

Overview of comorbid associations of allergic rhinitis

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Allergic rhinitis affects approximately 20% of the U.S. population. An association between allergic rhinitis and conditions including asthma, sinusitis, otitis media, nasal polyposis, respiratory infections, and even orthodontic malocclusions has been observed. Clinical research has identified shared pathogenic mechanisms, epidemiologic correlations, and findings from allergy testing to indicate that these conditions represent long-term physical consequences in allergic individuals. The positive response of patients afflicted with these conditions to antiallergic treatment further enhances the association between allergic rhinitis and other airway diseases. The use of nasal corticosteroids in patients with rhinitis and asthma reduces not only rhinitis symptoms but also asthma symptoms and airway reactivity to methacholine challenge. Similarly, antihistamines, with or without decongestants, result in improvement of objective measurements of pulmonary function. In the treatment of acute sinusitis, the combination of an intranasal corticosteroid and an antibiotic provides greater benefit than an antibiotic alone. Treatment strategies for allergic rhinitis should be directed at controlling the symptoms of allergic rhinitis and reducing the development of physical complications in susceptible persons. Three techniques for the treatment of allergic rhinitis are used, including avoidance of offending allergens, selection of appropriate pharmaceuticals, and allergy immunotherapy. Appropriate treatment may spare some patients of related airway diseases and may also reduce the overall cost of care. The broadened scope of allergic rhinitis and increased prevalence of IgE-mediated diseases have heightened awareness regarding the profound consequences of allergic rhinitis and the importance of effective treatment. (J Allergy Clin Immunol 1997;99:S773-80.)

Key words: Allergic rhinitis, asthma, sinusitis, otitis media, respiratory infections, nasal polyposis, antihistamines, decongestants, topical corticosteroids

Allergic rhinitis is not a trivial disease in its prevalence, discomfort, impact on the afflicted person, or its effect on related respiratory disorders. It also produces a significant economic impact. It is by far the most prevalent of the chronic allergic respiratory diseases and affects approximately 20% to 25% of the population.¹ Moreover, many studies suggest that this is an underestimate.²⁻⁸ For example, Wright et al.⁸ found that 42% of the children in their study, who were enrolled in a health maintenance organization in Tucson, had physician-diagnosed allergic rhinitis by the age of 6 years.

It is often not appreciated that patients with allergic rhinitis may experience fatigue, irritability, and mood and cognitive disturbances, in addition to the usual nasal, ocular, and throat symptoms. Indeed, allergic rhinitis can cause functional and physical impairments that can profoundly affect quality of life in both adults and adolescents.^{9,10} Although psychosocial dysfunction is an important potential effect of rhinitis, the thrust of part II of this supplement will deal with evidence that links chronic allergic rhinitis with the development and exacerbation of other airway disorders, such as asthma, otitis media, chronic sinusitis, nasal polyposis, and even orthodontic malocclusions in the pediatric population.¹¹

Abbreviations used

FEV ₁ :	Forced expiratory volume in 1 second
OME:	Otitis media with effusion
PEFR:	Peak expiratory flow rates

LINK BETWEEN RHINITIS AND OTHER CONDITIONS

For years investigators have noted an association between allergic rhinitis and asthma, sinusitis, otitis media, possibly nasal polyposis, and recurrent respiratory tract infection. Although the link may be predominantly an allergic one, nonallergic factors may also play a role (Fig. 1).

Relationship between allergic rhinitis and asthma

Several reports indicate that the incidence of allergic rhinitis in asthmatic adults can be as high as 58%.^{2-5,7} Saxon et al.¹² postulate that the higher prevalence may be related to the Industrial Revolution, because diesel particles seem to interact with allergens to produce a higher incidence. Indeed, if there is a higher prevalence on both allergic rhinitis and asthma together, there is also a suggested link between these two entities. For example, a Swiss population study showed an increased prevalence of hay fever in recent decades by analysis of the records of 18-year-old Swedish conscripts from 1971 and 1981. Indeed, the prevalence of allergic rhinitis

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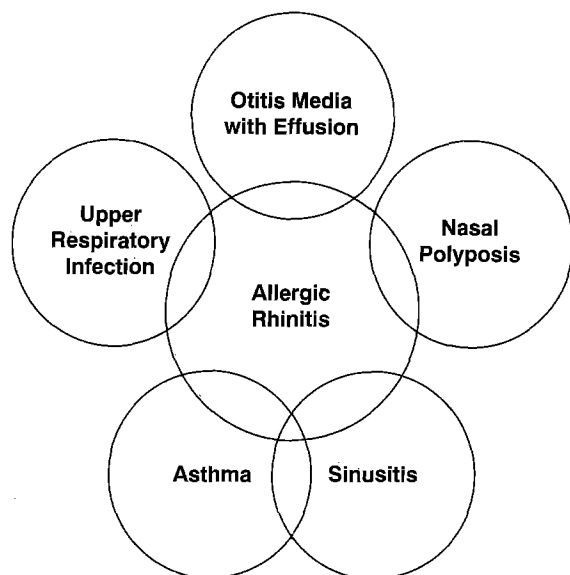


FIG. 1. Interrelationship between allergic rhinitis and associated airway diseases.

during this time increased from 4.4% to 8.4% and asthma increased from 1.9% to 2.8%.¹³

Historically, there clearly is a link between the triggers of asthma and allergic rhinitis, with mucosal inflammation a major feature in both diseases. For example, patients will often relate how, during the ragweed pollination season, their hay fever symptoms as well as cough and chest tightness will worsen, correspondingly. Exposure to allergens either experimentally or environmentally is associated with hyperreactive airways.¹⁴⁻¹⁶ Allergen exposure also seems to be a risk factor for the development of subsequent asthma.¹⁴

Hay fever has been linked to other allergic disorders such as eczema or digestive problems, but the association between asthma and hay fever has been studied extensively in terms of pathophysiology, epidemiology, and treatment.¹⁷ Studies have identified the frequent association between allergic rhinitis and asthma and that allergic rhinitis and positive skin tests are risk factors for the development of asthma.¹⁸⁻²¹ Of particular interest to clinicians are the studies showing that treatment of allergic rhinitis reduces the incidence and severity of asthma.²²⁻²⁵ In fact it has become evident that control of the upper airway is necessary to control the lower airway.

Relationship between allergic rhinitis and sinusitis

Approximately 31 million Americans develop sinusitis each year.²⁶ Investigators have linked allergy as a contributing factor in 25% to 30% of patients with acute maxillary sinusitis, with an expected incidence of 14% to 17% in control subjects.²⁷ During acute sinusitis there is swelling of mucous membranes, infiltration of eosinophils, and resulting ciliostasis and pooling of secretions that probably contribute to the subsequent infection.

These factors may play an even greater role in chronic sinusitis, whereby various investigators have associated sinusitis with diminution in ciliary beat frequency (i.e., ciliostasis). There is also ciliostasis because of the presence of major basic protein.²⁸ Interestingly, the eosinophil is a common cell found in allergic rhinitis, sinusitis, and bronchial asthma. Chronic inflammation blocks not only the ostiomeatal complex but restricts sinus drainage and causes mucous gland hypersecretion.

Newman et al.²⁹ found an association between extensive sinus disease, quantitated by computerized tomography, and allergy in 78% of patients, and asthma in 71% of patients. According to Scandinavian studies, allergy was an underlying factor in 40% to 67% of patients who had symptoms of chronic sinusitis with unilateral involvement.³⁰ If bilateral sinusitis was present, as many as 80% of patients were believed to be allergic.³¹ Other investigators^{32, 33} have also incriminated allergy as a risk factor for sinusitis.

One of the most suggestive experimental links is derived from a study reported by Pelikan et al.,³⁴ in which rhinomanometry was performed and maxillary sinus x-ray films were taken before and after nasal provocation tests. Of 73 separate provocation tests, 41 test results in 29 patients were positive. Thirteen of these revealed early-phase responses only, 18 indicated late-phase responses alone, and 10 reactions were early and late phase together. Thirty-two of these patients experienced increased sinus mucosal edema and opacification of the paranasal sinuses or other inflammation as revealed by sinus x-ray films. Concomitantly, increased pressure in the maxillary sinus, acute headaches, and associated otalgia were reported by patients. Nevertheless, three of the patients who did not have an obvious clinical response had thickened mucosa and subjective symptoms. In view of the difficulty in performing direct paranasal sinus challenges, these nasal challenges provide a link between rhinitis and sinusitis.

In addition, in sinusitis, bronchial hyperresponsiveness is correlated with extrathoracic airway hyperresponsiveness and reverses after treatment with antibiotics and nasal corticosteroids.³⁵

Link between allergic rhinitis and otitis media

Acute otitis media with effusion (OME) refers to a noninfectious inflammatory condition of the middle ear, usually accompanied by eustachian tube dysfunction, with accumulation of serous fluid. It is commonly associated with loss of hearing in children and may provide an ideal setup for a subsequent infection of the middle ear. Although infections are associated with acute otitis media or OME, the link of OME with allergic rhinitis is strong.³⁶⁻³⁹ The prevalence of nasal allergy in children with OME ranges from 35% to 50%,^{38, 39} depending somewhat on the age of the children studied. Conversely, about 21% of allergic children have OME.³⁸

An allergic association has been implied by the presence of higher levels of IgE³⁹ or eosinophil cationic protein in the middle ear of allergic children than the levels found in serum at the same time. The eustachian

tube is not only a conduit to the middle ear but may also be a target for allergy-related OME alone. A higher incidence of eustachian tube dysfunction occurs after nasal allergen challenge in atopic individuals compared with normal subjects.⁴⁰ This association has also been observed clinically.^{38, 40} In fact, during the peak ragweed and mold season, allergic children have more eustachian tube dysfunction than at other times.⁴⁰ Experimentally, pretreatment with an antihistamine/decongestant protects against the eustachian tube obstruction induced after an allergen challenge in adults with allergic rhinitis.⁴¹

Allergic rhinitis has also been associated with orthodontic malocclusions. A stuffy, blocked nose leads to mouth breathing, and the incidence of malocclusions is almost three times greater in mouth breathers than in nose breathers.¹¹ Considering the differential diagnosis of malocclusion, adenoid hyperplasia must also be considered, because removal of the adenoids may improve the occlusion.

Link between allergic rhinitis and respiratory infections

There is an interesting and possibly reciprocal relationship between respiratory tract infections and rhinitis. Epidemiologically, respiratory viral infections in childhood have lead to the development of allergic rhinitis and asthma.⁴²⁻⁴⁷ The timing and duration of a particular viral infection of the respiratory tract may influence the subsequent development of these other problems. In children infected during the first 6 months of age, the frequency of persistent wheezing from ages 7 to 8 years was directly related to the levels of respiratory syncytial virus IgE in their nasal secretions during the initial infections.⁴⁸ A rhinovirus infection can accentuate the response to an experimentally inhaled allergen or histamine challenge. After a controlled inoculation in allergic patients with rhinovirus 16, an increase in the immediate response to allergen and subsequent nonspecific hyperreactivity to histamine was observed. The rhinovirus infection also changed the pattern of allergic airway response toward that of a late-phase allergic reaction.⁴⁹

The association can also go the other way; Porro et al.⁵⁰ identified atopy as a trigger in childhood upper respiratory tract infections. Allergen exposure can induce the expression of intercellular adhesion molecule 1, which is the receptor for 90% of human rhinoviruses. This may in turn increase the susceptibility of atopic individuals to rhinovirus infections.

Link between allergic rhinitis and nasal polyps

Perhaps the link of these two entities is the most controversial, especially because there is a high incidence of nasal polyps in nonatopic asthmatic patients with "intrinsic" or corticosteroid-dependent asthma and in persons with cystic fibrosis or aspirin idiosyncrasy. Settupane and Chafee⁵¹ evaluated 211 patients with nasal polyps: 71% had asthma, 76% had positive skin tests, 29% had allergic or nonallergic rhinitis, and 14% had aspirin idiosyncrasy. Investigators have suspected

an allergic association with nasal polyps because of the presence of concomitant eosinophils, cytokines, and typical allergic inflammatory cells. The beneficial effect of steroids on polyps has also suggested their association. In fact mechanisms responsible for the accumulation and activation of nasal eosinophils are probably important in the development of the polyps.⁵² Perhaps one reason for the controversy regarding allergies and polyps is that there are multiple types of polyps, and some may have a more allergic basis than others. Polyp recurrence is more common in the presence of an underlying allergic diathesis. In fact the recurrence rate in a study of 140 patients was 36% in allergic individuals versus only 18% in nonallergic individuals.⁵³ Settupane⁵⁴ reported that the rate of repeated polypectomies increases with the rate of positive skin test to common allergens.

Clinical observation suggests that allergy control may improve the prognosis and decrease polyp recurrence and thereby reduce the overall cost of treatment.⁵⁵ As stated previously, if there is an increased incidence of rhinitis, one would anticipate an increased incidence of many of these associated comorbid conditions. Effective treatment might impact the associated problem as well as rhinitis. It is logical that economic savings can be realized with early intervention.⁵⁶⁻⁵⁸

Quality-of-life issues

Chronic allergy respiratory diseases can have a minor or profound effect on a person. Adults usually experience the consequences of chronic rhinitis with sleep disturbances and limitations of activity; however, decision making and psychomotor skills may also be diminished. In contrast, children may demonstrate behavioral problems, poor concentration, irritability, disinterest in educational and social activities, fatigue, and mood changes. Quality-of-life questionnaires bring out these associations with both asthma and hay fever. However, interestingly, Bousquet et al.,^{59, 60} who studied asthmatic patients compared with those with rhinitis, found that in all but three categories, allergic rhinitis sufferers experienced greater quality-of-life impairment than did asthmatic patients (Table I). In addition, a recent study⁶¹ showed that the use of a second-generation antihistamine improved quality of life for patients with perennial allergic rhinitis. Other investigators⁶⁵ have noticed that many indexes of cognitive skills and decision-making ability improved when allergic patients were tested at a time when they were free of seasonal allergic symptoms.

TREATMENT

The treatment of allergic rhinitis is based on three therapeutic techniques: avoidance of offending allergens, use of appropriate pharmaceutical agents, and allergy immunotherapy.

Avoidance

Because allergic triggers affect not only the nose but also many associated organs, it is important to implement avoidance procedures that are as simple yet as

TABLE I. Comparison of mean quality-of-life scores* in asthmatic patients and patients with chronic rhinitis based on generic health profile (SF-36) health status questionnaire

Health concept	Asthma (n = 252)	Chronic rhinitis (n = 111)
Physical functioning	80	89
Social functioning	84	73
Role limitations (physical)	66	61
Role limitations (emotional)	70	64
Mental health	66	65
Energy/fatigue	59	55
Pain	74	77
Change in health (1 yr)	55	50
General health perception	57	62

*Scale = 1 to 100; higher score indicates better health-related quality of life.

From Bousquet J et al. *Am J Respir Crit Care Med* 1994;149:371-5.

extensive as possible. Because some of the triggers may derive from outdoor activities at the height of the pollen season, changes in outdoor behavior may be necessary. Dealing with indoor triggers, especially the elimination of house dust mite, cockroach, and animal danders, can prove as effective, if not more so, than medications or immunotherapy. In fact studies have shown that symptoms of allergic rhinitis can improve, along with the twitchiness of the lower airways.²²⁻²⁴

PHARMACOTHERAPY

Antihistamines

As has been reviewed previously,^{63, 64} antihistamines control the symptoms of itching, sneezing, rhinorrhea, and eye irritation but not nasal congestion. Because of the adverse effects of sedating antihistamines on the central nervous system, nonsedating antihistamines are generally preferred (Table II).^{65, 66} Moreover, many of the sedating antihistamines impair performance and motor skills, and these side effects may not be apparent to the user.^{67, 68} The nonsedating antihistamines do not impair performance when used in recommended dosages.⁶⁹⁻⁷¹

Terfenadine and astemizole were linked to electrocardiographic QT prolongation and serious ventricular arrhythmias, including life-threatening torsade de pointes. These events are relatively rare and occur primarily in patients with elevated serum drug levels. Interactions of terfenadine and astemizole with certain macrolide antibiotics and imidazole antifungal agents have lead to an increased awareness of the possibility of significant drug interactions.

Oral decongestants

A decongestant is designed to relieve the symptoms of congestion or blockage. Oral preparations include pseudoephedrine, phenylpropanolamine, and phenylephrine, although the latter may not be very effective in

usual doses. As α -adrenergic agonists, they constrict blood vessels that supply the nasal mucosa, but they also constrict vessels throughout the body to some degree, raising the potential for side effects such as hypertension. Other side effects include restlessness, insomnia, headache, dry mucous membranes, and cardiovascular effects such as palpitations, tachycardia, or extrasystoles. Symptoms of bladder neck obstruction from prostate enlargement are often increased. Exacerbation of thyrotoxicosis or glaucoma can also occur; thus patients with these concomitant diseases should take oral decongestants with caution.

Nasal decongestants

Topical decongestants relieve nasal congestion more rapidly and more effectively than oral agents and are thereby susceptible to patient abuse. Examples of over-the-counter preparations include oxymetazoline, phenylephrine hydrochloride, naphazoline, and xylometazoline. Overuse of these compounds is associated with rebound nasal congestion and so-called rhinitis medicamentosa. Sufficient drug may be absorbed to exert systemic α -adrenergic effects on blood vessels, bladder, or ocular pressure.

Antihistamine/decongestant combinations

When a patient is experiencing the constellation of symptoms of rhinitis, a combination product of an antihistamine and long-acting α -adrenergic agonist is often preferable. Examples of such agents include a combination of pseudoephedrine with loratadine or terfenadine. Both combinations are available as formulations for twice-daily administration; however, loratadine/pseudoephedrine has just recently been approved in a once-daily formulation. A decrease in the number of medications and a convenient schedule should improve patient compliance. Although an antihistamine/decongestant combination may provide greater overall symptom relief than either agent alone,⁷² there is the potential side effect of jitteriness when a decongestant is added to an antihistamine.

Intranasal corticosteroids

Local administration of corticosteroids (Table II) minimizes systemic side effects associated with oral administration. Steroids serve as vasoconstrictors and reduce vascular permeability. They act on various components of the inflammatory cascade and thereby inhibit early- and late-phase allergen reactions.^{73, 74} They decrease the number of antigen-presenting cells, basophils, cytokines, and eosinophils.⁷⁵⁻⁷⁸ In comparative trials, intranasal corticosteroids are superior to antihistamines in relieving nasal symptoms.⁷⁹⁻⁸⁴ However, they usually do not relieve palatal or ocular itching as effectively^{22, 85}; therefore if these symptoms are present, an antihistamine is often added to the regimen.⁷⁹

Intranasal corticosteroids are particularly effective when used prophylactically, and they can be used once or twice daily in either an aqueous or aerosol formula-

TABLE II. Drug therapy for allergic rhinitis

Drug classification	Drug names	Administration schedule
Antihistamines	Nonsedating*	
	Astemizole	Once daily
	Fexofenadine	Twice daily
	Loratadine	Once daily
	Terfenadine	Twice daily
	Sedating	
	Cetirizine	Once daily
	Chlorpheniramine	Twice daily
	Clemastine	1-3 times/day
	Diphenhydramine	3-4 times/day
	Hydroxyzine	2-3 times/day
	Promethazine	Once daily
Decongestants	Oral	
	Phenylephrine	2-3 times/day
	Phenylpropanolamine	2-4 times/day
	Pseudoephedrine	1-4 times/day
	Nasal	
	Naphazoline	4 times/day
	Oxymetazoline	Twice daily
Antihistamine/decongestant	Phenylephrine HCl	4-6 times/day
	Xylometazoline	2-3 times/day
	Loratadine + pseudoephedrine	Once or twice daily
Intranasal corticosteroids	Terfenadine + pseudoephedrine	Twice daily
	Beclomethasone	1-4 times/day
	Budesonide	Once or twice daily
	Flunisolide	Twice daily
	Fluticasone	Once or twice daily
	Triamcinolone	Once daily
Others	Cromolyn	4 times/day
	Ipratropium bromide	4 times/day
	Oral corticosteroids	Once daily

*At recommended doses, sedation associated with these drugs is comparable to that reported with placebo.

tion. They are the treatment of choice for nonallergic rhinitis with eosinophilia (NARES syndrome), and they are useful in reducing small nasal polypoid lesions and the likelihood of polyp recurrence after surgery.

Potential disadvantages of intranasal corticosteroids include a possible cumulative effect when a person is receiving simultaneous oral corticosteroids, local irritation or bleeding, delayed onset of action compared with oral medications, lack of complete management of ocular or palatal symptoms, and inconvenience for persons who dislike use of nasal sprays. If nasal polyps or enlarged turbinates impede appropriate delivery to the nasal mucosa, pretreatment with topical decongestants or even oral steroids may be necessary for the intranasal steroid to exert its effect.

Cromolyn

Cromolyn is an antiinflammatory agent that relieves nasal itching, sneezing, hypersecretion, and congestion in patients with allergic rhinitis.⁸⁶ However, its effectiveness is generally less than that of intranasal corticosteroids in controlling allergic rhinitis.²² It blocks both the early- and late-phase hypersensitivity responses and serves as prophylaxis when given before exposure to a

known allergen. It is a safe compound, but the need for frequent administration (i.e., three or four times per day) mitigates ideal patient compliance. Its wide safety margin may prompt its use in elderly patients, children, and pregnant individuals.

Ipratropium bromide

Ipratropium bromide is an anticholinergic agent, derived from atropine, that inhibits cholinergic receptors involved in mucous secretions from glands. It can provide relief from excessive rhinorrhea associated with allergic and nonallergic rhinitis, including vasomotor rhinitis and gustatory rhinitis. It does not relieve sneezing, itching, or nasal congestion. The most common local side effects are minimal wheezing and nasal dryness, which may disappear with dosage adjustments.^{87, 88}

Systemic corticosteroids

Nasal symptoms of allergic rhinitis can be effectively controlled with systemic corticosteroids. Moreover, these agents have the advantage over nasal sprays because the drug reaches both the nasal and paranasal tissues. Unfortunately, their systemic side effects limit

their usefulness to temporary therapy for such problems as nasal polyps and severe nasal congestion.

IMMUNOTHERAPY

The effectiveness of specific immunotherapy for house dust, molds, pollens, mites, and danders has been clearly documented and recently reviewed.⁸⁹ Systemic therapy is also useful for reductions in symptoms involving other organ systems, such as the eyes or lungs. It is usually considered when environmental control measures and a reasonable trial of pharmacotherapy have proved insufficient to control symptoms. Potential systemic reactions, such as urticaria, laryngeal edema, bronchospasm, and even death, are highly unlikely with careful dose titration and monitoring.

EFFECTS OF NASAL THERAPY ON OTHER ORGAN SYSTEMS

In a study by Welsh et al.,²² three different antiinflammatory nasal preparations (i.e., beclomethasone dipropionate, flunisolide, and cromolyn sodium) relieved nasal symptoms of ragweed allergy as expected. However, when symptoms of asthma were assessed, it was apparent that lower airway symptoms were also reduced, with steroid aerosols more effective than cromolyn.

Watson et al.²⁴ examined 21 patients with both rhinitis and asthma who had hyperresponsiveness, as measured by methacholine reactivity, assessed by bronchial challenge. Patients were treated for 4 weeks with either nasal beclomethasone or placebo. The nasal corticosteroid significantly reduced rhinitis symptoms as expected but also reduced some asthma symptoms and methacholine reactivity in the airways compared with placebo. With use of an exercise-induced bronchoconstriction model, intranasal corticosteroids were also able to block exercise-induced bronchoconstriction, along with various subjective symptoms.⁹⁰

Corren et al.²³ first demonstrated that nasal allergen challenges could cause increased bronchial responsiveness, as measured by methacholine in patients with seasonal allergic rhinitis and asthma, and subsequently found that nasal beclomethasone could prevent the increase in bronchial responsiveness. In a recent study with fluticasone, European investigators²⁵ were also able to abrogate the symptoms of both rhinitis (as expected) and asthma (as measured by methacholine reactivity).

Antihistamines can also provide benefit to patients with concomitant rhinitis and asthma. Spector et al.⁹¹ studied 60 mg and 120 mg of terfenadine and found a significant bronchodilator effect, relative to placebo, that lasted at least 8 hours after a single dose. After 2 weeks of round-the-clock therapy with terfenadine, twice-daily administration, the bronchodilator effect was reduced, although patients showed no worsening of their asthma symptoms.

The effects of cetirizine were examined in a double-blind, placebo-controlled study.⁹² Cetirizine was administered in 5, 10, and 20 mg oral doses, with and without inhaled albuterol (180 mg), to 12 patients at 11 time

points over an 8-hour period. At the 20 mg dose, forced expiratory volume in 1 second (FEV₁) was generally greater than that seen with 10 or 5 mg doses, but the difference was statistically significant only at the 30-minute time point. All three doses provided significantly greater increases in FEV₁ than did placebo. The forced expiratory flow was increased by 25% to 75% for 8 hours, and peak expiratory flow rates (PEFRs) were significantly increased for 7 hours ($p < 0.02$). When added to the cetirizine regimen, albuterol appeared to have an additive effect on bronchodilation. When given alone, albuterol had the expected significant effect on pulmonary function variables between hours 1 and 5 compared with baseline. None of the cetirizine doses caused a worsening of pulmonary function.

Corren et al.⁹³ studied 193 subjects with both seasonal allergic rhinitis and asthma with a combination of 5 mg of loratadine and 120 mg of pseudoephedrine versus placebo, twice daily, for 6 weeks. Total nasal and asthma symptom severity scores improved significantly ($p < 0.05$) with loratadine plus pseudoephedrine compared with placebo throughout the 6-week study. Morning and evening PEFRs and FEV₁ were also significantly ($p < 0.05$) increased in patients who received loratadine plus pseudoephedrine in comparison with placebo-treated patients. Complete or marked relief of asthma symptoms was observed in 43% of patients treated with loratadine plus pseudoephedrine and in 23% of placebo-treated patients ($p = 0.01$). The recommended dose of loratadine plus pseudoephedrine provided effective control of symptoms of allergic rhinitis and also resulted in improvement in asthma severity and objective measurement of pulmonary function.⁹³

These studies help dispel old beliefs that antihistamines have negative effects in asthma. The mechanism by which this improvement occurs is not clear, although it appears to be another example of upper airway therapy improving the function of lower airways. An antihistamine/decongestant also may benefit patients susceptible to allergen-induced eustachian tube dysfunction⁴¹ presumably mitigating OME.

Systemic corticosteroids are known to benefit not only the symptoms of rhinitis but also the swelling and inflammation association with eustachian tube dysfunction, sinusitis (especially the polypoid variety) and bronchial asthma. One study reported that the beneficial effect of nasal steroids plus antibiotics was greater than that of antibiotics alone in the treatment of acute sinusitis.⁹⁴ Immunotherapy as a systemic treatment provides benefits not only to patients with allergic rhinitis but also to those with asthma or both. Its effect on nasal polyps has not been adequately studied. Preliminary findings of an ongoing multicenter European study on immunotherapy imply that immunotherapy might ameliorate or prevent the subsequent development of asthma.⁹⁵

In summary, upper airway problems have been linked pathophysiologically, epidemiologically, and therapeutically to associated organs. The diagnosis and treatment

of rhinitis are important not only for its own sake, but for its impact on other organ systems as well.

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