Rhinitis Subtypes, Endotypes, and Definitions



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KEYWORDS

• Rhinitis • Endotypes • Phenotypes • Pathophysiology • Symptoms

KEY POINTS

- Rhinitis endotypes are as numerous and diverse as the disease's phenotypes and are largely overlapping, making a clear demarcation challenging.
- Some rhinitis phenotypes previously considered important are now thought to be less relevant because of advances that have been made in understanding rhinitis subtypes.
- Consensus classification of rhinitis subsets is still an unmet need.
- Chronic rhinitis is a far more complex and burdensome condition than is generally acknowledged, and there is considerable need for research to better understand the pathobiology of nonallergic rhinitis and its interaction with allergic rhinitis.

INTRODUCTION

Chronic rhinitis (CR) is defined as an inflammation of the nasal mucosa, characterized by 2 or more symptoms of nasal congestion/obstruction, anterior or posterior rhinorrhea, and sneezing and itching for at least 1 hour daily and for more than 2 weeks.¹ CR is a prevalent pathologic condition with widespread morbidity associated with a considerable financial burden on health care systems.^{2,3} Its economic impact is further magnified because it is a risk factor for other comorbidities in adults, such as sinusitis and asthma, and also a precursor to serious conditions in children, such as learning disabilities, behavioral deviation, and psychological impairment.^{3,4} Nevertheless, it is an underestimated and often trivialized disease,

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often viewed as no more than a mere annoyance. Furthermore, the high variability in both underlying pathophysiologic mechanisms (endotypes) and clinical presentations (phenotypes) of CR has hindered efforts to develop clear guidelines for its diagnosis and treatment. Even the term rhinitis has been criticized because it connotes inflammation, whereas certain rhinitis endotypes seem to be devoid of an inflammatory component.⁵

The 3 most widely accepted rhinitis subgroups thus far are allergic rhinitis (AR), infectious rhinitis, and nonallergic noninfectious rhinitis (NAR).¹ However, this classification may be an oversimplification, because a combined (mixed) phenotype exists in many patients.^{3,6} In addition, there are numerous, mostly overlapping classification systems based on independent criteria such as age of onset, disease severity, symptoms, symptom pattern/frequency, causative agents, and underlying pathophysiology. For instance, from a clinical perspective, patients are classified as blockers, with nasal congestion as the prominent symptom, and runners, with rhinorrhea being predominant. Also, rhinitis caused by mechanical/structural abnormalities is included in the NAR subgroup by some investigators^{7,8} and excluded by others.⁹ Furthermore, occupational rhinitis can be either allergic or nonallergic, blurring the boundaries between the 3 widely accepted categories.¹⁰ Characterization of rhinitis phenotypes is further hampered by the scarcity of distinct biomarkers. Even for allergic rhinitis, for which the immunopathogenesis is more clearly delineated, clinical classification as proposed by Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines are frequently not adhered to by treating physicians who still do not prescribe or modify treatment based on phenotypic characteristics (eg, frequency or disease severity), contrary to the ARIA guidelines.^{11–14} These studies underscore the difficulty of using only the phenotype concept to classify CR and highlight the importance of developing a classification system that focuses on rhinitis endotypes.¹⁵

SUBTYPES, ENDOTYPES, AND DEFINITIONS *Rhinosinusitis and Overlapping Subtypes*

Rhinitis frequently coexists with sinusitis because the nose and sinuses share vascular, neuronal, and anatomic pathways. Therefore, the term rhinosinusitis is preferred in patients with symptomatic sinus inflammation.¹⁶ Rhinosinusitis can be acute or chronic.¹

The acute form of rhinosinusitis is infectious and predominantly of viral origin (around 90% of cases^{17,18}), with the usual causes being rhinovirus (common cold), coronavirus, adenovirus, parainfluenza virus, respiratory syncytial virus, or enterovirus. It is common that an acute viral rhinosinusitis is complicated by secondary bacterial superinfection that establishes a bacterial rhinosinusitis endotype (eg, *Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis*).

The chronic rhinosinusitis phenotype is more complicated for establishing a defined endotype because infection has a minor, if any, role. Chronic rhinosinusitis is characterized by nasal and sinus symptoms, such as nasal congestion, purulent discharge, facial pain, and impaired olfaction, which last longer than 12 weeks. Specifically, diagnosis requires:

- 1. The existence of 2 or more symptoms, one of which must be either nasal blockage or discharge and the other facial pain/pressure or impaired olfaction
- Either endoscopic signs (polyps, mucopurulent discharge, and/or edema/mucosal obstruction primarily in the middle meatus) and/or computed tomography findings (sinus mucosal changes)¹⁹

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