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Pharmacologic rationale for treating allergic and nonallergic rhinitis

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Allergic rhinitis (AR) and perennial nonallergic rhinitis (PNAR) represent conditions affecting millions of individuals across the world. Although the diagnosis of AR might be presumptively based on the types of symptoms and the history of allergen triggers, confirmation requires documentation of specific IgE reactivity. In contrast, PNAR is a condition with similar symptomatology but in which the patient has no identifiable specific allergic sensitivities. This review presents the diverse options of currently available pharmacologic agents for the treatment of AR and PNAR, including intranasal corticosteroids, H1-antihistamines, decongestants, cromolyn sodium, antileukotrienes, anticholinergics, capsaicin, anti-IgE, and intranasal saline. Furthermore, appropriate stepped-up, stepped-down pharmacotherapeutic algorithms are described for the various forms of rhinitis. (*J Allergy Clin Immunol* 2006;118:985-96.)

Key words: Allergic rhinitis, nonallergic rhinitis, nonallergic rhinitis with eosinophilia syndrome, perennial nonallergic rhinitis, pharmacotherapy, H1-antihistamines, intranasal corticosteroids, antileukotrienes, capsaicin, cromolyn sodium

Abbreviations used

AR: Allergic rhinitis
INS: Intranasal corticosteroid
NARES: Nonallergic rhinitis with eosinophilia syndrome
OTC: Over the counter
PNAR: Perennial nonallergic rhinitis
VMR: Vasomotor rhinitis

Rhinitis, an extremely common rhinopathy, is characterized by the presence of nasal pruritus, sneezing, rhinorrhea, and nasal congestion. However, these symptoms do not always reflect an underlying pathologic process. For example, up to 95% of healthy adults sneeze and blow their nose up to 4 times in a given day.¹ In addition, nasal cycling, which results in temporary unilateral nasal congestion, as well as exposure to cold air, which promotes rhinorrhea, are 2 examples of normal physiologic mechanisms that sometimes could be misinterpreted as being abnormal. Therefore the magnitude and persistence of the symptoms is an important parameter.

Rhinopathies can be classified as being structural, infectious, allergic, or nonallergic (Fig 1). The latter category is the most heterogeneous and includes drug- and hormonal-induced rhinitis, irritative-toxic rhinitis, and perennial nonallergic rhinitis (PNAR). This article will focus on allergic rhinitis (AR) and PNAR.

EPIDEMIOLOGY

The epidemiology of specific forms of rhinitis can be difficult to study because of the differences in classification and diagnostic assessments. AR has been reported to affect approximately 17% of the general population in the United States,² and in selected pediatric populations might be present in up to 42%.³ Less information is available on the demographics of nonallergic rhinitis in the general population. However, in an attempt to define the prevalence of various forms of rhinitis, the National Rhinitis Classification Task Force retrospectively analyzed 975 patients with rhinitis from a variety of allergy practices. They determined

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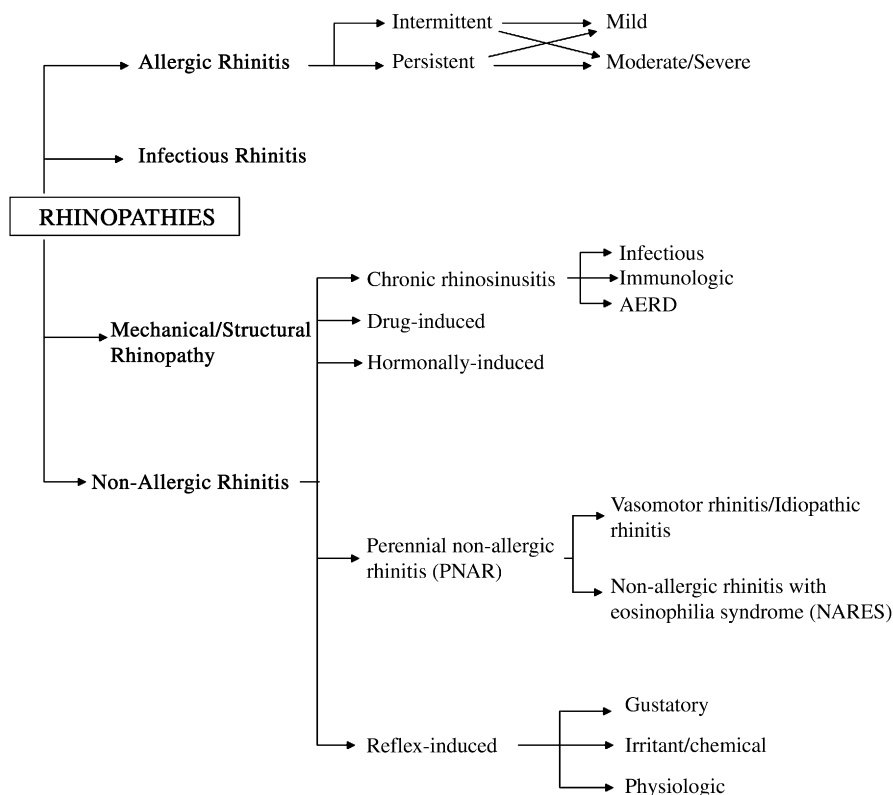


FIG 1. Rhinopathies: classification overview. AERD, Aspirin-exacerbated respiratory disease.

that in the surveyed cohort, 43% of patients had “pure” AR, 23% had “pure” nonallergic rhinitis, and 34% had mixed rhinitis.⁴ Thus 57% of the patients with rhinitis had nonallergic rhinitis either alone or of mixed form.

CLASSIFICATION AND DIAGNOSIS OF AR

AR, an inflammatory condition of the nasal mucosa mediated by an IgE-associated response to indoor and outdoor environmental allergens, has traditionally been classified as being seasonal or perennial, depending on whether an individual is sensitized to cyclic pollens or year-round allergens, such as dust mites, pets, cockroaches, and molds. This classification scheme has proved to be artificial and often inconsistent because, depending on the locale, allergic sensitization to multiple seasonal allergens can result in year-round disease, and conversely, allergic sensitization to perennial allergens, such as animal dander, can result in symptoms during only a limited period of time.

Although clinical research and regulatory agencies continue to use this nomenclature, recent global guidelines for classification and treatment of AR, as set forth by the Allergic Rhinitis and Its Impact on Asthma workshop, have proposed that allergic nasal disease be defined as being intermittent or persistent and mild or moderate-severe.⁵ Intermittent rhinitis is defined on the basis of symptoms that are present for less than 4 days per week or less than 4 weeks in duration. If symptoms are present for more than 4 days per week and are present for more

than 4 weeks, AR is defined as being persistent. Mild symptoms do not affect sleep, interfere with work or school, or impair daily activities, sports, and leisure and, although present, are not considered troublesome. Conversely, moderate-severe symptoms can result in impairment or disturbances of any or all of these activities or aspects of life. Although the duration categories of intermittent and persistent appear to be a practical system, further refinement of the severity categories would be valuable. In addition, development of a validated method for assessing rhinitis control would be useful to monitor the often variable course of a patient's disease.

The diagnosis of AR can be made presumptively based on the types of symptoms and the history of allergen triggers. Confirmation requires documentation of specific IgE reactivity through determination of allergen sensitivity by using skin prick testing or *in vitro* specific IgE determination. These procedures can help detect specific allergic sensitivities and provide information for directing environmental control interventions.

CLASSIFICATION AND DIAGNOSIS OF PNAR

PNAR is a condition in which the patient has no identifiable specific allergic sensitivities. Although it is controversial how to best subdivide PNAR, one previous approach has been to do so based on the presence or absence of nasal eosinophilia. Individuals with nasal eosinophilia and with no IgE sensitivity have traditionally

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