Allergic Rhinitis
Mechanisms and Treatment

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KEYWORDS

• Mechanisms • Allergic rhinitis treatment • Leukotrienes • Intranasal corticosteroids • Intranasal antihistamines • Subcutaneous immunotherapy • Treatment

KEY POINTS

- Allergic rhinitis is an immunoglobulin E (IgE) -mediated inflammatory disease.
- Allergic rhinitis has a significant impact on patient morbidity and is a major economic burden to society.
- There are several effective treatment modalities available for allergic rhinitis that target receptors of bioactive mediators or inflammation.
- Subcutaneous allergen immunotherapy induces tolerance to aeroallergens and is highly effective in mitigating symptoms and preventing progression of disease and comorbidities such as asthma.
- Sublingual immunotherapy formulations offer an alternative approach to subcutaneous immunotherapy, allowing for symptomatic relief to specific seasonal allergens also likely through tolerogenic mechanisms.

INTRODUCTION

Atopic diseases, including allergic rhinitis (AR), are very prevalent, especially in developed countries. Prevalence estimates of chronic rhinitis around the world range between 10% and 40%.[1–11] The impact of AR on quality of life is very significant. Allergic rhinitis is a major contributor to the total cost of health-related absenteeism (eg, missing work) and presenteeism (ie, showing up to work but having reduced productivity). For example, costs of AR and allergic conjunctivitis in the United States have been estimated at more than $6 billion per year.[12–14] Lamb and colleagues[15] estimated the productivity loss from AR to be the highest of 15 chronic conditions among employees in the United States.

There are multiple phenotypes and endotypes of rhinitis, but in recent years, rhinitis control has been increasingly emphasized.[16] AR has been traditionally categorized as

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Immunol Allergy Clin N Am 36 (2016) 261–278
http://dx.doi.org/10.1016/j.iac.2015.12.004 **immunology.theclinics.com**
0889-8561/16/$ – see front matter

seasonal allergic rhinitis (SAR), perennial allergic rhinitis (PAR), and mixed rhinitis (ie, combined allergic and nonallergic phenotype). AR has recently been classified via the ARIA (Allergic Rhinitis and its Impact on Asthma) guideline as mild versus moderate to severe and intermittent versus persistent (**Table 1**).[17,18] Regardless of the classification system, the main goal of treatment is to achieve control of nasal and ocular symptoms of SAR and PAR.

The 3 key elements of AR management are reduction of exposure to the sensitizing allergen, which includes a spectrum of environmental avoidance recommendations specific to the inciting allergen, targeted pharmacotherapy, and either subcutaneous or sublingual immunotherapy.[19,20] Environmental control should focus on avoidance of known allergens as well as nonspecific aggravating triggers, such as noxious odorants and chemical irritants (eg, fragrances, cleaning agents, environmental tobacco smoke) identified by medical history. Broad environmental control measures aimed at reducing allergen exposure (eg, house dust mite) should not be instituted without first confirming clinical relevance, which involves demonstrating sensitization by skin prick testing or serum-specific IgE and correlation of symptoms with exposure to the specific sensitizing allergen.[17,19] Often patients may exhibit sensitization but are not able to correlate their symptoms with exposure, and in these instances, nasal provocation testing using standardized methodologies to the specific allergen may be useful to confirm or exclude the clinical relevance of sensitization.[21,22] Diagnosis of AR is discussed more extensively elsewhere in this issue. (See Scadding GK, Scadding GW: Diagnosing Allergic Rhinitis, in this issue.) The importance of environmental determinants in causing AR and eliciting related symptoms with continuous or intermittent exposures is discussed more extensively elsewhere in this issue. (See Dunlop J, Matsui E, Sharma H: Allergic Rhinitis: Environmental Determinants, in this issue.) This article focuses on providing a brief overview of the mechanisms related to AR and current treatment options for this chronic and often debilitating condition.

Allergic Rhinitis Mechanisms

AR is caused by specific immunoglobulin E (IgE) -mediated reactions against inhaled allergens driven by type 2 helper T (Th2) cells. AR results in mucosal inflammation with tissue influx of eosinophils and basophils.[23,24] IgE constitutes a very small fraction of the total antibody amount in human serum, but its biological activity is enhanced by specific cell surface receptors whose affinity can vary in strength.[24] IgE is produced as a result of complex interactions between B cells, T cells, mast cells, and basophils and involves multiple cytokines, such as interleukin (IL) -4, IL-13, and IL-18.[25] On exposure of allergen into the upper respiratory tract, the allergen is taken up by antigen-presenting cells (ie, dendritic cells, B cells) and processed to a small peptide

Table 1
Rhinitis severity grading based on joint task force rhinitis guidelines

Rhinitis Severity	Medication Requirement Example
Step 1: Episodic	—
Step 2: Mild	1 medication
Step 3: Mild to moderate	2 medications or change to another medication
Step 4: Moderate to severe	2–3 medications and/or change of 1 or more medications
Step 5: Severe	Oral corticosteroid

Data from Wallace DV, Dykewicz MS, Bernstein DI, et al. The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol 2008;122(2 Suppl):S1–84.