Allergic Rhinitis

Allergic Rhinitis Guideline Team

Richard Orlandi, MD
Otolaryngology

James Baker, MD
Allergy

Margie Andreae, MD
Pediatrics

Daniel Dubay, MD
General Internal Medicine

Steve Erickson, PharmD
Pharmacy

Consultant:
Jeffrey Terrell, MD
Otolaryngology

Developed
July, 2002

UMHS Guidelines Oversight Team
Connie Standiford, MD
Lee Green, MD, MPH
Van Harrison, PhD

Literature search service
Taubman Medical Library

For more information call
GUIDES: 936-9771

UMHS Preferred Drugs version

Patient population: Adults and pediatrics

Objectives: The purpose of this guideline is to assist in the diagnosis and cost-effective treatment of allergic rhinitis.

Key Points:

Diagnosis. Allergic rhinitis is an antigen-mediated inflammation of the nasal mucosa that may extend into the paranasal sinuses. Diagnosis us usually made by history and examination ("itchy, running, sneezy, stuffy"). A symptom diary and a trial of medication may be helpful to confirm a diagnosis. Allergy testing is rarely helpful in diagnosis. Allergy testing is not commonly needed to make the diagnosis, but may be helpful for patients with multiple potential allergen sensitivities

Therapy. The goal of therapy is to relieve symptoms.

1. **Avoidance of allergens is the first step in this process. (see text for details). If avoidance fails:**
2. Over-the-counter (OTC) antihistamines and decongestants should be tried initially, as they provide relief in most cases. If symptoms persist, consider the following options:
3. Prescribed medications:
   - Nasal corticosteroids are considered the most potent medications available for treating allergic rhinitis *[A*]*. They control itching, sneezing, rhinorrhea, and stuffiness in most patients, but do not alleviate ocular symptoms. They have a relatively good safety profile, but long-term perennial use, as well as prolonged use in children, may be problematic. **UMHS preferred medications in this class are Flonase, Nasacort AQ, and Nasonex AQ.**
   - Oral antihistamines prevent and relieve itching, sneezing, and rhinorrhea, but tend to be less effective for nasal congestion *[A*]*. If an initial trial with a first-generation (OTC) antihistamine is unsuccessful or poorly tolerated, a second-generation antihistamine may be substituted. **UMHS preferred prescription antihistamines include Allegra and Zyrtec**. Second generation antihistamines are less sedating, but are expensive.
   - Intranasal antihistamines, while effective in treating the nasal symptoms associated with seasonal and perennial rhinitis and nonallergic vasomotor rhinitis, offer no therapeutic benefit over conventional treatment *[A*]*.
   - Oral decongestants decrease swelling of the nasal mucosa which, in turn, alleviates nasal congestion *[A*]*. They are contraindicated with monoamine oxidase inhibitors (MAOIs) and in uncontrolled hypertension and severe coronary artery disease. Geriatric patients may be more sensitive to the effects of decongestants.
   - Nasal cromolyn is less effective than nasal corticosteroids *[A*]*. Cromolyn is a good alternative for patients who are not candidates for corticosteroids. It is most effective when used regularly prior to the onset of allergic symptoms.

Referral. Appropriate criteria for referral to a colleague who specializes in the diagnosis and treatment of allergies may include *[D*]*:

- consideration of allergy skin/RAST testing for better allergen identification for avoidance and/or immunotherapy, because of:
  - failure of medical therapy
  - perennial allergic rhinitis that is moderate to severe
- associated conditions such as chronic or recurrent acute rhinosinusitis.
- any severe allergic reactions causing patient or parental anxiety.

Controversial Issues

Medication vs. immunotherapy**.** A formal risk/cost-benefit analysis of medication therapy versus immunotherapy (allergy shots) has not been performed; however, patients with moderate to severe symptoms that continue year round (i.e., perennial allergic rhinitis) may benefit most from immunotherapy *[D*]*.

* Levels of evidence reflect the best available literature in support of an intervention or test**:**
A=randomized controlled trials; B=controlled trials, no randomization; C=observational trials; D=opinion of expert panel.

Figure 1. Treatment of Allergic Rhinitis

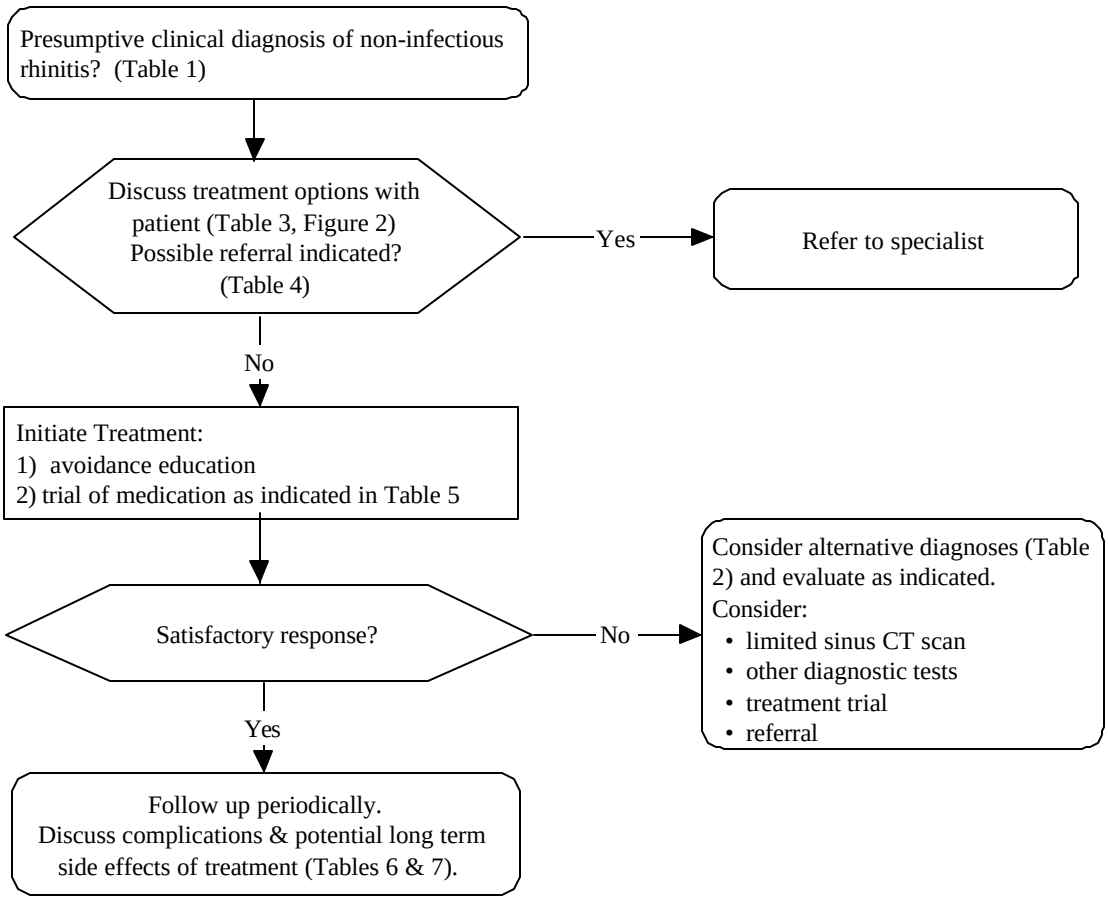

Table 1. Symptoms and Signs Suggestive of Allergic Rhinitis

Chronic or recurrent: sneezing, nasal congestion, pale or blue nasal mucosa, clear nasal discharge, morning cough, red watery eyes, ocular discharge/pruritus or pressure/pain in nose, palate, eyes, ears, or sinus pressure.
Family or personal history of: food allergy, atopic dermatitis, asthma, onset of symptoms with recurrent exposure
Patterns: Relief of symptoms (acute or chronic) with therapies, seasonality
Other: conjunctival infection or pharynx cobblestoning, allergic shiners, nasal salute (crease)

NOTE: chronic perennial allergies present with congestion and thick mucus more often than with itching or sneezing symptoms

Table 2. Alternative Diagnoses with Typical Characteristics

Alternative Diagnosis	Typical Characteristics
Acute rhinosinusitis	Facial pressure or pain, purulent nasal discharge; maxillary toothache; failure to respond to decongestants; fever or cough may be present; may follow an allergy flare-up or a viral URI
Chronic rhinosinusitis	Facial pressure or pain, purulent discharge; fever often absent; may be present in addition to allergic rhinitis; symptoms may wax and wane over time; chronic hyposmia.
Viral URI	Self-limited course with symptoms (clear rhinorrhea, cough, ache) usually resolving within 3-7 days
Septal deviation	Nasal obstruction is often constant and unilateral; deflection can often be seen on examination
Rhinitis medicamentosa	Also called "rebound rhinitis;" caused by overuse of topical decongestants; diagnosis is easily made by history; may mask another underlying condition such as septal deviation or allergic rhinitis.
Vasomotor rhinitis	Clear rhinorrhea, nasal obstruction, often depends on position (*e.g.*, supine), may be episodic. Pregnancy may exacerbate symptoms
Atrophic rhinitis	Also call "ozena;" caused by over-resection of turbinate tissue or poor mucus production, resulting in nasal dryness and crusting; foul odor may be present; rarely secondary to klebsiella ozaenae infection
Gastroesophageal reflux	Under-recognized cause of post-nasal drip, cough, and globus sensation; hoarseness or frequent throat clearing may also be present

Table 3. Advantages & Disadvantages of Treatment Options

Treatment Options	Advantages	Disadvantages
Environmental Control / Avoidance of Allergens	• Beneficial with minimal cost	• Difficult to assess with certainty whether exposure has been controlled • Effectiveness of chemical barriers requires repeated application
Medications (See also: Tables 5 & 6)	• Patient preference • Rapid onset • May control non-allergic rhinitis symptoms • Many choices (See Tables 5&6)	• Cost of medication • Individual medication side effects (e.g., sedation, nasal septal perforation with nasal steroids [rare]) • Potential unknown long term side effects
Allergy Testing (RAST or Skin testing)	• Beneficial in defining allergens in complex patients or to institute immunotherapy • May help direct avoidance therapy	• Anaphylaxis (rare with skin testing)
Immunotherapy	• Medication requirements usually reduced • Benefits may persist after therapy has stopped • May be less costly in long term	• Effectiveness of treatment is uncertain Frequent visits for years: - Year 1: Initial visit (exam & testing) + 26 weekly shot visits + 13 bi-weekly shot visits - Year 2: 26 bi-weekly shot visits - Years 3-5: 18 shot visits (21-day interval) • Potential unknown long term side effects • Anaphylaxis (rare)

Table 4. Possible Indications for Referral to Specialist

• Identify specific allergens in patients with unclear/multiple environmental allergies (RAST or skin testing)	• Moderate to severe symptoms of perennial rhinitis or presence of nasal polyps
• Intolerance to, or failure of medical treatment (See Table 7)	
• Associated comorbidities such as chronic or recurrent bacterial rhinosinusitis, or recurrent otitis media	• Any severe allergic reaction which causes patient or parental anxiety
• Need for improved allergen avoidance education	• Immunotherapy is a consideration (See also: Table 6)

Table 5. Pharmacologic Therapy for Allergic Rhinitis (UMHS Preferred Agents in Bold)

Generic Name	Brand Name	Usual Adult Dose	30 Day AWP Cost*	Usual Pediatric Dose	30 Day AWP Cost*
Oral Antihistamines – 1st Generation					
Chlorpheniramine	**Chlor-Trimeton**	4 – 12 mg hs or 2 - 12 mg BID	$1 g	≥ 12 yrs: 4 - 12 mg hs or 2 - 12 mg BID 6 to 11 yrs: 2 - 8 mg q d - BID, 12 mg/d max 2 to 5 yrs: 2 - 6 mg q d - BID	$1 g $1 g $1 g
Clemastine	**Tavist-1**	1.34 mg 2x / day	$7 g	6 to 11 yrs: 0.37 mg twice daily	$7 g
Diphenhydramine	Benadryl	25–50 mg q 6-8 h	$5 g	6 to 11 yrs: 12.5–25 mg every 4–6 hrs 2 to 5 yrs: 6.25 mg every 4–6 hrs	$4-$8 g $3 g
Brompheniramine	Dimetapp	4–8 mg 3–4x / day 12 mg q 12 h as extended-release tablet	$5-10 g $6	≥ 12 yrs: 4 mg q 4 hrs 12 mg q 12 h as extended release tablet 6 to 11 yrs: 2 mg q 4 hrs 2 to 5 yrs: two droppers full (1.6 mL) every 4–6 hrs	$7 g $6 $4 g $5
Dexchlorpheniramine	Polaramine	2 mg 4x / day or 4 mg 3x / day 6 mg as extended release tablet q 8 to 12 h	$16 g $18 g	≥ 12 yrs: 2 mg 4x / day or 4 mg 3x / day 6 mg as extended release tablet q 8–12 h 6 to 11 yrs: 1 mg 4x / day 2 to 5 yrs: 0.5 mg q 4–6 h	$16 g $18 g $22 g $11 g
Azatadine	Optimine	1-2 mg 2x / day	$60-$120	≥ 12 yrs: 1–2 mg 2x / day	$60-$120
Hydroxyzine	Atarax	25–100 mg 3–4x / day	$3-$10 g	6 to 11 yrs: 12.5–25 mg 4x / day 2 to 6 yrs: 0.5 mg/kg every 6 hrs (patient is 20 kg & syrup used)	$3 g $5 g
Phenindamine	Novahist	25 mg every 4 to 8 hours	$19–$38	6 to11 yrs: 12.5 mg every 4-6 hours /day 2 to 6 yrs: 6.25 mg every 4-6 hours/ day	$13–$19 $7–$9
Oral Antihistamines – 2nd Generation					
Fexofenadine	**Allegra**	60 mg twice daily or 180 mg once daily	$62	≥ 12 yrs: 60 mg 2x / day or 180 mg once daily 6 to 11 yrs: 30 mg 2x / day	$62 $31
Cetirizine	**Zyrtec**	5–10 mg once daily	$59–$109	6 and older: 5–10 mg once daily 2 to 5 yrs: 2.5 or 5 mg once daily	$59–$109 $30–$60
Fexofenadine and pseudoephedrine	**Allegra D**	60 mg twice daily	$70	NA	
Loratadine	Claritin	10 mg once daily	$75	≥ 6 yrs: 10 mg once daily	$75
Loratadine and pseudoephedrine	Claritin D Claritin D-24	1 tab q 12 hr (5 mg–120 mg) 1 tab q 24 hr (10 mg–240 mg)	$82 $82	NA NA	
desloratadine	Clarinex	1 tab q 24 hr (5 mg)	$66	≥ 12 yrs: 1 tab q 24 hr (5 mg)	$66
Oral Decongestants					
Pseudoephedrine	Various	30 - 60 mg q 4-6 h 120 mg as extended release tab q 12 h	$3-$5 g $19 g	6 to 11 yrs: 30 mg q 4-6 hrs 2 to 5 yrs: 15 mg q 4-6 hrs	$2 g $1 g

*** g = generic average wholesale acquisition cost**

(continued on next page)

Table 5. Pharmacologic Therapy for Allergic Rhinitis, Continued (UMHS Preferred Agents in Bold)

Generic Name	Brand Name	Usual Adult Dose	30 Day AWP Cost*	Usual Pediatric Dose		30 Day AWP Cost
Intra-Nasal Corticosteroids						
Fluticasone propionate	**Flonase**	4 sprays as a single daily dose or in 2 divided doses; may increase up to 8 sprays as single daily dose	$58	≥ 4 yrs:	2 sprays as single daily dose; may increase up to 4 sprays as single daily dose	$29-$58
Mometasone	**Nasonex**	4 sprays as single daily dose	$44	3 to 11 yrs:	2 sprays as single daily dose	$22
Triamcinolone acetonide	**Nasacort**	Nasacort aerosol: 4 sprays as single dose, may increase up to 8 sprays as single dose or divide into 2-4 doses	$51-$102	6 to 11 yrs:	4 sprays as single daily dose	$51
		Nasacort Nasal spray: 4 sprays as single daily dose	$54	6 to 12 yrs:	2-4 sprays as single daily dose	$27–$54
Flunisolide	Nasalide, Nasarel	8 sprays / day in 2 divided daily doses or as single dose	$48	≥ 12 yrs:	2 sprays as single dose, may increase up to 8 sprays as single dose	$48
				6 to 11 yrs:	2 sprays as single dose, may increase up to 4 sprays as single dose	$48
Beclomethasone dipropionate	Aerosol: Beconase, Vancenase Spray; B-AQ, V-AQ	Beconase aerosol: 4-8 sprays / day in 2-4 divided doses	$50	6 to 12 yrs:	6 sprays / day in 3 divided doses	$50
		Beconase AQ: 4-8 sprays / day in 2 divided doses	$51-$102	6 to 12 yrs:	4 sprays / day in 2 divided doses	$51
				≥ 6 yrs:	2 to 4 sprays as single dose	$57
		Vancenase AQ: 2-4 sprays / day as single dose	$57			
Budesonide	Rhinocort	Rhinocort aerosol: 8 sprays / day in 2 divided doses or as single daily dose	$42			
		Rhinocort Aqua Spray: 2 sprays as a single daily dose, may increase up to 8 sprays / day	$47-$94	6 to 11 yrs:	2 sprays as single daily dose, may increase to 4 sprays as single daily dose	$47
Intra-Nasal Antihistamine						
Azelastine nasal spray	Astelin	2 sprays EN (each nostril) 2x / day	$26	≥ 12 yrs:	2 sprays EN (each nostril) 2x / day	$26
				5 to 11 yrs:	1 spray EN 2x / day	$13
Intra-Nasal Decongestants (Drops Or Spray)						
Oxymetazoline	Afrin	2 or 3 drops or sprays of 0.05% BID	$3	6 to 12 yrs:	2 or 3 drops or sprays of 0.05% BID	$3
				2 to 5 yrs:	2- 3 drops 0.025% BID	$3
Intra-Nasal Mast Cell Stabilizers						
Cromoglycate, cromolyn sodium	Nasalcrom	1 spray EN 3-4x / day	$5	≥ 6 yrs:	1 spray EN 3-4 times daily	$5
Intra-Nasal Anticholinergic						
Ipratropium bromide	Atrovent	0.06% solution, 2 sprays EN 3-4x / day	$38	≥ 12 yrs:	0.06% solution, 2 sprays EN 3-4x / day	$38
				6 to 12 yrs:	0.03% solution, 2 sprays EN 2-3x / day	$44

*** g = generic average wholesale acquisition cost**

(continued on next page)

Table 5. Pharmacologic Therapy for Allergic Rhinitis, Continued (UMHS Preferred Agents in Bold)

Generic Name	Brand Name	Usual Adult Dose	30 Day AWP Cost*	Usual Pediatric Dose		30 Day AWP Cost*
Ocular Decongestants						
Naphazoline	Many (e.g., Albalon)	1-2 drops in affected eye(s) up to 4x / day	$3 g	NA		
Oxymetazoline	Visine LR, OcuClear	1-2 drops in affected eye(s) repeated as needed every 6 hrs or as directed by physician	$3 g	≥ 6 years:	1 or 2 drops in affected eye(s), may be repeated as needed q 6 h	$3 g
Phenylephrine	Many (e.g., Mydfrin)	1 drop in affected eye(s), repeat in 1 hr if necessary	$4	all ages	1 drop in affected eye(s), repeat in 1 hr if necessary (avoid 10% solution in infants)	$4
Tetrahydrozoline	Many (e.g., Visine)	1-2 drops in affected eye(s) up to 4x / day	$1 g	≥ 6 years:	1-2 drops in affected eye(s) up to 4x / day	$1 g
Ocular Antihistamines						
Levocabastine	Livostin	1 drop affected eyes up to 4x / day	5 ml $45	NA		
Emedastine	Emadine	1 drop affected eyes up to 4x / day	$44	≥ 4 yrs:	1 drop affected eye up to 4x / day	$44
Olopatadine	Patanol	1-2 drops in affected eyes 2x / day at interval of 6-8 h	$63	≥ 4 yrs:	1-2 drops in affected eye 2x / day at interval of 6-8 h	$63
Ocular Non-Prescription Antihistamine/Decongestant Combinations						
Naphazoline & pheniramine	Naphcon-A	1-2 drops in affected eye(s) up to 4x / day	$8	NA		
Naphazoline & antazoline	Vascon-A	1-2 drops in affected eye(s) up to 4x / day as needed	$6	NA		
Ocular Non-Steroidal Anti-Inflammatory Drugs (NSAIDS)						
Ketoralac	Acular	1 drop 4x / day	$50	NA		
Ocular Mast Cell Stabilizers						
Lodoxamide tromethamine	Alomide	1-2 drops in affected eye 4x / day	$57	≥ 2 yrs:	1-2 drops in affected eye 4x / day	$57
Cromolyn	Opticrom	1-2 drops affected eye 4-6x / day	$12 g	≥ 4 yrs:	1-2 drops in affected eye 4-6x / day	$12

Note: For brand drugs, Average Wholesale Price from First Data Bank, 11/2001. For generic drugs, Wholesale Acquisition Cost from Amerisource Bergen Wholesale Catalog, 11/2001

Table 6. Complications of Allergic Rhinitis

General Concerns / Complications	Adults	Children
Exacerbation of asthma	X	X
Deviations in facial growth		X
Hyposmia	X	
Incisor protrusion		X
Malocclusion (crossbite, high palatal arch)		X
Nasal polyps	X	?
Middle ear effusion: hearing loss	X	X
Sinusitis	X	X
Sleep Apnea	X	?

X = Possible; ? = Uncertain

Table 7. Possible Side Effects Associated with Medical Therapy for Allergic Rhinitis

Antihistamines

<u>Anticholinergic effects</u>
- blurred vision
- dry mouth
- urinary retention

<u>Central nervous system</u>
- drowsiness (decreased learning, increased accidents)
- cognitive impairment (any age; elderly)
- impaired reflexes (impaired performance, ↓ psychomotor performance)

<u>Gastrointestinal</u>
- constipation
- GI upset
- nausea

<u>Sensory</u>
- taste: bitter taste, loss of taste

<u>Weight gain</u>

Corticosteroids

Nasal/Topical Preparations

<u>Nasopharyngeal</u>
- coughing
- epistaxis
- nasal irritation: burning, crusting, dryness
- pharyngitis
- septal perforation

<u>Sensory</u>
- smell: reduced sense of smell
- taste: unpleasant taste, loss of taste

Ocular Preparations
- glaucoma (elevated intra-ocular pressure)
- infection:
  - secondary ocular infection
  - exacerbation of infection
- ophthalmic irritation: burning, dryness, Pruritus, stinging

Decongestants

General
- tachycardia
- palpitations
- nervousness
- headache
- insomnia
- drowsiness
- dizziness
- weakness

Intra-Nasal
- burning
- stinging
- increased discharge
- swelling
- sneezing

Ocular
- burning
- stinging
- transient pain
- conjunctivitis
- eyelid eczema / dermatitis

Mast Cell Stabilizers

Nasal Preparations

<u>Nasopharyngeal</u>
- epistaxis
- nasal irritation: burning, Stinging
- sneezing

<u>Sensory</u>
- taste: unpleasant taste

Ocular Preparations
- headache
- ophthalmic irritation: burning, dryness, pruritus, stinging

Clinical Background

Clinical Problem and Management Issues

Incidence. Allergic rhinitis, the most common form of rhinitis, affects 20-40 million people in the United States annually, including 10-30% of adults and up to 40% of children. Although the disease tends to be more prevalent among males during childhood, the gender ratio among adults is approximately equal.

The severity of allergic rhinitis ranges from mild to seriously debilitating; its social and financial impact is significant. It accounts for in excess of 2.7 billion dollars in direct and indirect medical costs (1995 dollars) and is often associated with other conditions such as asthma and chronic rhinosinusitis. When lost productivity due to drowsiness and cognitive/motor impairment related to over the counter antihistamine use were considered, the total cost estimate associated with allergic rhinitis increased to 5.3 billion dollars for 1996.

Diagnosis. Allergic rhinitis is primarily diagnosed on the basis of history, with physical examination providing additional clues. Because of the significant overlap of its symptoms with those of other nasal conditions, diagnosis may not be straightforward. Allergy testing may help in the diagnosis but must be properly performed in order to avoid false negative results.

Testing/referral. When history is not adequate for diagnosis, skin or RAST testing is helpful to (a) differentiate allergic from non-allergic rhinitis symptoms and (b) to identify specific allergens that may cause symptoms. Skin tests are more sensitive, faster, and more cost effective than RAST. However, skin testing needs to be performed by a trained physician using a cell-controlled process and interpreting results in light of local aeroallergens and their properties.

Treatment. Treatment options for allergic rhinitis include environmental control (allergen avoidance), pharmacotherapy, and immunotherapy ("allergy shots"). Most treatment regimens employ one or more of these options. While each option has been shown to be effective in treating allergic rhinitis, they have significant costs as well. Medications and changes in the home environment can result in sizable direct expenditures, while immunotherapy necessitates frequent office visits, often over a number of years.

The effectiveness of a medication is related to the route of administration. Medication administered through the ocular route only addresses ocular systems; while no data exist regarding the relief of ocular symptoms with oral medications, expert opinion indicates that systemic drugs do provide some relief.

Rationale for Recommendations

Definition

Allergic rhinitis is an allergy-driven inflammation of the membranes lining the nose. The disease is characterized by sneezing, congestion, clear rhinorrhea, and nasal or palatal itching. The disease may also coexist with allergic conjunctivitis (characterized by itchy, watery eyes that may also be red or swollen). Allergic rhinitis may be seasonal, perennial, or may occur sporadically after specific exposures.

Epidemiology

Allergic rhinitis manifests in two forms. Seasonal allergic rhinitis tends to be associated with cyclical changes in the environment. In contrast, perennial allergic rhinitis does not exhibit a seasonal pattern; this may reflect the patient's continuous exposure to the offending allergen (e.g., animal, house dust mites, occupational exposures). Distinguishing prevalence rates of seasonal versus perennial allergic rhinitis is complicated by two factors: first, epidemiologic studies have focused primarily on seasonal allergic rhinitis (e.g., hay fever), and second, the symptom complex of perennial allergic rhinitis overlaps with those of seasonal allergic rhinitis, chronic sinusitis, recurrent upper respiratory infections, and vasomotor rhinitis. Nevertheless, studies suggest that seasonal rhinitis (hay fever) occurs in 10-20% of the population.

Diagnosis

Adult, general. Assessment of a patient who presents with symptoms of allergic rhinitis begins with a detailed history regarding the pattern, frequency, duration, severity, and seasonality of symptoms (or lack thereof), response to medications, presence of coexisting conditions (especially atopic conditions), occupational exposure, environmental history, and identification of precipitating factors. Family history of atopic disease is often positive in patients with allergic rhinitis. An integral part of the assessment is an evaluation of the degree to which symptoms affect the patient's quality of life, physical and social functioning, mental health, energy level, and general health perception. Response to previous medication trials should be assessed.

Physical examination should be made of the external nose, nasal mucosa, secretions, turbinates, and septum. In the allergic patient, the nasal mucosa typically appears pale, swollen, and bluish-gray. Secretions tend to be clear and watery. Chronic or severe acute allergic rhinitis may be accompanied by a transverse crease across the bridge of the nose, particularly in children, as a result of the "allergic salute" (i.e., rubbing the nose to relieve nasal obstruction and itching). "Allergic shiners" (infraorbital dark skin discoloration) and facial pallor may also be present. Other causes for nasal obstruction should be sought or ruled out.

Pediatric. Symptoms exhibited by children and adolescents with allergic rhinitis are indistinguishable from those of adults with the exceptions that pediatric patients

have a greater frequency of the allergic salute and eye rubbing. These are linked to chronic nasal obstruction, which may lead to "the allergic facies," a complex of infraorbital darkening, facial maldevelopment, including overbite, palatal arching, and molar flattening.

Testing

Testing is not indicated in most allergic rhinitis cases. Skin tests and RAST (radioallergosorbent test) identify the presence of IgE antibody to a particular allergen. Testing is helpful to (a) differentiate allergic from non-allergic rhinitis symptoms and (b) to identify specific allergens that may cause symptoms. A small minority of patients who undergo testing may be candidates for immunotherapy. Nasal smears identify the presence of neutrophils and eosinophils, the latter of which suggests an allergic disease.

Skin tests are more sensitive, faster, and more cost effective than RAST testing. Antihistamines should be stopped 7-10 days (7 days to be safe) before skin testing, but do not need to be stopped prior to RAST serum tests.

Skin testing should be performed by a physician trained in allergy testing and interpretation. Effective testing requires a well-controlled process with consistent application technique and proper precautions for patients who react to skin testing (approximately 1-10% of patients). A controlled environment and proper technique are vital to producing accurate and reproducible results. Interpreting skin or in-vitro tests for a specific IgE requires knowledge of locally-present aeroallergens, their clinical importance, and their cross-reactivity with botanically-related species. The number of skin tests needed may vary with the patient's age, potential allergen exposures, and geographic region.

Treatment

Treatment by avoidance or environmental control. Avoidance of inciting factors (e.g., allergens, irritants, medications) is fundamental to the management of allergic rhinitis. Food allergies may cause rhinorrhea in young children but this is rarely the overriding symptom.

Triggers for allergic rhinitis may be grouped into five major categories: pollens, molds, house dust mites, animals, and insect allergens (e.g., cockroaches, bee venom). The effectiveness of control measures instituted is assessed primarily by patient symptoms and the necessity of medications.

Pollens. Pollen-triggering allergic rhinitis is principally derived from wind-pollinated trees, grasses, and weeds. In Michigan, the predominant sources of pollen vary with the season:

- April – May = tree pollen
- May – June – early summer = grass pollen
- August – September = weed pollen
- September – October = seasonal mold).

Reducing pollen exposure is important to the effective management of allergic rhinitis; this can be accomplished by closing doors and windows, using air conditioning (if necessary, on an indoor cycle), minimizing the use of window or attic fans, and limiting outdoor activity. Showering or bathing after outdoor activity removes pollen from the hair and skin and helps avoid contamination of bedding. In highly sensitive patients, effective allergen avoidance may require severely curtailing the patient's outdoor activity.

Molds. Molds proliferate in both indoor and outdoor environments; most mold allergens are encountered through inhalation of mold spores. Patients can avoid outdoor molds by remaining indoors and using air conditioning on an indoor cycle; however, it is important to note that air conditioning units themselves may be heavily contaminated with mold. Indoor mold is influenced by the age and construction of the building, presence of basement or crawl space, type of heating system, and use of humidifiers and air conditioning. Indoor mold can be controlled somewhat via chemical and physical measures such as fungicides, careful cleaning of humidifiers and vaporizers, and placement of a plastic vapor barrier over exposed soil in crawl spaces. Dehumidifiers in basements and other damp areas may help reduce mold levels. The overall effectiveness of these measures, however, is dependent upon reducing relative humidity and condensation levels.

House dust mites. Fecal residue from dust mites is the primary allergen in household dust. The dust mites' principle food source is exfoliated human skin; as such, mite concentrations are highest in bedding, fabric-covered furniture, soft toys, and carpeting. While no effective means currently exist in the US for permanently eliminating mites from upholstered furniture and carpeting, physical and chemical barriers offer some relief. Physical barriers may include allergen-proof encasings for mattresses, pillows, box springs, and bedding, using plastic, wood, or leather furniture in lieu of upholstered furniture, and replacing carpeting with wood or vinyl flooring. Chemical barriers include using 3% tannic acid solution to denature dust mites in upholstered furniture and treating carpeting with Arcarosan®, a compound containing benzyl benzoate. The effectiveness of chemical barriers depends upon their repeated application. Finally, while it is possible that air conditioning reduces mite numbers by lowering indoor humidity, evidence regarding the effect of air purifiers on alleviating dust mite allergy symptoms is either nonexistent (for electrostatic purifiers) or conflicting (for HEPA air purifiers). Similarly, cleaning heating ducts is of no demonstrated value.

Animal allergens. All warm-blooded animals, including birds, are capable of sensitizing a susceptible allergenic patient. While exposures to mice, rats, guinea pigs, and farm animals constitute occupational hazards for some, the most common manifestations of animal allergy are to cats and dogs. Cat and dog allergens are notable for the ease and extent of their dissemination, particularly through passive means (i.e., transport on clothing). While significant cleaning measures are required to reduce cat and dog allergen levels to those found in environments not inhabited by cats or dogs, their effectiveness is limited. Such measures may include washing the animal itself on a weekly basis. Evidence in support of this practice is mixed,

but washing should never be attempted by the allergic patient. If the allergenic animal is not to be removed from the home, confining it to an uncarpeted room with an electrostatic or HEPA air purifier may markedly reduce airborne allergens in the rest of the home.

Insect allergens. Sources of insect allergens include cockroaches, crickets, flies, midges, and moths. Debris from these insects is associated with allergic rhino-conjunctivitis and asthma. The most common of these, the cockroach allergen, is found on the insect's body and in its feces. While careful sanitation practices are often effective in reducing or eliminating cockroaches, heavy infestation may require application of pesticides by a professional exterminator.

Pharmacological therapy. Several classes of drugs comprise the mainstay of treatment of allergic rhinitis; of these, the primary ones are nasal corticosteroids and oral antihistamines.

Nasal Corticosteroids. A number of studies have shown these drugs to be the most effective treatment of the itching, sneezing, rhinorrhea, and stuffiness associated with allergic rhinitis. Their effect is not immediate, however; onset of relief is seen on day 2 to 3 with effects reaching their peak at 2 to 3 weeks. Regular, consistent use is required to maintain a maximum effect. Nasal corticosteroids do not treat ocular symptoms.

Nasal corticosteroids are well tolerated and have a relatively good safety profile. Newer, more potent formulations offer the advantages of once daily dosing, minimal to no systemic absorption, and demonstrated tolerability in pediatric patients. The incidence of adverse effects is between 5-10%; local effects most commonly reported include sneezing, stinging, and burning or irritation. However, these effects are generally mild and do not preclude the use of intranasal preparations. Aqueous formulations are preferred because they are less irritating to the nasal mucosa.

Oral antihistamines. Antihistamines are effective in reducing symptoms of itching, sneezing, and rhinorrhea and should be tried with most patients as first-line therapy for allergic rhinitis. Antihistamines also reduce symptoms of allergic conjunctivitis, which are often associated with allergic rhinitis. While they tend to be less efficacious overall compared to the nasal steroids, antihistamines appear to be equally effective in blocking histamine-mediated responses to allergens *[A*]*.

All antihistamines appear to be equally effective. It is therefore recommended that therapy be initiated with first generation, over the counter agents in patients who can tolerate them. Generic chlorpheniramine is inexpensive and effective. Usual dosing recommendations are based on obsolete data, however. The tissue half-life of chlorpheniramine is 24 hours +/- 6 hours. Therapy should be initiated at 2 - 4 mg at bedtime, and increased by 2 - 4 mg every 2 - 3 days. The maximum single dose is 12 mg for adults, or 24 mg divided BID. There is no rationale for sustained-release chlorpheniramine. In patients who cannot tolerate a sedating antihistamine during the daytime, giving chlorpheniramine in the evening only, or use of fexofenadine or cetirizine is recommended. Roughly 10% of patients experience sedation even with "non-sedating" antihistamines. No data indicate that combining an antihistamine and a nasal steroid produces improved symptomatic relief.

Decongestants. Decongestants act on adrenergic receptors to produce vasoconstriction and decrease swelling of the nasal mucosa which, in turn, alleviates nasal congestion. Oral decongestants may be used until symptoms resolve. Although they have not been found to affect blood pressure significantly in patients with *stable* hypertension, oral decongestants (including combination products containing a decongestant—see below) should be used with caution in patients with unstable hypertension, ischemic heart disease, glaucoma, prostatic hypertrophy, or diabetes mellitus. Urinary retention in elderly males is a common side effect. Oral decongestants are contraindicated in patients using monoamine oxidase inhibitors (MAOIs) or having uncontrolled hypertension or severe coronary artery disease. In addition, geriatric patients may be more sensitive to the side effects of oral decongestants. Topical decongestants do not exhibit significant systemic absorption in usual doses, but due to the risk of rebound vasodilation (*rhinitis medicamentosa)* or atrophic rhinitis with chronic use, these agents have no role in the treatment of allergic rhinitis.

Combination antihistamine/decongestant. Patients for whom an antihistamine or decongestant alone fails to provide complete relief may benefit from an antihistamine/ decongestant combination; studies have show improved allergy symptom control when a decongestant has been added to antihistamine therapy *[A*]*. Decongestant-containing products are approved only for patients 12 years of age and older; the cautions enumerated above for decongestant use also apply to combination products.

Nasal cromolyn. Although less effective than intranasal corticosteroids, cromolyn is a good alternative for patients who are not candidates for corticosteroids. It is most effective when used regularly prior to the onset of allergic symptoms. The four times daily dosing can cause compliance problems. Adverse effects are minimal and include nasal irritation, sneezing, and unpleasant taste.

Anticholinergics. Ipratropium bromide (Atrovent) is an effective anticholinergic spray for patients with severe vasomotor symptoms (profuse thin rhinorrhea). Anticholinergics decrease the production of mucus and diminish rhinorrhea. Both topical medications and oral preparations (usually first-generation antihistamines) have been shown to be effective. While it is plausible that thickening of the mucus could impair its clearance from the sinuses (thereby possibly precipitating acute rhinosinusitis), this phenomenon has not been documented despite numerous clinical trials with anticholinergic medications. The therapeutic effect of antihistamines is due to their anticholinergic properties. Therefore newer, less-sedating antihistamines are less likely to be effective.

Nasal Antihistamines (Astelin). Intranasal antihistamines are effective in treating the nasal symptoms associated with seasonal and perennial rhinitis and nonallergic vasomotor rhinitis. When administered intranasally, the primary adverse effects are nasal burning and altered taste (i.e., bitter or metallic taste). While effective in the symptomatic treatment of seasonal allergic rhinitis, Astelastine offers no therapeutic benefit over conventional treatment.

Ocular Medications. Ocular medications are available as topical solutions or suspensions. They contain antihistamines, decongestants, combination antihistamines / decongestants, corticosteroids, or mast cell stabilizers (cromolyn sodium and lodoxamide). Side effects of ocular medications (except corticosteroids) are generally mild and include a brief stinging, burning sensation. Topical antihistamines can be used as needed for acute symptomatic relief and prophylaxis of allergic rhinitis with minimal systemic side effects.

Sodium cromolyn has been shown to be effective for the treatment of seasonal allergic rhinitis and allergic conjunctivitis and should be administered on a regular basis. Lodoxamide has been shown to be as effective or more effective than sodium cromolyn in vernal conjunctivitis. Contact lens users should consult their eye care provider regarding the use of these products.

Nasal saline. Saline sprays theoretically moisten the nasal cavity and promote mucous clearance. Many preparations, however, contain benzalkonium chloride, a preservative implicated in the rebound irritation seen in *rhinitis medicamentosa*. Steam inhalation may give some symptomatic relief, but there is some evidence of rebound congestion with this remedy as well.

Immunotherapy. Allergen immunotherapy is defined as the repeated administration of specific allergens to patients with IgE-mediated conditions, for the purpose of providing protection against the allergic symptoms and inflammatory reactions associated with natural exposure to these allergens. Well-controlled clinical trials have demonstrated that allergen immunotherapy is beneficial in the treatment of seasonal pollinosis caused by trees, grasses, weeds, and in the treatment of mold-induced rhinitis. Clinical studies have also demonstrated the efficacy of allergen immunotherapy in perennial allergic rhinitis caused by dust mites and animal sensitivity. Allergen immunotherapy should also be considered for patients who have experienced insect-induced hypersensitivity reactions after exposure to insect allergens. See Table 3 for advantages and disadvantages.

Referral/Consultation

Appropriate criteria for referral to a colleague who specializes in the diagnosis and treatment of allergies may include:

- Failure of oral/nasal medications
- Moderate-severe perennial symptoms
- Allergy skin/RAST testing to better identify allergens, to improve avoidance therapy, or initiate immunotherapy
- Associated conditions such as atopic dermatitis, asthma, or chronic or recurrent acute rhinosinusitis
- Any severe allergic reaction causing patient or parental worry.

Special Considerations

Pediatrics

For children with occasional symptoms, antihistamines can be taken on days when symptoms are present or expected. Children experiencing daily symptoms achieve the most relief when taking antihistamines continuously throughout the pollen season. If drowsiness becomes a problem, consider decreasing the dose temporarily until the child becomes tolerant of the regular dosage (usually 1 to 2 weeks). A second-generation less-sedating antihistamine may be an option for children over age 2.

Pregnancy

Allergic rhinitis has no predictable pattern during pregnancy; it may worsen, improve, or stay the same. Some of the hormonal changes associated with pregnancy may exacerbate symptoms. Rising progesterone and estrogen levels during pregnancy may increase glandular secretions, and vasodilation and increased blood volume may cause nasal vascular pooling. These changes may cause symptoms to worsen. In contrast, increased serum levels of free cortisol during pregnancy could improve symptoms of allergic rhinitis.

Pregnancy risks associated with agents used to treat allergic rhinitis are grouped in two categories. The first category includes agents for which animal studies have not demonstrated a risk to the fetus, but for which there are no adequate studies in pregnant women. Among these, intranasal cromolyn should be considered a first-line agent in view of its topical application and reassuring gestational animal data. Chlorpheniramine should be considered the antihistamine of choice during pregnancy; if chlorpheniramine proves to be ineffective, tripelennamine should be tried next. Second-generation antihistamines should be reserved for women who clearly need an antihistamine but who have experienced unacceptable side effects with first-line antihistamines. Ideally, second-generation drugs should be used only after the first trimester.

Finally, immunotherapy for allergic rhinitis may be continued during pregnancy as long as it provides benefit and does not cause systemic reactions, which could be harmful to both mother and fetus. Generally, immunotherapy should not be started during pregnancy.

Severe Asthmatics

Rhinitis can exacerbate asthma. However, desensitization does not improve asthma control, and other allergy treatments have not been shown to improve asthma control either.

Severe Atopic Dermatitis Patients

Patients with atopic dermatitis tend to be severely allergic and should be referred if initial therapy is unsuccessful.

Controversial Areas

Testing

Cytotoxicity testing, provocative and neutralization testing carried out by either intracutaneous or subcutaneous injection or sublingual administration, and measurement of specific and non-specific IgG4 have not been validated by accepted standards of scientific evaluation and as such are considered unproven, controversial, and inappropriate for diagnostic use.

Treatment Strategy and Cost

Pharmacologic control of allergic rhinitis is expensive and may carry some long term side effects, especially in children. Immunotherapy (allergy shots) may provide significant long-term control of symptoms at a reduced cost and without the risks of medication, but requires multiple office visits, which compromises patient compliance. These issues must be weighed when considering treatment options.

Strategy for Literature Search

The literature search for this project was conducted in 1998 using the major keywords of: *allergic rhinitis, avoid, control triggers, clinical trials-- phase IV, cohort studies, controlled clinical trials, multicenter studies, randomized controlled trials, observational trial, meta analysis,* on Medline. The search was a single cycle. When possible, conclusions were based on prospective randomized clinical trials. In the absence of randomized controlled trials, observational studies were considered. If none were available, expert opinion was used.

Related National Guidelines

The UMHS Clinical Guideline on Allergic Rhinitis is consistent with the Joint Council on Allergy, Asthma, and Immunology *Executive Summary of Joint Task Force Parameters on Diagnosis and Management of Rhinitis* (1998). (See "Annotated References" below.)

Disclosures

The University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

Team Member	Company	Relationship
Richard Orlandi, MD	Bayer Pharmaceuticals	Consultant
Daniel Dubay, MD	(none)	
Margie Andreae, MD	(none)	
James Baker, MD	Pfizer, Merck, Adventis, Schering	Consultant
Steve Erickson, PharmD	(none)	
Jeffrey Terrell, MD	(none)	

Annotated References

Stroebel R, Graft D, Takahashi M, et al. Health Care Guideline: Rhinitis. Bloomington, MN: Institute for Clinical Systems Improvement (ICSI), 2000. [www.icsi.org/guidelst.htm#guidelines]

Evidence based guideline and algorithms for treatment of allergic and non-allergic rhinitis.

Dykewicz MS, Fineman S, Nicklas R, et al. Diagnosis and Management of Rhinitis: Parameter Documents of the Joint Task Force on Practice Parameters in Allergy, Asthma, & Immunology. Annals of Allergy, Asthma, and Immunology, 1998; 81 (Part II): 463-468

Special issue reporting summary statements, guidelines, and algorithms prepared by the Joint Task Force on Practice Parameters in Allergy, Asthma, and Immunology.

Baker JR (ed.). Primer on Allergic and Immunologic Diseases (4th Edition). JAMA, 1997; 278 (22): 1799-2034.

Special issue published every 5 years and devoted to many aspects of allergic, immunologic, and asthmatic disorders. In this issue, the discussions of immuno-deficiency diseases and definition of immune dysfunction reflect advances in knowledge regarding genetic defects at specific points in the immune response. Also included are expanded treatments of immune physiology, cells of the allergic response, and cost –benefits of therapeutic alternatives.