Allergic Rhinitis

Allergic Rhinitis Guideline Team

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These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

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 is 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 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. The over-the-counter (OTC), non-sedating antihistamine loratadine (Claritin) should be tried initially, as it will provide relief in most cases. If symptoms persist, consider the following options:
3. Prescribed medications:
   - Intranasal 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 long-term safety profile. **UMHS preferred intranasal corticosteroids for adults are generics: fluticasone (Flonase) and flunisolide (Nasarel). Mometasone (Nasonex AQ) is preferred for children.**
   - Oral, non-sedating antihistamines prevent and relieve itching, sneezing, and rhinorrhea, but tend to be less effective for nasal congestion *[A*]*. **UMHS preferred prescription antihistamine is fexofenadine (Allegra)**.
   - Oral decongestants decrease swelling of the nasal mucosa which, in turn, alleviates nasal congestion *[A*]*. However, they are associated with appreciable side effects, especially in geriatric patients, and should only be considered when congestion is not controlled by other agents. They are contraindicated with monoamine oxidase inhibitors (MAOIs), in uncontrolled hypertension and in severe coronary artery disease.
   - Leukotriene inhibitors are less effective than intranasal corticosteroids *[A*]* but may be considered for patients that cannot tolerate the first line agents or have co-morbid asthma.
   - Intranasal cromolyn (OTC) is less effective than intranasal 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.
   - Intranasal antihistamines (Astelin), 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*]*.
   - Ocular preparations should be considered for patients with allergic conjunctivitis who are not adequately controlled with or can not tolerate an oral antihistamine.

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 or seasonal allergic rhinitis that is moderate to severe
- associated comorbidities (Table 5).
- 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 (seasonal or 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

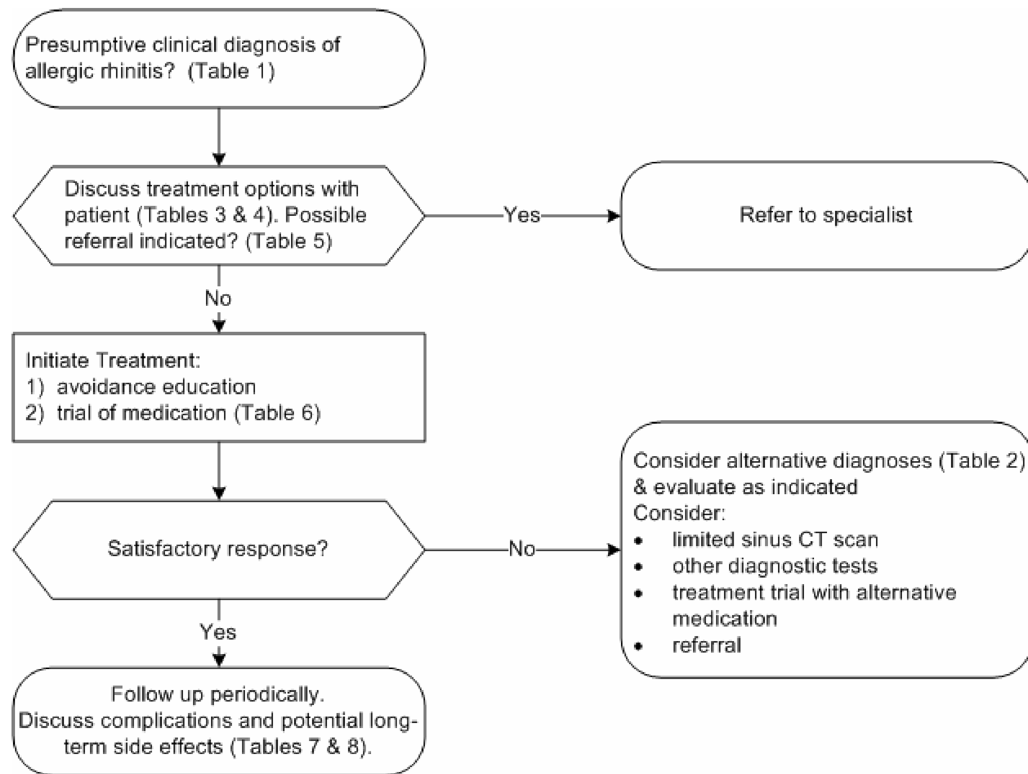

Table 1. Symptoms and Signs Suggestive of Allergic Rhinitis

Symptoms	Seasonal, perennial or episodic (associated with exposure, e.g., cat) itching of eyes, ears, nose, palate; sneezing, nasal congestion, chronic sniffling, clear rhinorrhea, post nasal drip, pressure of nose or over paranasal sinus', morning cough. Red, watery eyes or ropy discharge.
Family or personal history	Atopic dermatitis, asthma, food allergy.
Physical findings	Ocular-allergic shiners, Dennie's lines, scleral injection with corkscrewing of vessels, conjunctival erythema with possible cobblestoning. Nasal-transverse nasal crease (salute), congestion, pale pink or bluish mucosa, clear or thick mucoid discharge, presence of nasal polyps, pharyngeal cobblestoning.

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; typically follows 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, low grade fever) usually resolving within 3-7 days
Structural abnormalities	Include nasal septal deviation, nasal polyps, enlarged turbinates, adenoidal hypertrophy. Obstruction may be unilateral or bilateral and may or may not be seen on routine nasal 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 called "ozena", caused by over-resection of nasal turbinate tissue or poor mucus production, resulting in nasal dryness and crusting. Foul odor may be present.
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 6 & 7)**	• Patient preference • Rapid onset • May control non-allergic rhinitis symptoms • Many choices (See Tables 6 & 7)	• Cost of medication • Medication side effects (e.g., sedation, impaired performance, nasal septal perforation with nasal steroids [rare]) • Potential unknown long term side effects
Allergy Testing, Skin Testing (preferred) or RAST Testing	• Beneficial in defining allergens in complex patients or to institute immunotherapy • May help direct avoidance therapy	
Immunotherapy	• Only disease remitting therapy available • Medication requirements usually reduced • Benefits may persist after therapy has stopped • May be less costly in long term • May prevent polysensitization and onset of asthma in children	• Benefits of therapy not seen until several months of treatment • Requires patient commitment • Anaphylaxis (rare)

Table 4. Order of Medication Addition Based on Presenting Symptoms

Addition Sequence	Nasal Obstructive Symptoms	Rhinorrhea without Obstruction	Comorbid Persistent Asthma
First	Intranasal corticosteroid	Antihistamine +/- decongestant	Intranasal corticosteroid
Second	Antihistamine +/- decongestant	Intranasal corticosteroid	Leukotriene inhibitors OR Antihistamine +/- decongestant
Third	Leukotriene inhibitors	Leukotriene inhibitors	If intranasal corticosteroid use above, ADD antihistamine +/- decongestant If antihistamine +/- decongestant, ADD intranasal corticosteroid
Fourth	Intranasal antihistamine	Intranasal antihistamine	Intranasal antihistamine
Fifth	Intranasal mast cell stabilizer	Intranasal mast cell stabilizer	Intranasal mast cell stabilizer
Sixth	Intranasal anticholinergics	Intranasal anticholinergics	Intranasal anticholinergics

Table 5. Possible Indications for Referral to Specialist

- Identify specific allergens for patients
- Intolerance to, contraindication of, or failure of medical management (See Table 8)
- Symptoms interfere with daily activities, or sleep
- Associated comorbidities such as chronic or recurrent bacterial rhinosinusitis, or recurrent otitis media, nasal polyps, asthma, atopic dermatitis, ocular symptoms
- Need for improved allergen avoidance education
- Moderate to severe symptoms of seasonal or perennial rhinitis or presence of nasal polyps
- Any severe allergic reaction that causes patient or parental anxiety
- Immunotherapy is a consideration (See also: Table 7)

Table 6. Pharmacologic Therapy for Allergic Rhinitis (UMHS Preferred Agents in Bold)

Generic Name	Brand Name	Usual Adult Dose	30 Day Cost* Brand	30 Day Cost* Generic	Usual Pediatric Dose (syrup concentration if available)	30 Day Cost* Brand	30 Day Cost* Generic
Intranasal Corticosteroids							
Fluticasone propionate	**Flonase**	1 spray each nostril (EN) 2x/day or 1–2 sprays EN 1x/day	43	27	≥ 4 yrs: 1–2 sprays EN 1x/day	22	14
Mometasone **	**Nasonex AQ**	2 sprays EN 1x/day	41	N/A	2 to 11 yrs: 1 spray EN 1x/day ≥ 12 yrs: 2 sprays EN 1x/day	21 41	N/A N/A
Triamcinolone acetonide	Nasacort AQ	2 sprays EN 1x/day	42	N/A	≥ 6 yrs: 1–2 sprays EN 1x/day	21-42	N/A
Flunisolide	**Nasalide, Nasarel**	2 sprays EN 2x/day	17	14	6 to 14 yrs: 2 sprays EN 2x/day	17	14
Beclomethasone dipropionate	Beconase AQ-42	Beconase AQ: 1–2 sprays EN 2x/day	34-68	N/A	6 to 12 yrs: 1–2 sprays EN 2x/day	34-68	N/A
Budesonide	Rhinocort Aqua	1–4 sprays EN 1x/day	21-82	N/A	6 to 11 yrs: 1–2 sprays EN 1x/day ≥ 12 yrs: 1–4 sprays EN 1x/day	21-42 21-82	N/A N/A
Oral Antihistamines – 2nd Generation (prescription benefit coverage may vary by insurer and product)							
Loratadine OTC	**Claritin**	10 mg once daily	32	11	≥ 6 yrs: 10 mg once daily 2-5 yrs: 5 mg once daily (1mg/mL, $9/ 4 oz)	16 15	11 10
Loratadine and pseudoephedrine OTC	Claritin D-12 Claritin D-24	1 tab q 12 hrs (5 mg–120 mg) 1 tab q 24 hrs (10 mg–240 mg)	50 57	42 30	≥ 12 yrs: 1 tab q 12 hrs (5-120mg) ≥ 12 yrs: 1 tab q 24 hrs (10-240mg)	50 57	42 30
Fexofenadine	**Allegra**	60 mg twice daily or 180 mg once daily	80-92	53-60	≥ 12 yrs: 60 mg 2x/day or 180 mg once daily 6 to 11 yrs: 30 mg 2x/day (6 mg/mL, $16 / 4oz)	80-92 46	53-60 31
Fexofenadine and pseudoephedrine	Allegra D-12 Allegra D-24	1 tab q 12 hrs (60-120 mg) 1 tab q 24 hrs (180-240 mg)	103 103	N/A N/A	≥ 12 yrs: 1 tab q 12 hr (60-120mg) ≥ 12 yrs: 1 tab q 24 hr (180-240mg)	103 103	N/A N/A
Cetirizine	Zyrtec	5–10 mg once daily	69	N/A	≥ 6 yrs: 5–10 mg once daily or divided BID 2 to 5 yrs: 2.5 or 5 mg once daily (1mg/mL $34 / 4 oz)	69 35-64	N/A N/A
Cetirizine and pseudoephedrine	Zyrtec D-12	1 tab q 12 hrs (5-120 mg)	69	N/A	≥ 12 yrs: 1 tab q 12 hr (5-120mg)	69	N/A
Desloratadine	Clarinex	5 mg once daily [liquid 0.5mg/mL]	94	N/A	6 to 11 months: 1 mg once daily, 2mL of 0.5mg/mL 1-5 yrs: 1.25 mg once daily 2.5mL of 0.5mg/mL 6-11 yrs: 2.5 mg once daily, 5mL of 0.5mg/mL (0.5 mg/mL $38 / 4oz) ≥ 12 yrs: 5 mg once daily	10 38 100 94	N/A N/A N/A N/A
Desloratadine and pseudoephedrine	Clarinex D-12 Clarinex D-24	1 tab q 12 hr (2.5-120 mg) 1 tab q 24 hr (5-240)	128 100	N/A N/A	≥ 12 yrs: 1 tab q 12 hrs (2.5-120mg) ≥ 12 yrs: 1 tab q 24 hrs (5-240mg)	65 100	N/A N/A

* Pricing information for brand products based on average wholesale price (AWP) – 10% found in the Amerisource Bergen 2/07 catalog. Pricing information for generic products is based on the Blue Cross Blue Shield Maximum Allowable Cost (MAC) price + $3 as posted on 1/07. EN=each nostril, MDA=Metered Dose Actuator

** Mometasone is the only nasal steroid with indication down to age 2, therefore, preferred in pediatric patients.

Table 6. Pharmacologic Therapy for Allergic Rhinitis, Continued (UMHS Preferred Agents in Bold)

Generic Name	Brand Name	Usual Adult Dose	30 Day Cost* Brand	30 Day Cost* Generic	Usual Pediatric Dose (syrup concentration if available)	30 Day Cost* Brand	30 Day Cost* Generic
Oral Antihistamines – 1st Generation (For use only in special circumstances as described)							
Chlorpheniramine	**Chlor-Trimeton** Various	4–12 mg hs or 2–12 mg 2x/day	9-20	1-5	≥ 12 yrs: 4 mg q 4-6 hr or SR 12 mg q 12 hrs, max 24 mg daily 6 to 11 yrs: 2 mg q 4-6 hr, (2mg/5mL $6 /4 oz), max 12 mg daily 2 to 5 yrs: 1 mg q 4-6 hr, (2mg/5mL $6 / 4 oz)	9-20 5-17 5-10	1-5 1-3 1-3
Clemastine OTC	Tavist-1	1.34 mg 2x/day	23	15	6 to 11 yrs: as fumarate 0.67-1.34 mg BID (0.67 mg/5mL $10 / 4oz)	N/A	6
Pseudoephedrine	Various	30 - 60 mg q 4–6 h 120 mg as extended release tab q 12 h	20-40 26	7-14 18	≥ 12 yrs: 60 mg q 6 hrs, SR 120 mg q 12 hrs or 240 mg once daily, max 240 mg daily 6 to 12 yrs: 30 mg q 6 hrs 2 to 5 yrs: 15 mg q 6 hrs (30 mg/5ml $5/4 oz; 15 mg/5 ml)	20 9 N/A	7 4 5
Leukotriene Inhibitors							
Montelukast	Singulair	10 mg hs	103	N/A	1 to 5 yrs: 4 mg hs 6 to 14 yrs: 5 mg hs > 14 yrs: 10 mg hs	103 103 103	N/A N/A N/A
Intranasal Antihistamine							
Azelastine nasal spray	Astelin	1–2 sprays EN 2x/day	23-37	N/A	5 to 11 yrs: 1 spray EN 2x/day ≥ 12 yrs: 1-2 sprays EN 2x/day	13 23-37	N/A N/A
Intranasal Mast Cell Stabilizers							
Cromolyn sodium	Nasalcrom	1 spray EN 3–6x/day	8-13	8-13	≥ 2 yrs: 1 spray EN 3-6 x/day	8-13	8-13
Intranasal Anticholinergic							
Ipratropium bromide	Atrovent 0.3% Atrovent 0.6%	0.03% solution, 2 sprays EN 2-3x/day 0.06% solution, 2 sprays EN 4x/day for up to 3 weeks	22-66 112	N/A N/A	≥ 6 yrs: 0.03% solution, 2 sprays EN 2-3x/day ≥ 5 yrs: 0.06% solution, 2 sprays EN 4x/day for up to 3 weeks	22-66 112	N/A N/A
Ocular Antihistamines							
Azelastine	Optivar	1 drop affected eye(s) up to 2x/day max 8 weeks	83	N/A	≥ 3 yrs: 1 drop affected eye(s) up to 2x/day max 8 weeks	83	N/A
Olopatadine	Patanol	1-2 drops in affected eye(s) 2x day every 6-8 hrs max 6 wks	82	N/A	≥ 3 yrs: 1-2 drops in affected eye(s) 2x/day at interval of 6-8 hrs for up to 6 weeks	82	N/A
Ketotifen	Zaditor	1 drop affected eye(s) up to 2x/day for up to 8 weeks	69	15	≥ 3 yrs: 1 drop affected eye(s) up to 2x/day max 8 weeks	69	15
Ocular Mast Cell Stabilizers							
Lodoxamide tromethamine	Alomide	1-2 drops in affected eye(s) 4x/day	80	N/A	≥ 2 yrs: 1-2 drops in affected eye(s) 4x/day	80	N/A
Cromolyn	Opticrom	1-2 drops affected eye(s) 4-6x/day	N/A	18	≥ 4 yrs: 1-2 drops in affected eye(s) 4-6x/day	N/A	18
Nedocromil	Alocril	1-2 drops affected eye(s) 2x/day	84	N/A	≥ 3 yrs: 1-2 drops in affected eye(s) 2x/day	84	N/A

Table 7. Complications of Allergic Rhinitis

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

X = Possible; ? = Uncertain

Table 8. Possible Side Effects Associated with Medical Therapy for Allergic Rhinitis

Oral Antihistamines (1st generation)

Anticholinergic effects
- blurred vision
- dry mouth
- urinary retention

Central nervous system
- drowsiness (increased accidents)
- cognitive impairment (any age)

Gastrointestinal
- constipation
- GI upset
- nausea

Sensory
- taste: bitter taste, loss of taste

Oral Antihistamines (2nd generation)

General (rare)
- GI upset
- headache
- drowsiness (1-3%)
- myalgias

Intranasal Corticosteroids

Nasopharyngeal
- nasal irritation
- epistaxis
- pharyngitis, coughing
- septal perforation

Sensory
- smell: reduced sense of smell
- taste: unpleasant taste, loss of taste

Oral Decongestants

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

Leukotriene Inhibitors

General
- headache
- rash (uncommon)
- dream abnormalities
- gastritis, dyspepsia
- dental pain
- respiratory tract infections

Intranasal Mast Cell Stabilizers

Nasopharyngeal
- epistaxis, sneezing
- nasal irritation: burning, stinging

Sensory
- taste: unpleasant taste

Ocular Preparations
- headache
- ophthalmic irritation: burning, dryness, pruritus, stinging
- possible contact lens irritation (consult with eye care provider)

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 physician trained in using a well-controlled process and in interpreting results relevant to the patient.

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 IgE-antigen and mast cell mediated 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 10-30% 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 (especially the inferior turbinates), the nasal mucosa typically appears pale pink, swollen, and may have a bluish-gray tinge. Secretions in acute allergies may be thin and clear, but with chronic allergies may be thick and clear/white. There may be polypoid changes along the anterior end of the middle turbinate. 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), Dennie’s lines (an accentuated fold below the lower eyelid) 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, crossbite, narrow arched palate, and molar flattening.

Testing

Testing is not indicated in many allergic rhinitis cases. For other allergic symptoms 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, (b) to identify specific allergens that may cause symptoms, and (c) identify allergens for immunotherapy.

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. Intranasal corticosteroids, leukotriene inhibitors, decongestants, oral corticosteroids **do not** need to be stopped for skin testing. Patients who cannot stop their antihistamines because of symptoms should keep their appointment with the allergist.

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). Proper technique is 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. Nasal smears, although rarely performed, identify the presence of neutrophils and eosinophils, the latter of which suggests an allergic disease.

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 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). Removing the offending animal from the household is preferred. While significant cleaning measures are required to reduce cat and dog allergen levels to those found in environments not inhabited by cats or dogs, if the animal is still present, the effectiveness of cleaning is limited. Cleaning 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 un carpeted 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 intranasal corticosteroids and oral antihistamines.

Intranasal 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. Patient education for the correct use of intranasal pump sprays is essential. Intranasal corticosteroids do not treat ocular symptoms.

Intranasal 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 intranasal steroids, antihistamines appear to be equally effective in blocking histamine-mediated responses to allergens *[A*]*.

All antihistamines appear to be equally effective; however, first generation agents adversely affect cognition and performance *[A*]*. It is therefore recommended that therapy be initiated with generic loratadine, the only current OTC second generation agent. Some patients may get better symptom relief with cetirizine; however, it is more sedating than loratidine and requires a prescription. For patients that cannot afford OTC loratadine, generic, OTC, chlorpheniramine is inexpensive and effective. It is the least sedating of the 1st generation antihistamines; however, it must still be used with caution in patients requiring mental alertness in the workplace and in driving.

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 maintenance treatment of allergic rhinitis. They may be used short-term (3-5 days) for the severely congested patient to improve initial drug delivery with intranasal corticosteroids.

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; however, pseudoephedrine can be added as a separate agent in children as young as 2 years of age. The cautions enumerated above for decongestant use also apply to combination products.

Leukotriene inhibitors. Leukotriene inhibitors are the newest class of medications used for allergic rhinitis. They reduce allergy symptoms through inhibition of inflammation and also have proven efficacy for control of asthma. Several large studies have evaluated montelukast and have shown a reduction in itching, sneezing, rhinorrhea, and congestion. Efficacy appears comparable to oral antihistamines but studies demonstrate that inhaled corticosteroids have superior improvement in nasal obstructive symptoms compared to leukotriene inhibitors.

Combination therapy of leukotriene inhibitors and antihistamines improved intranasal symptom compared to monotherapy, but were again less effective when compared to inhaled nasal steroids alone *[A*]*. Leukotriene inhibitors may have a role as first line therapy in patients with comorbid persistent asthma to control both diseases and reduce medication costs.

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 or atrophic rhinitis (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. One therapeutic effect of the first generation antihistamines is related to their anticholinergic properties. Therefore newer, less-sedating antihistamines are less likely to produce this benefit.

Nasal Antihistamines. 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, intranasal antihistamines offer no therapeutic benefit over conventional treatment.

Ocular Medications. Ocular medications for allergic conjunctivitis are available as topical solutions or suspensions. They contain antihistamines or mast cell stabilizers. Side effects of ocular medications are generally mild and include a brief stinging, burning sensation. Ocular antihistamines can be used as needed for acute symptomatic relief and prophylaxis of allergic symptoms with minimal systemic side effects.

Sodium cromolyn has been shown to be effective for the treatment of seasonal allergic conjunctivitis and should be administered on a regular basis. Lodoxamide has been shown to be as effective as or more effective than sodium cromolyn in vernal conjunctivitis. Soft contact lens users and patients with sensitivities to certain preservatives should consult their eye care provider or refer to specific product information regarding the use of these products

Nasal saline. Saline sprays theoretically moisten the nasal cavity and promote mucociliary clearance. Saline solutions also contain magnesium, which possibly reduces inflammation in the nasal mucosa.

One small comparative study showed that intranasal hypertonic saline spray improved symptoms of allergic rhinitis, but saline was not as effective as intranasal corticosteroids. Therefore, saline solution can be an effective adjunctive medication for mild-to-moderate allergic rhinitis.

Immunotherapy. Allergen immunotherapy is the repeated administration of specific allergens to patients with IgE mediated conditions for the purpose of desensitizing them to the offending allergens. It is the only disease remitting agent available. Well controlled clinical trials have demonstrated its effectiveness for seasonal and perennial allergic rhinitis, seasonal asthma, and ocular allergy. It may prevent polysensitization to other allergens in children and prevent the development of asthma. No long term effects have been reported.

Omalizumab (Xolair). A recombinant DNA derived IgG1 monoclonal antibody that selectively binds to circulating IgE and limits the amount of IgE available to bind to FCR1 receptors on mast cells. This limits the release of mediators and modifies the allergic response. It decreases the number of FCR1 receptors on basophils. Studies in patients with allergic rhinitis have shown a decrease in mediators released, decrease in symptoms and need for rescue medication, and improved quality of life scores. Long term effects are not known. The drug is expensive and is currently not approved for use in clinical practice.

Surgical therapy. For patients who have persistent nasal obstruction after adequate trial of medical therapy (including or not including immunotherapy), referral to a surgical specialist should be considered for possible surgical reduction of the inferior turbinates, which has been demonstrated to lead to objective and subjective improvements in airflow symptoms *[B*]*.

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 seasonal or 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, nasal polyps, or ocular allergy.
- Persistent nasal obstruction despite medical therapy (surgical evaluation).
- 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. Second-generation, less-sedating, antihistamines should be used for school-age children. Intranasal corticosteroids, especially mometasone, have demonstrated an excellent safety profile in children with minimal systemic absorption and no evidence of growth retardation. *[A*]*

Pregnancy

Allergic rhinitis does not follow a predictable pattern during pregnancy; it may worsen, improve, or stay the same. Hormonal changes associated with pregnancy may exacerbate symptoms. Rising progesterone and estrogen levels may increase glandular secretions and vasodilation, and increased blood volume may cause nasal vascular pooling. In contrast, increased serum free cortisol during pregnancy could improve symptoms.

Medications should be prescribed during pregnancy when the apparent benefit of the drug outweighs the apparent risk. Agents used to treat allergic rhinitis in pregnancy are either category B (presumed safe based on animal studies, but without adequate data in humans), or category C (of uncertain safety, with no demonstrated adverse effects in animals or humans). If possible, medication should be avoided in the first trimester because of the potential risk of congenital malformations. In general, it is considered safe to continue immunotherapy during pregnancy.

For mild to moderate nasal symptoms of allergic rhinitis, nasal saline irrigation is safe and effective. Providers could also choose intranasal cromolyn (category B) but this is not as effective as intranasal corticosteroids. For more severe or persistent symptoms, intranasal budesonide (category B) can be prescribed; all other intranasal corticosteroids are rated category C. A recent study showed no increased risk of adverse fetal outcomes with maternal exposure to inhaled budesonide, and intranasal budesonide should be at least as safe because of the lower systemic exposure.

If prescribing an oral antihistamine, the provider should choose either:

- first-generation antihistamine chlorpheniramine (category B) or
- second-generation agents, loratadine or cetirizine (both category B).

Severe Asthmatics

Rhinosinusitis can exacerbate asthma. However, desensitization generally does not improve asthma control for most patients, but may have some benefit for a subset of selected patient with extrinsic (allergic) asthma. Consider referral if rhinitis or asthma is poorly controlled.

Severe Atopic Dermatitis Patients

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

Complementary and Alternative Medicine

Complementary and alternative medicine (CAM) is widely practice by patients to treat allergic rhinitis. Many patients that use CAM report improvement in symptoms. However, no evidence definitively supports the efficacy of CAM in the treatment of allergic rhinitis. In addition, CAM may have side effects and some of the medications used may interact with other drugs.

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 update began with the results of the literature search performed for the 2002 version of this guideline. A search for literature published since that time was performed. The search on Medline was conducted prospectively for literature published from 1/1/99 to 7/31/06 using the major keywords of: *allergic rhinitis, human (adult and pediatric), English language, clinical guidelines, avoid, clinical trials-- phase IV, cohort studies, controlled clinical trials, multicenter studies, randomized controlled trials, observational trial, meta analysis.* Separate searches were performed for: *history ((inciting factors, seasonality, family history, severity & severity scoring), physical exam, signs, symptoms (nasal exam for changes in mucosa, conjunctival changes), laboratory (nasal smear for presence of eosinophyls, skin testing; avoid: RAST), Diagnosis – other references, avoid or control triggers, corticosteroids (intra-nasal, ocular), antihistamines (intra-nasal, oral, ocular), leukotriene inhibitors/modulators, decongestants (intra-nasal, ocular, oral), mast cell stabilizers (intra-nasal, ocular), non-steroidal anti-inflammatory (ocular), anticholinergics (intra-nasal), omalizumab, saline irrigation to remove allergens (nasal spray, eye wash), immunotherapy/allergy shots or inhaler, turbinate reduction surgery, integrative/*

alternative/ complementary medicine [9/1/05 – 7/31/06 only], pregnancy & lactation), treatment or management – other references.

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with recent clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was a single cycle. Conclusions were based on prospective randomized clinical trials if available, to the exclusion of other data; if RCTs were not available, observational studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

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.

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Annotated References

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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 immunodeficiency 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.