Chapter 6
Allergic Rhinitis: Diagnosis and Treatment

Amber N. Pepper and Dennis K. Ledford

Introduction

Rhinitis is a syndrome defined by the symptoms of nasal congestion, postnasal drip, rhinorrhea, sneezing, and nasal itching, usually with physical findings of turbinate edema and increased secretions. The term implies inflammation as an essential component of the pathophysiology, but inflammation may not always be evident or confirmed in the pathophysiology of all rhinitis syndromes. Nevertheless, rhinitis, rather than rhinopathy or another term, is generally used to describe the constellation of symptoms listed. Classification of severity is generally based on symptom intensity and duration rather than physical examination or laboratory findings. Rhinitis may be subdivided into more than nine groups based on probable etiology or associations. These include allergic, idiopathic perennial nonallergic (sometimes referred to as vasomotor rhinitis), infectious, medication related (rhinitis medicamentosa), hormonal, atrophic, polypoid or hyperplastic, and rhinitis associated with systemic diseases. Some authorities divide nonallergic rhinitis into subgroups based on triggers (e.g., weather, odor, alcohol ingestion, or irritants among others), but the symptoms and physical findings of these rhinitis subgroups tend to be more alike than dissimilar, prompting others to classify all into one category, perennial nonallergic rhinitis (PNAR). Occupational rhinitis is a classification sometimes used, referring to irritant, nonallergic rhinitis or allergic rhinitis related to work environments. This chapter focuses on allergic rhinitis and includes the differential diagnosis of other rhinitis syndromes (Table 6.1)

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Table 6.1 Differential diagnosis of rhinitis

Allergic rhinitis
Seasonal/intermittent
Perennial/persistent
Local allergic rhinitis[a]
Perennial nonallergic rhinitis (PNAR or vasomotor rhinitis)
Gustatory rhinitis
Irritant/occupational rhinitis
Mixed rhinitis (concomitant allergic and nonallergic rhinitis)
Atrophic rhinitis
Nonallergic rhinitis with eosinophilia syndrome (NARES)
With or without polyps
Infectious rhinitis
Viral
Adenovirus, influenza virus, parainfluenza virus, respiratory syncytial virus, rhinovirus
Bacterial
Haemophilus, Klebsiella, Mycobacterium, Staphylococcus, Streptococcus, Treponema
Allergic fungal rhinosinusitis
Rhinitis medicamentosa
Topical therapies
Cocaine, oxymetazoline, phenylephrine
Systemic therapies
α-Antagonists, β-blockers, estrogen or oral contraceptives, NSAIDS
Systemic diseases
Endocrine/hormonal
Diabetes mellitus, hypothyroidism, pregnancy/breast-feeding
Inflammatory/autoimmune
Cicatricial pemphigoid, eosinophilic granulomatosis with polyangiitis, granulomatosis with polyangiitis, relapsing polychondritis, reticular histiocytosis, sarcoidosis, Sjögren disease
Infiltrative
Amyloidosis
Structural disorders
Adenoid hyperplasia/cyst
Choanal atresia
Concha bullosa
Nasal polyps
Nasal septal deviation
Neoplasm
Angiofibroma (adolescent boys)
Esthesioneuroblastoma
Lymphoma
Sarcoma
Squamous cell carcinoma (smokers)
Ciliary defects

Table 6.1 (continued)

Foreign body
Cerebrospinal fluid rhinorrhea
Gastroesophageal reflux
Cystic fibrosis

NSAID nonsteroidal anti-inflammatory drugs
[a]Allergic rhinitis pathogenesis with eosinophilia but the absence of detectable systemic specific IgE and evidence of locally produced specific IgE

Table 6.2 Mediators and allergy symptoms

Mediators	Symptoms
Histamine	Itching
Prostaglandins	
Histamine	Sneezing
Prostaglandins	
Histamine	Nasal congestion/swelling (due to microvascular leakage)
Prostaglandins	
Leukotrienes	
Platelet-activating factor (PAF)	
Kinins	
Substance P	
Histamine	Mucous production
Leukotrienes	
Platelet-activating factor (PAF)	
Kinins	

Pathophysiology and Specific IgE

The pathophysiology of rhinitis is well defined for allergic, infectious, some medication related, and select systemic disease-associated rhinitis syndromes. The pathophysiology of allergic rhinitis stems from the degranulation of mast cells and the subsequent mucosal recruitment of inflammatory cells, particularly eosinophils. The role of mast cell degranulation has been confirmed by nasal allergen challenge, nasal lavage with analysis of mediators, nasal cytology, and nasal biopsy. Inflammation, characterized by recruitment of eosinophils into the nasal mucosa, is an essential component of the pathology of allergic rhinitis.

The symptoms of allergic rhinitis result from the combined effects of inflammatory cell recruitment and of the actions of mediators on receptors, for example, histamine 1 (H1) receptor or leukotrienes (LT), specifically LTD4, with the cysteinyl LT receptor 1. The mediators released from mast cells are responsible for the acute symptoms of allergic rhinitis, primarily itching and sneezing (Table 6.2 and Fig. 6.1). The mucosal inflammation is primarily a result of eosinophil immigration, activation, and persistence, due largely to factors released by the mast cell. The mast

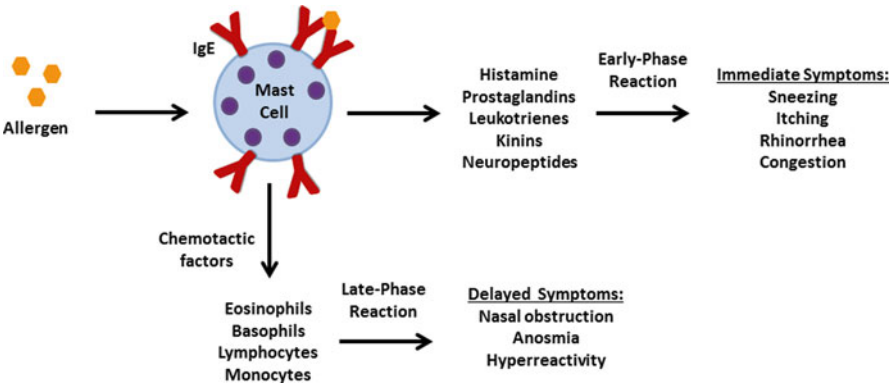

Fig. 6.1 Pathogenesis of allergic rhinitis

cell degranulates when high-affinity IgE receptors are cross-linked by antigen (allergen). IgE specific for a causal allergen is bound to the mast cell via the high-affinity IgE receptor, enabling the triggering of degranulation on exposure to specific allergen. The production of specific IgE is a result of the complex interaction of genetic predisposition and the environment. Exposure to environmental allergens, which is a risk factor for sensitization, does not result in uniform immune responses, even in subjects with similar, or even identical, genetic backgrounds. Modulation of the IgE response depends on variables such as the type of allergen, the route and dose of exposure, the timing of exposure (e.g., childhood versus adulthood), and concomitant or preceding exposure to infectious organisms or adjuvants, such as endotoxin. Genetic factors affect the epitope or specific portion of the antigen to which the individual responds (some epitopes are more likely to evoke an IgE response) as well as the immunologic regulation that modulates the tendency to produce IgE. Interactions between antigen-presenting cells, such as dendritic cells and B lymphocytes, T-regulatory cells (T_{reg}), group 2 innate lymphoid cells (ILC2), epithelial cells, and T helper 1- (Th1-) and Th2-like cells, determine the probability of specific IgG antibody formation versus IgE antibody formation versus tolerance to a specific allergen. To further complicate the understanding of this process, individuals may simultaneously be sensitized and tolerant to different allergens, for example, dust mite and cat, emphasizing that antigen properties, variation in exposure characteristics, and genetic factors regulate individual antigen responses. Finally, the blood concentration of specific IgE for a selected allergen or the magnitude of a skin test response with allergen does not generally correlate with the severity of symptoms on exposure to that allergen but rather the likelihood that the allergen is contributing to symptoms. Thus, a simple, unifying explanation of the allergic response or a measurable parameter that will consistently predict symptoms is not available.

The importance of specific IgE in the development of allergic rhinitis is confirmed by nasal challenge with allergen in subjects with specific IgE, correlation of symptoms with the level of allergen exposure, the predictive value of specific IgE in

determining response to specific allergen immunotherapy, evidence of mast cell degranulation with allergen contact, and the improvement of allergic rhinitis with anti-IgE monoclonal therapy. Local production of IgE, which would not be recognized by blood or skin tests, and non-IgE mechanisms of mast cell degranulation are hypotheses offered to explain allergic-like rhinitis in subjects without measurable, systemic specific IgE. Local allergic rhinitis is a distinct entity that presents with eosinophilia with evidence of locally produced specific IgE, but the absence of detectable systemic specific IgE.

Epidemiology

The prevalence of atopic disease in general and of allergic rhinitis in particular has increased during the past century. Currently, the prevalence of allergic rhinitis worldwide is between 20 and 30 %, increased from approximately 10–15 % at the midpoint of the twentieth century. The increase is more apparent in affluent socioeconomic circumstances, particularly Western Europe, North America, Australia, and New Zealand. Explanation for this increase remains elusive, with a variety of hypotheses summarized in Table 6.3. The hygiene hypothesis, as first suggested by Salzman and colleagues in 1979, is probably the most widely accepted explanation. This hypothesis proposes that reduced infections and endotoxin exposure in infancy diminish the stimuli to convert the Th2-like immune response (allergic-like with a predominance of interleukin 4 [IL-4] and IgE production) present at birth to a Th1-like response (nonallergic with gamma interferon production and reduced IgE). The endotoxin association suggests that the innate immune system and Toll-like receptors (TLRs) are important in the conversion of Th-2 to Th-1-like immune responses. The data supporting this is found both in epidemiologic studies as well as experimental work. For example, urban children with similar ethnic and genetic backgrounds to those in rural farming areas have a higher occurrence of allergic rhinitis.

Table 6.3 Theories for the increase of atopic diseases in the past century

Hygienic changes leading to decreased exposure to infections
Clean water
Introduction of broad-spectrum antibiotics
Use of vaccinations
Decrease in parasitic infections
Improved food preparation
Lifestyle changes
Increased time indoors with more exposure to indoor allergens
Urbanization with decreased exposure to farm animals
Increase in obesity and more sedentary way of life
Dietary changes (high in calories, low in nutrients)
Reduction in family size with fewer older siblings
Reduced breast-feeding

Furthermore, the occurrence of allergic rhinitis correlates inversely with exposure to farm animals and to endotoxin in early childhood. Conflicting data are a reminder that the hygiene hypothesis is not proven, and additional explanations for the increased prevalence of allergic rhinitis are likely.

There is a bimodal age variation in the prevalence of allergic rhinitis: one peak occurring in either the mid to late teenage years or late childhood and the second peak occurring in the mid-1920s. Most affected subjects initially develop symptoms prior to adulthood. However, a notable proportion of people with allergic rhinitis report symptom onset after the age of 30 years. The prevalence of allergic rhinitis diminishes progressively as the population ages, but an individual may develop allergic rhinitis at any age.

The importance of allergic rhinitis is its prevalence and impact on the quality of life of affected subjects. Individuals with symptomatic allergic rhinitis do not learn or process information as well as those unaffected. Sleep quality and sense of vitality are also commonly diminished. The treatments used, particularly sedating or first-generation antihistamines, may compound these problems. Allergic rhinitis is also associated with a variety of other airway diseases or symptoms, including otitis media, sinusitis, cough, and asthma, and with other allergic conditions, including atopic dermatitis and food allergy. Treatment of allergic rhinitis improves asthma and may reduce the development of asthma in those predisposed. Treatment of rhinitis may also decrease other associated conditions, including sinusitis, otitis media, and sleep disturbance. Thus, the importance of diagnosing and treating allergic rhinitis extends beyond the simple relief of nasal complaints.

Classification of Allergic Rhinitis

Traditionally, allergic rhinitis has been separated into perennial allergic rhinitis (responsible allergens found indoors, such as dust mites, cockroach, mouse, dogs, and cats) with year-round symptoms or seasonal allergic rhinitis (responsible pollen allergens found seasonally outdoors, such as trees in the spring, grass in the summer, and weeds in the fall in temperate climates in the Northern Hemisphere). The Allergic Rhinitis and its Impact on Asthma (ARIA) Workshop, in collaboration with the World Health Organization, recommended a different classification in 2001, using the terms intermittent and persistence and the severity classifications of mild and moderate/severe. Intermittent is defined as having symptoms for less than 4 days a week or less than four consecutive weeks of the year. Mild is defined as not affecting quality of life or normal daily activities. Most subjects who seek medical care are expected to be in the moderate/severe, persistent category because over-the-counter products are available for treatment of less severe disease. Published studies report that the ARIA classification is more useful in clinical assessments than the seasonal and perennial terminology, suggesting that persistent rhinitis as defined is not equivalent to perennial rhinitis and intermittent is not equivalent to seasonal. Both classifications are used clinically and in the medical literature.

Differential Diagnosis of Allergic Rhinitis

Allergic rhinitis is the most prevalent form of rhinitis and should be considered in any individual presenting with nasal complaints. Other possible diagnoses are listed in Table 6.1. The principal factors used in distinguishing allergic rhinitis from nonallergic rhinitis are summarized in Table 6.4, with history being the most important. The diagnosis of allergic rhinitis is presumptive until specific allergic sensitivity is identified by epicutaneous or percutaneous testing or in vitro-specific IgE testing. Immediate wheal and flare skin tests remain the most cost-effective means of identifying specific IgE. The value of intradermal allergy testing is primarily to exclude the diagnosis with negative results, with positive intradermal results providing only tenuous support for a diagnosis of allergic rhinitis. The evidence of specific IgE should be correlated with exposure and symptoms to support the diagnosis. Identifying environmental factors that trigger nasal symptoms is important in distinguishing allergic rhinitis from nonallergic or mixed rhinitis (components of both allergic and nonallergic rhinitis). For example, worsening symptoms from odor

Table 6.4 Diagnosis of allergic versus nonallergic rhinitis

	Allergic rhinitis	**Nonallergic rhinitis**
Age of onset	Usually <20 years of age	Usually >30 years of age
Triggers	Allergen exposure	Odor, irritants, temperature/weather changes, alcohol, food (gustatory)
Symptoms	Sneezing (>4 in succession) Pruritus Rhinorrhea (watery) Nasal congestion	Nasal congestion Rhinorrhea (clear or mucoid) Postnasal drip Sinus pressure Sneezing (<4 in succession)
Seasonal variation	Usually seasonal (if sensitized to outdoor allergens) May be perennial (if sensitized to indoor allergens)	Usually no seasonal association, although changes in symptoms with weather/temperature variation may be confused for seasonality
Family history of atopy/allergies	Presence of atopic disease	Absence of atopic disease
Associated atopic features	Allergic conjunctivitis Atopic dermatitis (eczema)	None
Physical exam findings	Transverse nasal crease Variable nasal mucosa but classically described as pale and boggy	Erythematous nasal mucosa with edema of turbinates Watery or mucoid secretions
Confirmatory tests	Nasal eosinophilia Positive specific IgE testing	Nasal eosinophilia only present in NARES, otherwise absent Negative specific IgE testing

NARES nonallergic rhinitis with eosinophilia syndrome

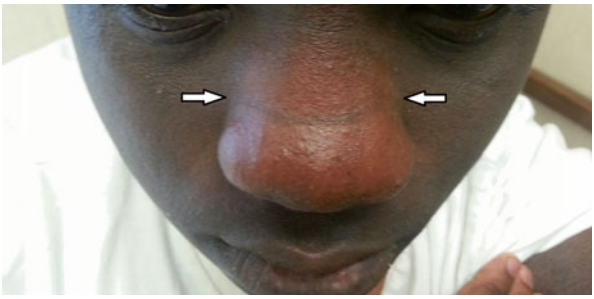

Fig. 6.2 Transverse nasal crease. Transverse nasal crease of allergic rhinitis. This photograph shows the transverse nasal crease (*arrows*) that is characteristic of allergic rhinitis. This linear change occurs from repetitive rubbing of the nose vertically, pushing the tip of the nose cephalad

would be attributed to nonallergic rhinitis, rather than allergic. If odor affects symptoms in a subject with allergic rhinitis, the individual has mixed rhinitis (i.e., coexistence of two rhinitis syndromes).

Congestion is the most common symptom prompting physician evaluation of nasal complaints but is nonspecific (Tables 6.2 and 6.4). Itching, particularly with rubbing of the nose vertically, is typical of allergic disease. The repetitive rubbing results in the characteristic "nasal crease" of allergic rhinitis (Fig. 6.2). Additional supportive historical features for allergic rhinitis include rubbing the tongue on the roof of the mouth, producing a "clucking" sound, and paroxysmal or episodic sneezing, particularly four or more in succession. Itching and sneezing are more common with intermittent or seasonal than persistent or perennial allergic rhinitis. The less frequent symptoms of itching and sneezing in persistent or perennial allergic rhinitis make it more challenging to diagnose.

The secretions in allergic disease typically are clear or white, but severe disease may result in cloudy mucus. Allergic rhinitis symptoms should be bilateral, with lateralizing complaints or findings suggesting an alternative diagnosis or a complication. The presence of other allergic diseases, particularly allergic conjunctivitis or atopic dermatitis, would also be strong support for the diagnosis of allergic rhinitis. Finally, family history is important because one immediate family member increases the likelihood of allergic rhinitis to approximately 40–50 %. Having two affected immediate family members makes the probability of having allergic rhinitis greater than 60 %.

Treatment of allergic rhinitis is reviewed in the next section.

Chronic or Perennial Nonallergic Rhinitis (Vasomotor Rhinitis)

Chronic or perennial nonallergic rhinitis (PNAR) is a term used to designate a heterogeneous group of disorders that share clinical features. The pathophysiology is not completely defined, and nasal histology does not correlate with symptoms.

PNAR is common, representing 30–60 % of subjects referred to an allergy/immunology or otolaryngology clinic for evaluation. PNAR coexists with allergic rhinitis in more than 50 % of adults with allergic rhinitis, a condition referred to as mixed rhinitis. Mucosal inflammation is less evident in PNAR than allergic rhinitis, making the term rhinitis sometimes a misnomer. However, the symptoms are consistent with other inflammatory nasal diseases, and inflammation may be present in a subset of PNAR.

The typical presentation of PNAR is complaints of nasal obstruction, with or without rhinorrhea or postnasal drip, exacerbated by physical stimuli such as odor (particularly floral smells), air temperature changes, air movement, body position change, food, beverage (particularly alcoholic drinks such as wine), or exposure to airborne irritants such as cigarette smoke. Paroxysmal sneezing and itching are less common in PNAR than allergic rhinitis. A variant of PNAR, with copious rhinorrhea associated with eating or meal preparation, is termed gustatory rhinitis. Exercise often improves the symptoms of PNAR, contrasting with allergic rhinitis.

Non-IgE degranulation of nasal mast cells, by physical stimuli such as cold, dry air, and hyperosmolar mucosal fluid, is not likely a critical part of the pathophysiology of PNAR because the symptoms of nasal itching, sneezing paroxysms, and mucosal eosinophilia are typically absent. However, mast cell degranulation has been demonstrated with cold air challenge of the nose in PNAR. Neurogenic mechanisms may play a pathophysiologic role in PNAR because some affected subjects hyperrespond with nasal congestion following challenge with cholinergic agents, suggesting a type of nasal hyperreactivity similar to that occurring in the bronchial airway with asthma.

The diagnosis of PNAR is suggested by the symptom history, the nature of provoking stimuli, adult onset, and the absence of a family history of allergy. The nasal mucosa is variable in appearance but generally is congested with normal to erythematous color. The secretions are usually clear and do not contain a significant number of eosinophils or neutrophils. Other causes of nasal symptoms should be excluded because of the lack of a confirmatory diagnostic test for PNAR. The exclusion of perennial allergic rhinitis is particularly important because the symptoms of the two are similar, and some subjects have both conditions. Sinusitis should also be considered because many symptoms are common to both.

The treatment of PNAR is symptomatic because the pathophysiology is unknown. The physician should focus the therapy on the primary symptom. Decongestants, nasal saline to lavage irritants from the mucosa or to dilute secretions, and topical ipratropium bromide 0.03 % (Atrovent Nasal) for rhinorrhea are often helpful. Oral antihistamine therapy offers limited benefits, although the anticholinergic effects of first-generation, sedating antihistamines may be helpful for rhinorrhea. Topical antihistamine therapy with azelastine is efficacious and approved for treatment of PNAR, contrasting with the lack of approval for any oral antihistamine. Topical nasal corticosteroid therapy relieves symptoms of PNAR, probably by reducing glandular secretion and blood flow to the nose. An anti-inflammatory effect of corticosteroid is not likely important in PNAR since mucosal inflammation is not consistently present. The response to topical nasal corticosteroids is variable and not as

predictable as with allergic rhinitis. Although only select nasal corticosteroids have a US Food and Drug Administration (FDA) indication for PNAR, most likely all work and all are generally used. Nasal corticosteroids with a detectable odor, for example, fluticasone (Flonase), may aggravate symptoms, suggesting a preference for sprays without smell. Intranasal capsaicin, a substance which depletes the neurokinin substance P and the active component of Sinus Buster, significantly improves symptoms in patients with PNAR as demonstrated by a placebo-controlled, clinical trial. Regular aerobic exercise, 20–30 min two to three times a week, may help reduce PNAR symptoms, at least temporarily, and is good for general health. Nasal congestion and sinus pressure are often the most bothersome symptoms, so emphasis on avoidance of regular topical decongestants is important because this may lead to rhinitis medicamentosa or rebound worsening of congestion. Oral lozenges containing menthol may affect the perception of nasal congestion but have no measurable effect on congestion. Finally, affected subjects need reassurance and empathetic care to reduce "doctor shopping," unnecessary surgery, overuse of antibiotics, and overinterpretation of allergy tests.

Nonallergic Rhinitis with Eosinophilia

Nonallergic rhinitis with eosinophilia (NARES) is a syndrome generally distinguished from PNAR by the presence of eosinophils in the nasal secretions or mucosa. The symptoms cannot be distinguished readily from PNAR, and the family history is generally negative for atopy, increasing the clinical confusion between NARES and PNAR. Affected subjects suffer from perennial nasal congestion, rhinorrhea, sneezing, and pruritus, but do not have specific IgE for allergens, an increase in total IgE, or a personal or family history of atopy. The nasal secretions contain eosinophils, which distinguishes this condition from other forms of PNAR. The lack of an atopic personal and family history in NARES makes an undefined allergy unlikely as the cause. The condition may be part of the spectrum of eosinophilic rhinitis and nasal polyposis. Subjects with the aspirin triad or aspirin-exacerbated respiratory disease (AERD; nasal polyps with eosinophils, asthma, and aspirin sensitivity) experience eosinophilic rhinorrhea and nasal congestion prior to the development of nasal polyps, suggesting a spectrum of eosinophilic nasal disease (Fig. 6.3). However, most subjects with NARES do not develop AERD.

Allergic rhinitis and nasal polyposis are the principal diagnoses to be excluded when assessing a subject with NARES. Treatment is symptomatic with topical nasal corticosteroid therapy, generally the most effective pharmacologic agent. Symptom relief may require a higher dosage of nasal corticosteroid than generally required for allergic rhinitis. Titrating the dose of nasal corticosteroid against the presence of nasal eosinophils may be of clinical value in determining the appropriate dose. Azelastine reduces eosinophil chemotaxis in vitro, but has not been studied in NARES.

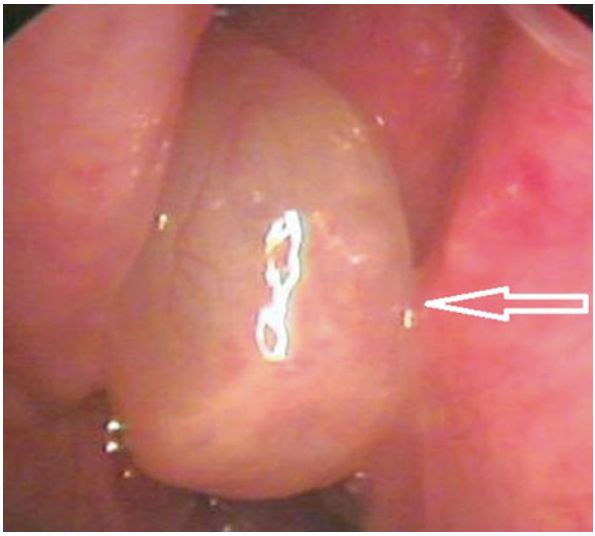

Fig. 6.3 Nasal polyp. This is a view from the rhinoscope in the left nostril. The septum is on the left, and the polyp is the pale soft tissue between the middle and inferior turbinate (*arrow*). Nasal polyps are associated with chronic inflammatory sinus disease, usually eosinophilic. Nasal polyps are not consistently found in subjects with allergic rhinitis but could explain persistent congestion. Cystic fibrosis is also associated with nasal polyps although not generally with eosinophilic inflammation

Rhinitis Induced by Drugs or Hormones (Rhinitis Medicamentosa)

Topical use of α-adrenergic decongestant sprays for more than 5–7 days in succession may result in a rebound nasal congestion following discontinuation of treatment or after the immediate effects have waned. Continued use of the decongestant to control withdrawal congestion can lead to an erythematous, congested nasal mucosa termed rhinitis medicamentosa. Regular intranasal cocaine use will have an even greater effect and should be considered in the differential diagnosis. Other systemic medications or hormone changes may also be associated with nasal symptoms, although the nasal mucosa may not always appear the same with each medication.

The mechanisms responsible for nasal symptoms associated with medications or hormones are variable. Antihypertensive therapies with β-blockers and α-adrenergic antagonists, less commonly calcium channel blockers and angiotensin-converting enzyme inhibitors, probably affect nasal blood flow. Oral α-adrenergic antagonists are also commonly used for symptom relief of prostate enlargement. Topical ophthalmic β-blocker therapy may also result in nasal congestion by the same mechanism. Oral phosphodiesterase inhibitors used for treatment of erectile dysfunction also are associated with nasal congestion, likely due to the enhancement of vasodilation from locally produced nitric oxide. Nasal congestion and/or rhinorrhea may

also result from changes in estrogen, and possibly progesterone, either from exogenous administration, pregnancy, or menstrual cycle variations. Hypothyroidism is associated with nasal congestion, rhinorrhea, and a pale, allergic-like nasal mucosa. Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) may result in congestion and rhinorrhea, primarily in subjects with AERD. Subjects with intermittent symptoms associated with aspirin or NSAIDs may be part of the evolving spectrum of chronic eosinophilic rhinosinusitis with nasal polyps (see section "Nonallergic Rhinitis with Eosinophilia").

The primary treatment of rhinitis medicamentosa is discontinuation of the offending agent or correction of the hormonal imbalance, if possible. Symptomatic treatment may be helpful. Treatment of rebound nasal congestion associated with topical decongestant use may require 5–7 days of oral prednisone or equivalent, 20–30 mg per day, followed by high-dose, topical, intranasal corticosteroid therapy. Reassurance that the nasal symptoms are the result of the medications or hormonal changes may be sufficient to discourage other unnecessary investigations if the medical treatments causing the rhinitis are essential.

Atrophic Rhinitis

Atrophic rhinitis usually occurs in late middle-aged to elderly patients. The cause of atrophic rhinitis is unknown with the leading theory being age-related mucosal atrophy, sometimes complicated by secondary bacterial infection. Primary atrophic rhinitis resembles the rhinitis associated with Sjögren syndrome or previous nasal surgery, particularly extensive turbinectomy. Examination generally reveals a patent nasal airway with atrophic erythematous turbinates, despite the symptoms of congestion.

Some subjects with atrophic rhinitis report crusting of the nasal airway and a bad smell (ozena). Ozena is associated with bacterial overgrowth of the mucosa, particularly by *Klebsiella ozaenae* or *Pseudomonas aeruginosa*. The appearance of ozena may resemble chronic granulomatous disease, such as granulomatosis with polyangiitis (Wegener granulomatosis) or sarcoidosis, or the effects of previous local irradiation. The prevalence of ozena is variable with a greater occurrence in select geographic areas, such as southeastern Europe, China, Egypt, and India, and a lower prevalence in northern Europe and the United States.

Symptomatic treatment of atrophic rhinitis with low-dose decongestants and nasal saline lavage is minimally effective. Individuals with confirmed sicca complex or Sjögren syndrome (Table 6.5) may benefit from oral cevimeline, 30 mg three times daily, keeping in mind that bronchospasm and arrhythmias are potential side effects. Oral antibiotic therapy is necessary for ozena. Topical antibiotic therapy, such as gentamicin or tobramycin, 15 mg/mL, or ciprofloxacin, 0.15 mg/mL in saline, may offer some benefit for subjects with atrophic rhinitis and recurrent mucosal infections or sinusitis, although no well-designed clinical studies are

Table 6.5 Potentially helpful tests in the diagnosis of systemic diseases with nasal symptoms

Disease	Laboratory tests and imaging studies
Common variable immunodeficiency	Quantitative immunoglobulins
Cystic fibrosis	Sweat chloride test CFTR genotyping
Eosinophilic granulomatosis with polyangiitis (Churg-Strauss vasculitis)	ANCA (specifically p-ANCA)
Granulomatosis with polyangiitis (Wegener granulomatosis)	ESR ANCA (specifically c-ANCA)
Hypothyroidism	TSH
Immotile cilia syndrome	Saccharine taste test[a] Nasal fractional exhaled nitric oxide
Relapsing polychondritis	ESR CRP
Sarcoidosis	ESR Angiotensin-converting enzyme level Chest radiograph
Selective IgA deficiency	Quantitative immunoglobulins
Sjögren syndrome	ANA Anti-Ro (SSA), anti-La (SSB) Schirmer tear test[b]
Syphilis	RPR VDRL
Tuberculosis	Tuberculin skin testing Interferon-gamma release assays Chest radiograph

ANA antinuclear antibody, *ANCA* antineutrophil cytoplasmic antibody, *CFTR* cystic fibrosis transmembrane conductance register, *CRP* c-reactive protein, *ESR* erythrocyte sedimentation rate, *RPR* rapid plasma reagin, *TSH* thyroid-stimulating hormone, *VDRL* Venereal Disease Research Laboratory (test)

[a]Saccharine is placed with a cotton swab on the inferior turbinate, at the junction of the anterior and middle thirds of the turbinate. The time required for tasting is recorded, with normal usually less than 20 min. Greater than 30 min before tasting is considered indicative of dysfunction of ciliary motility. The patient must be instructed not to sniff, blow the nose, or use any topical nasal therapies during the test (Stanley et al., Corbo et al.).

[b]A 5 × 35 mm piece of sterile filter paper is folded 5 mm from the end and inserted over the inferior eyelid at the junction of the middle and lateral third. The eye is gently closed for 5 min, and the length of wetting is measured after removal. Less than 5 mm indicates significant dryness; normal is more than 15 mm (Available from Alcon Laboratories, Fort Worth, TX)

available to validate this treatment. The addition of propylene glycol, 3–15 %, or glycerin to nasal saline may prolong the benefits of topical moisturization by reducing the water's surface tension or reducing the irritation from irrigation. Application of petrolatum or petrolatum with eucalyptus/menthol (Vicks ointment) to the nasal mucosa at night may help reduce nasal bleeding. Topical shea butter (Butter Bar Moisture Therapy), an over-the-counter herbal therapy, also may be of some benefit but likewise is unproven.

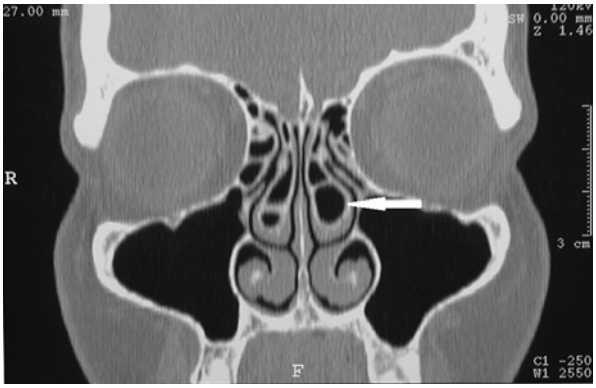

Fig. 6.4 Concha bullosa. This figure shows a coronal computed tomography scan image of the paranasal sinuses. The *arrows* point to the concha bullosa in each middle turbinate. In this case, septae divide the concha bullosa into more than one air space. The usual result of the concha bullosa is enlargement of the turbinate, usually resulting in chronic nasal congestion. Infection may occur in the concha bullosa. Frequently, the septum is deviated away from a unilateral concha bullosa. Therefore, this entity should be considered in a patient complaining of chronic congestion

Rhinitis Associated with Systemic Diseases or Anatomic Defects

The presence of systemic findings or the persistence of nasal symptoms despite treatment should prompt consideration of systemic diseases or anatomic problems resulting in nasal symptoms. Structural problems typically present with a predominance of unilateral symptoms or initially unilateral symptoms. Nasopharyngoscopy, paranasal computed tomography, and/or otolaryngologic consultation is an essential consideration with lateralizing nasal complaints, bleeding noted from one nasal airway, or unremitting congestion. Nasal septal deviations are the most common anatomic nasal variants noted, but often septal deviation is not primarily responsible for the symptoms, unless the deviation is very severe or coupled with mucosal disease such as allergic rhinitis or PNAR. A concha bullosa is an anatomic variant in which an air cell or cells occur within a nasal turbinate, often resulting in enlargement of the turbinate with congestion (Fig. 6.4). Profuse rhinorrhea should prompt testing of the secretions for glucose or for β-2 transferrin (β-trace protein) to exclude cerebral spinal fluid rhinorrhea.

Granulomatosis with polyangiitis (GPA or Wegener granulomatosis) may present initially with upper airway complaints, particularly hearing loss, intractable sinusitis, and persistent nasal congestion associated with purulent or bloody nasal discharge. Sarcoidosis of the nasal airway may appear similarly, although not usually as necrotizing. Persistent sinusitis or recurring infectious complications should prompt consideration of cystic fibrosis, partially cleft or submucosal cleft palate, humoral immunodeficiency, or ciliary dysfunction. Table 6.5 lists potentially useful tests to discriminate among the systemic possibilities.

Treatment of Allergic Rhinitis

The treatment of allergic rhinitis is three pronged—allergen exposure modification or avoidance, allergen immunotherapy (allergy shots or sublingual treatment), and pharmacotherapy. A stepwise approach to the treatment of allergic rhinitis is shown in Fig. 6.5. Clinical studies confirming efficacy of various therapies use symptoms as primary outcome variables. More objective means of assessing allergic rhinitis would be desirable, but such measures have not supplanted symptom scores in clinical trials or clinical care. Potential objective assessments include acoustic rhinometry, rhinomanometry, nasal peak flow, nitric oxide levels in exhaled air, concentration of mediators in nasal lavage, nasal cytology, and nasal histology. These assessments show promise, but difficulties with reproducibility, necessity of patient cooperation or mastering the technique, sampling error, and cost combine to reduce their utility. Using symptom scores as the primary outcome variable limits the ability to compare treatments, because the magnitude of response is not always consistent from study to study.

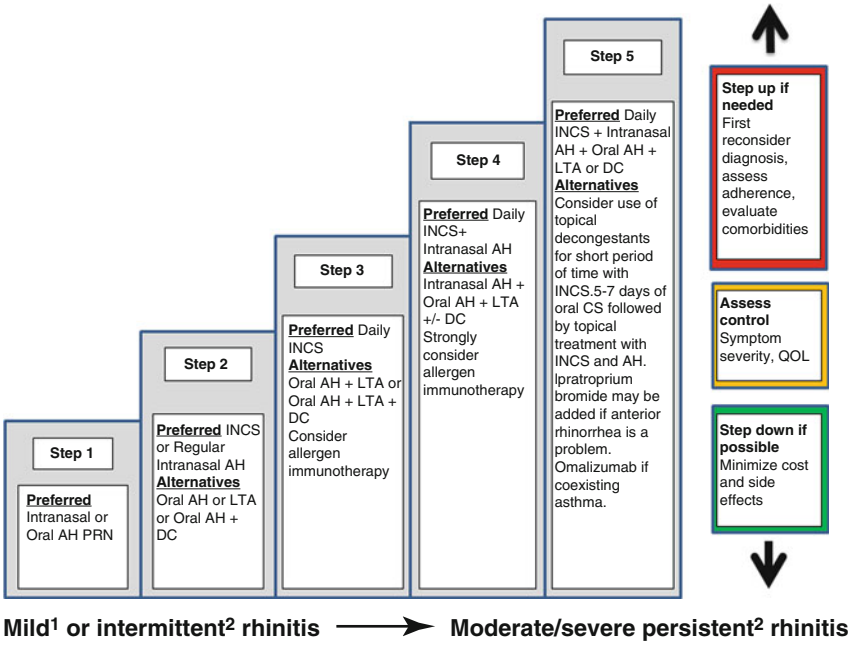

Fig. 6.5 Stepwise approach to the treatment of rhinitis (Adapted from Reference). *Legend*: *AH* antihistamines, *PRN* as needed, *LTA* leukotriene antagonists, *INCS* intranasal topical corticosteroid, *DC* oral decongestant, *CS* corticosteroid, *QOL* quality of life. [1]Mild indicates the absence of sleep disturbance, impairment of daily activities, impairment of school or work productivity. Symptoms are noted but not troublesome. [2]Intermittent is defined by ARIA as symptoms for 4 days or less a week or less than 4 consecutive weeks; persistent is greater than 4 days a week or 4 weeks

Allergen Avoidance

Avoidance is primarily helpful for indoor, domestic allergens, although occasionally modifiable occupational exposures, such as animal contact or colophony fumes during soldering, may be effective. Indoor avoidance focuses primarily on dust mite allergen reduction (encasing the pillow, mattress, and box springs with a material that does not allow dust mite movement) and washing all bedding in water at a temperature greater than 130 °F. Washing removes the allergen, which is primarily digestive enzymes present in dust mite excrement. The hot water is essential to control dust mite populations, the source of the allergen. Studies to show benefit of dust avoidance have failed when hot water washing was not assured. Air filter systems probably do not have a significant role in allergen avoidance, although high-efficiency particulate air (HEPA) filters may be helpful for homes with animals and possibly help with indoor mold spore reduction. Very little data support the use of filtration.

Allergen Immunotherapy

Specific allergen immunotherapy can be administered subcutaneously or sublingually. Indications include severe or persistent symptoms, poor response to medications, intolerance to or side effects from medications, or reluctance to take medications (Fig. 6.5). The main advantage of allergen immunotherapy, in addition to symptom improvement, is that the treatment alters the immune response. Immunotherapy shifts the immune response from Th2-like (pro-allergic) to Th1-like (nonallergic) upon exposure to an allergen, resulting in an increase in specific IgG, with some studies showing a switch from specific IgG1 to IgG4. This immunomodulation may reduce the development of additional sensitivities and minimize the occurrence of asthma in subjects with allergic rhinitis. Pharmacotherapy, aimed solely at symptom improvement, does not achieve these goals. Finally, immunotherapy offers the potential of treating allergic airway disease beyond the nose with improvement in allergic conjunctivitis and/or asthma.

Subcutaneous Immunotherapy (SCIT)

Traditionally, specific allergen immunotherapy has been administered subcutaneously. Subcutaneous immunotherapy (SCIT) is used for the treatment of seasonal and perennial allergic rhinitis, allergic asthma, and venom sensitivity with systemic reactions. SCIT provides a 50 % reduction in medication and symptoms if sufficient doses of the major allergens are administered to significantly (epicutaneous or percutaneous positive skin tests) allergic subjects. This improvement is confirmed by the majority of controlled trials with SCIT in both seasonal and perennial allergic

rhinitis. Duration of SCIT is based on clinical experience and limited evidence. In general, 3–5 years of maintenance treatment, usually administered every 3–4 weeks, is necessary to minimize reoccurrence of symptoms after discontinuation. Optimal duration minimum is likely longer for indoor, perennial allergens, suggested minimum of 4 years, compared to outdoor, seasonal allergic sensitivity, suggested minimum of 3 years.

The major impediments to SCIT are the inconvenience and cost of the therapy as well as the risk of anaphylaxis. Analyses have shown that high-dose allergen immunotherapy is cost-effective because of the reduction of regular medication use. Anaphylaxis following SCIT occurs in 0.1–3 % of treated subjects. This risk, which is minimized by identification and treatment of anaphylaxis, requires that SCIT be administered under the immediate supervision of a physician or health professional trained in the treatment of anaphylaxis. Treated subjects should remain under observation for 30 min after receiving SCIT to minimize risk of reaction after departure. Relative contraindications to SCIT include uncontrolled asthma, β-blocker therapy, and possibly angiotensin-converting enzyme inhibitor therapy. Some clinicians are less inclined to suggest SCIT in a subject with unstable autoimmune disease because of the theoretical, unproven possibility that autoimmune disease could be aggravated by the SCIT. SCIT should be initiated and supervised by a trained specialist but can be administered by any physician who is prepared to treat anaphylaxis, the most serious adverse effect of the treatment.

Sublingual Allergen Immunotherapy (SLIT)

In 2014, three sublingual tablets gained FDA approval in the United States for the treatment of allergic rhinitis, with or without allergic conjunctivitis, due to specific outdoor allergens. Two of the tablets are directed against grass pollens and the other against short ragweed. Oralair (Stallergenes) contains five northern grass pollens (Kentucky bluegrass, orchard, perennial rye, sweet vernal, and Timothy). Grastek (Merck) contains Timothy grass pollen. The third approved product, Ragwitek (Merck), contains short ragweed. A sublingual liquid containing short ragweed extract has also been studied. Appropriate candidates for sublingual immunotherapy (SLIT) must have documented positive epicutaneous or percutaneous skin test or in vitro-specific IgE testing to the allergen contained in the tablet. The first dose of each of these tablets must be administered under the supervision of a healthcare professional to monitor for anaphylaxis, but if tolerated, subsequent doses can be given at home. Given the inconvenience of recurrent office or clinic visits required with SCIT, the home administration of SLIT is attractive to patients. Grastek has the youngest approved age indication of 5 years. Oralair is approved for children and adults aged 10 through 65 years, and Ragwitek is approved for adults aged 18 through 65 years. Oralair and Grastek have an FDA Class B rating in pregnancy, while Ragwitek is Class C. SLIT can be given co-seasonally (initiated before the season and continued throughout the season) or year-round. If used co-seasonally,

Oralair should be started 4 months before grass pollen season. Grastek and Ragwitek should be started 12 weeks before the start of grass pollen season and ragweed pollen season, respectively.

Side effects of SLIT are generally localized to the mouth and gastrointestinal tract. Pruritus of the mouth and ears and throat irritation are the most common adverse reactions, but cases of eosinophilic esophagitis are reported. Sublingual immunotherapy may cause anaphylaxis, less than 1 case per million doses, and patients should be prescribed auto-injectable epinephrine during home administration. All of the tablets are contraindicated in patients with a history of severe uncontrolled asthma, anaphylaxis, or eosinophilic esophagitis.

In terms of efficacy, further evidence is needed to definitively compare SCIT and SLIT. However, some evidence suggests SCIT is superior to SLIT in the treatment of allergic rhinitis. Also, SCIT offers the advantage of treating multiple allergen sensitivities with a single injection, while SLIT is likely more effective for treatment of a limited number of allergens. Currently, there is no approved SLIT product in the United States which can be used in combination or contains multiple, non-cross-reacting allergens. The advantages and disadvantages of each administration modality should be discussed in order to choose the most appropriate immunotherapy for each individual patient.

Pharmacotherapy

Pharmacotherapy may be divided into two broad classes—topical or oral (Fig. 6.5). Advantages of topical therapy are greater efficacy for nasal complaints and limited adverse effects. Patient acceptance due to nasal irritation or taste is the major objection. Advantages of oral therapy include the potential to address the systemic nature of the allergic response and greater patient acceptance compared to sprays.

Topical Therapy of Allergic Rhinitis

Topical corticosteroids offer 70% improvement in approximately three-fourths of treated subjects, with the greatest response generally in allergic rhinitis. In addition, topical nasal corticosteroids improve symptoms in nonallergic rhinitis and subjects with nasal polyps, conditions that typically do not respond to oral therapy, other than corticosteroids and decongestants. Response with topical corticosteroids may occur within 7–12 h, but maximum effect requires days to weeks. Differences among the various products are minimal, although some agents (ciclesonide, fluticasone, mometasone) have a greater first-pass clearance of swallowed drug with less oral bioavailability. Almost 80% of a nasally administered drug is swallowed, but the relatively low dosage used in nasal therapy limits potential systemic side effects. However, studies with triamcinolone (Nasacort AQ) and beclomethasone dipropionate (Beconase or Vancenase) at recommended dosage demonstrated a significant, but small, reduction in growth of children. This is a reminder that systemic side

effects may occur with topically applied medications. Mometasone (Nasonex), triamcinolone (Nasacort AQ), and fluticasone furoate (Veramyst) have the youngest, approved age indication, 2 years of age, and budesonide (Rhinocort) has the safest Food and Drug Administration (FDA) classification for pregnancy, Class B, with other agents Class C. The most common side effect with nasal corticosteroid therapy is nasal bleeding. Bleeding is minimized by instructing the patient to administer the spray in a lateral direction or toward the ipsilateral ear, to minimize septal deposition. Mucosal atrophy does not occur with topical corticosteroids, but the anterior nasal septum and anterior inferior turbinate have a squamous epithelium, with a possibility of irritation, ischemia, and very rarely septal perforation with topical corticosteroid application.

Other topical nasal treatments include antihistamines (azelastine and olopatadine), ipratropium, and cromolyn sodium. Olopatadine reduces mast cell degranulation and is approved for seasonal allergic rhinitis. Azelastine seems to have anti-inflammatory properties when applied topically. These effects include inhibition of mast cell degranulation and inflammatory cell recruitment and reduction of adhesion receptors necessary for cell trafficking. Azelastine nasal spray is approved for both seasonal allergic rhinitis and nonallergic rhinitis. Presumably, the anti-inflammatory effects, rather than antihistamine properties, are important in the improvement of nonallergic disease because histamine does not seem to be an important mediator in nonallergic rhinitis. Thus, oral antihistamine therapy is ineffective for nonallergic rhinitis. Topical azelastine may provide symptom improvement within 30 min to an hour in allergic rhinitis, making this an ideal therapy for intermittent or as-needed use. A combination nasal spray containing both azelastine and fluticasone (Dymista) is approved for the treatment of seasonal allergic rhinitis in patients greater than 6 years of age. This combination therapy improves nasal symptoms significantly more than either treatment alone. Ipratropium nasal spray minimizes rhinorrhea by inhibiting muscarinic receptors. The indication is for both allergic and nonallergic rhinitis, but the treatment is not as effective for mucoid secretions as for watery secretions. Nasal sodium cromolyn is available over the counter. This product must be used every 4–6 h to be significantly effective because sodium cromolyn does not treat existing symptoms but rather reduces subsequent symptoms from mast cell mediator release. Nasal sodium cromolyn is likely to be useful in circumstances in which the affected subject can predict exposure to a known allergen and use the product before exposure. For example, an animal-allergic individual could use topical sodium cromolyn to suppress allergic rhinitis if the medications were applied prior to visitation of the home with the animal and if the sodium cromolyn is reapplied every 4–6 h. The requirement for regular administration makes sodium cromolyn relatively ineffective for chronic disease.

Oral Therapy of Allergic Rhinitis

Oral antihistamines, with or without decongestants, are the most commonly utilized approach in allergic rhinitis (Table 6.6). The second- and third-generation antihistamines offer excellent relief of itching and sneezing without the side effects of

Table 6.6 Oral antihistamines used in the treatment of rhinitis

Antihistamine	Generation	Availability[a,b]
Cetirizine (Zyrtec)	Second	OTC
Chlorpheniramine (Aller-Chlor; Chlor-Trimeton)	First	OTC
Clemastine (Tavist Allergy)	First	OTC
Cyproheptadine (Periactin)	First	Prescription only
Desloratadine (Clarinex)	Third	Prescription only
Diphenhydramine (Benadryl)	First	OTC
Fexofenadine (Allegra)	Third	OTC
Hydroxyzine (Atarax, Vistaril)	First	Prescription only
Levocetirizine (Xyzal)	Third	Prescription only
Loratadine (Claritin)	Second	OTC

OTC over the counter; trade name in parentheses
[a]Availability information for the United States of America
[b]Antihistamines listed are all available as generic

excessive sedation, dryness, constipation, or bladder dysfunction. Thirty percent improvement in 50 % of treated subjects is the approximate expected clinical response. The explanation for the reduced magnitude of response with oral antihistamine therapy, compared to topical nasal corticosteroids, is the general lack of improvement in congestion and inflammation and limited, if any, effect on nonallergic rhinitis. Nonallergic rhinitis may coexist with allergic rhinitis in up to 50 % of affected adults. In addition, symptoms of allergic rhinitis are the result of multiple mediators, limiting the benefits of a single inhibitor (Table 6.2 and Fig. 6.1).

Selecting an oral antihistamine therapy is often predicated on formulary coverage, cost, prior therapeutic trials, tolerance, degree of functional impairment, and personal bias. Sedating oral antihistamines, such as hydroxyzine or diphenhydramine, are very effective H1 inhibitors but are limited by anticholinergic side effects and sedation. Second- and third-generation antihistamines cause less anticholinergic side effects and sedation. Cetirizine, desloratadine, fexofenadine, levocetirizine, and loratadine are the second- and third-generation oral antihistamines available in the United States. Distinguishing these agents is a challenge and subject to individual opinion more than evidence. Several antihistamines are available over the counter, including diphenhydramine, cetirizine, loratadine, and fexofenadine. Others, including hydroxyzine, levocetirizine, and desloratadine, are available by prescription only. A complete list is shown in Table 6.6. Cetirizine, desloratadine, levocetirizine, and loratadine have the youngest approved age indication, 6 months. One study shows some benefit in 50 % of subjects after changing oral antihistamine therapy in individuals who have noted declining benefit with chronic antihistamine treatment. This supports the commonly reported phenomenon of “resistance” or tolerance to oral antihistamine therapy, without evidence of measurable change in the histamine receptor. Adding an oral decongestant to an antihistamine may improve the clinical response, particularly by reducing nasal congestion, but also may result in side effects of nervousness, sleep disturbance, increase in blood

pressure, tremor, and bladder dysfunction. This is a popular alternative due to the primal importance of nasal congestion among affected subjects.

Oral montelukast is also effective for seasonal and perennial allergic rhinitis and associated with minimal side effects. The degree of improvement is difficult to compare to oral antihistamine therapy but is probably equivalent to slightly less effective. An advantage of oral montelukast is a greater effect on asthma than oral antihistamines at approved doses. Montelukast may be particularly useful in a subject with cough, attributed to upper airway disease, but who may have a component of asthma as well.

Oral corticosteroid therapy of relatively short duration is effective for severe rhinitis associated with congestion such that topical therapy is limited by the inability to deliver the treatment to the affected mucosa. Oral corticosteroid therapy is also helpful for nasal polyps and rhinitis medicamentosa. Treatment is generally limited to 5–7 days to minimize side effects, and the dose is generally 0.5 mg/kg/day of prednisone or equivalent.

Future Therapeutic Options for Allergic Rhinitis

Future therapies for allergic rhinitis may include immunomodulators such as monoclonal anti-IgE (omalizumab), inhibitors of inflammatory cell immigration into the nasal mucosa, and anti-inflammatory therapies. Omalizumab binds to soluble IgE and also results in a reduction in the high-affinity receptor for IgE on mast cells and basophils and probably on select dendritic cells and B lymphocytes. Omalizumab is currently FDA approved for the treatment of moderate to severe, persistent asthma and chronic idiopathic urticaria unresponsive to oral antihistamine therapy. It is not approved for allergic rhinitis. Despite lacking FDA approval, omalizumab significantly improves symptoms and quality of life in patients with poorly controlled allergic rhinitis. Histamine 3 (H3) and histamine 4 (H4) receptor antagonists are considerations for the treatment of allergic rhinitis. H3 receptors modulate vascular patency in the nasal mucosa, and H4 receptors are expressed on mast cells, basophils, and eosinophils, making these receptors attractive targets for allergic rhinitis therapy. Modulation of TLRs is under investigation for the treatment of allergic rhinitis. Other potential therapies include cytokine inhibitors and phosphodiesterase 4 inhibitors. The potential of more rapid application of this cutting-edge science to allergic rhinitis is greater than other diseases due to the relative ease of applying these therapeutics to the nasal mucosa.

Conclusion

Allergic rhinitis is a common condition that significantly impacts the quality of life of affected subjects and occurs coincidentally with a variety of other airway, systemic, or allergic conditions. The application of an appropriate differential diagnosis and targeting therapy to the predominant symptom of the patient will allow the

physician to make a major difference in the lives of affected subjects. Nasal disease is complex in scope, but the two most common conditions, allergic rhinitis and perennial nonallergic rhinitis, can be assessed with a modest degree of investigation. As with most medical conditions, the history is paramount because the physical findings in rhinitis are somewhat limited or nonspecific. Consideration should always be given to systemic diseases other than allergy, particularly if the clinical data are inconsistent or initial response to therapy is disappointing. Appropriate allergy testing is essential to confirm the diagnosis of allergic rhinitis. Knowledge of the environment and the important allergens in a particular area are critical to understanding the results of allergy testing. Many of the "panels" offered by commercial laboratories are not targeted to specific environments. Allergists/immunologists have a unique advantage in the assessment of affected subjects because their training encompasses both the immunologic and environmental factors that affect the upper airway.

Evidence-Based Medicine

Tsabouri S, Tseretopoulou X, Priftis K, Ntzani EE. Omalizumab for the treatment of inadequately controlled allergic rhinitis: a systematic review and meta-analysis of randomized clinical trials. J Allergy Clin Immunol Pract. 2014;2(3):332–40.e1.

Omalizumab, a monoclonal antibody which binds and neutralizes IgE, shows promise in the treatment of poorly controlled seasonal and perennial allergic rhinitis. This systematic review examines 11 randomized controlled trials including 2,870 subjects. Omalizumab significantly improved nasal symptoms and quality of life and reduced the use rescue medications. However, the magnitude of reduction in nasal symptoms was somewhat modest, especially when considering the substantial cost of this therapy.

Chelladurai Y, Suarez-Cuervo C, Erekosima N, Kim JM, Ramanathan M, Segal JB, Lin SY. Effectiveness of subcutaneous versus sublingual immunotherapy for the treatment of allergic rhinoconjunctivitis and asthma: a systematic review. J Allergy Clin Immunol Pract. 2013;1(4):361–9.

Dretzke J, Meadows A, Novielli N, Huissoon A, Fry-Smith A, Meads C. Subcutaneous and sublingual immunotherapy for seasonal allergic rhinitis: a systematic review and indirect comparison. J Allergy Clin Immunol. 2013;131(5):1361–6.

Although both subcutaneous and sublingual immunotherapy are useful in the treatment of allergic rhinitis, the superiority of one mode of administration over the other is an area of active debate. Two systematic reviews attempted to assess if SCIT or SLIT is more effective. Dretzke et al. stated more head-to-head trials are needed to make a conclusion about the relative effectiveness of SCIT versus SLIT. However, Chellandurai et al. concluded there is moderate-grade evidence that SCIT is superior to SLIT in reducing allergic rhinitis and rhinoconjunctivitis symptoms. Continued research is needed to elucidate the comparative effectiveness of SCIT versus SLIT.

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