Allergic rhinitis: Treating the adult

Jonathan Corren, MD  Los Angeles, Calif

Allergic rhinitis is now recognized as a chronic medical condition that markedly affects patient quality of life and is a cause of substantial medical care expenditures. Effective treatment of adults with allergic rhinitis usually requires an integrated regimen that combines allergen avoidance measures, pharmacotherapy, and possible specific-allergen immunotherapy. This approach can control bothersome symptoms with minimal adverse effects in most patients. New medications, such as anti-immunoglobulin E therapy and cytokine antagonists, may provide relief to patients who are refractory to or do not tolerate currently available treatments. (J Allergy Clin Immunol 2000;105:S610-15.)

Key words: Allergic rhinitis, antihistamine, decongestant, intranasal corticosteroid, pharmacotherapy, specific-allergen immunotherapy

Allergic rhinitis is the most common of all atopic diseases and has been estimated to affect up to 20% of the adult population in the United States.1 Although allergic rhinitis can develop at any age, most patients report the onset of symptoms before 30 years of age, during some of the most productive years of life. Whereas rhinitis was once considered to be a medical condition of trivial importance, it is now recognized to substantially affect quality of life and to impair both physical and cognitive functioning in adults. Therefore it is not surprising that allergic rhinitis accounts for at least 1.9 billion dollars in annual health care spending, along with costly but undetermined indirect expenses.2

In view of the social and medical impact of this disorder, appropriate therapy of nasal allergy is important to both primary care and specialty physicians. In this article, I will review a stepped care approach to adult patients with allergic rhinitis, including recommended care for special populations.

ALLERGEN AVOIDANCE MEASURES

In patients with perennial symptoms attributable to indoor allergens (eg, dust mites, furry animals, indoor molds, cockroaches), avoidance of the allergen is a critical first step in treatment. Environmental control programs should always be based on accurate assessments of both sensitization (by skin or in vitro testing) and exposure. These strategies are particularly helpful to patients who are sensitized only to indoor allergens with no evidence of allergy to pollens or outdoor molds.

Dust mites

House-dust mites Dermatophagoides farinae and D pteronyssinus are ubiquitous throughout the world (except in dry or alpine regions), and approximately 30% to 40% of patients with allergic rhinitis are allergic to allergens produced by these mite species.3 Although a large number of clinical trials have established the efficacy of mite avoidance measures in patients with asthma, there have been only a limited number of studies in patients with allergic rhinitis. In general, these studies have demonstrated that mite avoidance must be aggressive to be effective and should include (1) encasement of pillows and mattresses in impermeable covers, (2) washing of all bedding in hot (>130°F) water, and (3) elimination of carpeting in favor of tile or hardwood floors.4 Frequent cleaning of floors with vacuum cleaners equipped with double-reservoir bags and/or a high-efficiency particulate air (HEPA) filter attached to the exhaust port is also helpful in the elimination of settled dust.5 The application of acaracidal and denaturing solutions6 and the installation of free-standing HEPA filters7 into bedrooms have not proved effective in reducing symptoms caused by mite exposure.

Animals

Virtually any furry pets may result in allergic sensitization and ultimately symptoms of rhinitis. However, most of the available clinical data regarding the efficacy of animal avoidance measures come from studies of indoor cats and their major allergen, Fel d I. Contrary to patients’ wishes, effective avoidance of cat allergen requires removal of the pet from the inside of the home. Even after this is accomplished, it may take several months or longer for indoor concentrations of Fel d I to return to low levels; this process is markedly expedited by the removal of indoor carpeting and aggressive cleaning.8 One study suggested that a combination of noncarpeted floors, plastic or leather furniture, frequent vacuuming, high-flow air filtration, and frequent washing of the cat substantially reduced indoor levels of Fel d I.9 However, long-term studies with clinical end points are needed before this approach can be advocated. One recent study that examined the effects of

Abbreviations used

CNS: Central nervous system
HEPA: High-efficiency particulate air
OTC: Over the counter
the removal of the cat from the bedroom (but not from the house) plus the use of a HEPA filter in the bedroom failed to demonstrate any clinical benefits.\textsuperscript{10}

**Indoor mold**

Identification of homes with mold growth is often difficult. Indoor mold spores from species of Aspergillus and Penicillium are most likely to emanate from potentially damp areas such as crawl spaces (because of defective plumbing or poor drainage), attics (because of roof leaks), and under sinks.\textsuperscript{11} The presence of a musty smell and the visual presence of mold confirm the problem. Occasionally, however, wall spaces, carpet backing, and other areas with limited access may harbor mold growth, and identification of the mold may be delayed or even missed. Complete correction of all plumbing, drainage, and construction defects must be undertaken to eliminate significant mold problems. In some cases of extensive mold growth, major portions of a house may have to be rebuilt. More limited measures, such as the application of bleach or fungicides, have not been shown to be beneficial.

**Cockroach**

Although cockroach allergy has been most heavily implicated as a pathogenic factor in children with asthma, it may play a substantial role in perennial allergic rhinitis as well.\textsuperscript{12} The best indicator of a significant cockroach infestation is the presence of emanations on the floor. Cockroach exposure is usually not limited to the kitchen or dining room but may affect all living areas because allergen is passively transferred on shoes and clothing. Pesticide application is only temporarily effective, and problems will recur unless food and garbage are appropriately packaged and handled.\textsuperscript{13}

**Outdoor seasonal allergens**

Plant pollens and outdoor molds (eg, species of Alternaria and Cladosporium) are responsible for the symptoms of seasonal allergic rhinitis and are generally very difficult to avoid completely. During indoor activities, keeping all windows and doors shut and the use of an air-conditioner eliminate most pollen from the inside of the house. Because outdoor pollen counts are highest between 11:00 AM and 3:00 PM, especially on hot, sunny days, avoidance of outdoor activities during these times may be helpful. Certain mold spore counts tend to be highest late in the evening or early in the morning, especially in damp climes, and this may be a consideration for patients who are mold allergic. However, altering schedules and activities is undesirable for most patients, and, for this reason, avoidance measures play a limited role in allergic rhinitis caused by outdoor allergens.

**PHARMACOLOGIC THERAPY**

Patients with significant symptoms of seasonal allergic rhinitis will usually require medication to relieve the symptoms. Whereas environmental control measures may reduce the intensity of perennial rhinitis because of indoor allergens, in most cases supplemental medical therapy will also be needed. Several different classes of medication are now available for the treatment of allergic rhinitis.

**H\textsubscript{1} antihistamines**

H\textsubscript{1} antihistamines are the most commonly prescribed class of medication for allergic rhinitis. Although these drugs act primarily by blocking the H\textsubscript{1}-histamine receptor, many of the agents have also been shown to have mild anti-inflammatory properties (eg, reduction in expression of adhesion molecules). As a general rule, H\textsubscript{1} antihistamines reduce symptoms of sneezing, itching, rhinorrhea, and ocular injection but have little effect on nasal congestion.\textsuperscript{14} Because most antihistamines have a relatively rapid onset of action (1 to 3 hours), these agents are frequently and effectively used on an intermittent, as-needed basis. Whereas chronic use of these drugs was once thought to result in therapeutic subsensitivity, recent studies have failed to support this contention.\textsuperscript{15}

First-generation antihistaminic compounds were the first to be developed, and most are available over the counter (OTC), either alone or in combination with a decongestant. These drugs readily cross the blood-brain barrier and bind not only to the H\textsubscript{1}-histamine receptor but in many cases to dopaminergic, serotonergic, and cholinergic receptors.\textsuperscript{16} These characteristics help account for the adverse effects of these agents, which include both central nervous system (CNS) effects (eg, sedation, fatigue, dizziness, impairment of cognition and performance) and anti-cholinergic effects (eg, dryness of the mouth and eyes, constipation, inhibition of micturition, potential precipitation of narrow-angle glaucoma). Although tolerance to sedation may occur over a period of several days, substantial effects on intellectual functioning and performance may persist without the patient’s knowledge.\textsuperscript{17} This is well exemplified in studies of driving performance, which have demonstrated marked impairment with the use of single doses of triprolidine 50 mg.\textsuperscript{18} It may also help explain the reason that serious work accidents are more closely associated with first-generation antihistamines than any other class of medication.\textsuperscript{19} Therefore first-generation antihistamines must be prescribed with great caution in all adult patients but should be absolutely avoided in patients who pilot planes, drive extensively, or operate heavy or dangerous machinery; who have pre-existing intellectual impairment; who have benign prostatic hypertrophy or other forms of bladder-outlet obstruction; or who have elevated intraocular pressure.

Although alternative forms of therapy for allergic rhinitis are preferably in many situations, patients who do not have medical insurance or formulary coverage often resort to self-medication with OTC first-generation antihistamines. A recent strategy to avoid drug side effects and to contain costs has been to use a potentially sedating, first-generation antihistamine at night coupled with a short-acting, non-sedating antihistamine in the morning. However, one study has demonstrated that adverse CNS effects occur with this regimen as well, even after several days of dosing.\textsuperscript{20}
Second-generation antihistamines have been shown to be at least as clinically effective as first-generation agents for the treatment of allergic rhinitis (Table I). Importantly, they are larger and more lipophobic than first-generation drugs and therefore do not readily cross the blood-brain barrier. In addition, they bind specifically to the H1-histamine receptor and have little affinity for other receptors. For these reasons, the second-generation agents cause little or no somnolence, do not affect performance, and have no anticholinergic effects.

Select second-generation antihistamines (ie, terfenadine, astemizole) were found to cause blockade of the slow potassium channel and subsequent prolongation of the electrocardiographic QT interval in certain patients. When combined with other drugs that are metabolized by the cytochrome P-450 system (eg, macrolide antibiotics, azole antifungals), these 2 drugs resulted in multiple cases of torsades de pointes ventricular arrhythmia and occasional sudden cardiac death. Neither of these agents is currently available in the United States.

Most recently, third-generation antihistamines have been developed. These drugs represent metabolites of second-generation agents and appear to have substantial advantages, including an absence of effects on cardiac conduction tissue. Fexofenadine (terfenadine metabolite) has been approved for use, whereas desloratadine (loratadine metabolite) and norastemizole (astemizole metabolite) are currently in phase II and III clinical trials. All of these agents will provide therapeutic efficacy equivalent or greater to their parent compounds along with excellent safety profiles.

### Decongestants

A number of α-adrenergic agonists are available for oral use, including pseudoephedrine, phenypropanolamine, and phenylephrine. These drugs primarily reduce nasal congestion and to some extent rhinorrhea but have no effect on sneezing, itching, or ocular symptoms. Therefore they are most helpful in allergic rhinitis when combined with an antihistamine. Most common side effects of oral decongestants include CNS (eg, nervousness, insomnia, irritability, headache) and cardiovascular (eg, palpitations, tachycardia) symptoms. In addition, these drugs may elevate blood pressure, raise intraocular pressure, and aggravate urinary obstruction. This group of medications should be used very cautiously in elderly patients and should be avoided in patients with ischemic heart disease, glaucoma, and any form of bladder-outlet obstruction. Although clinical studies have demonstrated that short-term use of oral decongestants does not increase blood pressure in patients with controlled hypertension, other agents (eg, intranasal corticosteroids) are preferable in these individuals.

Topical intranasal decongestants continue to be widely used by patients with allergic rhinitis and include phenylephrine, oxymetolazine, xylometolazine, and naphephrine. When topical decongestants are used for longer than 3 to 5 days, many patients will experience rebound congestion after withdrawal of the drug. If patients continue to use these medications over several months, a form of rhinitis (rhinitis medicamentosa) will develop, which can be difficult to treat effectively.

### Antihistamine-decongestant combinations

The combination of an oral H1 antihistamine and decongestant is one of the most popular OTC remedies for allergic rhinitis. The second-generation antihistamines loratadine and fexofenadine are both available in combination with long-acting pseudoephedrine and provide better symptom relief than does an antihistamine alone.

---

**TABLE I.** Dosing of second- and third-generation antihistamines

<table>
<thead>
<tr>
<th>Antihistamine</th>
<th>Generation</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azelastine</td>
<td>2</td>
<td>2 sprays each nostril, bid</td>
</tr>
<tr>
<td>Cetirizine</td>
<td>2</td>
<td>10 mg, qd</td>
</tr>
<tr>
<td>Fexofenadine</td>
<td>3</td>
<td>60 mg, bid</td>
</tr>
<tr>
<td>Loratadine</td>
<td>2</td>
<td>10 mg, qd</td>
</tr>
</tbody>
</table>

bid, Twice daily; qd, daily.
Intranasal corticosteroids

Topical intranasal corticosteroids have made a significant impact on treatment of both seasonal and perennial allergic rhinitis. These drugs appear to exert their effects through multiple mechanisms, including vasoconstriction and reduction of edema, suppression of cytokine production, and inhibition of inflammatory cell influx.26 (Fig 1). Physiologically, prophylactic treatment before nasal allergen challenge reduces both the early- and late-phase allergic responses.27

This class of agents works best when taken regularly on a daily basis. However, because of their rapid onset of action (within 12 to 24 hours with many agents), there is increasing evidence that they may also be moderately effective when used intermittently.28 A number of glucocorticoid compounds are now available for intranasal use in both aerosol and aqueous formulations (Table II).21,29 Although the topical potency of these agents varies widely, clinical trials have been unable to demonstrate significant differences in efficacy in either seasonal or perennial allergic rhinitis.30 The most important pharmacologic characteristic differentiating these agents is systemic bioavailability. After intranasal application, the majority of the dose of a glucocorticoid is swallowed. Most of the available compounds (including beclomethasone dipropionate, budesonide, flunisolide, and triamcinolone acetonide) are absorbed readily from the gastrointestinal tract into the systemic circulation and subsequently undergo significant first-pass hepatic metabolism (Table II).21,29 The resulting bioavailabilities can be as high as 50%. However, neither fluticasone propionate nor mometasone furoate is well absorbed through the gastrointestinal tract, and the small amount of drug that reaches the portal circulation is rapidly and thoroughly metabolized.29,31 These low systemic drug levels may represent an advantage in adult patients who are prone to systemic effects of corticosteroids, such as those with developing cataracts or elevations in intraocular pressure. The low systemic availabilities of these 2 newer agents may be most important in growing adolescents and in patients who are already using medium-to-high doses of inhaled corticosteroids for bronchial asthma.

Patients using intranasal corticosteroids experience dryness and irritation of the nasal mucous membranes in 5% to 10% of cases and mild epistaxis in approximately 5%. For mild symptoms, the dose of corticosteroid may be reduced if tolerated, and/or saline nasal spray should be instilled before spraying the drug. Because there have been case reports of nasal septal perforation, patients who use these agents continuously for perennial rhinitis should be seen at yearly intervals, and evidence of superficial erosions or significant crusting or bleeding should prompt discontinuation of the drug.

Ipratropium bromide

Topical intranasal ipratropium bromide, 0.03% solution, reduces the volume of watery secretions, but has little or no effect on other symptoms.32 Therefore ipratropium is most helpful in allergic rhinitis when rhinorrhea is refractory to topical intranasal corticosteroids and/or antihistamines. The most common side effects include nasal irritation, crusting, and occasional mild epistaxis.

Leukotriene modifiers

Sulfidopeptide leukotrienes are released into the nose after allergen challenge; it is suspected that leukotriene C4 contributes to nasal congestion in allergic rhinitis.33 It is therefore not surprising that symptoms of allergic rhinitis are reduced by the leukotriene D4 receptor antagonists zafirlukast34 and montelukast.35 Although these drugs are not currently indicated for the primary treatment of rhinitis, they may play a helpful role in nasal allergy in patients who are being treated for concomitant asthma.

Cromolyn sodium

Topical intranasal cromolyn sodium has an extensive record of use for allergic rhinitis.36 When given 4 times daily, it is as effective as antihistamines in controlling sneezing, rhinorrhea, and itching. Although the drug has no significant side effects, the necessity of frequent dosing limits the usefulness of cromolyn in adult patients with chronic, daily symptoms. Intranasal cromolyn is most useful as a prophylactic treatment before a known allergen exposure when antihistamines are not tolerated.
ALLERGEN IMMUNOTHERAPY

Specific-allergen immunotherapy (allergy vaccine therapy) continues to be a useful and important treatment for many patients with severe allergic rhinitis. Research performed during the past decade has demonstrated that allergy immunotherapy induces a state of allergen-specific T-lymphocyte tolerance with a subsequent reduction in mediator release and tissue inflammation. When administered to appropriately selected patients, immunotherapy is effective in most cases. In addition to short-term benefits, recently published data suggest that the improvement in rhinitis symptoms persists for several years after the treatment is discontinued (Fig 1). Immunotherapy should be considered in patients who (1) do not respond to a combination of environmental control measures and medications, (2) experience substantial side effects with medications, (3) have symptoms for a significant portion of the year that require daily therapy, or (4) prefer long-term modulation of their allergic symptoms.

CONSIDERATIONS IN SPECIAL GROUPS

Selected populations have unique needs that must be considered when a treatment regimen is established.

Elderly patients

As people grow older, structural changes in the nose result in increased nasal airflow resistance and dryness and atrophy of the mucous membranes. These normal changes in nasal anatomy and physiologic condition contribute to the symptoms of pre-existing allergic rhinitis and may make treatment more difficult. Often, nasal saline solution helps eliminate dryness and reduces the need for antiallergy drugs.

Patients older than 60 years of age frequently use a number of medications that can be primary or contributing factors in chronic rhinitis. Antihypertensive drugs are most commonly implicated, including angiotensin-converting enzyme inhibitors, β-blockers, methyldopa, prazosin, reserpine, guanethidine, and phentolamine. Nonsteroidal anti-inflammatory drugs have been noted to cause nasal congestion and rhinorrhea, often but not always, associated with sinusitis, nasal polyps, and asthma. In the event that any one of these drugs may be contributing to significant nasal symptoms, consideration should be made to switching the patient to an alternative agent.

As mentioned earlier, elderly patients are more likely to experience a number of comorbid conditions that contraindicate the use of first-generation antihistamines and oral decongestants. Second- or third-generation antihistamines and intranasal steroids or corticosteroids have fewer adverse effects and are better choices in this population.

Pregnancy

Allergic rhinitis can worsen considerably during pregnancy. For symptoms of rhinorrhea, sneezing, or itching, intranasal cromolyn has an excellent safety profile and should be considered as first-line therapy. If cromolyn is ineffective for these symptoms or is poorly tolerated, an oral antihistamine should be given. Chlorpheniramine and tripelennamine have an extensive record of use in pregnant women and remain the antihistamines of choice during pregnancy. If nasal congestion is prominent, intranasal corticosteroids are both safe and effective. If an oral decongestant is desired, pseudoephedrine is the drug of choice. However, patients should be advised to avoid oral and topical decongestants during the first trimester because of the risk of infant gastrochisis (abdominal wall defect).

FUTURE THERAPIES

A variety of new treatments are emerging that may be available in the near future.

Anti-IgE therapy

A recombinant, humanized monoclonal IgG antibody directed against the Fc portion of IgE has recently been demonstrated to cause substantial reductions in the circulation of IgE levels, immediate skin test reactivity, and the immediate nasal reaction to allergen challenge. Importantly, long-term studies have demonstrated the treatment to be safe and well tolerated, with fewer adverse events than currently available allergen-specific immunotherapy. Although this new treatment offers a safe and effective alternative to both pharmacotherapy and immunotherapy, it is unknown whether long-term administration will result in a lasting modulation of the immune system.

Anticytokine treatments

IL-4 and IL-5 are key regulators of allergic sensitization and inflammation. Now in early-phase studies in allergic asthma, the soluble receptor for IL-4 appears to be safe and effective when used topically on a weekly basis. IL-5–receptor antagonists and anti–IL-5 monoclonal antibodies are also in development for asthma. If effective in bronchial asthma, all of these new drugs will probably also play roles in the treatment of allergic rhinitis.

SUMMARY

In adults with allergic rhinitis, physicians should be alert to the frequency and severity of specific symptoms and how these symptoms affect the daily functioning of the patients. A stepped care approach that involves environmental manipulations, drug therapy, and possible immunotherapy should be considered and used in all patients with nasal allergy. As new therapies are developed, patients with severe symptoms of allergic rhinitis may be able to lead more comfortable and productive lives.

REFERENCES


