Chapter e14: Allergic Rhinitis

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CHAPTER SUMMARY FROM THE PHARMACOTHERAPY HANDBOOK

For the Chapter in the Schwinghammer Handbook, please go to Chapter 78, Allergic Rhinitis.

KEY CONCEPTS

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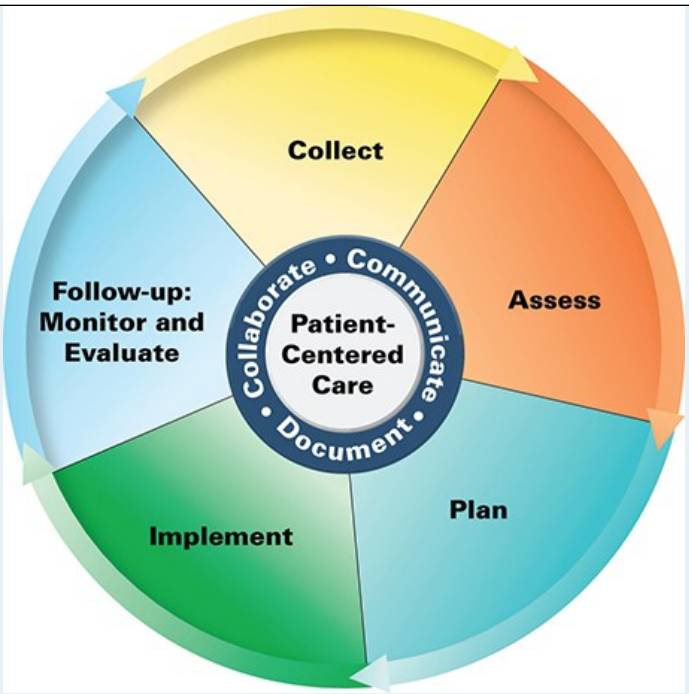
1. Allergic rhinitis is a common disease. Prevention measures and treatment are justified in most cases because of the potential for complications.
2. Because an immune response to allergens results in release of inflammatory mediators that cause allergic rhinitis symptoms, patients must understand the rationale for proper timing and administration of prophylactic regimens.
3. Avoidance of allergens is difficult and it may be impractical to expect full success.
4. Antihistamines offer an effective option for treating both seasonal and persistent allergic rhinitis.
5. Intranasal steroids are highly effective in patients who use them properly.
6. While immunotherapy is the only disease-modifying treatment of allergic rhinitis, expense, potential risks, and the major time commitment required make patient selection critical.

PATIENT CARE PROCESS

Patient Care Process for Management of Allergic Rhinitis



Collect

- Primary complaint(s) (sneezing, clear rhinorrhea, postnasal drip, nasal congestion, ocular or otic symptoms, pruritic nose or palate)
- Patient characteristics (eg, age, race, sex, pregnant)
- Past medical history, allergy testing, medications
- Patient family, social history—dietary habits; presence of pets, mold, or wall-to-wall carpeting; times of year, situations, or locations (indoor or outdoor) when symptoms are worse
- Current over-the-counter (OTC) products, prescription medications, dietary supplements; past medications or interventions used for treating rhinitis symptoms
- Past or current use of environmental controls of potential allergens (eg, removal of carpeting or pets, air-filtration systems)
- Objective data
  - Presence of allergic “shiners” (dark circles under eyes) or “salute” (crease across nose caused by constant rubbing)
  - Labs when available (eg, immunoglobulin E [IgE], serum eosinophil count)
  - Other diagnostic tests when available (eg, allergy testing)

Assess

- Presence of concomitant atopic disorders (eg, asthma, atopic dermatitis)
- Presence of complications of allergic rhinitis (eg, acute otitis media, middle ear effusion, sinusitis, epistaxis)
- Timing of symptoms—seasonal or persistent (see Table e14-2)
- Usefulness for environmental controls of allergens (primarily for persistent cases)

- Which symptoms to control (eg, nasal congestion, clear rhinorrhea, sneezing, pruritus, ocular conjunctivitis)
- Current or past medications and patient response to those
- Appropriateness and effectiveness of current regimen

Plan*

- Nonpharmacologic interventions (eg, allergen avoidance, nasal rinses, nasal strips; see Table e14-3)
- Drug therapy regimen including specific agent(s), dose, route, frequency, and duration; specify the continuation and discontinuation of existing therapies (see Table e14-2 and Fig. e143-2)
- Patient education (eg, purpose of treatment, allergen avoidance, nonpharmacologic interventions, drug therapy, and the potential need for referral to physician or allergist for prescription or immunologic treatment).
- Self-monitoring of symptoms and adverse effects—where and how to record results
- Referrals to other providers when appropriate (eg, physician, allergist)

Implement*

- Provide patient education regarding all elements of treatment plan
- Use motivational interviewing and coaching strategies to maximize adherence
- Schedule follow-up if needed

Follow-up: Monitor and Evaluate

- Monitoring parameters including efficacy (eg, bothersome symptoms), safety (eg, drowsiness, anticholinergic effects, effects on blood pressure; medication-specific adverse effects [see Table e14-8])
- Patient perception of control of bothersome symptoms
- Presence of adverse effects
- Continued presence of physical signs of nasal and ocular pruritus
- Patient adherence to treatment plan using multiple sources of information
- Referrals to other providers when appropriate (eg, physician, allergist)

**Collaborate with patient, caregivers, and other healthcare professionals.*

BEYOND THE BOOK

Review the patient monitoring recommendations for the most common allergic rhinitis pharmacotherapy options (antihistamines, intranasal steroids, topical and systemic decongestants, mast cell stabilizers, and leukotriene receptor antagonists) in a standard drug information compendium (eg, Facts & Comparisons). This activity is useful to enhance student understanding of the PLAN step in the patient care process.

INTRODUCTION

Allergic rhinitis involves inflammation of the nasal mucous membrane. In a sensitized individual, allergic rhinitis occurs when inhaled allergenic particles contact mucous membranes and elicit a specific response mediated by immunoglobulin E (IgE). This acute response involves the release of inflammatory mediators and is characterized by sneezing, nasal itching, and watery rhinorrhea, often associated with nasal congestion. Itching of the throat, eyes, and ears frequently accompanies allergic rhinitis.

Allergic rhinitis may be regarded as seasonal allergic rhinitis, commonly known as *hay fever*, or persistent allergic rhinitis (formerly known as perennial rhinitis). Seasonal rhinitis occurs in response to specific allergens usually present at predictable times of the year, during plants' pollination (typically the spring or fall). Seasonal allergens include pollen from trees, grasses, and weeds. Persistent allergic rhinitis is a year-round disease caused by nonseasonal allergens, such as house dust mites, animal dander, and molds, or multiple allergic sensitivities. It typically results in less variable, chronic symptoms. Many patients have a combination of these two types of allergic rhinitis, with symptoms year-round and seasonal exacerbations.

EPIDEMIOLOGY AND ETIOLOGY

1 Allergic rhinitis is one of the most common diseases affecting adults and is the most common chronic disease in children in the United States, generating $2 to $5 billion in direct healthcare cost each year.[1] Prevalence rates are 14% in adults and 13% in children when using a physician-confirmed diagnosis.[2] Actual sensitization to inhaled allergens is likely higher and is increasing with estimates of 15% to 30% in the United States.[3] Patients may be limited in their ability to carry out normal daily functions; higher levels of general fatigue, mental fatigue, anxiety, depressive disorders, and learning disabilities (secondary to sleep loss and fatigue) are possible.

In addition, the impact of allergic rhinitis goes well beyond these CNS issues. Allergic rhinitis is associated with several other serious medical conditions, including asthma, chronic rhinosinusitis, otitis media, nasal polyposis, respiratory infections, and orthodontic malocclusions.

The development of allergic rhinitis is determined by genetics, allergen exposure, and the presence of other risk factors. A family history of allergic rhinitis, atopic dermatitis, or asthma suggests that rhinitis is allergic. The risk of developing allergic disease appears to increase if one parent is atopic and further increases if two are allergic; however, small sample sizes and the lack of reproducibility prevent generalization.[4]

Allergen exposure is another necessary factor. For allergic rhinitis to occur, an individual must be exposed over time to a protein that elicits the allergic response in that individual. Many potential sufferers never develop symptoms because they do not come into contact with the allergen that would produce symptoms in them.

Microbial exposure in the first years of life could help prevent allergic disease by stimulating a nonatopic immune response.[5] Farm children are exposed to higher concentrations of endotoxin, derived from cell walls of gram-negative bacteria, in barns and dust around the farmhouse. Consumption of nonpasteurized farm milk may cause further exposure. These observations have led to the idea that allergic disease could be prevented by proactively increasing exposure to harmless bacteria early in life (see section "Alternative Treatment Options" below). This could explain why positive skin tests indicating allergen sensitization have been observed more frequently for people in higher income groups and for people who live in suburban areas.

Other predisposing factors include an elevated serum IgE (>100 international units/mL [kIU/L]) before the age of 6 years, eczema, and heavy exposure to secondhand cigarette smoke.[6]

Allergens that produce seasonal rhinitis include protein components of airborne pollen grains, often enzymes, from a variety of trees, grasses, and weeds. Ragweed and grass pollen are the most common offenders in the United States; however, this varies with the geographic region. In general, tree pollens cause symptoms in the spring, grass pollens cause symptoms in the late spring and summer, and weed pollens are the culprits from late summer through fall. Patients who are hypersensitive to all three may have overlapping problem periods and may be described as having persistent rhinitis when they are actually experiencing prolonged seasonal rhinitis. For this reason and the fact that most patients with seasonal problems are sensitive to at least some of the perennial allergens, there is little practical difference between the two types of allergic rhinitis. To complicate matters further, the antigenic components of many grasses—including fescue, Kentucky bluegrass, orchard, redtop, and timothy—cross-react extensively. By contrast, most tree allergens are antigenically distinct. Trees with allergenic pollen include ash, beech, birch, cedar, hickory, maple, oak, poplar, and sycamore. Flowering plants that depend on insect pollination do not cause allergic rhinitis because their pollen is too heavy and sticky and is not carried in the air.

Smaller mold spores are also important but cause allergy much less frequently. Various spores are present year-round; however, mold growth on decaying vegetation increases seasonally. Just walking through uncut fields or raking leaves can increase exposure. Thus, mold spores can be responsible for both perennial and seasonal allergies.

Indoor allergens are always present. Most important among these are house-dust mite fecal proteins, animal dander, cockroaches, and certain mold species. Dust mite levels are on the rise, possibly because of the construction of energy-efficient homes and offices with reduced ventilation and increased humidity, use of wall-to-wall carpeting, and the popularity of cool-water detergents and cold-water washing.[4]

PHYSIOLOGY AND MECHANISMS OF DISEASE

Knowledge of nasal physiology aids in the understanding of allergic rhinitis. The nose performs three “air conditioning” functions to prepare incoming gases for the lungs. During the fraction of a second that air is in the nose, it is heated, humidified, and cleaned. The cleaning process plays a role in the development of allergic rhinitis. As the air passes through the nose, the turbulence throws particulate matter against a mucous blanket. The rhythmic movements of the nasal cilia cause the mucous blanket to move posteriorly at approximately 9 mm/min, where it is eventually swallowed; thus, trapped foreign particles are removed via the GI tract and do not reach the lungs. It also concentrates foreign protein material into the posterior nasopharynx, where lymph tissues identify them and produce most of the allergic antibody that drives allergic rhinitis.

The vascular tissue in the nose is erectile. Stimulation of sympathetic fibers causes vasoconstriction, reduction in erectile tissue size and the size of the membranes and turbinates, and airway widening. Parasympathetic stimulation causes opposite effects.

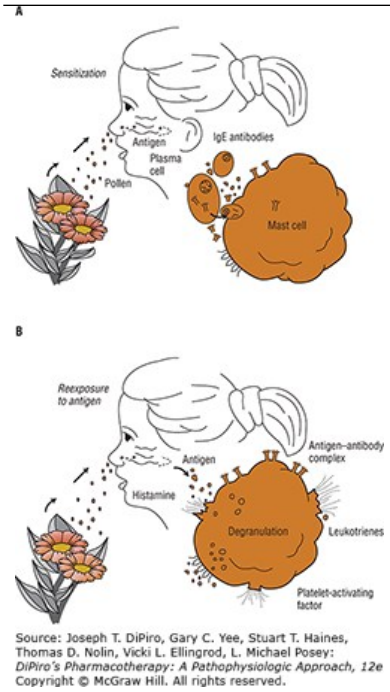
Mast cells, in the nasal membranes, participate in the regulation of nasal patency by releasing mediators such as histamine. These are described below.

Immune Response to Allergens

Allergic reactions in the nose are mediated by antigen–antibody responses when allergens interact with specific IgE molecules bound to nasal mast cells and basophils. In allergic people, these cells are increased in both number and reactivity. During inhalation, airborne allergens enter the nose and are processed by lymphocytes, which produce antigen-specific IgE, thereby sensitizing genetically predisposed hosts to those agents. Upon nasal reexposure, IgE bound to mast cells interacts with airborne allergen, triggering release of inflammatory mediators in vastly increased quantities (Fig. e14-1).[7]

FIGURE e14-1

Allergen sensitization and the allergic response. (*A*) exposure to antigen stimulates IgE production and sensitization of mast cells with antigen-specific antibodies. (*B*) Subsequent exposure to the same antigen produces an allergic reaction when mast cell mediators are released.



Source: Joseph T. DiPiro, Gary C. Yee, Stuart T. Haines, Thomas D. Nolin, Vicki L. Ellingrod, L. Michael Posey: *DiPiro's Pharmacotherapy: A Pathophysiologic Approach, 12e*

Both immediate- and late-phase reactions are observed after allergen exposure. The immediate reaction occurs within seconds to minutes, resulting in the rapid release of preformed mediators and newly generated mediators from the arachidonic acid cascade as the mast cell membrane is disturbed (Table e14-1). These mediators of immediate hypersensitivity include histamine, some leukotrienes, prostaglandin D_2, tryptase, and kinins.[7] In addition, the mast cell has been found to be a source of several cytokines that probably are relevant to the chronicity of the mucosal inflammation that characterizes allergic rhinitis.[8] Sensory nerve stimulation produces itching, and sneezing occurs via reflex stimulation of efferent vagal pathways. Neuropeptides substance P and calcitonin gene-related peptide from nonandrenergic, noncholinergic nerves affect vascular engorgement directly and via modulation of sympathetic tone. Histamine produces rhinorrhea, itching, sneezing, and obstruction, with the obstruction only partially blocked by H_1- or H_2-blocking agents.[9] Nasal obstruction is also caused by kinins, prostaglandin D_2, and leukotrienes C_4/D_4. Kinins, when directly administered, produce pain rather than itching.[10] These inflammatory mediators also produce vasodilation, increased vascular permeability, and production of increased nasal secretions.[11]

TABLE e14-1

Mast Cell Mediators

Mediators	Effects
Preformed and rapidly released histamine	Stimulates irritant receptors
	Pruritus
	Increased vascular permeability
	Increased mucosal permeability
	Smooth muscle contraction
Neutrophil chemotactic factor	Influx of inflammatory cells
Eosinophil chemotactic factor	Influx of inflammatory cells

Kinins	Increased vascular permeability
N-α-tosyl L-arginine methyl esterase	Increased vascular permeability
Newly generated	
Leukotrienes	Smooth muscle contraction
	Increased vascular permeability
	Mucus secretion
	Chemotaxis
	Neutrophil chemotaxis
Thromboxanes	Smooth muscle spasm
Platelet-activating factor	Mucus secretion
	Increased airway permeability
	Chemotaxis
	Increased vascular permeability
Granule matrix contents	
Heparin	Anti-inflammatory
Tryptase	Protein hydrolysis
Kallikrein	Protein hydrolysis

Four to eight hours after the initial exposure to an allergen, a late-phase reaction occurs symptomatically in 50% of allergic rhinitis patients.[12] This response, thought to be caused by cytokines released primarily by mast cells and thymus-derived helper lymphocytes, is characterized by profound infiltration and activation of migrating cells. This inflammatory response likely is responsible for the persistent, chronic symptoms of allergic rhinitis, including nasal congestion. The inflamed mucosa becomes hyper-responsive, a state characterized by exacerbation of nasal reactions to nonspecific or irritant triggers. In this state, the patient also reacts to increasingly lower amounts of the same allergen.[13] The process also causes significant increases in nonspecific irritability (as seen in asthma) and the notion among patients that they have become “allergic to everything.”

PATIENT CARE PROCESS

Collect Information

The patient with allergic rhinitis typically complains of clear rhinorrhea, paroxysms of sneezing, nasal congestion, postnasal drip, and pruritic eyes, ears, nose, or palate. Symptoms of allergic conjunctivitis are associated more frequently with seasonal than persistent allergic rhinitis, because a majority of the perennial allergens, such as dust mites and molds, are indoors, where air velocity is too low for substantial deposition of allergenic

particles on the conjunctivae. However, with heavy exposure from animal or mold allergens, allergic conjunctivitis can be pronounced.

Symptoms secondary to the late-phase reaction, predominantly nasal congestion, begin 3 to 5 hours after antigen exposure and peak at 12 to 24 hours. Subsequent symptoms, both allergic and irritant, are elicited more easily because of the priming effect. For instance, a ragweed-sensitive patient, when exposed to ragweed pollen out of season, responds with modest symptoms and may be very tolerant of irritants such as air pollution or tobacco smoke. During the ragweed season, however, when the nasal mucosa is already inflamed, exposure to small doses of pollen or to irritants to which the patient is usually tolerant elicits a response clinically indistinguishable from the patient's allergy.

Assess the Patient

Allergic rhinitis is distinguished from other causes of rhinitis by a thorough history, physical examination, and certain diagnostic tests. The medical history consists of a careful description of symptoms, environmental factors and exposures, results of previous therapy, use of other medications, previous nasal injuries, previous nasal or sinus surgery, family history, and the presence of other medical problems and medications. Historical identification of specific causative allergens may be difficult. For example, a reaction induced by mowing the lawn may not be caused by grass pollens but may be caused by the disturbance of various weeds, molds, or other plants in the lawn. With perennial allergic rhinitis, the cause-effect and temporal relationships are less clear, making the diagnosis of specific causes more difficult, especially with such covert allergens as house dust mites and molds.

In children, physical examination may reveal allergic shiners—a transverse nasal crease caused by repeated rubbing of the nose—and adenoidal breathing. Pale, bluish, edematous nasal turbinates coated with thin, clear secretions are characteristic of a purely allergic reaction. Tearing, conjunctival injection and edema, and periorbital swelling may be present. Physical findings are generally less clear-cut for adults.

Allergy testing can help determine whether a patient's rhinitis is caused by an allergen. Immediate-type hypersensitivity skin tests are used for the diagnosis of allergic rhinitis. These include skin tests performed by the percutaneous route, where the diluted allergen is pricked or scratched into the skin surface, or by the intradermal route, where a small volume (0.01-0.05 mL) of diluted allergen is injected between the layers of skin. Percutaneous tests are more commonly performed and are safer and more generally accepted, with intradermal tests reserved for patients requiring confirmation in special circumstances.

In all allergy testing, a positive control (histamine) and a negative control are essential for correct interpretation. After 15 minutes of the application of the allergen, the site is examined for a positive reaction (defined as a wheal-and-flare reaction). Because correct testing is done with extremely minute doses, undetectable by nonsensitized individuals, this reaction is evidence of the presence of mast cell–bound IgE specific to the allergen tested. Many, but not all, common allergens are available as standardized allergenic extracts.

Antihistamines and a few other medications interfere with the wheal-and-flare reaction. First-generation antihistamines should be stopped at least 3 to 5 days before testing, and second-generation, nonsedating antihistamines should be stopped at least 7 days before testing.[14] Medications with antihistamine properties (eg, sympathomimetic agents, phenothiazines, and tricyclic antidepressants) should be discontinued if possible before skin testing. The patient's physician should be contacted before stopping any prescription medications.

The radioallergosorbent test (RAST) was the first commonly used method for detecting IgE antibodies in the blood that are specific for a given allergen. Several other quantitative assays that include a reference curve calculated against standardized IgE are available. These tests are highly specific but may be slightly less sensitive than percutaneous tests.

Complications

Not only is allergic rhinitis aggravating, it frequently leads to further complications, particularly if the patient does not receive adequate treatment. Symptoms of untreated rhinitis may lead to disturbed sleep, chronic malaise, fatigue, and poor work or school performance. Patients often are plagued by loss of smell or taste, with sinusitis or polyps underlying many cases of allergy-related hyposmia. Postnasal drip with cough, hoarseness, and even vocal polyps also can be bothersome.

The role of allergic rhinitis in the development of acute otitis media or chronic middle ear effusion is often less clear. Children with allergic rhinitis appear to be at greater risk of these conditions because of nasal obstruction and negative middle ear pressure. Hearing problems in children related to middle ear effusion may lead to delayed development of language in young children or to school problems in older children.

Permanent facial disfigurement can result from chronic allergic rhinitis.[15,16] The chronic edema and venous stasis may contribute to the development of a high-arched, V-shaped palate. Mouth breathing caused by nasal obstruction can be responsible for dental malocclusion and orthodontic problems. Constant upward rubbing of the nose (allergic salute) can cause a transverse crease across the lower nose; nasal congestion often leads to venous pooling and dark circles under the eyes known as *allergic shiners*.

Allergic rhinitis is clearly associated with asthma. The prevalence of asthma in patients without rhinitis is less than 2%, while the prevalence of asthma in patients with rhinitis is 10% to 40%. It is not known if allergic rhinitis is an early clinical manifestation of asthma or if the nasal disease itself is causative for asthma.

Recurrent sinusitis and chronic sinusitis are relatively common complications of allergic rhinitis. The structure of the mucus blanket breaks down, with decreased water production by serous glands, leaving hair cells trapped in the thicker mucus layer. This greatly reduces the clearance of trapped bacteria and offers ideal breeding grounds for the bacteria. Nasal polyps are less common but nonetheless bothersome; they require specific therapy but may improve with management of the underlying allergic state. Epistaxis also can be a problem; it is related to mucosal hyperemia and inflammation.

Plan for Treatment or Referral

A number of options exist for the treatment of allergic rhinitis, both nonpharmacologic and pharmacologic. Many of the pharmacologic options are available OTC requiring that patients receive guidance in the selection process by a healthcare professional to obtain the most appropriate therapy. Both OTC and prescription choices must be guided by patient-specific symptomatology and patient characteristics as described in this chapter.

The therapeutic goal for patients with allergic rhinitis is to minimize or prevent symptoms and prevent long-term complications. This goal should be accomplished with no or minimal adverse medication effects and reasonable medication expenses. The patient should be able to maintain a normal lifestyle, including participating in outdoor activities, yard work, and playing with pets as desired.

General Approach to Treatment

Once the causative allergens and the specific symptoms are identified, management consists of three possible approaches: (a) allergen avoidance, (b) pharmacotherapy for prevention or treatment of symptoms, and (c) specific immunotherapy. The pharmacotherapy for symptoms approach includes several options that are based on patient-specific information (Table e14-2). Figure e14-2 depicts an algorithm for treatment options.

FIGURE e14-2

Treatment algorithm for allergic rhinitis.

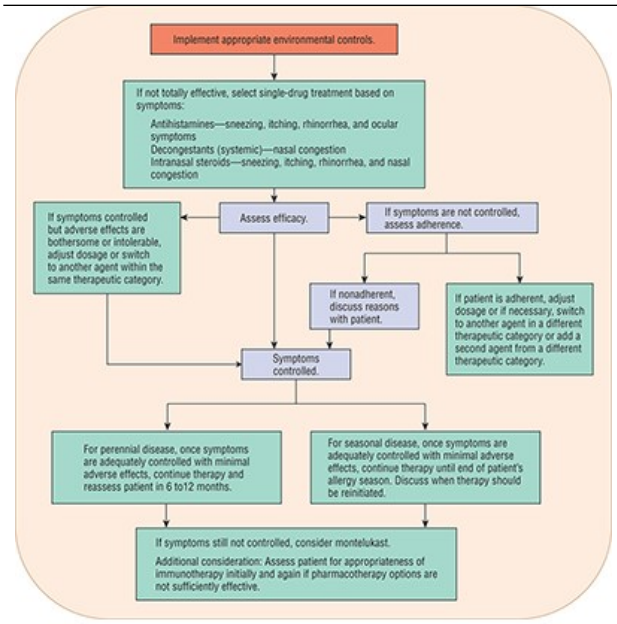


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TABLE e14-2

Pharmacotherapeutic Options for Allergic Rhinitis

Medication Classes	Symptoms Controlled	Comments
Antihistamines		
Systemic	Sneezing, rhinorrhea, itching, conjunctivitis	For seasonal allergic rhinitis, begin treatment before allergen exposure. Nonsedating agents should be tried first. If ineffective or too expensive for the patient, the older agents may be used. For perennial allergic rhinitis, use an intranasal steroid as an alternative to or in combination with systemic antihistamines
Ophthalmic	Conjunctivitis	Logical addition to nasal steroids if ocular symptoms are present
Intranasal	Sneezing, rhinorrhea, nasal pruritus	Option for seasonal allergic rhinitis. Warn patients of potential drowsiness
Decongestants		
Systemic	Nasal congestion	Only needed when nasal congestion is present
Topical	Nasal congestion	Only needed when nasal congestion is present. Do not exceed 3-5 days
Intranasal corticosteroids	Sneezing, rhinorrhea, itching, nasal congestion	For seasonal allergic rhinitis, an option when congestion is present. Must begin therapy before allergen exposure. Excellent choice for persistent allergic rhinitis
Mast cell stabilizers	See comments	Prevents symptoms; therefore, for seasonal allergic rhinitis, use before offending allergen's season starts. For persistent allergic rhinitis, improvement may not be seen for up to 1 month
Intranasal anticholinergics	Rhinorrhea	Reserve for use when above therapies fail or cannot be tolerated
Leukotriene receptor antagonists	See comments	When combined with antihistamines, more effective than antihistamines alone. May be used as monotherapy in children with asthma and coexisting allergic rhinitis

Nonpharmacologic Therapy

3 Avoidance of offending allergens is the most direct method of preventing allergic rhinitis, but it is often the most difficult to accomplish, especially for perennial allergens. Mold growth can be reduced by maintaining household humidity below 50% and removing obvious growth with bleach or disinfectant. Patients sensitive to animals will benefit most by removing pets from the home.[17] However, most animal lovers are reluctant to comply with this approach. Dog and cat allergens may produce symptoms in sensitized individuals.[8] After removing a cat from the home, it may take as long as

20 weeks for the home to reach allergen levels of a pet-free home. Washing cats weekly may reduce allergens but studies are inconclusive.[7] Some dogs display antigens more profusely than do others; clinically, a sensitized person may tolerate one animal better than another.

Evidence to support avoidance measures for house dust mites suggests that accepted notions for reducing exposure have little practical effect.[17] While some evidence shows allergen levels can be reduced by washing bedding on a hot cycle, replacing carpets with hard flooring and using vacuum cleaners with HEPA filters, there is no documented evidence for a clinical benefit. Only encasing bedding in impermeable covers has some clinical benefit in children but not adults. Future studies are needed to determine if environmental control of allergens may be helpful in forestalling further rhinitis and preventing later asthma.

General recommendations have been made to prevent poor air quality in homes.[18] Steps include avoiding wall-to-wall carpeting, using moisture control to prevent the accumulation of molds, and controlling sources of pollution such as cigarette smoke. Patients with seasonal allergic rhinitis should keep windows closed and minimize time spent outdoors during pollen seasons. Immediate hair washing and change of clothes are recommended upon returning indoors. Use of fans that direct outside air into the house should be avoided. Filter masks can be worn while gardening or mowing the lawn. Avoidance of upholstery and stuffed toys in the bedroom are easy steps to accomplish.

A couple of nonpharmacologic options available OTC can prove useful. Nasal saline irrigations represent a well-tolerated, inexpensive, and safe nonpharmacologic option for allergic rhinitis. Improvement in nasal symptoms and a reduction in medicine consumption have been demonstrated.[19] Adhesive nasal strips can facilitate breathing and can reduce nasal obstruction.[20]

Table e14-3 summarizes recommendations for environmental control and other nonpharmacologic options. These measures are intended to be a part of a comprehensive treatment strategy that will likely include pharmacotherapy and, in selected cases, immunotherapy.

TABLE e14-3

Nonpharmacologic Options for Allergic Rhinitis

Avoidance
Pollens • Keep windows and doors closed during pollen season • Avoid fans that draw in outside air • Use air conditioning • If possible, eliminate outside activities during times of high pollen counts • Shower, shampoo, and change clothes following outdoor activity • Use a vented dryer rather than an outside clothesline
Molds • Use similar controls as above • Avoid walking through uncut fields, working with compost or dry soil, and raking leaves • Clean indoor moldy surfaces • Fix all water leaks in home • Reduce indoor humidity to <50% if possible
House dust mites • Encase mattress, pillow, and box springs in an allergen-impermeable cover • Wash bedding in hot water weekly • Remove stuffed toys from bedroom • Minimize carpet use and upholstered furniture • Reduce indoor humidity to <50%, if possible

Animal allergens (if removal of pet is not acceptable) • Keep pet out of patient's bedroom • Isolate pet from carpet and upholstered furniture • Wash pet weekly
Cockroaches • Keep food and garbage in tightly closed containers • Take out garbage regularly • Clean up dirty dishes promptly • Use roach traps
Other recommendations • Do not allow smoking around the patient, in the patient's house, or in the family car • Minimize the use of wood-burning stoves and fireplaces
Over-the-counter options
Saline Rinses • Products include sodium chloride packets that are placed in containers or squeeze bottles and diluted then used to irrigate the nasal passages and sinuses.
Nasal Strips • Adhesive strips used externally on the nose to widen the nasal passages

Data from References 4, 19, and 20.

Pharmacologic Therapy

Table e14-4 summarizes the guidelines for treatment of allergic rhinitis with levels of evidence for each treatment strategy.[1,21] Therapeutic modalities for treating allergic rhinitis are generally directed at relief of symptoms as previously described in Table e14-2. Historically, antihistamines and decongestants (both oral and topical) were generally used first in treating allergic rhinitis with medications. Several options in these two categories are available without a prescription, but patients will need sound advice to make appropriate choices. Knowledge of pathophysiology, the inflammatory state, and analysis of published evidence has led to moving intranasal steroids to an option for first-line therapy. Several products are available OTC. Patients should receive counseling on the use of intranasal steroids to maximize their effects as described in the below Implement section.

TABLE e14-4

Evidence-Based Treatment Recommendations for Allergic Rhinitis

Recommendation	Level of Evidence[a]
Environmental factors	B
• Avoidance of known allergens	

• Environmental controls (removal of pets, air filters)	
• May consider this approach as optional	
Note: Even though good evidence exists, this may be hard to achieve.	
See text for limitations of this approach.	
Nasal steroids	A
• Benefits include symptom control, improved quality of life, better sleep, cost-saving if used as monotherapy, targeted local effect. Patient preference will play a large role.	
Oral antihistamines	A
• Second-generation (nonsedating) agents should be used in patients with primary complaints of sneezing and itching. Relief of eye symptoms, OTC status, and the availability of lower cost generics may be advantages.	
Intranasal antihistamines	A
• Evidence is strong but studies were of short duration. May consider these agents as optional.	
Oral leukotriene receptor antagonists	D
• For initial treatment of seasonal allergic rhinitis in patients >15 years, an intranasal steroid should be recommended over this class. (strong recommendation).	
• Clinicians should not recommend these agents as primary therapy for allergic rhinitis.	
• Patients with allergic rhinitis and asthma may benefit from this therapy.	
Combination therapy	Variable
• Oral antihistamines and oral decongestants: Several studies show benefit but must be weighed against potential risks: increased insomnia, headache, dry mouth, nervousness, and increased blood pressure. Tolerance may develop with long-term use of oral decongestants.	
• Oral antihistamines and intranasal steroids: No evidence to support the combination. For initial treatment of seasonal allergic rhinitis, monotherapy with an intranasal steroid rather than a combination should be used (strong recommendation).	
• Intranasal steroids and intranasal antihistamines: For patients who tolerate a nasal agent but have inadequate control of symptoms with a single agent, this combination is an effective option.	

• Intranasal steroids and topical decongestants: Combination more effective than intranasal therapy alone; however, see text regarding risk of rhinitis medicamentosa.	
Immunotherapy	
• Recommended in patients who have inadequate response to with pharmacologic therapy with or without environmental controls	A
• See text for information on sublingual versus subcutaneous therapy	

[a]Levels of evidence: A, a strong recommendation or recommendation based on excellent evidence where benefits clearly outweigh harms. B, a strong recommendation or recommendation based on good evidence that benefits outweigh harms. C, recommendation where evidence is not as strong or high-quality evidence is impossible to obtain. D, an optional therapy for some patients but quality of evidence is suspect, or no recommendation because there is a lack of pertinent evidence and an unclear balance between benefits and harm. For each level of evidence, see comments for further clarification of recommendations.

TABLE e14-5

Relative Adverse-Effect Profiles of Antihistamines

Medications	Relative Sedative Effects	Relative Anticholinergic Effects
Alkylamine class, nonselective		
Brompheniramine maleate	Low	Moderate
Chlorpheniramine maleate	Low	Moderate
Dexchlorpheniramine maleate	Low	Moderate
Ethanolamine class, nonselective		
Carbinoxamine maleate	High	High
Clemastine fumarate	Moderate	High
Diphenhydramine hydrochloride	High	High
Phenothiazine class, nonselective		
Promethazine hydrochloride	High	High
Piperidine class, nonselective		
Cyproheptadine hydrochloride	Low	Moderate
Phthalazinone class, peripherally selective		
Azelastine (nasal only)	Low to none	Low to none
Bepotastine (ophthalmic only)	Low to none	Low to none
Piperazine class, peripherally selective		
Cetirizine	Low to moderate	Low to none
Levocetirizine	Low to moderate	Low to none
Piperidine class, peripherally selective		
Desloratadine	Low to none	Low to none
Fexofenadine	Low to none	Low to none
Loratadine	Low to none	Low to none
Olopatadine (nasal only)	Low to none	Low to none

Antihistamines

4 Antihistamines are much more effective in preventing the actions of histamines and essentially do not reverse these actions once they have taken place. Reversal of symptoms is largely caused by the anticholinergic properties of these drugs. This activity is responsible for the drying effect of antihistamines, which reduces the problem of nasal, salivary, and lacrimal gland hypersecretion. Antihistamines antagonize increased capillary permeability, wheal-and-flare formation, and itching.

In general, the antihistamines are well absorbed, have large volumes of distribution, and are metabolized by the liver. Serum half-lives vary considerably between patients. In addition, the therapeutic effects of these agents are more prolonged than might be predicted by their half-lives.

Drowsiness is usually the chief complaint of patients who take antihistamines. It can interfere with a patient's ability to drive a car or operate machinery and may interfere with the patient's ability to function adequately at the workplace. Remember that these problems can also be a reflection of the disease itself. For this reason, many recommend the use of peripherally selective agents as first-line treatment for any patient who is at high risk for the development of adverse events. This includes patients with renal or hepatic impairment, those with small weights (for whom adult doses may provide larger-than-recommended doses on a milligram-per-kilogram basis), patients with preexisting CNS or cardiac disorders, patients who require higher doses, and patients who have shown a tendency to overuse nonprescription or prescription medications (Table e14-5).[22]

The sedative effects of antihistamines can be useful for patients who suffer from sleeplessness caused by the symptoms of allergic rhinitis. In these patients, a bedtime dose may prove beneficial. However, they may cause residual daytime sedation, decreased alertness, and performance impairment.

The logic of preferentially using the second-generation agents is not clear-cut. A meta-analysis of performance-impairment trials did not show a clear and consistent distinction between diphenhydramine and the peripherally selective agents.[23] Another study showed that tolerance to sedation secondary to diphenhydramine developed by day 4 of treatment, becoming indistinguishable from placebo,[24] but sedation must be distinguished from impairment since the two are not equivalent. Despite this evidence, guidelines recommend the nonsedating agents.[1,17]

Anticholinergic (drying) effects contribute to the agents' therapeutic efficacy, but they also cause most adverse effects. Dry mouth, difficulty in voiding urine, constipation, and potential cardiovascular effects may be troublesome. Keep in mind that the differences may be small. Patients with a predisposition to urinary retention (eg, older men and those on concurrent anticholinergic therapy) should use antihistamines with caution. Caution also should be used for patients with increased intraocular pressure, hyperthyroidism, and cardiovascular disease.

Other adverse effects of oral antihistamines include loss of appetite (and paradoxically, weight gain with increased appetite), nausea, vomiting, and epigastric distress.

Antihistamines are only fully effective when taken approximately 1 to 2 hours before anticipated exposure to the offending allergen. This must be discussed with patients who face exposure daily during a pollen season and with those who have indoor perennial allergens where daily scheduled use is necessary. If tolerance develops to the therapeutic effect, a change to an agent in a different chemical class is usually effective.

Patients should be counseled about the proper use of antihistamines. Adverse effects, especially drowsiness, should be emphasized. Patients should be warned against taking other CNS depressants, including the use of alcohol. Patients should be told not to take a double dose when a dose is missed. Taking the antihistamine with meals or at least a full glass of water will help prevent GI adverse effects such as nausea, vomiting, and epigastric distress. Patients should check with their healthcare professional and read labels before taking nonprescription medications. Many cold products and sleep aids contain antihistamines. Patients should be instructed not to use more than one antihistamine at a time. Table e14-6 lists the recommended dosages of the commonly used agents with their availability status (prescription only vs OTC).

TABLE e14-6

Medication Dosing for Allergic Rhinitis

Drugs	Dosages	Comments
Antihistamines		
Oral, nonselective		

Chlorpheniramine	*Adolescents and adults (>12 years)*	
	4 mg every 6 hours (plain)	OTC, available as liquid
	12 mg every 12 hours (extended release)	OTC
	Pediatrics	
	2-5 years: 1 mg every 4-6 hours	
	6-11 years: 2 mg every 4-6 hours	
Diphenhydramine	*Adolescents and adults (>12 years)*	
	25-50 mg every 4-6 hours	OTC, available as liquid
	(max = 300 mg daily)	
	Pediatrics (6-11 years only)	
	12.5-25 mg every 4-6 hours (max = 150 mg daily)	
Oral, peripherally selective		
Cetirizine	*Adolescents and adults (>12 years)*	
	5-10 mg once daily	OTC, available as liquid
	Pediatrics	
	6 months to 5 years: 2.5 mg daily	
	6 years to 11 years: 5-10 mg daily	
Fexofenadine	*Adolescents and adults (>12 years)*	
	60 mg every 12 hours or 180 mg once daily	OTC, available as liquid
	Pediatrics	
	2-11 years: 30 mg twice daily	
Levocetirizine	*Adolescents and adults (>12 years)*	
	5 mg once daily (in the evening)	Rx, available as liquid
	Pediatrics	
	6 months to 5 years: 1.25 mg daily (in the evening)	
	6-11 years: 2.5 mg daily (in the evening)	

Loratadine	*Adolescents and adults (>12 years)*	
	10 mg once daily	OTC, available as liquid
	Pediatrics	
	2-5 years: 5 mg daily	
	6 years and older: 10 mg once daily or 5 mg twice daily	
Intranasal	Note: dose is per each nostril	
Azelastine	*Adolescents and adults (>12 years)*	
	1-2 sprays once or twice daily (depending on brand)	Rx
	Pediatrics	
	6 months to 11 years: 1 spray twice daily	
Olopatadine	*Adolescents and adults (>12 years)*	
	2 sprays twice daily	Rx
	Pediatrics	
	6-11 years: 1 spray twice daily	
Ophthalmic		
Bepotastine	*Adolescents and adults (>12 years)*	
	1 drop to affected eye(s) twice daily	Rx
	Pediatrics	
	2-11 years: 1 drop to affected eye(s) twice daily	
Decongestants		
Oral		
Pseudoephedrine	*Adolescents and adults (>12 years)*	
	60 mg every 4-6 hours	OTC, available as liquid
	120 mg every 12 hours (sustained release)	
	240 mg every 24 hours (controlled release)	
	Pediatrics	

	2-5 years: 15 mg every 4-6 hours	
	6-11 years: 30 mg every 4-6 hours	
Phenylephrine	*Adolescents and adults (>12 years)*	
	10-20 mg every 4 hours	OTC, available as liquid
	Pediatrics	
	2-5 years: 2.5 mg every 4 hours	
	6-11 years: 5 mg every 4 hours	
Nasal	Note: dose is per each nostril	
Oxymetazoline	*Adolescents and adults (>12 years)*	
	2-3 sprays, twice daily (max = 3 days)	OTC
	Pediatrics	
	6–11 years: same as adult dose (max = 3 days)	
Phenylephrine	*Adolescents and adults (>12 years)*	
	2-3 sprays every 4 hours (max 3 days), 0.25%-1%	OTC
	Pediatrics	
	2-5 years: 2-3 sprays every 4 hours (max 3 days), 0.125%	
	6-11 years: 2-3 sprays every 4 hours (max 3 days), 0.25%	
Intranasal Steroids	Note: dose is per each nostril	
Beclomethasone	*Adolescents and adults* (>12 years)	
	42-84 mcg twice daily (42 mcg/spray)	Rx
	160 mcg once daily (80 mcg/spray)	
	Pediatrics	
	6-11 years: 42 mcg twice daily (42 mcg/spray)	
	4-11 years: 40 mcg once daily (40 mcg/spray)	
Budesonide	*Adolescents and adults (>12 years)*	
	32 mcg (1 spray) once daily	OTC

	Pediatrics	
	6-11 years: 32 mcg (1 spray) once daily	
Flunisolide	*Adolescents and adults (>15 years)*	
	50 mcg (2 sprays) twice daily	Rx
	May increase to three times daily	
	Pediatrics	
	6-14 years: 50 mcg (2 sprays) twice daily	
Fluticasone	*Adolescents and adults (>12 years)*	
	1-2 sprays once daily (either salt)	OTC
	Pediatrics propionate = 50 mcg/spray	
	4-11 years: 1 spray once daily (propionate) furoate = 27.5 mcg/spray	
	2-11 years: 1 spray once daily (furoate)	
Mometasone	*Adolescents and adults (>12 years)*	
	100 mcg (2 sprays) once daily	Rx
	Pediatrics	
	2-11 years: 50 mcg (one spray) once daily	
Triamcinolone	*Adolescents and adults (>12 years)*	
	110 mcg (2 sprays) once daily	OTC
	Pediatrics	
	2-11 years: 55 mcg (1 spray) once daily	
Other Nasal Medications	Note: dose is per each nostril	
Cromolyn	*Adolescents and adults* (>12 years)	
	5.2 mg (1 spray) three to four times daily	OTC
	Pediatrics	
	2-11 years: 5.2 mg (1 spray) three to four times daily	
Ipratropium	Persistent allergic rhinitis:	Rx

	Adolescents and adults (>12 years)	
	2 sprays (21 mcg/spray) 2 or three times daily	
	Pediatrics	
	6 years and older: 2 sprays (21 mcg/spray) two or three times daily	
	Seasonal allergic rhinitis	
	Adolescents and adults (>12 years)	
	2 sprays (42 mcg/spray) three or four times daily	
	Pediatrics	
	5 years and older: 2 sprays (42 mcg/spray) four times daily	
Leukotriene-Receptor Antagonist, oral		
Montelukast	*Adolescents and adults (>12 years)*	
	10 mg once daily	Rx
	Pediatrics	
	6-14 years: 5 mg once daily	
	2-5 years: 4 mg once daily	
	6-23 months: 4 mg once daily	

Many patients respond to and tolerate the older agents quite well. Because many of the older agents are available generically, they are much less expensive. Patient cost for many of the older nonprescription agents is less than $5 for a 30-day supply, compared with more than $20 for some of the nonprescription selective agents. Although cost is a concern, patient safety should be the first consideration.

The selective agents are preferred over nonselective antihistamines, according to a survey of pharmacists.[25] Among the 2 million antihistamine recommendations, the top three were loratadine (41%), cetirizine (33%), and fexofenadine (15%) followed by the nonselective agents diphenhydramine (9%) and chlorpheniramine (2%).

Intranasal or ophthalmic antihistamines are possible options but these products are available by prescription only. For seasonal and persistent allergic rhinitis, the intranasal antihistamine azelastine is available. The 0.1% product can be used in children for seasonal allergies, while the 0.15% product is labeled for adults only for either type of allergic rhinitis. Despite this labeling, recent guidelines favor the use of the intranasal route for seasonal but not persistent allergic rhinitis.[17] Azelastine has been used successfully for patients who did not respond to loratadine.[26] Using the nasal route offers an alternative to switching to another oral antihistamine. Patient satisfaction has been varied because while the product produces rapid symptom relief, patients complain of drying effects, headache, and diminished effectiveness over time. Patients should be warned of the medication's potential to produce drowsiness, as its systemic availability is approximately 40%.[27,28] Olopatadine, another intranasal antihistamine, may cause less drowsiness as it is a selective H_1-receptor antagonist.

Allergic conjunctivitis, often associated with allergic rhinitis, can be treated with ophthalmic antihistamines such as levocabastine or bepotastine.

Because systemic antihistamines usually are also effective for allergic conjunctivitis, one of these ophthalmic agents may be a logical addition to nasal steroids when ocular symptoms occur.

Decongestants

Topical and systemic decongestants are sympathomimetic agents that act on adrenergic receptors in the nasal mucosa, producing vasoconstriction. Decongestants shrink swollen mucosa and improve ventilation. When nasal congestion occurs with allergic rhinitis, decongestants work well in combination with antihistamines.

Topical Decongestants

Topical decongestants are applied directly to swollen nasal mucosa via drops or sprays. Table e14-7 lists the common topical decongestants and their durations of action. The use of these agents results in little or no systemic absorption.

TABLE e14-7

Duration of Action of Topical Decongestants

Medications	Durations of Action (hours)
Short acting	
Phenylephrine hydrochloride	Up to 4
Intermediate acting	
Naphazoline hydrochloride	2-6
Tetrahydrozoline hydrochloride	
Long acting	
Oxymetazoline hydrochloride	Up to 12
Xylometazoline hydrochloride	

Because these agents are extremely effective and are available to patients without a prescription, they are widely used. However, prolonged use of these agents (for more than 3-5 days) can result in a condition known as *rhinitis medicamentosa*, or *rebound vasodilation*, with even more severe congestion. Patients who develop this condition use increasingly more spray more often with less response. Although the methods used to treat this "addiction" have not been studied formally, several are used commonly. Abrupt cessation works, but it is difficult because of rebound congestion that may leave the patient congested for several days or weeks. Sleeping may become difficult. Nasal steroids have been used successfully, but they take several days to work. Weaning the patient off topical decongestants can be accomplished by decreasing the dosing frequency or the concentration over several weeks. Combining the weaning process with nasal steroids may prove useful. Ultimately, the success of any plan depends on the patient's resolve and clear understanding of the importance of stopping the drug to end the problem.

Other adverse effects of topical decongestants include burning, stinging, sneezing, and dryness of the nasal mucosa.

Patients should be counseled on the use of topical decongestants to prevent rhinitis medicamentosa. Patients should be instructed to use as small a dose as possible as infrequently as possible and only when absolutely necessary (eg, at bedtime to aid in falling asleep). Duration of therapy always should be limited to 3 days or less.

Systemic Decongestants

Oral decongestants are not as effective on an immediate basis as the topical agents, but their effects sometimes last longer and they cause less local irritation. In addition, rhinitis medicamentosa is not a problem with oral agents. The most commonly used agent is pseudoephedrine. Table e14-6 lists the usual doses for the regular and sustained-release versions. The use of phenylephrine is increasing because of regulations related to pseudoephedrine described below.

Concerns of safety have greatly limited the systemic decongestant options. Legal requirements for the sale of pseudoephedrine were put into place to combat the misuse of the drug as a component in making methamphetamine. Pseudoephedrine must now be sold behind the counter, and the monthly amount a patient can purchase is limited. Until this requirement, pseudoephedrine was the most frequently used systemic decongestant, and it was considered the safest. Doses of 180 mg produce no measurable change in blood pressure or heart rate.[29] In higher doses (210-240 mg), pseudoephedrine has raised both blood pressure and heart rate.[30] Pseudoephedrine can cause mild CNS stimulation, even at therapeutic doses. Stroke, related to use of oral decongestants such as pseudoephedrine, can occur in patients with hypertension and/or vasospasm.[31] Although stroke complications seem to be associated with higher-than-recommended doses, there is also a stroke risk when these agents are taken properly. Severe hypertensive reactions can occur when pseudoephedrine is given concomitantly with monoamine oxidase inhibitors. Hypertensive patients should, unless necessary, avoid systemic decongestants.

Combination Products

Numerous products combine an antihistamine with a decongestant. While the combination may be rational because of the different mechanisms of action, remember that antihistamines must be taken on a regular schedule, but decongestants should only be used when needed. Both nonselective and peripherally selective antihistamines are available in such combinations. As mentioned previously, patients should read labels to avoid therapeutic duplication. Consideration should be given to how often and how severely the patient is congested before recommending these combinations. Only a short course of a combination product should be used.

Nasal Steroids

5 Nasal steroids are an excellent choice for treating persistent rhinitis, and can be an excellent choice in seasonal rhinitis, especially if begun in advance of symptoms. Nasal steroids appear to be effective with minimal adverse effects. Recent guidelines suggest that nasal steroids should be recommended as initial therapy.[21] Multiple mechanisms are involved with the effects of nasal steroids on the nasal mucosa: reducing inflammation by reducing mediator release, suppressing neutrophil chemotaxis, reducing intracellular edema, causing mild vasoconstriction, and inhibiting mast cell-mediated late-phase reactions. Table e14-6 lists the available nasal steroids and their usual doses.

Topical steroids produce only minor adverse effects, most commonly sneezing, stinging, headache, and epistaxis. Despite concerns about safety of systemic steroids, nasal steroids have been found to have no significant association with hypothalamic–pituitary axis suppression, cataract formation, glaucoma, or bone mineral density changes in the doses used for allergic rhinitis. Growth suppression remains a question with some evidence showing that nasal steroids with higher bioavailability (eg, beclomethasone) may have a greater growth-suppression effect than less bioavailable agents.[32] These findings require more study. Most likely, all currently available nasal steroids are safe in the majority of patients, and their clinical benefits outweigh any small growth suppressive effect. Other concerns include local infections with *Candida albicans*, which occur rarely.

Patient preference studies suggest some patients tolerate the fluticasone furoate better than fluticasone propionate or mometasone in characteristics such as taste, odor, gentleness, and nasal irritation.[34] While fluticasone furoate is more expensive, it should be considered if patients complain about these characteristics of the other products.

The therapeutic benefits of topical steroids are not immediate, and they are not decongestants. Patients need to understand this to ensure cooperation and continuation of therapy. Some patients notice improvement in a few days, but peak responses may not be observed for 2 to 3 weeks. Once a response is achieved, the dosage may be reduced. Blocked nasal passages should be cleared with a decongestant or saline irrigation before administration to ensure adequate penetration of the spray. Patients should be advised to avoid sneezing or blowing their noses for at least 10 minutes after administration. Topical steroids should not be used for patients with nasal septum ulcers or recent nasal surgery or trauma.

One additional benefit of nasal steroids in treating allergic rhinitis in individuals with asthma and upper airway conditions is that they may confer some protection against exacerbations of asthma, leading to fewer emergency room visits. The overall relative risk for an emergency visit among asthma

patients who received intranasal steroids was 0.7.[33] No effect was seen for patients receiving antihistamines.

Other Inhalant Medications

Cromolyn sodium and ipratropium bromide offer two additional approaches for treating allergic rhinitis. While neither of these agents appears in the latest treatment guidelines, they are mentioned here for completeness. Cromolyn sodium is a mast cell stabilizer. Increased interest in this product has resulted from it becoming available without a prescription. Ipratropium bromide is an anticholinergic agent that may be useful in perennial allergic rhinitis.

Cromolyn sodium nasal spray is used for the symptomatic prevention and treatment of allergic rhinitis. It curtails antigen-triggered mast cell degranulation and release of the mediators of allergic reactions, including histamine. Cromolyn sodium has no direct antihistaminic, anticholinergic, or anti-inflammatory properties. Similarly to topical steroids, the most common adverse effects—sneezing and nasal stinging—result from local irritation. Dosing information is given in Table e14-6. Cromolyn sodium must cover the entire nasal lining; therefore, patients should be instructed to clear nasal passages before administration. Inhaling gently through the nose during administration aids in this process. Dosing must be repeated at 6-hour intervals to maintain the effect.

For seasonal rhinitis, treatment with cromolyn sodium should be initiated just before the usual start of the offending allergen's season and continued throughout the season. In perennial rhinitis, the effects may not be seen for 2 to 4 weeks; therefore, antihistamines or decongestants may be needed during this initial phase of therapy. As cromolyn sodium begins to work, the need for these medications should decrease.

Ipratropium nasal spray is an anticholinergic agent that exhibits antisecretory properties when applied locally. It provides symptomatic relief of rhinorrhea associated with allergic and other forms of chronic rhinitis. Dosing information is given in Table e14-6. The optimal dose should be determined based on the specific patient's symptoms and response. Adverse effects are mild, with the most common being headache, nosebleeds, and nasal dryness.

Immunotherapy

6 Experience with immunotherapy has reached the one-century mark, as the first report of the successful use of grass pollen extract injections to treat allergic rhinitis was published in 1911.[34] Until recently, immunotherapy was only available for via subcutaneous injections. Sublingual dosage forms are now available for a very limited number of antigens as will be described later. The therapy was first called *desensitization*; however, this did not seem appropriate because skin reactivity sometimes remained. The name was later changed to *hyposensitization*. Although this term is still used today, *immunotherapy* is used more commonly and is less confusing.

Immunotherapy is the process of administering doses of antigens responsible for eliciting allergic symptoms into a patient with the hope of inducing tolerance to the allergen when natural exposure occurs. Several mechanisms have been proposed to explain the beneficial effects of immunotherapy, including induction of IgG-blocking antibodies, reduction in specific IgE (long-term), reduced recruitment of effector cells, altered T-cell cytokine balance (a shift from T-helper type 1 to T-helper type 2), T-cell anergy, and alteration of regulatory T-cell actvitiy.[35]

Immunotherapy is moderately expensive, has significant potential risks, and for subcutaneous therapy, a major time commitment is required from the patient. However, the cost of immunotherapy may be covered by insurance, including Medicaid. Long-term savings can be realized since decades of treatment with medication can be averted through successful immunotherapy. Candidates for immunotherapy should have significant symptoms unsuccessfully controlled by avoidance and pharmacotherapy or should stand to benefit in other significant ways, such as with asthma. Immunotherapy may postpone the onset of asthma or possibly even prevent it.[36] Patients who are unable to tolerate the adverse effects of properly managed drug therapy also should be considered. Patients must be committed to the necessary regular office visits required to complete a course of subcutaneous therapy over several years.

The effectiveness of immunotherapy for seasonal allergic rhinitis appears to be better than that seen with persistent rhinitis, in part because it is more difficult to determine which allergen is responsible for persistent symptoms, and it is more often due to multiple sensitizations. Effectiveness has been shown in a number of clinical studies using a variety of pollen extracts, even for patients with severe disease resistant to pharmacotherapy.[36] Data indicate that for some patients, 3 years of subcutaneous immunotherapy may be sufficient to give lasting benefit[37]; however, many require longer treatment.

The selection of antigens should be based on patient history and skin test results. Numerous regimens for administration of selected allergens have been suggested. In the beginning of subcutaneous immunotherapy, very dilute solutions are given initially to one to two times per week. The concentration is increased until the maximum tolerated or highest planned or effective dose is achieved. This maintenance dose is continued in slowly increasing intervals over several years, depending on clinical response. Because of the present understanding of the immunologic results of immunotherapy, it should be given year-round rather than seasonally.

Sublingual dosage forms for a very limited number of allergens are now available in the United States. Sublingual immunotherapy is available for ragweed and certain grass allergies. Because the types of allergens are limited, patient selection should be done carefully to ensure that those receiving this route of immunotherapy are the most likely to benefit. These products are started 12 weeks before the allergen season and continued throughout the season. House dust mite allergen is available in the United States. Because house dust mites cause persistent allergic rhinitis, this product is given year round. The first dose is administered in the physician's office to allow observation of the patient for 30 minutes for hypersensitivity reactions. The patient places the tablet under the tongue where it dissolves. Patients should not swallow for at least 1 minute. After the first dose is administered without incident, patients can take sublingual immunotherapy at home. However, patients must be prescribed an autoinjectable epinephrine.

Adverse reactions can occur with immunotherapy and range from mild to life threatening. Among the most common are mild local reactions with subcutaneous injections, consisting of induration and swelling at the site of the injection. These may be immediate or delayed. Other more serious reactions (eg, generalized urticaria, bronchospasm, laryngospasm, and vascular collapse) occur rarely; deaths can result from anaphylactic reactions. Severe reactions are treated with epinephrine as well as other modalities recommended for anaphylaxis. Because of this potential risk, subcutaneous immunotherapy should not be given without adequate direct observation in a medical facility. With sublingual immunotherapy, the most common reactions are pruritus of the mouth, ears, and tongue, throat irritation, and mouth edema.

Several patient types are poor candidates for immunotherapy, including patients with any medical condition that would compromise the ability to tolerate an anaphylactic-type reaction, patients with impaired immune systems, and patients with a history of nonadherence to therapy. Sublingual immunotherapy is only approved for patients 18 years and older.

Leukotriene Receptor Antagonists

Leukotriene receptor antagonists inhibit the cysteinyl leukotriene receptor. The cysteinyl leukotrienes are one type of inflammatory mediators released from mast cells in allergy. Montelukast is approved for the treatment of perennial allergic rhinitis in children as young as 6 months and for seasonal allergic rhinitis in children as young as 2 years. Montelukast is considered a third choice behind antihistamines and nasal steroids.[17]

Leukotriene receptor antagonists are no more effective than peripherally selective antihistamines and less effective than intranasal steroids. However, when combined with antihistamines, they are more effective than the antihistamine alone.[38] In children with mild persistent asthma and coexisting allergic rhinitis, montelukast as monotherapy has been recommended.[1] Table e14-6 lists dosage regimens.

Alternative Treatment Options

A few other alternative options have been suggested for treatment of allergic rhinitis. As mentioned earlier in this chapter, microbial exposure in the early years of life could help prevent allergic disease by favoring a nonatopic immune response.[5] However, the use of probiotics may be limited to treatment or prevention of childhood eczema as available evidence shows little benefit in allergic airway diseases.[39] Butterbur, with the active ingredient petasin that exhibits antileukotriene and antihistamine activity, has shown some success but is not recommended for most patients.[17,40] Acupuncture is listed as an optional therapy in the latest guidelines, but high-quality evidence supporting the intervention is not available.[1]

Implement the Plan

The two primary pharmacotherapy options for the treatment of allergic rhinitis in adults and children are antihistamines and intranasal steroids. Patient preference should play a role when selecting between these two options. While limited evidence supports intranasal steroids over antihistamines, some patients may prefer simple oral therapy. Either choice requires clear patient counseling to ensure appropriate timing of therapy and expectations of effect.

For patients (both adults and children) who are not immunocompromised, have a high likelihood for adherence, and have adequate insurance and/or financial resources, subcutaneous specific immunotherapy is an excellent choice for treatment of seasonal allergic rhinitis and allergic rhinitis secondary to house dust mites. In some children, immunotherapy may prevent development of asthma. Sublingual immunotherapy may be beneficial to patients who are sensitive only to ragweed or certain types of grasses.

For patients experiencing an exacerbation of nasal congestion as part of their allergic rhinitis picture, decongestants can be used for short term.

Leukotriene receptor antagonists should not be recommended as primary therapy for allergic rhinitis; however, patients with allergic rhinitis and asthma may benefit from this therapy.

Cromolyn is another alternative that is effective, but many patients may find its frequent daily dosing (up to six times daily) difficult.

Follow-up: Monitoring and Evaluating Outcomes

More supportive evidence is needed to determine which patients, if any, would benefit from the other alternative options mentioned earlier.

With allergic rhinitis, major outcomes include the effect of the disease on a patient's life, the efficacy and tolerability of treatment, and patient satisfaction. Consideration must be given to how the condition is affecting the patient's job or school performance, family and social interactions, and other aspects of quality of life. Drug therapy should prevent or minimize symptoms with few adverse effects. The patient should not have difficulty obtaining needed medication for financial or other reasons. Patients should be questioned about their satisfaction with the management of their allergic rhinitis. The management should result in minimal disruption to their lives.

A drug monitoring summary is shown in Table e14-8. Intranasal and ophthalmic antihistamines may be helpful for specific symptoms not relieved by first-line choices. An intranasal anticholinergic such as ipratropium is specifically useful for rhinorrhea.

TABLE e14-8

Monitoring of Medications for Allergic Rhinitis

Drug	Adverse Reaction	Monitoring Parameter	Comments
• Antihistamines	• Drowsiness • Gastrointestinal effects • Anticholinergic effects	• Caution patient about the potential for drowsiness, even with nonsedating and intranasal products • Counsel patient to take with a meal or full glass of water • Watch for dry mouth and difficulty with urination. Caution patient about other medications with anticholinergic effects	• Do not mix with alcohol or other CNS depressants • Switching to an antihistamine with less anticholinergic effects may be necessary

• Decongestants
  ○ Topical
  ○ Systemic
	• Rebound vasodilation
	• Local irritation
	• Hypertension
	• CNS stimulation
		• Watch for decreased response to topical agent
		• Watching for burning, stinging, sneezing, and dryness of mucosa
		• If used in a patient with hypertension, monitor blood pressure regularly and discontinue if the pressure increases
		• Usually mild but discuss with
			• Avoid prolonged use (>3-5 days)
			• Self-limiting due to short-term use. May try nasal saline for dryness
			• Usually not an issue for patients without preexisting hypertension.
			• Use lowest effective dose

		patient	
• Nasal steroids	• Local effects such as sneezing, stinging, and epistaxis	• These effects may vary among products.	

• Other intranasal agents
  ○ Cromolyn
  ○ Ipratropium
	• Local effects such as sneezing, burning, or coughing
	• Headache, nosebleeds, and nasal dryness
		• Usually mild but tell patient to report bothersome symptoms
		• Usually mild, tell patient to report bothersome symptoms
			• If patient cannot tolerate local reactions, choose an alternative agent
			• If patient cannot tolerate local reactions, choose an alternative agent

• Montelukast	• Behavioral changes	• Monitor for mood and behavioral changes including suicidal ideation	• Rare but should be monitored
• Immunotherapy, SC • Immunotherapy, SL	• Local reactions • Allergic reactions • Pruritis of ear, oral itching, mouth edema, throat irritation	• Watch for induration or swelling at site of injection • Monitor for signs of anaphylaxis • Caution patient about these reactions as they are fairly common	• Anaphylaxis rare, but should only be given under direct medical supervision with epinephrine available • First dose giving in physician's office so patient can be observed for 30 minutes. Prescription must be accompanied by a prescription for an epinephrine autoinjector.

Methods for assessing patient-reported outcomes and health-related quality of life in clinical trials related to allergy have been recommended.[41] These tools go beyond measuring improvement in symptoms and include such items as sleep quality, nonallergic symptoms (eg, fatigue, poor concentration, and others), emotions, and participation in a variety of activities. How well each of the current treatment modalities performs and how they compare in improving patient outcomes remain to be determined.

Clinicians caring for allergic rhinitis patients should develop a comprehensive pharmaceutical care plan that addresses several areas. Discuss and agree on therapeutic end points for allergic rhinitis, including the patient's acceptable level of symptom relief, onset of symptom relief expectations, and seasonal starts and stops. Discuss adverse drug reaction self-monitoring and prevention based on treatment selection. Assess patient attitude toward adherence to and persistence with oral, ocular, intranasal, or immunologic therapies. Ensure proper matching of treatment to symptoms and intervene with the prescriber if necessary. Conduct seasonal or annual review with patient.

The therapeutic goal for all patients with allergic rhinitis is to minimize or prevent symptoms. Evaluation of success is accomplished primarily through the discussions with the patient, in whom both relief of symptoms and tolerance of drug therapy must be discussed.

CONCLUSION

Allergic rhinitis is a common disease with symptoms ranging from mild to severe. If avoidance measures are unsuccessful, allergic rhinitis should be

treated to improve quality of life and prevent long-term complications. Timing of treating is essential. Treatment regimens should be individualized based on patient symptoms and response. Care should be taken to correctly identify allergy as the cause of the patient's rhinitis before committing them to chronic treatment.

ABBREVIATIONS

IgE	immunoglobulin E
RAST	radioallergosorbent test

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SELF-ASSESSMENT QUESTIONS

1. Sensitization to inhaled allergens in the United States is estimated to be

   A. 5%

   B. 13% in children and 14% in adults

   C. 15%-30 %

   D. 25%-50%

   E. >50%

2. Persistent allergic rhinitis is a year-round disease that can be caused by which of the following?

   A. Dust mites

   B. Oak tree pollen

   C. Animal dander

   D. Ragweed pollen

   E. Both A and C

3. Inflammatory mediators produce all of the following in the nose except:

   A. Decreased vascular permeability

   B. Rhinorrhea

   C. Nasal congestion

   D. Sneezing

   E. Vasodilation

4. Which of the following are possible complications of allergic rhinitis?

   A. Dental malocclusion and orthodontic problems

   B. Poor work or school performance

   C. Allergic shiners resulting from venous pooling under the eyes

   D. All of the above

   E. Only A and C

5. Prior to allergen skin testing, which of the following drugs should be stopped for at least 10 days?

   A. Olopatadine

   B. Pseudoephedrine

   C. Intranasal fluticasone

   D. Cetirizine

   E. All of the above

6. Which of the statements regarding nonpharmacologic management of allergic rhinitis is true?

   A. Avoidance of the offending allergens is effective in most patients.

   B. Increasing humidity in the home above 50% helps with reactions to indoor allergens.

   C. If removal of a pet is unacceptable, keeping the pet out of the patient's bedroom and washing the pet weekly may be beneficial.

   D. Saline washes for nasal passages and sinuses are almost never helpful.

   E. Smoking in the house is acceptable but smoking in the car with the patient should be avoided

7. Which of the following statements is true regarding antihistamines?

   A. An antihistamine is more effective at reversing allergic rhinitis symptoms than preventing them.

   B. For most patients, peripherally selective agents are recommended over nonselective agents because they do less sedation.

   C. There is no need to counsel patients on the use of antihistamines because most are available OTC.

   D. A and B are true.

   E. None of the above are true.

8. Which of the following have a high level of evidence for their effectiveness for initial treatment of allergic rhinitis?

   A. Nasal steroids.

   B. Oral leukotriene receptor antagonists.

   C. A nasal steroid combined with an oral antihistamine.

   D. Avoidance.

   E. A, C, and D all have a high level of evidence to support their use.

9. Patients experiencing allergic conjunctivitis while receiving nasal steroids may benefit from having what drug added to their regimen?

   A. Azelastine

   B. Cromolyn sodium

   C. Levocarbastine

   D. An intranasal decongestant

   E. A systemic decongestant

10. Rhinitis medicamentosa may be a complication of which of the following drugs if used for more than 3 days:

    A. Diphenhydramine

    B. Sublingual immunotherapy

    C. Fluticasone

    D. Oxymetolazone

    E. Loratadine

11. Intranasal fluticasone:

    A. Provides immediate relief of allergic rhinitis symptoms

    B. Does not require patient counseling because it is available OTC.

    C. May cause growth suppression in children and this effect outweighs the clinical benefit so this agent is not recommended in children under the age of 12.

    D. Is likely to cause local infections with *Candida albicans;* therefore should not be used in patients over the age of 65.

    E. Has had no significant association with hypo-pituitary axis suppression.

12. Which of the following statements are false regarding cromolyn sodium?

    A. It has no direct antihistaminic properties.

    B. It has no direct anticholinergic properties.

    C. It has no anti-inflammatory properties.

    D. Patients should be instructed to clear nasal passages before administration.

E. For seasonal allergic rhinitis, it should be started just before the offending allergen's season and continued throughout the season.

13. The following statements about subcutaneous immunotherapy are true except:

A. Candidates should have a history of symptoms controlled by antihistamines and/or nasal steroids.

B. It is a slow gradual process.

C. Effectiveness has been demonstrated in clinical trials using pollen extracts.

D. Three years of immunotherapy may be sufficient to give some patients lasting benefits.

14. Which of the following is true regarding sublingual immunotherapy

A. The tablets are dissolved under the tongue and swallowed immediately.

B. Prescriptions may be accompanied with a prescription for an epinephrine pen only if the physician considers the patient high risk.

C. For pollen allergens, they must be given year round to maintain effect.

D. The first dose must be given in the physician's office where the patient is observed for 30 minutes.

15. Key elements of evaluation of the therapeutic outcome of a patient with allergic rhinitis include:

A. The effect of the disease on the patient's life

B. The efficacy of the treatment regimen

C. The tolerability of the treatment regimen

D. The patient's satisfaction of the treatment regimen

E. All of the above

SELF-ASSESSMENT QUESTION-ANSWERS

1. **C.** Allergic rhinitis is one of the most common diseases affecting adults and children in the United States. While prevalence rates using physician-confirmed diagnosis are 13% in children and 14% in adults, actual sensitization to inhaled allergens is estimated to be higher.

2. **E.** Persistent allergic rhinitis is caused by allergens that are present year round, such as house dust mites, animal dander, cockroaches, and certain mold types. Pollens are released in the fall or spring.

3. **A.** A variety of mediators such as histamine, kinins, leukotrienes, and others cause *increased* vascular permeability.

4. **D.** Untreated allergic rhinitis can lead to complications that seem unrelated to typical symptoms of runny and stuffy nose, sneezing, and pruritic eyes. These symptoms may disturb sleep resulting in fatigue and poor work or school performance. Mouth breathing due to the chronic nasal congestion can lead to orthodontic problems. Chronic nasal congestion can also lead to venous pooling and dark circles under the eyes.

5. **D.** Any oral antihistamine the patient is taking should be stopped at least 10 days prior to allergen skin testing as they can decrease the sensitivity of the test by blocking or decreasing the skin reaction (positive result).

6. **C.** Nonpharmacologic approaches to treating allergic rhinitis are difficult and are rarely effective alone (see Table e14-3) for potential options. Most patients will not want to get rid of their pet. Keeping the pet out of the patient's bedroom, off carpet and upholstered furniture, and washing the pet weekly may be difficult but can be beneficial.

7. **B.** Antihistamines are much more effective in preventing allergic rhinitis symptoms; therefore, counseling patients about taking them before

allergen exposure is helpful. Also, patients must be fully aware of potential adverse effects. Peripherally selective antihistamines are less sedating and are recommended as first line.

8. **A.** The strongest evidence for initial treatment of allergic rhinitis exists for intranasal steroids alone or peripherally selective antihistamines alone.

9. **C.** Nasal steroids have little effect on ocular symptoms of allergic rhinitis since they act primarily in the nasal passages. Adding an ocular antihistamine may prove beneficial.

10. **D.** Intranasal decongestants, such as oxymetazoline, if used for more than 3 days can cause rebound vasodilation resulting in even more severe nasal congestion than the patient was initially experiencing. This leads to higher and more frequent doses that may provide some temporary relief, but the rebound congestion worsens.

11. **E.** Intranasal steroids are minimally absorbed so the worrisome effects of systemic steroids are not a concern with local use. These agents take over a week to be effective and are more effective if taken just prior to the start of allergy season, so patients should be counseled about these points and on the proper administration technique.

12. **E.** To be effective, cromolyn must be started just before the usual start of the allergen's season and continued throughout the season. If not, it may take 2 to 4 weeks to provide any relief.

13. **A.** The best candidates for immunotherapy are those that have not responded to other pharmacotherapeutic options.

14. **D.** With sublingual immunotherapy, the first dose must be given in the physician's office where the patient can be observed for at least 30 minutes. The risk of anaphylaxis is low but care must be taken to see how the patient will respond since anaphylaxis is a life-threatening condition. For this reason, an autoinjectable epinephrine must be provided with the prescription for the sublingual product.

15. **E.** All of these items are important and must be considered.