

The Patient with Allergies

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KEYWORDS

• Allergy • Adult allergy • Atopy • Allergic rhinitis

Allergy is extremely common in the United States, with 20% to 25% of the general adult population affected by some form of chronic allergic respiratory disease.¹ Among children, allergic disease is more common, with some sources estimating that it affects up to 40% of children.² The social and economic burden of allergic disease is substantial, with allergic rhinitis alone responsible for 3.5 million missed days of work³ and more than \$6 billion spent on prescription medications alone for its treatment in 2000.⁴ This does not take into account loss of productivity, physician office visits, over-the-counter medications, or other costs associated with additional manifestations of allergic disease.

Allergic diseases are ubiquitous in the United States, affecting all ages and walks of life, and they account for a large number of physician visits annually. Simplified, allergy is the undesirable clinical manifestation of an exaggerated immunologic response to an otherwise harmless antigen. These responses also are known as hypersensitivity reactions and are classified further into several different types, depending on the immunologic mechanism of the reaction. The focus of this article involves the manifestations of the most familiar and best understood of the hypersensitivity reactions, type 1 hypersensitivity, also termed immediate hypersensitivity. Type 1 hypersensitivity reactions are immunoglobulin (Ig)E-mediated, and the process of IgE production in response to exposure to an allergen is termed atopy. While type 1 hypersensitivity can be caused by ingestion of food antigens or pharmaceuticals, this article will focus on IgE-mediated allergic disease caused primarily by inhalant allergens.

Inhalant allergic diseases may manifest in many organ symptoms. Allergic complaints, however, often are centered around the head and neck and upper airways, and because the myriad of symptoms all relate back to a single common pathogenesis, all allergic complaints frequently are gathered under the term allergic rhinitis. Much of the allergy literature centers around the diagnosis and management of allergic rhinitis, although the disease manifestations typically are not limited to the nose.

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Frequently, patients with allergic disease will state on initial presentation that they “have allergies.” This self-diagnosis is often inaccurate. A patient’s self-diagnosis should not be passively accepted without further query to establish the likelihood of allergy disease. Nonallergic triggers may cause symptoms that are identical to allergic rhinitis. These triggers include changes in the weather (or in temperature and humidity), air pollution, smoke, perfumes, fumes from household cleaning chemicals, or others. A patient with the previously mentioned triggers is more likely to have nonallergic rhinitis. However, it is just as common for patients to be completely unaware that the main cause of their symptomology is allergy. A good example is the patient with frequent sinus complaints who often feels ill from repeated infections. Many times, the cause is an underlying allergic pathology, not sinusitis.

An in-depth discussion of allergic disease and its many aspects of evaluation, diagnosis, and treatment is beyond the scope of this article. What follows is an overview of the most common manifestations of inhalant atopic disease in the head and neck, possible diagnostic options, and potential treatment choices.

HISTORY

For any patient with chronic or recurrent upper respiratory complaints, the diagnosis of inhalant allergic disease should be considered. The patient’s history is the single most important source of information in making the diagnosis of atopy.⁵ Additionally, there are various inflammatory conditions of the head and neck for which allergy may be a contributing factor to the underlying disease process. For some patients with head and neck symptoms, complete improvement may not occur unless the associated allergic issues also are addressed.

Sneezing, itchy or watery eyes, and clear rhinorrhea are common, well known allergic symptoms. However, other less specific symptoms also may indicate allergy such as complaints of nasal congestion, frequent sinus infections, change in hearing, ear pressure or pain, the feeling of ears being stopped up, or itchy throat. In addition, other disease processes, such as obstructive sleep apnea, eustachian tube dysfunction, asthma, and chronic rhinosinusitis can be exacerbated by inhalant allergies, so it is critical that the practitioner investigate the presence of allergic symptoms.

Timing and onset of symptoms are helpful to establish in diagnosing allergy. The onset of true inhalant allergies is rare in the infant and geriatric populations, but more common in the teen and young adult ages, peaking at around age 30.⁵ However, a significant change in environment, such as a cross-country move, with exposure to new allergens, can be factor in the development of allergies in the adult population, so it is important to elicit this history when seeing a new patient with allergic-type symptoms. Whether the symptoms are present year-round or only during certain seasons is very helpful in diagnosing perennial versus seasonal allergic disease.

Family history and environmental exposures are also key historical information. Allergic disease is hereditary, and other family members usually will be affected by the same or similar complaints as the patient. The list of environmental exposures can be exhaustive when considering home, outdoor, and occupational environments, but key things to inquire about are the presence of pets (indoor or outdoor) or livestock, tobacco use, hobbies, stuffed animals, carpeting or draperies in the domicile, and type of heating or air conditioning, indications of mold or humidity, and nearby landscaping. Certainly it is impossible during one session to investigate all possible exposures, but if the allergic patient is not improving with appropriate treatment, it can be highly beneficial to review additional environmental exposures.

SIGNS AND SYMPTOMS

Ear

Otitis media with effusion is an inflammatory condition of the middle ear mucosa without evidence of infection. Otitis media with effusion is the accumulation of serous fluid in the middle ear space, which can be the result of or merely accompanied by eustachian tube dysfunction. The serous fluid in the middle ear space may cause a conductive hearing loss and a feeling of fullness of the ear, both of which are often the major otologic complaints in atopic diseases. Multiple authors⁶⁻⁸ have established the relationship between IgE-mediated eosinophilic reactions and the presence of otitis media with effusion. Higher levels of IgE and eosinophil cation protein have been found in the middle ear of allergic children when compared with serum levels.⁹ Although most of the literature linking otitis media to allergic diseases is in children, a strong pathophysiological link is well established and thought to carry over into adulthood.

Eustachian tube dysfunction is thought to contribute to the development of otitis media with effusion also. This epithelium-lined tube connects the middle ear space to the nasopharynx and is responsible for both drainage of and aeration of the middle ear space. The eustachian tube normally stays closed, but is transiently opened upon swallowing, yawning, sneezing, or crying by contraction of the tensor veli palatini muscle. This transiently opens the eustachian tube and equalizes pressure across the tympanic membrane.

Therefore, the eustachian tube is uniquely positioned to be a connecting source and cause of changes in the middle ear secondary to changes in the nasal cavity. It has been shown that patients with allergic rhinitis can develop eustachian tube obstruction after provocation tests.¹⁰ It has been postulated that allergy may contribute to the development of otitis media with effusion in one or more of the following ways:

- Middle ear mucosa as a target organ for IgE-mediated inflammation
- Inflammation and edema of the eustachian tube leading to obstruction
- Inflammation and edema of the nasopharynx and nasal cavity
- Reflux or insufflation of infected nasopharyngeal secretions into the middle ear space.¹¹

Eyes

Perhaps one of the most common presentations of allergic symptoms is that of rhinoconjunctivitis, or a combination of allergic nasal and ocular symptoms. The marriage of the two symptoms is quite astonishing; in studies of allergic rhinitis, more than 75% of patients had coexistent allergic conjunctivitis.¹² The eye is somewhat different than other target organs in that it has no mechanical barrier to prevent interaction with allergens. Conjunctivitis is sometimes largely thought of as a minor component of the allergic response, but 70% of seasonal allergy patients report that their ocular symptoms are at least as severe as their rhinitis symptoms.¹³

During the physical examination of a patient with suspected atopy, it is important to stress that in the examination of the allergic eye, close attention should be made not only to the ocular tissues themselves, but also to the surrounding periorbital skin.¹⁴ In allergic conjunctivitis, the eyelids and eyelashes are notable for erythema, swelling, thickening, and discoloration (**Fig. 1**). The conjunctiva should be examined for hyperemia, scarring, and chemosis (clear swelling). The presence or absence of discharge from the eye should be noted, and any discharge should be documented with a description of its color, amount, location, and quality. Corneal injury is unlikely in

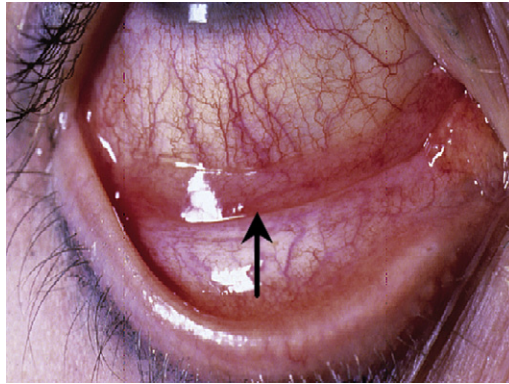


Fig. 1. Allergic conjunctivitis. Arrow indicates area of chemosis in the conjunctiva. (From Adkinson. Middleton's allergy: principles and practice. 7th edition. Philadelphia (PA): Mosby; 2008; with permission.)

acute forms of allergic conjunctivitis, but is common in more chronic forms of ocular allergy.

Perhaps one of the most striking ocular physical findings in the periorbital region of atopic patients has been termed allergic shiners.⁵ The allergic shiner is a dark discoloration that appears below the lower eyelids, similar to how a black eye or traumatic shiner would appear (**Fig. 2**). This discoloration, which also can be hereditary, can present throughout any point in life, and if left untreated, the discoloration can become permanent. Another, more subtle ocular finding that frequently accompanies allergic shiners is Dennie-Morgan lines, or simply Dennie lines.⁵ These are creases or folds that appear on the lower eyelids, underneath the lower eyelid margin (see **Fig. 2**). Both allergic shiners and Dennie lines occur from venous congestion in the orbital region as a result of nasal congestion. The venous congestion results in discoloration of the overlying skin, and it is hypothesized that localized hypoxia causes spasms of Muller muscle, which appear as Dennie lines. Leakage of hemosiderin can cause the allergic shiner discoloration to become permanent, with the possibility of Dennie lines becoming permanent also.

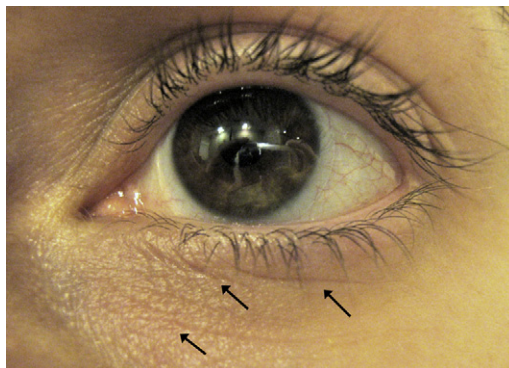


Fig. 2. Allergic shiner. Arrows indicate Dennie lines.

Should the general practitioner find these symptoms of ocular allergy, the standard treatment regimes are similar to other allergic diseases. However, it is highly recommended that one seek the expertise of an ophthalmologist if the patient does not improve quickly with routine treatment.¹⁴

Nose

Allergic rhinitis, commonly referred to as hay fever, is defined simply as an IgE-mediated inflammation of the mucous membranes of the nasal cavity. Although there is not a single etiologic or genetic factor, there are some predisposing factors. Multiple authors^{15,16} have agreed that a family history of atopy, elevated serum IgE levels in childhood (before age 6), cigarette smoke exposure, indoor allergen exposure, and a higher socioeconomic status predispose one to allergic rhinitis. Additionally, there has been agreement that the risk of allergic rhinitis is lessened in the presence of a large family, involvement in a day care setting in childhood, infectious exposures during childhood, and the avoidance of antibiotics for childhood sicknesses.^{15,16}

Allergic rhinitis can be categorized into two broad categories: seasonal allergic rhinitis and perennial allergic rhinitis according to the offending allergen. Seasonal allergens are pollens of trees, grasses, and weeds affecting patients living in more temperate climates. Because of their predictable pattern, these often can be controlled more easily with anticipatory treatment before the allergen season. Perennial allergic rhinitis typically is caused by molds, dust mites, cockroach allergens, and animal dander. As one might imagine, major sources of perennial allergic disease in the United States are dog and cat dander.

Classic manifestations of allergic rhinitis are sneezing, watery rhinorrhea, nasal itching, nasal congestion, and nasal obstruction.¹⁷ While these are the most common symptoms, allergic rhinitis is often accompanied by atopic ocular disease, ear complaints, laryngeal complaints, and, perhaps the most serious, asthma.

Physical examination provides distinctive clues to the diagnosis of allergic rhinitis. Optimal examination occurs with a nasal speculum and an adequate light source. Often clear rhinorrhea can be easily appreciated as well as edematous, boggy nasal mucosa. The inferior turbinates can be classically seen as swollen, thereby blocking nasal airflow, and can be said to have a purplish or bluish hue.¹⁵

With excessive rhinorrhea, patients will have evidence of the allergic salute. Although this is more commonly seen in children, this physical examination finding can be appreciated in the adult population also. In dealing with their rhinorrhea, patients develop a characteristic maneuver of wiping their nose with the palm of their hand and displacing the nasal tip superiorly. Over time, this creates a horizontal crease just above the nasal tip.

Lower Airways

The diagnosis of lower airway hyper-responsiveness or even a definitive diagnosis of asthma has been linked to allergic diseases repeatedly. Several large cohort studies^{18,19} have shown that the prevalence of atopic diseases early in life may be a heralding sign that they may follow a fairly predictable pattern from atopic dermatitis to allergic rhinitis to asthma, the so-called atopic march. It has been objectively shown that these phenomenon are intimately linked; nasal symptoms, nasal airflow and inflammation markers directly correlate with lower forced expiratory volume in the first second of expiration (FEV₁).²⁰

Fortunately, it seems that allergic rhinitis and asthma have a therapeutic relationship also. Treatment of allergic rhinitis has been shown in a few studies to reduce the incidence and severity of asthma. There has been a concept of priming introduced in the

literature, whereby a certain threshold of upper airway inflammation is reached and triggers lower airway changes during nasal challenge tests.²¹ In fact, some have said that control of the upper airway is necessary to control the lower airway.²²

Although there are disputes over the exact pathophysiology of the connections between atopic diseases, allergic rhinitis, and asthma, the coexistence cannot be denied. When considering the patient with allergic disease, lower airway hyper-responsiveness must be considered.

TREATMENT OPTIONS

Environmental Control

Although complete avoidance of all allergens is impossible, control and relative avoidance of known allergens may be effective and achievable. Patients who have seasonal allergies to pollens should be aware of their seasonal cycle and reduce outdoor activity during the pollen season (**Fig. 3**).

Indoor allergens are far more difficult to avoid. House dust mites, animal dander, and insect allergens are the major offending indoor allergens.² Main living areas such as bedrooms and living rooms should be free of carpet. If this is not possible and in those rooms with carpet remaining, frequent vacuuming with a double filtration system should be used. Air conditioning can often reduce humidity and can help curtail indoor mold growth, although infrequent changes of filters can promote mold growth and increase antigenic exposure. Mattresses and pillows should be enclosed in zippered, allergen-proof covers, and bed linens should be washed in hot water at least every 2 weeks and dried on a hot dry cycle.²³ Stuffed animals also can be placed in the drier on high heat weekly to reduce the burden of dust mite allergens. Perhaps the most difficult indoor allergen to control is animal dander; the only totally effective measure of control is to remove the pet from the home. Such a measure is often difficult for most patients to do. However, simply preventing the animal from entering the patient's bedroom can have a significant impact on symptoms from indoor pet allergens.

Antihistamines

Oral antihistamines are the most commonly used agents for the treatment of allergic rhinitis. Antihistamines have been shown^{21,22} to control the symptoms of nasal itching, rhinorrhea, sneezing, and ocular irritation, but have not been shown to be as effective at relieving nasal congestion.

The major difference between first- and second-generation antihistamines is the ability of the first-generation, older agents to cross the blood-brain barrier (**Table 1**). This quality makes them well known for their sedative effects. This quality has been shown to have a significant impact on school and work performance.² Second-generation antihistamines have little to no sedation effect when compared with the first-generation medications. It is notable that cetirizine is a second-generation antihistamine and is considered less-sedating because of the variability of its mild sedative quality in patients.

Oral antihistamines are first-line therapy for mild-to-moderate allergic disease and specifically for allergic rhinitis. They are also very effective at alleviating ocular symptoms and are used commonly in combination with topical antihistamines.²⁴ Additionally, it has been shown that antihistamines may be used alone to treat allergic conjunctivitis but the addition of a topical vasoconstrictive agent is more effective than either agent alone.²⁵

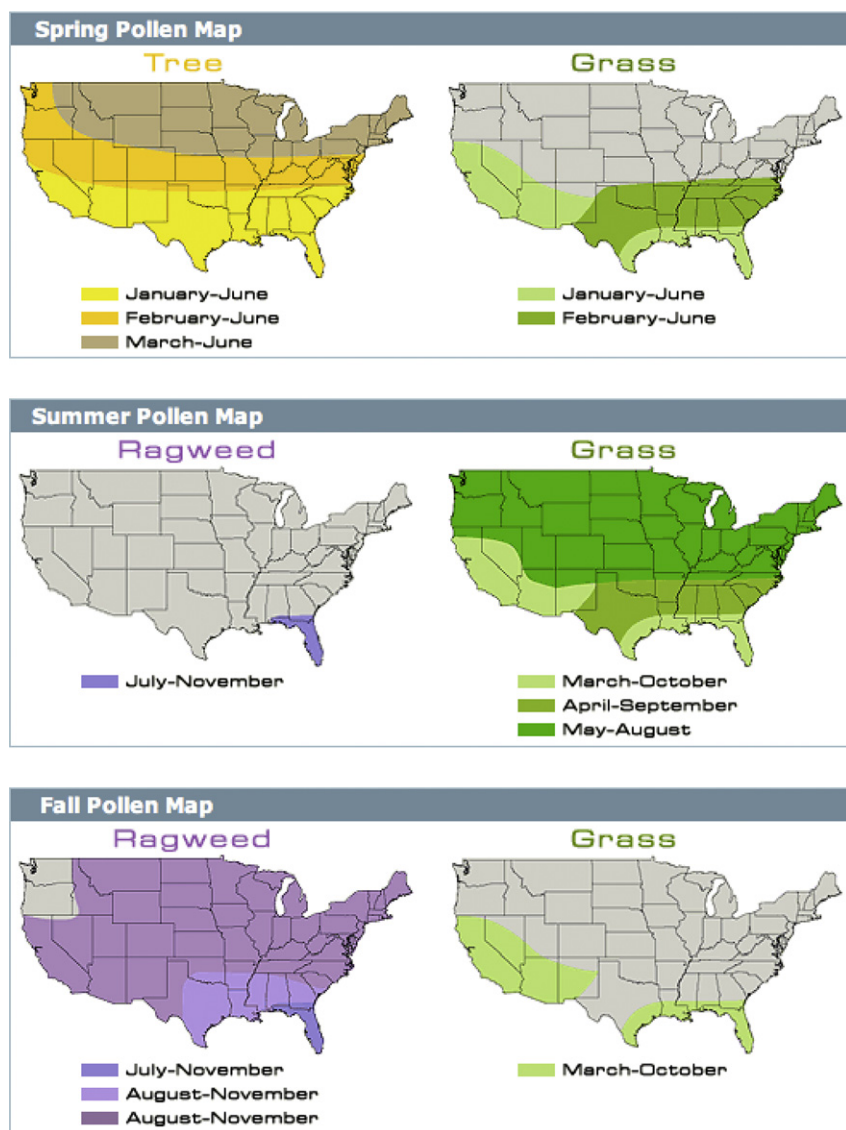


Fig. 3. Seasonal pollen map of the contiguous United States. (From AAOA Web site. Available at: <http://www.aaof.org>; with permission.)

Decongestants

Antihistamines are effective against a host of symptoms in allergic disease and allergic rhinitis. As previously mentioned, antihistamines have not been proven to be very effective against nasal congestion; therefore, combination therapy using an oral antihistamine and an oral decongestant has developed to target the full spectrum of symptoms. Decongestants such as pseudoephedrine and phenylephrine can be obtained over the counter. They are not without harmful effects, including insomnia, anorexia, and stimulation, causing difficulties with arrhythmias and exacerbation of

Table 1
Antihistamines used in treating allergic rhinitis

Drug Name		Dose	
Generic	Trade	Adults	Children
Oral Nonsedating Antihistamines			
Flexofenadine hydrochloride	Allegra Capsules ^a	1 capsule (60 mg) twice daily: 1 tablet (180 mg) daily	≥ 12 y: same as adults
Loratadine	Claritin Tablets ^b	1 tablet (10 mg) daily	≥ 12 y: same as adults
	Claritin Reditabs ^b	1 Reditab (10 mg) daily	
	Claritin Syrup ^b	2 teaspoons (5 mg/5 mL) daily	6–11y: 1–2 teaspoons daily 2–5 y: 1 teaspoon daily
Desloratadine	Clarinx Tablets ^b	1 tablet (5 mg) daily	≥ 12 y: same as adults
Oral Less-Sedating Antihistamines			
Cetirizine hydrochloride	Zyrtec Tablets ^c	1–2 tablets (5 mg) daily or 1 tablet (10 mg) daily	≥ 12 y: same as adults
	Zyrtec Syrup ^c		6–11 y: 1–2 teaspoons daily 2–5 y: start with 0.5 teaspoon (2.5 mg) daily; may increase to 1 teaspoon daily or 0.5 teaspoon twice daily
Oral Nonsedating Antihistamine–Decongestant Combinations			
Flexofenadine/pseudoephedrine HCl	Allegra-D Tablets ^a	1 tablet (60 mg/120 mg) twice daily (every 12 h)	≥ 12 y: same as adults
Loratadine/pseudoephedrine HCl	Claritin-D Tablets ^b	1 tablet (5 mg/120 mg) twice daily (every 12 h)	≥ 12 y: same as adults
	Claritin-D Tablets ^b	1 tablet (10 mg/240 mg) daily	≥ 12 y: same as adults
Oral less-sedating antihistamine–decongestant combinations		1 capsule (8 mg/60 mg) four times daily (every 4–6 h)	≥ 12 y: same as adults
Acrivastine/pseudoephedrine Semprex-D Capsules ^d HCl			

^a Aventis Pharmaceuticals, Bridgewater, NJ, USA.

^b Schering Corporation, Kenilworth, NJ, USA.

^c Pfizer Inc, New York, NY, USA.

^d Celltech Pharmaceuticals Inc, Rochester, NY, USA.

From Rosenwasser LJ. Treatment of allergic rhinitis. Am J Med 2002;113(9A):205; with permission.

coronary artery disease. Although antihistamines with or without the addition of a decongestant are the most commonly employed agents for allergic rhinitis, they are not as effective as intranasal steroid sprays at relieving overall symptoms of nasal congestion.^{25–27}

Intranasal Corticosteroids

While oral antihistamines are a mainstay for mild to moderate allergic disease, intranasal corticosteroids can provide effective first-line treatment also, and some consider them the most effective single agents for total symptom control for allergic rhinitis.² Intranasal corticosteroids are successful in ameliorating the inflammatory effects of allergic processes and are therefore effective in relieving nasal congestion in allergic rhinitis, as well as rhinorrhea, sneezing, and itching.²⁸ They typically are used once daily, but some are prescribed as twice-daily therapy. Often patients will use the intranasal steroid without immediate benefit and conclude that is ineffective. It is necessary to emphasize to patients that intranasal steroids may require up to at least 2 weeks to see significant benefit. It is important to note that intranasal corticosteroids have not been found to control ocular allergic disease as well as oral antihistamines, but they can still reduce ocular allergy symptoms.

Often there is concern from patients regarding fear of taking steroids. It is important to educate patients on the pharmacology of intranasal corticosteroids and the differences from systemic corticosteroids. There is very little systemic absorption, thereby relieving many of the concerns with long-term systemic corticosteroid use. The most common adverse effect of these medications is epistaxis, and this is most commonly caused by patients spraying the steroid toward the septum. There have been reports of septal perforation, and patients should be directed to spray away from the septum for this reason also.

DIAGNOSTIC TESTING AND IMMUNOTHERAPY

Not all patients with allergic rhinitis or atopic disease require confirmatory diagnostic testing. The patient's history and physical examination are sufficient to make the diagnosis of allergic disease in most cases. If appropriate medical therapy is instituted and it controls the patient's symptoms, then no further workup or testing is needed. However, if medical therapy fails or incompletely resolves the patient symptoms, the patient wishes to implement environmental control measures, or wishes to receive allergy immunotherapy, then a referral to an allergy practitioner is appropriate for diagnostic testing.

Diagnostic allergy testing for inhalant allergens can involve skin testing or in vitro testing. Skin testing generally involves prick testing, intradermal testing, or a combination of the two testing methods. Prick testing involves placing an antigen concentrate on the patient's skin after small, superficial punctures have been made to the epidermis, and intradermal testing involves injecting dilute solutions of antigenic material into the patient's dermis. Skin testing has the advantage of providing the patient an immediate answer to which allergens do or do not cause their symptoms but is time-consuming, carries the risk of anaphylaxis, and involves some discomfort. In vitro testing for inhalant allergens is an equally acceptable method of diagnostic testing. It has the advantages of no risk of anaphylaxis and much less discomfort as only a single needle stick to draw blood is needed; however, the test generally requires the blood be sent out to a laboratory for analysis, so it does not give the immediate answers that skin testing can give.

Immunotherapy is a very viable and effective option for some patients. Its effectiveness has been proven, especially for pollens and household allergens that are difficult to avoid.²⁹ Patient selection is critical, as there are some patients who are not suitable for immunotherapy. Patients taking beta antagonists or ace inhibitors are ineligible for immunotherapy given the difficulty in treating them for any possible anaphylaxis. It is appropriate in patients who:

- Have failed adequate medical therapy or are having significant side effects from the prescribed regimen
- Demonstrate IgE-mediated disease either through skin testing or in vitro testing
- Will commit to a 3- to 5-year process of immunotherapy escalation and maintenance
- Are controlled on medical therapy, but the regimen is too burdensome
- Are younger with allergic rhinitis with concerns about possibility preventing progression to asthma.⁵

Additionally, some patients may desire allergy testing with or without immunotherapy simply to elucidate the offending allergens for the purpose of environmental control.

These and many other clinical situations are opportunities wherein a referral to an allergist likely would provide great benefit to the patient. The allergist would be able to provide further testing and offer immunotherapy based on the clinical symptomatology. Furthermore, one of the major advantages of immunotherapy is that it is systemic therapy and has been shown to improve symptoms across multiple organ systems.

SUMMARY

Allergic disease accounts for a large number of physician visits annually in this country and diminishes the quality of life and productivity of its sufferers. Allergic disease affects multiple systems through one common immunologic mechanism of IgE-mediated response, and its symptoms can range from annoying to life threatening. Predictable symptom patterns and physical examination findings will lead clinicians to the diagnosis of allergic disease. The treatment of allergic disease includes allergen avoidance, pharmacotherapy, and immunotherapy.

REFERENCES

1. Sibbald B, Rink E. Epidemiology of seasonal and perennial rhinitis: clinical presentation and medical history. *Thorax* 1991;46:895-905.
2. Dykewicz MS, Fineman S, Skoner DP, et al. Diagnosis and management of rhinitis: complete guidelines of the Joint Task Force on practice parameters in allergy, asthma, and immunology. *Ann Allergy Asthma Immunol* 1998;81: 478-518.
3. Kay GG. The effects of antihistamines on cognition and performance. *J Allergy Clin Immunol* 2000;105:S622-7.
4. Stempel DA, Woolf R. The cost of treating allergic rhinitis. *Curr Allergy Asthma Rep* 2002;2:223-30.
5. King HC, Mabry RL, Mabry CS, et al. Interaction with the patient. In: *Allergy in ENT practice: the basic guide*. 2nd edition. New York: Thieme Medical Publishers; 2005. p. 67-104.

6. Hurst DS, Venge P. The presence of eosinophil cationic protein in middle ear effusion. *Otolaryngol Head Neck Surg* 1993;108:711–22.
7. Tomonaga K, Kurono Y, Mogi G. The role of nasal allergy in otitis media with effusion: a clinical study. *Acta Otolaryngol* 1988;458:S41–7.
8. Bernstein JM. The role of IgE-mediated hypersensitivity in the development of otitis media with effusion. *Otolaryngol Clin North Am* 1992;25:197–211.
9. Bernstein J, Lee J, Conboy K, et al. Further observations on the role of IgE-mediated hypersensitivity in recurrent otitis media with effusion. *Otolaryngol Head Neck Surg* 1985;93:611–5.
10. Friedman RA, Doyle WJ, Casselbrant ML, et al. Immunologic-mediated eustachian tube obstruction: a double-blind crossover study. *J Allergy Clin Immunol* 1993;71:442.
11. Fireman P. Otitis media and eustachian tube dysfunction: connection to allergic rhinitis. *J Allergy Clin Immunol* 1997;99:S787–97.
12. Bousquet J, Knani J, Hejjaoui A, et al. Heterogeneity of atopy. I. Clinical and immunologic characteristics of patients allergic to cypress pollen. *Allergy* 1993;48(3):183–8.
13. Wuthrich B, Brignoli M, Canevascini M, et al. Epidemiological survey in hay fever patients: symptom prevalence and severity and influence on patient management. *Schweiz Med Wochenschr* 1998;128(5):139–43.
14. Bielroy L. Allergic diseases of the eye. *Med Clin North Am* 2006;90:129–48.
15. Skoner DP. Allergic rhinitis: definition, epidemiology, pathophysiology, detection, and diagnosis. *J Allergy Clin Immunol* 2001;8:S2–8.
16. Ceuppens J. Western lifestyle, local defenses and the rising incidence of allergic rhinitis. *Acta Otorhinolaryngol Belg* 2000;54:391–5.
17. Rachelfsky GS. National guidelines needed to manage rhinitis and prevent complications. *Ann Allergy Asthma Immunol* 1999;82:296–305.
18. Gustafsson D, Sjöberg O, Foucard T. Development of allergies and asthma in infants and young children with atopic dermatitis: a prospective follow-up to 7 years of age. *Allergy* 2000;55:240–5.
19. Rhodes HL, Thomas P, Sporik R, et al. A birth cohort study of subjects at risk of atopy: twenty-two-year follow-up of wheeze and atopic status. *Am J Respir Crit Care Med* 2002;165:176–80.
20. Ciprandi G, Cirillo I, Vizzaccaro A, et al. Airway function and nasal inflammation in seasonal allergic rhinitis and asthma. *Clin Exp Allergy* 2004;34:891–6.
21. Spector SL. Overview of comorbid associations of allergic rhinitis. *J Allergy Clin Immunol* 1997;99:S773–80.
22. Corren J, Rachelefsky GS. Interrelationship between sinusitis and asthma. *Immunol Allergy Clin North Am* 1994;14:171–84.
23. Rosenwasser LJ. Treatment of allergic rhinitis. *Am J Med* 2002;113(9A):17S–24S.
24. Abelson MB, Paradis A, George MA, et al. Effects of vasocon-A in the allergen challenge model of acute allergic conjunctivitis. *Arch Ophthalmol* 1990;108:520–4.
25. van Cauwenberge P, Juniper EF. Comparison of the efficacy, safety, and quality of life provided by fexofenadine hydrochloride 120 mg, loratadine 10 mg, and placebo administered once daily for the treatment of seasonal allergic rhinitis. *Clin Exp Allergy* 2000;30:891–9.
26. Horak F, Stubner P, Ziegelmayer R, et al. Controlled comparison of the efficacy and safety of cetirizine 10 mg o.d. and fexofenadine 120 mg o.d. in reducing symptoms of seasonal allergic rhinitis. *Int Arch Allergy Immunol* 2001;125:73–9.

27. Horak F, Stubner UP, Ziegelmayer R, et al. Effect of desloratadine versus placebo on nasal airflow and subjective measures of nasal obstruction in subjects with grass pollen-induced allergic rhinitis in an allergen-exposure unit. *J Allergy Clin Immunol* 2002;109:956–61.
28. Bousquet J, van Cauwenberge P, Khaltaev N, et al, for the World Health Organization. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol* 2001;108:S147–336.
29. Nicklas R. Joint Task Force on practice parameters. Practice parameters for allergen immunotherapy. *J Allergy Clin Immunol* 1996;98:1001–11.