# Nonallergic Rhinitis
## Mechanism of Action

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**KEYWORDS**

• Nonallergic rhinitis • Neurogenic • Reactivity • Histamine • Cold-dry air

**KEY POINTS**

- Cellular inflammation is not a consistent finding in patients with nonallergic rhinitis.
- Neuropeptides play an important role in the pathophysiology of nonallergic rhinitis.
- Transient receptor potential ion channels have an important role in mediating the response of patients with nonallergic rhinitis to environmental stimuli.
- Patients with nonallergic rhinitis exhibit various degrees of nasal reactivity to certain nonspecific stimuli, such as histamine, cold-dry air, and capsaicin.

### INTRODUCTION

Nonallergic rhinitis (NAR) is a chronic condition of the nasal mucosa that predominantly involves symptoms of nasal congestion and rhinorrhea with no evidence of allergic sensitization (ie, negative skin testing and/or serum-specific immunoglobulin E [IgE] testing). Although the primary and most common symptoms are congestion and anterior and posterior rhinorrhea, other associated symptoms include throat clearing, cough, eustachian tube dysfunction, sneezing, decreased sense of smell, and facial pain/pressure.[1] Itching of the eyes, throat, and ears is not a common symptom. The timing of symptoms may be perennial/persistent, intermittent, and/or precipitated by recognized triggers. Some of these include cold air, changes in environmental temperature and humidity, changes in barometric pressure, strong smells (perfumes, food, chemical odors), environmental tobacco smoke, pollutants and chemicals, ingestion of certain foods (gustatory rhinitis), and alcohol.

Unlike allergic rhinitis (AR), which is the most common chronic condition in children, NAR presents predominantly with adult onset; the female to male incidence varies

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between 2:1 and 3:1. Data from rhinitis epidemiologic studies suggest that the prevalence of AR is around 3 times more than that of NAR (AR:NAR = 3:1).[2] Thus, based on our knowledge of the prevalence of AR in the United States and the aforementioned ratios, one can estimate the number of Americans with NAR as 20 million or 7% of the population.

The classification of NAR has been unsolidified over the years and its pathophysiology relatively unexplored. Although *vasomotor rhinitis* was a common term used to describe such an entity, this term is no longer favored and is mostly replaced by NAR. It is important to realize that there are other types of rhinitis that are nonallergic but have specific and identifiable precipitating factors and triggers. These types include chronic rhinosinusitis with and without nasal polyps; NAR with eosinophilia syndrome (NARES); aspirin-exacerbated rhinosinusitis; infectious rhinitis/rhinosinusitis such as triggered by viral, bacterial, or fungal infections; rhinitis of pregnancy; and drug-induced rhinitis. Furthermore, the presence of inflammation in the nasal mucosa of patients with NAR is not ubiquitous leading some investigators to consider the term *rhinopathy* instead of rhinitis to refer to this entity. In the following pages, the author attempts to discuss available information that pertains to the pathophysiology of this disease and mostly centers around a description of inflammation in the nasal mucosa in NAR as well as neurogenic mechanisms thought to be important for this disease process. The author also details various methods of nasal provocation the results of which might shed some light on pathophysiologic processes involved in NAR.

## INFLAMMATION

Van Rijswijk and colleagues[3] performed nasal biopsies in patients with chronic rhinitis symptoms but negative evidence of allergic cause and compared those with the results of biopsies obtained from a normal control group with no nasal symptoms and negative skin test results. They evaluated various markers of lymphocytic cells, mast cells, Langerhans cells, macrophages, IgE+ cells, and eosinophils using immunohistochemistry. Most biopsies had a negligible number of eosinophils, which suggests that local AR and NARES were probably not a large contributor to this group. There were essentially no significant differences in the number of inflammatory cells between the rhinitis and control groups suggesting that cellular inflammation was not a prominent factor in this group of patients with NAR. The investigators also failed to show any relation between the number of immunocompetent cells in the nasal mucosa and nasal complaints in those patients when treated with either an intranasal corticosteroid or capsaicin.[4–6] In those studies, the intranasal corticosteroids resulted in a reduction of inflammatory cells but no improvement in symptoms and capsaicin reduced nasal symptoms without affecting the number of nasal inflammatory cells or mediators.

Powe and colleagues[7] performed similar investigations with different results. They evaluated nasal turbinate tissue obtained at the time of turbinectomies from patients with perennial allergic rhinitis, idiopathic rhinitis, and normal controls (undergoing surgery for mechanical, posttraumatic nasal obstruction) with no evidence of rhinitis. Using immunohistochemistry, they evaluated mast cells, IgE+ cells, eosinophils, and plasma cells and showed that both disease groups had essentially equivalent inflammatory cellular content, which was higher than that of the control, nonrhinitic subjects. The allergic group had a higher number of IgE+ cells and plasma cells compared with the group of patients with NAR. As mentioned earlier, the nonallergic group probably included subjects with local AR or NARES, as the number of