Nonallergic Rhinitis
Diagnosis

Justin Greiwe, MD[a,b], Jonathan A. Bernstein, MD[a,b,*]

KEYWORDS

• Nonallergic rhinitis • Differential diagnosis • Triggers • Symptoms • Provocation • Subtypes • Classification

KEY POINTS

- Nonallergic rhinitis (NAR) is a heterogeneous disorder that is difficult to characterize because there is very little consensus in the literature regarding its definition and mechanisms of action.
- The symptoms and physical findings of patients with allergic rhinitis (AR) are not pathognomonic, because patients with NAR often present with similar features and up to 50% suffer of AR patients have a non-allergic component termed mixed rhinitis (MR).
- NAR is currently diagnosed based exclusively on patients being nonatopic with symptoms in response to odorant and irritant triggers in the absence of a specific cause.
- Assessing treatment response remains a useful tool for differentiating among AR, MR, and NAR.
- More information regarding the mechanisms of NAR is needed, which will lead to more specific and effective therapeutic approaches.

INTRODUCTION

The practicing allergist manages several common clinical disorders, but none more prevalent than chronic rhinitis. Although asthma, atopic dermatitis, conjunctivitis, and sinusitis continue to afflict large proportions of the general population, they pale in scope to chronic rhinitis. This latter condition affects upward of 70 million individuals in the United States, making it one of the most prevalent medical disorders in the country.[1] Consequently, chronic rhinitis is associated with a considerable economic impact and can have major implications on quality of life, especially when one considers the various associated concomitant disorders. Although there is an

No funding was required for this research.
[a] Bernstein Allergy Group, 8444 Winton Rd, Cincinnati, OH 45231, USA; [b] Division of Allergy, Immunology and Rheumatology, University of Cincinnati, 231 Albert Sabin Way, Cincinnati, OH 45267, USA
* Corresponding author. Division of Allergy, Immunology and Rheumatology, University of Cincinnati, 231 Albert Sabin Way, ML 563, Cincinnati, OH 45267-0563.
E-mail address: Jonathan.Bernstein@uc.edu

Immunol Allergy Clin N Am 36 (2016) 289–303
http://dx.doi.org/10.1016/j.iac.2015.12.006 **immunology.theclinics.com**
0889-8561/16/$ – see front matter

extensive differential diagnosis for chronic rhinitis, the most ubiquitous and well known subtypes are seasonal and perennial allergic rhinitis (AR). In the United States, AR is estimated to affect approximately 10% to 30% of adults and 40% of children, with estimated direct costs of $11.2 billion, which overshadows other chronic illnesses, such as asthma, diabetes, and coronary heart disease.[2,3] Lost productivity at work estimated as a decrease of $600 per employee per year further magnifies the economic burden this condition has in the United States. A similar economic impact of AR has been reported for Europe and emerging economies.[4–6] Unfortunately, the economic and societal impact of chronic rhinitis is often underestimated and underappreciated.

Although millions of Americans believe they suffer from AR symptoms, the diagnosis of this condition is not always supported by serologic or skin testing identifying specific IgE responses to aeroallergens that correlate with their clinical history. In fact, a substantial proportion of patients that suffer from rhinitis symptoms turn out not to be sensitized, but instead suffer from a condition referred to as nonallergic rhinitis (NAR). NAR is a heterogeneous disorder that is difficult to characterize because there is very little consensus in the literature regarding its definition and mechanisms of action. However, emerging theories posit competing mechanisms including dysautonomia (autonomic dysfunction) resulting in diminished sympathetic activity and/or parasympathetic overactivity and altered expression or activity of transient receptor potential channels.[7]

A more detailed look at mechanism of action is addressed elsewhere (See Baroody FM: Non-Allergic Rhinitis: Mechanism of Action, in this issue). This article provides a framework for evaluation and accurate diagnosis of NAR. Development of a consensus opinion for diagnosis of this rhinitis subtype will improve clinical outcomes and provide a clearer pathway for investigation of underlying mechanisms and novel targeted therapies.

Classifying Chronic Rhinitis

Several attempts have been made to provide a classification system of chronic rhinitis subtypes to help guide the clinician in their diagnosis and treatment of these conditions. In 2009, a panel of key opinion leaders formed a consensus opinion on the classification of NAR subtypes based on the existing literature and consensus opinions.[8–10] They concluded that NAR should be classified into eight different subtypes because of their unique clinical presentation, summarized in **Box 1**.[4]

There are several other conditions excluded from this classification worth mentioning including mixed rhinitis (MR), localized AR or entopic rhinitis, rhinosinusitis with and without polyps, infectious rhinitis (bacterial and chronic rhinosinusitis), and occupational rhinitis, because they are not always purely nonallergic or are mediated through different mechanistic pathways that have been attributed to NAR. The lack of a consensus clinical phenotype for NAR may have hindered previous genetic studies that have investigated the role of cytokines (ie, interferon-γ and inducible T-cell tyrosine kinase) and olfactory receptor gene segments to establish more specific NAR endotypes.[11–14] The indeterminate results of these genetic studies may indicate that either these pathways in NAR or the clinical criteria used to enroll subjects may not be relevant or too heterogeneous, respectively. Therefore, one focus has been to determine better ways to characterize patients with NAR to make a more accurate diagnosis of this condition. This article reviews the different approaches that have been investigated to better differentiate NAR from other chronic rhinitis subtypes.