisting asthma
  - Common pathophysiologic mechanisms and epidemiology
- Approved in patients 6 months and up
  - Rx only
  - Only LTRA approved for rhinitis treatment
  - Chewable and non-chewable formulations
- Evidence (A)
  - No significant difference in efficacy vs antihistamines
  - Potential additive efficacy when combined w/**antihistamines**, but less effective than intranasal corticosteroids

Vignola et al. Allergy 1998;53:833-9.

## Intranasal Anticholinergics

Ipratropium bromide (Atrovent) (Rx)

- Approved for treating **rhinorrhea** in patients >5 years of age
- Evidence (A)
  - Mainly reduces **rhinorrhea**
  - Concomitant use w/ intranasal corticosteroid more effective than monotherapy
  - Minimal adverse effects
    - Nasal membrane dryness
    - Epistaxis

## Decongestants

- Guideline Recommendations (C)
  - Use **CAUTIOUSLY!**
- Symptoms Targeted
  - Nasal **congestion**
- Evidence
  - Oral (A)
    - **Insomnia, irritability, palpitations**
  - Topical (C)
    - Xylametazoline superior to intranasal corticosteroids at 28 days
    - **Short-term/intermittent** use not well studied
    - **Not for regular daily use** due to risk for **rhinitis medicamentosa**
  - May assist w/ delivery of other intranasal agents if significant nasal mucosal edema present

Wallace et al. J Allergy Clin Immunol 2008;122:S1-84.
Barnes et al. Rhinology 2005;43:291-5.

## Decongestants

- Oral (pseudoephedrine, phenylephrine)
  - Adverse effects: **Insomnia, irritability, palpitations**
- Topical (oxymetazoline (Afrin®), xylometazoline, naphazoline)
  - **3-5 days MAX**
  - **Rhinitis medicamentosa** (rebound congestion)
    - As early as 3-4 day onset
    - Initial α receptor effect → vasoCONSTRICTION
    - Latent β receptor effect → vasoDILATION
- Be Cautious/Avoid in:
  - **Older** adults
  - **Young** children
  - **Pregnant** women (oral) in first trimester (D)
  - Hx of cardiac arrhythmia, angina pectoris, cerebrovascular disease, hypertension, bladder neck obstruction, glaucoma, hyperthyroidism.

Morris et al. Am J Rhinol 1997;11:109-15.

## Case

AB is exhibiting nasal congestion symptoms. Would you consider recommending decongestants *as-needed* for AB?

1. No, she should use it on a long-term scheduled basis during her season
2. No, she should avoid decongestants
3. Yes

## Cromolyn sodium (NasalCrom®)

- Guideline recommendations (A)
  - Effective in prevention and treatment
- Symptoms Targeted
  - **Helps prevent allergic event** vs symptom reduction
- Evidence (A)
  - Minimal side effects
  - Less effective than corticosteroids
  - Very limited data comparing with other classes

Wallace et al. J Allergy Clin Immunol 2008;122:S1-84.

# Cromolyn sodium (NasalCrom®)

- Anti-inflammatory
  - Mast cell stabilizer → prevents mediator release
- **High** dose frequency
  - **3-6** times daily
- Use **regularly**
  - Start at least **1 week before** symptoms typically appear or **ASAP** before known allergen exposure
  - Onset 4-7 days
  - Peak benefit in 2-4 weeks of *continued* use
- Category **B**: favorable role in pregnancy

# Case

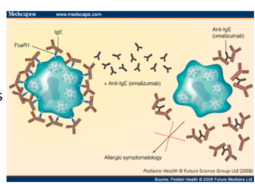
Which of the following "2nd-line" therapies would be reasonable for AB to try if she is inadequately controlled with "1st-line" therapies?

1. Montelukast
2. Ipratropium
3. Cromolyn sodium
4. Decongestants

# Omalizumab (Xolair®)

Humanized monoclonal anti-IgE antibody → ↓ circulating IgE

- Evidence
  - **Efficacy** in ↓ bronchial response to inhaled aeroallergen challenges
  - No evidence demonstrating superiority to other classes
- FDA approved for **allergic asthma**
- Administered under **medical supervision**
  - **Subcutaneous** injection q2-4 weeks
  - **Hypersensitivity** reactions
  - Epi-Pen required
- Expensive




Wallace et al. J Allergy Clin Immunol 2008;122:S1-84.

# Immunotherapy

- Guideline Recommendations (A)
  - **Consider** if evidence for **specific IgE antibodies**
  - Use **depends on degree of symptom control** w/ avoidance + medication use + patient-specific considerations (ex: comorbid conditions)
- Evidence
  - **Effective** for treatment (A)
    - Improved symptom score
    - Improved QOL measures
    - Improvement in provoked challenges
  - May **modify disease course** (B)
    - **Prevent** development of **new** allergen sensitizations
    - **Reduce risk** of **future asthma** development
    - Potentially **long duration** of action → years – lifelong

Wallace et al. J Allergy Clin Immunol 2008;122:S1-84.

# Complementary/Alternative Medicine

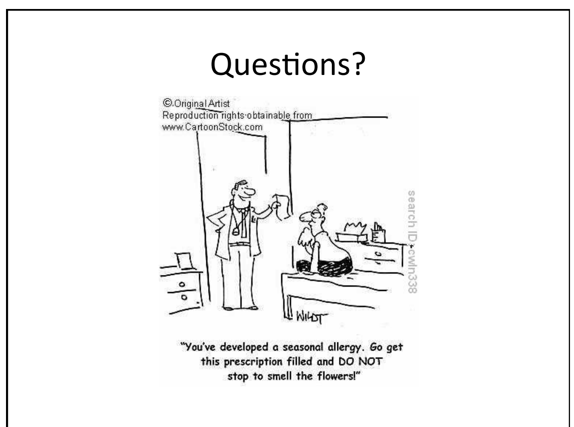
- **Not addressed by guidelines**
- **Poor** evidence → **AVOID!!**
  - Several meta-analyses **failed** to show statistically significant benefit
- Common agents
  - Ephedra (ma huang): Banned by FDA
  - Feverfew: Anti-inflammatory properties not proven; possible mouth ulceration, GI upset
  - Butterbur
  - Grapeseed
  - *P. hybridus*
  - Physical techniques: chiropractic, acupuncture, yoga, osteopathy, spinal manipulation
  - Phytotherapy: aromatherapy
  - Behavioral therapy: biofeedback
  - Bioresonance, chromotherapy, Hopi candles

Passalacqua et al. J Allergy Clin Immunol 2006;117:1054-62
Man L. Curr Opin Otolaryngol Head Neck Surg 2009;17:226–231
Resnick et al. Curr Allerg Asthma Rep 2008;8:118–125

# The Pharmacist's Role

- **Product selection**
  - No proven superiority within classes
  - Evidence showing efficacy between classes
  - Pharmacist knowledge of what agents will target specific symptoms and product cost
- **Patient education**
  - **Key** in promoting adherence and optimizing treatment outcomes (D)
  - Initial relief within 3-4 days, complete relief up to 2-4 weeks
  - Correct use and administration of medication
- **Patient Assessment**
  - Change dose?
  - Modify regimen?
  - Symptom changes requiring need for referral?

# Questions?

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