Allergic Rhinitis—Clinical Pathophysiology, Diagnosis, and Treatment

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Abstract

Although the term rhinitis implies inflammation of the nasal mucous membranes, inflammatory cell infiltrates are not characteristic or found in all disorders considered to be rhinitis. As a clinical term, rhinitis refers to a heterogeneous group of nasal disorders characterized by one or more of the following symptoms: sneezing, nasal itching, rhinorrhea, and nasal congestion. The symptoms of rhinitis may not be evident at all in infants and children. Rhinitis can be caused by allergic, non-allergic, infectious, hormonal, occupational, and other factors. Allergic rhinitis is the most common type of chronic rhinitis, but 30–50 % of patients with rhinitis have non-allergic triggers and the majority of these patients may have mixed rhinitis. Worldwide, the prevalence of allergic rhinitis continues to increase. Studies suggest that seasonal allergic rhinitis (hayfever) is found in approximately 10–20 % of the general population, with an even greater prevalence in children. Severe allergic rhinitis has been associated with diminished quality of life, disordered sleep (in as many as 76 % of patients), obstructive sleep apnea, and impairment in work performance. In addition, rhinitis can contribute to sinusitis and is frequently associated with asthma. Persistent allergic rhinitis has been associated with nasal remodeling.

Keywords

Rhinitis, allergic rhinitis, allergic

Allergic rhinitis (AR) is the most common type of chronic rhinitis. By definition, AR is an inflammatory disease of the nasal mucosa characterized by sneezing, itching, rhinorrhea, and nasal congestion induced by an immunoglobulin E (IgE)-mediated response.[1,2]

Epidemiology

Epidemiologic studies and recent surveys suggest that the prevalence of AR is increasing worldwide. Approximately 10–20 % of the general population and up to 40 % in children have AR.[1–5] The majority of children become symptomatic and are diagnosed by six years of age. About 80 % of all patients with AR have symptoms before 20 years of age. However, symptoms of AR can be present before two years of age.[6] Preliminary data suggest that 44–87 % of patients with rhinitis might have mixed rhinitis, a combination of allergic and non-allergic rhinitis,[7,8] although this is not entirely accepted as we know that the so-called 'non-allergic component' in mixed rhinitis may represent different forms of nasal sensitivity or hyper-reactivity and neurogenic inflammation. In addition, rhinitis can contribute to sinusitis[9,10] and is frequently associated with asthma.[10,11] Persistent AR has been associated with nasal remodeling.[12,13]

Quality of Life and Socioeconomic Impact

Quality of life studies reveal that patients with AR may have sleep disorders, irritability, persistent cough from post-nasal drip, headache and fatigue, and impaired learning ability and work performance, and is a major cause of school and work absenteeism.[14–16] The financial burden of AR is high. The direct and indirect costs of AR in the US were estimated to be $11.85 billion.[17,18] The at-work productivity loss resulted not from absenteeism but rather from the use of sedating over-the-counter antihistamines.[19]

Classification of Allergic Rhinitis

Although the term rhinitis implies inflammation of the nasal mucosal membrane, inflammatory cell infiltrates are not characteristic or found in all disorders considered to be rhinitis.[7] Rhinitis can be caused by allergic, non-allergic, infectious, hormonal, occupational, and other factors (see *Table 1*). AR has been traditionally classified as seasonal and perennial. Ten years ago, the international working group Allergic Rhinitis and its Impact on Asthma (ARIA)[11] suggested a new classification based on intermittent or persistent symptoms, putting patients into one of four categories: mild intermittent, mild persistent, moderate/severe intermittent, and moderate/severe persistent. However, Van Hoecke and her group[20] propose a modification to the ARIA classification, with patients subdivided into three different groups according to their impairment of quality of life: mild persistent, moderate persistent, and severe persistent (see *Table 2*).

Pathogenesis

The nose plays an important role in air-conditioning and host defense. Micro-organisms and allergens in sensitized people can activate resident

Allergic Rhinitis

Table 1: Classification of Allergic Rhinitis

Class	Types/Causes
I. Allergic rhinitis	A. Intermittent
	B. Persistent
	C. Episodic
II. Non-allergic rhinitis	A. Vasomotor rhinitis (non-allergic rhinopathy)
	1. Irritant-triggered (e.g. chlorine)
	2. Cold air/dry air
	3. Exercise (e.g. running)
	4. Undetermined or poorly defined triggers
	B. Food-induced/gustatory rhinitis
	C. Infectious (viral, bacterial, fungal, parasitic)
	D. Non-allergic rhinitis with eosinophilia syndrome)
III. Occupational rhinitis	A. Protein and chemical allergens; immunoglobulin E-mediated
	B. Chemical respiratory sensitizers; immune mechanisms uncertain
	C. Work-aggravated rhinitis
IV. Other rhinitis syndromes	A. Hormonally induced
	1. Pregnancy rhinitis
	2. Menstrual-cycle-related
	B. Drug-induced
	1. Rhinitis medicamentosa
	2. Oral contraceptives
	3. Antihypertensive and cardiovascular agents
	4. Aspirin/non-steroidal anti-inflammatory drugs
	5. Other drugs
	C. Atrophic rhinitis
	D. Rhinitis associated with inflammatory/immunologic disorders
	1. Granulomatous infection
	2. Wegener's granulomatosis
	3. Sarcoidosis
	4. Midline granuloma
	5. Churg–Strauss syndrome
	6. Relapsing polichondritis
	7. Amyloidosis

Source: Bousquet et al., 2008.[11]

inflammatory cells, leading to a localized immune response.[2,7,9] The nasal cavity and turbinates are lined with mucosa composed of pseudostratified columnar ciliated epithelium that overlies a basement membrane and the submucosa (lamina propria). The submucosa consists of serous and seromucous nasal glands, nerves, extensive vasculature, and cellular elements. Overlying the nasal epithelium is a thin layer of mucus that dynamically moves by means of ciliary action to the posterior nasopharynx. Infections (viral or bacterial) and allergic inflammation impair mucociliary clearance. Because nasal tissues are highly vascular, vascular changes can lead to significant nasal obstruction. Vasoconstriction and consequent decreases in nasal airway resistance result from sympathetic nerve stimulation. Parasympathetic nerve stimulation promotes secretion from nasal airway glands and nasal congestion. The nasal mucosa also contains nerves of the nonadrenergic noncholinergic system. Neuropeptides from the latter nerves (substance P, neurokinin A and K, and calcitonin gene-related peptide) are thought to play some role in vasodilatation, mucus secretion, plasma extravasation, neurogenic inflammation, and mast cell nerve interactions, amplifying the immune and allergic response.[1,2,7]

Pathophysiology—Mechanisms of Allergic Rhinitis

Common allergens causing AR include proteins and glycoproteins in airborne dust mite fecal particles, cockroach residues, animal dander, molds, and pollens. On inhalation, allergen particles are deposited in nasal mucus, with subsequent elution of allergenic proteins and diffusion into nasal tissues. In addition, small-molecular-weight chemicals in occupational agents or drugs can act as haptens that react with self-proteins in the airway to form complete allergens. Once in the nasal tissues, common aeroallergens not only undergo antigen processing to elicit allergen-specific allergic responses but also promote development of allergic airway disease through their inherent properties. Protease activities of several common aeroallergens can facilitate allergen access to antigen-presenting cells by cleaving tight junctions in the airway epithelium and through activation of protease-activated receptors on epithelial cells.[21,22] Activated epithelial cells then produce cytokines, chemokines, and thymic stromal lymphopoietin, which interact with interepithelial and subepithelial dendritic cells to skew T-cell development and adaptive allergic sensitization.

In the nose, allergens are processed by antigen-presenting cells (dendritic cells 'DC2' expressing CD1a, CD11c, and macrophages) in the nasal epithelial mucosa, with subsequent presentation of allergenic peptides by major histocompatibility complex class II molecules to T-cell receptors on resting CD4+ T lymphocytes in regional lymph nodes. With co-stimulatory signals, allergen-stimulated T cells proliferate into TH2-biased cells that release interleukin-3 (IL-3), IL-4, IL-5, IL-13, and other cytokines. These cytokines lead to a cascade of events that promotes B-cell isotype switching, with subsequent local and systemic production of allergen-specific IgE antibody production by plasma cells, eosinophilic infiltration into the nasal epithelium and mucosa, and mast cell proliferation and infiltration of airway mucosa.[7,9,21]

Mediators of Hypersensitivity

Early-phase and late-phase responses may be seen in AR. Both the early-phase and late-phase responses in AR are characterized by symptoms of sneezing, rhinorrhea, and nasal congestion. However, nasal congestion is predominantly a late-phase response. Mediators released from eosinophils during the late phase contribute to tissue damage. Stimulation of sensory nerves results in the perception of nasal congestion and itching and can provoke systemic reflexes, such as sneezing paroxysms, and can also contribute to vascular engorgement.[1,2,7,9–11] Continuing inflammation persists even when symptoms of rhinitis are quiescent (minimal persistent inflammation). This has important implications for treatment strategies and has led to the concept of the need for long-term anti-inflammatory treatment.[1,2,7,9]

Priming Effect

The amount of allergen necessary to elicit an immediate response is reduced when allergen challenges are given repeatedly, a phenomenon called the priming effect.[7,9,23] During continuing, prolonged allergen exposure and repeated late-phase/inflammatory responses, the nasal mucosa becomes progressively more inflamed and responsive to allergen. Clinically, the priming effect can explain why patients might have increasing symptoms despite decreasing aeroallergen levels as a season progresses, and also provides the rationale for initiating effective anti-

inflammatory rhinitis therapies before a pollen season or before other chronic or repetitive aeroallergen exposures. In addition, the priming effect from allergen is also associated with mucosal hyper-responsiveness and hypersensitivity to non-antigenic triggers, such as strong odors and cigarette smoke.

Sensory Nerves in Allergic Rhinitis

Activation of sensory nerves is important in the generation of acute symptoms of rhinitis.[24–26] Sensory nerves may produce inflammation by an antidromic axon reflex, which causes the release of neuropeptides such as substance P and neurokinin A. Nerve growth factor, which is responsible for the maturation and development of sensory nerves, is present in the nasal fluid of patients with AR and is increased after allergen challenge. Increased nasal sensitivity and irritation even with the slightest touch of the nasal mucosa found in AR patients correlates significantly with increased nerve fiber expression and increased subepithelial innervation.[27] The increased nerve fiber expression of sensory sodium channels Nav 1.7–1.9 in AR patients contributes to the hypersensitive state, irrespective of the degree of active inflammation. Increased allergen-induced target-organ hyper-responsiveness associated with late responses and continuing allergic disease is likely to result from a combination of inflammation and heightened sensory nerve activation.[24,28]

Local Allergic Rhinitis

Several studies have shown the existence of local AR with nasal production of specific IgE (sIgE) antibodies in the absence of atopy in over 40 % of non-AR patients. This entity is supported by the clinical symptoms, local production of sIgE, and a leukocyte–lymphocyte inflammatory pattern, with an increase in the nasal fluids of eosinophils, mast cells, and T lymphocytes during natural exposure to aeroallergens; there is also a positive immediate and dual response to a nasal allergen provocation test with local production of tryptase and eosinophil cationic protein and an increase of nasal sIgE to inhalant allergens.[7,13,29]

Association with Conjunctivitis

AR is often accompanied by allergic conjunctivitis (a complex referred to as allergic rhinoconjunctivitis), which results in conjunctival injection and chemosis and symptoms of itchy eyes and tearing.[1,2,10] The prevalence and severity of conjunctival symptoms associated with AR vary depending on several factors, but one study found allergic conjunctivitis symptoms in more than 75 % of patients with seasonal AR.[9,30]

Association with Asthma

Allergic asthma and rhinitis are comorbid conditions that are associated pathophysiologically and epidemiologically.[1,2,7–11] Both are airway diseases in which IgE antibody sensitization to aeroallergens is a prominent feature. There is evidence that systemic trafficking of inflammatory cells from local inflammation in one portion of the respiratory tract can induce inflammatory changes in the other; segmental bronchial allergen challenge in patients with AR has been shown to result in both bronchial and nasal inflammatory responses.[1,31] A substantial proportion of children with perennial AR has diminished forced expiratory flow 25–75 values and reversible airway obstruction. Nasal corticosteroids improve pulmonary function tests in these children with impaired lung function.[32–34] More than 80 % of people with allergic asthma have AR, and AR is a clear risk factor for the eventual development of asthma.[1]

Table 2: Modified Classification of Allergic Rhinitis According to Severity of Symptoms and Quality of Life Impairment

Type	Clinical Characteristics
Intermittent	Symptoms are present on fewer than four days a week and for less than four weeks
Persistent	Symptoms are present on more than four days a week and for more than four consecutive weeks
Mild	None of the following two domains is present: • sleep disturbance; or • impairment of daily activities, leisure and/or sport; impairment in school or work Or symptoms present but do not affect quality of life
Moderate	One of the following two domains is present: • sleep disturbance; or • impairment of daily activities, leisure and/or sport; impairment in school or work
Severe	Both of the following two domains are present: • sleep disturbance; or • impairment of daily activities, leisure and/or sport; impairment in school or work

Bousquet et al., 2008[11] and Van Hoecke et al., 2006.[20]

Table 3: Differential Diagnosis of Rhinitis—Conditions that Might Mimic Symptoms of Rhinitis

Pathology	Causes
Nasal polyps	Eosinophilic
	Neutrophilic (cystic fibrosis)
Structural/mechanical factors	Deviated septum/septal wall abnormalities
	Adenoidal hypertrophy
	Trauma
	Foreign bodies
	Nasal tumors: • benign; or • malignant
	Choanal atresia
	Cleft palate
	Pharyngeal reflux (laryngopharyngo-nasal reflux): • acidic; or • non-acidic
	Acromegaly (excess of growth hormone)
Cerebrospinal rhinorrhea	
Ciliary dyskinesia syndrome	

Source: Bousquet et al., 2008.[11]

Comorbidity

A considerable proportion of patients with AR will have middle ear symptoms. Otitis media with effusion is frequently encountered, as is hearing impairment owing to disturbance of the normal function of the Eustachian tube or allergic inflammation. During seasonal exposure, cough thresholds are decreased. The association of AR with cough may be amplified by the presence of posterior nasal discharge. Gastroesophageal reflux, which is known to trigger laryngeal symptoms, has also been implicated as a possible cause of inflammation of the nasopharynx, with associated rhinitis syptoms.[1,2,7,10]

Very commonly, rhinitis is linked with sinusitis and is referred to as rhinosinusitis. Conversely, sinusitis is a common complicating feature of

AR. The edema that accompanies AR will have an impact on sinus drainage. Nasal polyps may also complicate rhinitis. Nasal polyps are characterized by abundant eosinophilic infiltrate, local synthesis of IgE, and abundance of IL-5 and eotaxin. Although not attributable to allergy, nasal polyps may exist on a background of AR. Polypoid disease may be further complicated by sinusitis, which may be caused by a physical barrier to sinus drainage. More recently, the presence of *Staphylococcus aureus* enterotoxin as a superantigen has been implicated as the cause of local IgE production and steroid-insensitive inflammation. It is important to recognize this considerable overlap between rhinological diseases.[1,2,9,10]

Diagnosis

Always rule out anatomic abnormalities that may be present with prominent obstructive symptoms. Diagnosis might require fiber optic rhinopharyngoscopy or computed tomography scanning.[1,2,7,10,35,36] Nasal polyps can cause invariant unilateral or bilateral nasal obstruction and loss of smell or rhinorrhea. Polyps are infrequent in children, except for those with cystic fibrosis. Unilateral nasal polyps should raise consideration of a possible neoplasm.[35] Tumors can manifest as nasal obstruction. Juvenile angiofibromas often present with bleeding in adolescent males. Nasal carcinoma can present with unilateral epistaxis and nasal pain. Adenoidal hypertrophy in young children causes bilateral nasal obstruction and is often associated with nocturnal mouth breathing and snoring.[35,36] Wegener's granulomatosis can present with nasal and sinus complaints, including purulent rhinorrhea and, occasionally, septal erosions and perforations. Sjögren syndrome can cause nasal dryness, congestion, and crusting. Sarcoidosis can present with nasal congestion (see *Table 3*).[1,9,11]

Evaluation of the Patient with Allergic Rhinitis

Full evaluation of a patient with rhinitis should include assessment of specific symptoms bothersome to the patient and other symptoms that may be related, coming from the eyes, ears, throat, larynx, and lower respiratory tract, as well as the pattern of symptoms (infrequent/intermittent, seasonal, and perennial) that might affect therapeutic choices, identification of precipitating factors that might be avoided, previous response to medications, co-existing conditions, and a detailed environmental history, including home and occupational exposures.[1,2,7,9–11] Nasal itching is more suggestive of AR than non-AR. As AR is frequently associated with allergic conjunctivitis, the presence of eye pruritus and lacrimation is a helpful indication that a patient's rhinitis has an allergic basis. Family history is an important clue in making the diagnosis of AR in children. A handheld otoscope or headlamp with nasal speculum permits viewing of the anterior third of the nasal airway. Treatment with a topical decongestant improves visualization of the nasal cavity. However, some nasal polyps, septal deviation, adenoids, and masses can be missed because of the inability to visualize the posterior and superior nasal airways.[35–37]

Investigations

Determination of specific IgE antibodies to known allergens by means of skin testing or *in vitro* tests is indicated to provide evidence of an allergic basis for the patient's symptoms, to confirm or exclude suspected causes of the patient's symptoms, or to assess sensitivity to a specific allergen for avoidance measures, allergen immunotherapy, or both.[1,9,11] Skin testing is preferred for its simplicity, ease, and rapidity of performance, low cost,

and high sensitivity. In patients with perennial rhinitis, history is usually insufficient for distinguishing allergic from non-AR, and testing is of added importance. Neither total serum IgE levels nor total circulating eosinophil counts are routinely indicated in the diagnosis of rhinitis because they are neither sensitive nor specific for AR.[1,9,11] Nasal cytology is useful in differentiating AR and non-AR with eosinophilia syndrome from other forms of rhinitis, such as vasomotor or infectious rhinitis, if the correct procedure is followed and the appropriate stains are used.[1,2,10,36] Today, the proper use of flexible or rigid nasal endoscopes provides considerable information regarding the nose, nasopharynx, and larynx, and is an invaluable tool in the difficult-to-diagnose patient.[7,35–37]

Nasal airway measurements such as inspiratory peak flow, acoustic rhinometry, or rhinomanometry to assess airway function might be useful in evaluating patients presenting with rhinitis symptoms and persistent nasal congestion; the use of tympanometry for evaluating otitis media with effusion, a common finding in chronic rhinitis, is becoming more prominent nowadays.[2,7,10,37] Exhaled nasal nitric oxide is a sensitive marker of inflammation. Nitric oxide levels are raised in patients with AR[7] and decreased in those with sinusitis. Levels have also been shown to be low in patients with severe nasal obstruction and primary ciliary dyskinesia. Olfactory thresholds and odor identification tests are useful when smell dysfunction is suspected.[26] Although rarely used, nasal allergy challenge has an important role in establishing the causative agent in occupational rhinitis, or in the difficult case when a strong history exists despite negative skin-prick test or radioallergosorbent tests. Pulmonary function tests become important in all rhinitis patients presenting with chronic cough and for evaluating possible association with asthma.[1,2,7,9–11]

Treatment

The treatment of AR can be categorized into environmental control (allergen avoidance), patient education, pharmacotherapy, and immunotherapy.

Environmental Control and Patient Education

Allergists need to educate their patients so they understand the nature of AR, the identification of triggers, and how to implement measures for avoidance. Reducing contact with indoor/outdoor allergens, irritants, and triggers will reduce the symptoms and the continuing allergic inflammation.[38]

Pharmacotherapy

Management of AR with symptomatic and/or anti-inflammatory medications is needed when environmental control is ineffective. Selection of the appropriate medication should be individualized based on type of rhinitis, rhinitis symptoms, severity, patient age and preference (intranasal versus oral), individual response, and cost.

Oral Medications

Oral antihistamines are effective for symptoms of nasal itch, sneeze, and rhinorrhea. Their effect on nasal congestion is limited. They are ineffective for non-AR, less effective than intranasal steroids (INS) for AR, and have similar effectiveness to INS for associated ocular symptoms. Oral antihistamines are appropriate for as needed use in episodic or intermittent AR because of their relatively rapid onset of action. To avoid sedation (often not perceived by the patient), performance impairment, or

the anticholinergic effects of first-generation antihistamines, second-generation or new antihistamines with greater h1-receptor selectivity are preferred.[1,3,39–44] Oral corticosteroids are recommended only in a short course (five to seven days) in patients with moderate to severe nasal and/ocular symptoms or comorbidities not controlled by other treatments.[3,45] Oral decongestants alone or in combination with antihistamines are not recommended for treatment of AR because of a low added effect and significant adverse effects (insomnia, irritability, palpitations, hypertension). Oral decongestants should be avoided in children below six years of age.[1,3,46] Leukotriene receptor antagonists are approved for AR and reduce symptoms of nasal congestion, rhinorrhea, and sneezing. However, their effects are modest and less predictable than those of INS or antihistamines. When concomitant asthma is present, the use of leukotriene receptor antagonists has the potential to improve both nasal and bronchial symptoms. Combined with oral antihistamines, leukotriene receptor antagonists are no more effective than INS.[1,3,47–50]

Intranasal Medications
Local intranasal antihistamines are as effective as oral antihistamines for symptoms of AR but are superior in controlling nasal congestion. They are less effective than INS for nasal symptoms. These agents are approved for use in vasomotor rhinitis. Local intranasal antihistamines are appropriate for as needed use in episodic AR owing to their significantly rapid onset of action. Adverse effects are bitter taste and somnolence.[1,3,51–55] An anticholinergic (ipratropium bromide) is recommended for control of rhinorrhea in patients with AR and non-AR, although nasal dryness can occur.[56,57] INS are the most effective medications for the treatment of all allergic and non-AR symptoms, and are also effective for ocular symptoms accompanying AR. Adverse effects depend on the timing, dose, and type of INS used, with the exception of beclometasone which has shown growth restriction and should be avoided in children; at recommended dosages INS are safe and not associated with relevant systemic side adverse effects.[58–62] Cromolyn sodium has limited efficacy and short effect: it needs to be administered six times a day and needs weeks to show its full benefit. However, cromolyn sodium is effective for the prevention of symptoms of AR and other types of rhinitis and has a good safety profile. It is less effective than INS, and there are inadequate data for comparison with leukotriene antagonists and antihistamines.[1,3,63] Local decongestants are suggested for very short-term therapy (three to five days) for severe nasal congestion, but are inappropriate for daily use because of a very high risk for rhinitis medicamentosa.[64–67]

Saline Solution
Isotonic and hypertonic saline solutions are beneficial in chronic rhinorrhea and rhinosinusitis when used as a sole modality or for adjunctive treatment improving mucous rheology.[68,69]

Other Medications
Monoclonal antibodies such as omalizumab have been shown to be effective in a dose-dependent manner at controlling AR and ocular allergy symptoms by decreasing circulating IgE levels.[70,71]

Comparison of Different Pharmacotherapeutic Agents
In a recent meta-analysis (11 studies) evaluating approved medications to treat AR and their efficacy for nasal symptoms by class, antileukotrienes reduced the overall mean daily rhinitis symptom scores by 5 % compared with placebo. In the same analysis, antihistamines resulted in a 7 % reduction and INS a 17 % reduction[43] This demonstrates that not all allergic patients show the same therapeutic response. There are intrinsic differences and there may be endophenotypes that need to be understood to make the treatment of patients with AR more efficient.[72]

Immunotherapy
Allergen Immunotherapy
Subcutaneous (SCIT) or sublingual (SLIT) administration has been proved to be an effective therapeutic resource for AR with or without asthma. SCIT and SLIT potentially alter the natural course of allergic diseases, reduce the development of new sensitizations, and reduce the risk of future development of asthma in children.[73] In contrast to pharmacotherapy, the clinical benefits of immunotherapy may be sustained years after discontinuation of treatment. SLIT and SCIT are effective and safe in AR sensitized to pollen and dust mite allergy.[74–77] No life-threatening anaphylactic reactions have been reported with SLIT.[78] Although not common, serious anaphylactic reactions (some fatal) have been reported with SCIT.[79]

Surgery
Surgical procedures are indicated for the management of structural and mechanical problems or comorbid conditions of AR, such as nasal polyps and adenoidal hypertrophy.[80–82] Recent studies recommend a trial of inhaled corticosteroids before undertaking adenoidectomy.[80]

Special Considerations
Pregnancy
The clinician should consider the US Food and Drug Administration risk categories when considering treatment options in a pregnant woman with AR. Cromolyn sodium, montelukast, nasal corticosteroids, and maintenance immunotherapy are safe during pregnancy.[83,84]

Elderly Patients
Age-related anatomic and physiologic changes have to be taken in consideration for medication use. Intranasal glucocorticosteroids are safe at the recommended dose.[85]

Athletes
Antihistamines, antileukotrienes, immunotherapy, ipratropium bromide, and disodium cromoglycate are permitted by the World Anti-Doping Agency.[86]

Conclusion
Allergic rhinitis is a significant cause of widespread morbidity, medical treatment costs, reduced work productivity, and lost school days. Although sometimes mistakenly viewed as a trivial disease, symptoms of allergic and also non-allergic rhinitis may significantly affect a patient's quality of life and can be associated with conditions such as fatigue, headache, cognitive impairment, and sleep disturbance. Appropriate management of rhinitis may be an important component in effective management of coexisting or complicating respiratory conditions, such as asthma, sinusitis, and sleep apnea. Management of allergic rhinitis involves avoidance, many pharmacologic options, and, in appropriately selected patients, allergen immunotherapy. The patients that present a moderate or severe disease or persistent symptoms must be fully evaluated by a trained allergy/immunology/rhinology physician. ■

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