

Types of Rhinitis

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KEYWORDS

- Rhinitis • Allergic • Nonallergic • Occupational • Vasomotor
- Irritant • Atrophic

Key Points: TYPES OF RHINITIS

- Chronic rhinitis can be broadly classified into allergic, infectious, or nonallergic or non-infectious.
- Because of overlapping symptoms, the types of rhinitis are distinguished mainly by a careful history and, when indicated, allergy testing.
- The pathophysiology of nonallergic rhinitis likely involves a combination of inflammatory and neurogenic mechanisms that are poorly understood.
- The differential diagnosis is broad, and causes may include both local and systemic factors.
- Treatment involves having the patient avoid the offending agent, when possible, and use appropriate medications to control the predominant symptoms.

Rhinitis is a familiar disorder well known to primary care and specialty clinics alike. It affects up to 20% of the general population¹ and is one of the most common reasons for presentation to an otolaryngologist's office.²

Rhinitis is defined as inflammation of the nasal mucosa. This inflammation may be caused by a variety of factors, including infectious agents, allergies, irritants, medications, and hormones, among others. Associated symptoms may include excessive mucus production, nasal congestion, pain, pressure, sneezing, and pruritus. Acute rhinitis is often caused by infectious agents, such as viruses or bacteria, and is commonly associated with sinus inflammation as part of acute rhinosinusitis. More commonly, rhinitis presents as ongoing persistent symptoms, termed chronic rhinitis.

Chronic rhinitis can be broadly classified into allergic, infectious, or nonallergic-noninfectious. Allergic rhinitis (AR) is defined as IgE-mediated inflammation of the

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nasal mucosa after allergen exposure. It is definitively diagnosed through allergy testing, with either skin testing or serum-specific IgE antibody testing. Nonallergic rhinitis (NAR) is diagnosed when the history and physical examination are consistent and proper allergy testing is negative. Of patients seen with chronic rhinitis, approximately 50% of them will have allergic rhinitis as demonstrated on allergy testing.³ The remainder are given the diagnosis of nonallergic rhinitis. The latter is a broad category that includes a myriad of causes, some known, and some unknown.

Nasal symptoms characteristic of NAR are often indistinguishable from those that occur in AR. A careful history is important in establishing a diagnosis and distinguishing the two entities. Within the category of nonallergic rhinitis are various described entities relating to the causative factor. These include irritant, medication-induced, hormonal, atrophic, nonallergic rhinitis with eosinophilia syndrome (NARES), and smoking. When no causative agent is found, the patient is given the diagnosis of idiopathic rhinitis.

PATHOPHYSIOLOGY

The mechanisms that cause symptoms of rhinitis are complex and are likely multifactorial. Proposed contributions include chronic inflammatory and neurogenic sources.

Chronic Inflammation

It is well established that in allergic rhinitis, there is an influx of inflammatory cells and mediators into the nasal mucosa as they respond to the offending antigen. These mediators result in venous engorgement, increased nasal secretions and tissue edema, causing the classic symptoms of nasal congestion, sneezing, rhinorrhea, and pruritus.^{4,5} There are likely similarities in nonallergic rhinitis patients as well, though the relation is not as clear-cut.

Powe and colleagues⁶ examined inferior turbinectomy specimens from allergic, nonallergic, and normal patients. They found significantly more nasal mucosa mast cells and eosinophils in the rhinitic patients compared with the normal individuals. They concluded that idiopathic and allergic rhinitic mucosa show similarities in their inflammatory infiltrate suggesting that both groups share a similar cellular immunopathology.

In contrast, a study by van Rijswijk and colleagues⁷ found no difference in nasal mucosal lymphocytes, antigen-presenting cells, eosinophils, macrophages, monocytes, mast cells, and other IgE-positive cells between idiopathic rhinitis patients and controls.

Neurogenic Mechanisms

The sensory nerves of the nose arise from the olfactory nerves as well as from the ophthalmic (through the ethmoidal nerve) and maxillary (through the nasopalatine nerve) branches of the trigeminal nerve. In the neurogenic model of rhinitis, exaggerated responses to environmental or endogenous stimuli occur because neural activity is upregulated as a result of a pathologic process, primarily of an inflammatory nature. In this case, a stimulus of average intensity generates exaggerated symptoms. This phenomenon is known as neural hyperresponsiveness and is believed to play an important role in the clinical presentation of nasal disease.

The neural regulation of the upper airways is complex and consists of a number of interacting nervous systems. Sensory, parasympathetic, and sympathetic nerves regulate epithelial, vascular, and glandular processes in the nasal mucosa. The sensory, parasympathetic, and sympathetic neural systems contain heterogeneous

populations of nerve fibers with unique combinations of neurotransmitters and neuropeptides.

In 1959, Malcomson⁸ stated that idiopathic rhinitis was caused by an autonomic imbalance. Normally, increased sympathetic tone in nasal blood vessels leads to vasoconstriction.⁹ Underactivity of the sympathetic nervous system leads to nasal obstruction. Overactivity of the parasympathetic system also leads to rhinorrhea.¹⁰

In addition, perivascular and intraepithelial nonadrenergic, noncholinergic, sensory nerve fibers contain neuropeptides. These neuropeptides are locally released from peptidergic neurons (unmyelinated C-fibers or “pain fibers”) in the nasal mucosa after activation by nonspecific stimuli, and can be responsible for the symptoms of idiopathic rhinitis.^{11,12,13}

Progression to Allergic Rhinitis

Patients diagnosed with NAR typically have persistent symptoms, yet they are generally not followed up with further allergy management. Rondon and colleagues¹⁴ studied patients diagnosed with nonallergic rhinitis on the basis of rhinitis symptoms and negative skin prick testing and negative serum specific IgE on initial testing. They were reevaluated 3 to 7 years later with clinical questionnaires, spirometry, skin prick testing, and measurement of serum-specific IgE to common aeroallergens. They found that patients with NAR generally experienced worsening disease (52%), with an increase in the persistence (12%), severity of nasal symptoms (9%), and new comorbidities (24%) over time. The most frequent comorbidities at reevaluation were asthma (increasing from 32% to 55%) and conjunctivitis (from 28% to 43%), followed by chronic rhinosinusitis. Sensitization to aeroallergens not present at the initial evaluation was detected by means of skin prick testing, serum-specific IgE measurement, or both in 24% of the patients. They concluded that NAR may progress to AR over time and recommended that these patients be periodically reevaluated for allergy.

CLASSIFICATION

The classification of rhinitis is broad and, as previously mentioned, the most important diagnostic tool is the history. After excluding allergic rhinitis through history and appropriate allergy testing as indicated, a diagnosis of nonallergic rhinitis can be made. Often the term “vasomotor rhinitis” is used after ruling out allergy as the underlying cause: this term should only be used for cases that are idiopathic and after other causes of nonallergic rhinitis are excluded. Rhinitis can be classified based on multiple criteria and associated factors. The most common and clinically important forms are presented in **Box 1**. Although this is not exhaustive, it will give the reader a firm basis of understanding of these disorders.

Allergic Rhinitis

Allergic rhinitis is the most common type of rhinitis. It can be categorized into three basic subgroups: seasonal, perennial, and occupational. IgE mediates immunologic responses to different allergens. Tree, grass, and weed pollens generally cause seasonal symptoms. Mold spores may cause seasonal and perennial symptoms. Indoor allergens such as dust mites, pet dander, and molds usually cause perennial symptoms. Occupational rhinitis is triggered by exposure to allergens or irritants in the workplace.

Allergic rhinitis symptoms include early and late responses. Seasonal or intermittent allergy exposures yield classic “acute phase” symptoms such as pruritus, sneezing,

Box 1**Classification of rhinitis**

- Allergic rhinitis
 - Perennial rhinitis
 - Seasonal rhinitis
- Nonallergic rhinitis
 - Atrophic rhinitis
 - Surgery
 - Cocaine abuse
 - Aging
 - Emotional rhinitis
 - Exercise-induced rhinitis
 - Gustatory rhinitis
 - Hormone-related rhinitis
 - Hypothyroidism
 - Pregnancy
 - Menstrual cycle
 - Oral contraceptives
 - Idiopathic (vasomotor) rhinitis
 - Infectious rhinitis
 - Acute (usually viral)
 - Chronic (rhinosinusitis)
 - Irritant- or chemical-induced rhinitis
 - Temperature
 - Humidity
 - Perfumes
 - Cleaning agents
 - Cosmetics
 - Air pollution
 - Tobacco smoke
 - Medication-related rhinitis
 - Rhinitis medicamentosa
 - Other drugs
 - Nonallergic rhinitis with eosinophilia syndrome (NARES)
 - Systemic diseases
 - Autoimmune disorders
 - Vasculitides
 - Hormone disturbances

watery rhinorrhea, and acute conjunctivitis. On the other hand, perennial antigens such as cat dander or dust mite antigen can yield a more subtle presentation, with year-round “late-phase” symptoms such as congestion and rhinorrhea. Seasonal and perennial allergic rhinitis can be associated with systemic symptoms, including malaise, weakness, and fatigue. Patients with seasonal and perennial allergic rhinitis also may have asthma and eczema. Inasmuch as classic acute phase allergic symptoms may be blunted with constant antigen exposure, allergy testing may be beneficial in cases with only the more subtle late phase symptoms.

Hormone-related Rhinitis

Hormone-related rhinitis has been described in multiple disease processes as well as physiologic states. A neurogenic mechanism is proposed but is unclear. Disturbances in thyroid hormone (mainly hypothyroidism) and growth hormone (acromegaly) may have prominent nasal congestion and rhinorrhea. Estrogen and progesterone assert at least part of their effects on vascular smooth muscle, and hormonal rhinitis can develop during the menstrual cycle, puberty, or more commonly pregnancy. Pregnancy-induced rhinitis is probably the most common and well-known form of hormone-related rhinitis. It is diagnosed in a pregnant patient with rhinitis lasting 6 or more weeks without other causative agents, which disappears after delivery.¹⁵ Estrogen levels are correlated with the severity of rhinitis symptoms and are the most severe in the second trimester.¹⁶

Medication-related Rhinitis

Medication-induced rhinitis is related to the neurogenic mechanism or local inflammatory effects of the offending agent and can be difficult to diagnose given the broad range of drugs available to patients.¹⁷ Broad categories of medications include the antihypertensives, antidepressants, psychotropics, phosphodiesterase type 5 inhibitors (eg, sildenafil, vardenafil), and antiinflammatories. Many of these medications act at receptors that are ubiquitous throughout the body, including the nasal mucosa. The antiinflammatories exert a local effect and have a well-known mechanism of increased leukotriene production, leading to asthma and reactive airway disease in susceptible patients. This is termed aspirin-exacerbated respiratory disease (AERD).¹⁷

Intranasal decongestants such as oxymetazoline deserve specific mentioning. Extended use of topical α -adrenergic medications may result in rebound nasal congestion, termed “rhinitis medicamentosa.” These patients also have characteristic-appearing erythematous nasal mucosa, which may be prone to bleed, as opposed to other drug-induced rhinitis.¹⁸ Cocaine can act in a similar mechanism, resulting in rebound congestion. As mentioned previously, exogenous estrogen or progesterone agents can lead to rhinitis, which is reversible with discontinuation of medications.

Irritant-related Rhinitis

Irritant-related rhinitis involves an occupational or environmental exposure that causes symptoms. In this case, the agent causes an irritation rather than an allergic response. A spatial and temporal relationship of the exposure and associated symptoms is usually necessary to make the diagnosis, although sometimes it can be a difficult part of the history to assess. Some of the more common culprits are industrial chemicals, wood dust, tobacco smoke, paint fumes, hairspray, perfumes, and other fragrances. The diagnosis can be further strengthened by concurrent lower respiratory symptoms. Confirmation can be performed with a nasal provocation test under a controlled setting in clinic.¹⁹ Environmental exposures, including weather or

pressure changes, air pollution, cleaning agents, exercise, or even emotional situations, have been described. Ingestion of foods causing rhinitis characterized primarily by profuse, clear anterior rhinorrhea is termed gustatory rhinitis and is more common with spicy foods.²⁰

Atrophic Rhinitis

Atrophic rhinitis is characterized by atrophy of the nasal mucosa, including mucus glands and nerves. It can be primary or secondary and is due to the replacement of the normal ciliated columnar epithelium of the nasal mucosa by stratified squamous epithelium. Primary atrophic rhinitis can occur as the result of aging, heredity, infection, or even nutritional deficiencies.²¹ In Western civilization, the most common risk factor for primary atrophic rhinitis is age, with the majority of patients being diagnosed after 40.²² Secondary atrophic rhinitis can be due to surgery (excessive removal of turbinates), radiation, longstanding cocaine abuse, or infections (eg, leprosy, syphilis, rhinoscleroma). These factors may cause destruction of nasal structures leading to atrophic changes. With chronic changes in airflow patterns and mucous secretion, there is decreased stimulation to the olfactory mucosa as well as the trigeminal afferents leading to a sense of congestion.²² In addition to rhinitis, patients may present with foul smelling crusts or nasal obstruction with sensations of pain and pressure.

Systemic Diseases

Numerous systemic diseases can affect the nose, resulting in rhinitis. Granulomatous diseases (Wegener granulomatosis, sarcoidosis, Churg-Strauss syndrome), autoimmune diseases (lupus, Sjögren syndrome, pemphigoid), cystic fibrosis, tuberculosis, and ciliary dyskinesia all can have nasal manifestations of rhinitis.²³ When a patient's symptoms are not controlled with maximal medical management or the nasal mucosa demonstrates unusual features such as scarring (pemphigoid), excessive bleeding, and crusting (Wegener), or submucosal cobblestoning (sarcoidosis), other systemic causes must be considered.

Signs of granulomatous disease include persistent inflammation and crusting (Wegener), ulceration, nasal masses, submucosal nodules or cobblestoning (sarcoid), extranasal manifestations, and systemic symptoms. Autoimmune diseases can involve the complex process of antigen-antibody interaction in the nose and may result in mucosal ulceration (pemphigoid, lupus), dryness and crusting (Sjögren), and recurrent infections.²⁴ Sinonasal involvement in cystic fibrosis varies with the mutation status of the patient. Nasal polyps are present in most patients with the most common mutation $\Delta F508$ and is frequently associated with the presence of bacterial biofilm infections, usually *Staph aureus* or *Pseudomonas*. Tuberculosis commonly affects the nasopharynx and can result in nasal inflammation and rhinorrhea.²⁵ Primary ciliary dyskinesia results in nasal symptoms as the patient cannot clear the mucus produced. It should be suspected in patients with stagnant clear secretions on the floor of the nose. The diagnosis can be confirmed with a mucociliary transport saccharine test.

NARES

NARES exhibits symptomatology similar to allergic rhinitis (nasal congestion, sneezing, rhinorrhea, nasal and ocular pruritus), but allergy testing is negative.^{26,27} A distinguishing feature of NARES is the presence of eosinophils, usually 10% to 20% on nasal smears.²⁸ Although the overactivation of mast cells in the setting of chronic inflammation plays a role in the development of NARES, there is a lack of understanding of the exact pathophysiology. NARES patients can develop nasal

polyposis and aspirin sensitivity, but this is not always the case.²⁸ NARES has also been associated with the severity of obstructive sleep apnea.²⁹ The diagnosis is made by history, physical examination, and negative serologic or skin testing, and is confirmed by the presence of prominent eosinophilia within the nasal mucosa on cytology. On physical examination, the turbinates of NARES patients often appear pale and boggy. These patients are more responsive to treatment with nasal corticosteroids compared with other patients with nonallergic rhinitis. The differentiation is important to aid in adequate symptom relief.³⁰

Idiopathic Rhinitis

Idiopathic rhinitis (aka vasomotor rhinitis) should be a diagnosis of exclusion after an exhaustive history and physical examination. The pathogenesis of this condition is unclear. Increased sensitivity to environmental factors (eg, climate change, pollution, strong odors, perfumes) may trigger symptoms. This is the most common diagnosis within the subtypes of nonallergic rhinitis. On examination of nasal cytology, there is typically an absence of eosinophils, plasma cells, and mast cells compared with allergic rhinitis.³¹ Without typical causative factors, vasomotor rhinitis is thought to be due to an imbalance of the neurogenic mechanisms described previously.^{9,31}

DIAGNOSIS

Differentiating AR from NAR is important, but can be challenging, given the similarity in presentation and overlapping symptoms. However, a comprehensive history usually suggests the correct diagnosis. History-taking should focus on symptom onset, duration, chronicity, and severity. Rhinitis that appears later in life is more likely to be nonallergic.³ Environmental and occupational triggers should be sought. Seasonal variation, environmental influences, and exposures should be elucidated. Medical history, comorbidities, and family history are all important and help to differentiate NAR from AR. Previous treatments and their efficacy are also important to elicit.

The differential diagnosis for acute symptoms lasting only a few days is relatively small and often suggests a viral origin. An acute exposure to an irritant or allergen can also give these acute symptoms, as can a nasal foreign body (especially if unilateral in children). The differential diagnosis of chronic rhinitis, however, is much broader.

An environmental trigger, whether allergic or irritant, should be sought. Seasonal variations in symptoms suggest allergic rhinitis. Age can help to differentiate AR from NAR (80% of allergic rhinitis patients have the onset before age 20).³ Family history is important because allergic rhinitis and asthma both run in families. Comorbidities, especially those relating to atopy (asthma and eczema), can help steer the diagnosis. Finally, the success of past and current treatments may help identify the cause and direct future treatment.

A focused physical examination should follow the history. Acute viral rhinitis will tend to cause more generalized symptoms, including fevers, muscle aches, and fatigue. Patients with chronic allergic symptoms may have allergic shiners (ie, blue-gray or purple discoloration under the lower eyelids) or they may breathe preferentially through their mouths. Conjunctivitis can be a component of allergic rhinitis or acute viral upper respiratory infection (URI). A careful examination of the nose is important to identify structural abnormalities, polyps, mucosal swelling, foreign bodies, and discharge. Nasal endoscopy can enhance visualization and allow examination for signs of nasal polyps or sinusitis, but it is not always necessary. Examining the pharynx for enlarged tonsils or postnasal drip also can help identify viral causes or

chronic drainage from chronic rhinitis. Lymphadenopathy with associated symptoms may suggest a viral or bacterial cause of rhinitis. Wheezing or eczema suggests an allergic cause.

Allergy Testing

There is debate as to when allergy testing is indicated in the rhinitic patient. Gendo and Larson³² performed an extensive systematic review of the evidence on allergy testing and recommended that in general, physicians should select tests that will change outcomes or treatment plans; that empiric treatment is appropriate in patients with classic symptoms; that diagnostic tests may be appropriate if severe symptoms or an unclear diagnosis is present, or if the patient is a potential candidate for allergen avoidance treatment or immunotherapy; and that observation may be appropriate for patients with mild symptoms or an unclear history.

Allergy testing is useful to identify IgE-mediated disease, as this can have an effect on management. It usually involves one or more of the following methods: skin prick testing, intradermal testing, and allergen-specific IgE antibody testing. There are advantages and disadvantages to each, and the ultimate decision on which method to use often depends on the familiarity and preference of the physician and patient. The diagnosis of nonallergic rhinitis is made after eliminating allergic or IgE-mediated causes, often through allergy testing.

TREATMENT

As there are a myriad of causes of rhinitis, so there are a myriad of treatments. The treatment chosen for the specific patient is dictated by the underlying cause. Because the cause is not always apparent, as in idiopathic rhinitis, the treatment should be tailored toward the most troublesome symptoms of the patient.

If a cause is identified, such as an offending trigger, patient education regarding environmental modification and avoidance, if possible, should be employed. For temporary conditions, such as rhinitis of pregnancy, reassurance and counseling may be all that is needed. For those who desire pharmacologic treatment, several classes of drugs can be used.

Intranasal corticosteroids (INS) are FDA-approved for the treatment of rhinitis. The mechanism of action, presumably, relates to its antiinflammatory effects on the nasal mucosa. Fluticasone was shown to decrease the number of CD3+ cells, the amount of major basic protein, and the number of tryptase-positive cells in subjects with nonallergic rhinitis. It also lowered mRNA expression for interleukin (IL)-4 and IL-5.³³ In randomized clinical trials, INS have been shown to be effective in reducing symptoms, though it can take several weeks to reach maximal treatment effect.^{34,35} This treatment is especially effective for NARES patients. However, for many NAR patients, INS alone is not as effective as in AR.

Oral antihistamines have not been shown to be effective in treating NAR. However, the intranasal antihistamine azelastine is FDA-approved for both AR and NAR.³⁶ In clinical trials, azelastine has been shown to reduce symptoms of rhinitis, including postnasal drainage, sneezing, rhinorrhea, and congestion.³⁷ These multicentered, placebo-controlled trials studied azelastine for the treatment of nonallergic vasomotor rhinitis. Over 200 patients were evaluated. The response rate of between 82% and 85% was significantly higher than the placebo response of 73%. The high placebo response is expected because saline nasal spray also has been shown to have a beneficial effect in this disorder.

Given that NAR is a non-IgE-mediated condition, the mode of action of azelastine in NAR is not clear, partially because the pathophysiology of this condition itself is uncertain. However, there are several possible mechanisms, including a decrease in neurokinin,³⁸ the prevention of mast cell degranulation,³⁹ a reduction in eosinophil accumulation associated with a decrease in expression of adhesion molecules,⁴⁰ and a decrease in the synthesis of inflammatory cytokines and nitric oxide via an effect on transcription mediated through NF-kB.⁴¹

Patients with predominantly secretory or rhinorrhea symptoms, especially vasomotor rhinitis, may benefit from an anticholinergic agent such as ipratropium nasal spray, 80 mcg up to four times a day.⁴² Intranasal cromolyn has not been shown to be effective in treating this disorder. For those patients with congestion, a slow-release oral decongestant may provide relief, though significant side effects may result.⁴³ Even a simple intranasal saline spray may be all that is required for symptomatic improvement.

Patients with rhinitis medicamentosa attributable to over-use of topical α -adren-ergic agonist medications should be weaned off these agents over 7 to 10 days while using an intranasal steroid. The patient may also require a short course of oral pred-nisone tapering over 7 to 10 days. Nonallergic rhinitis with eosinophilia syndrome is best treated with intranasal steroids. Treatment of rhinitis associated with a systemic disease should be directed at the underlying disease process. Management of atro-phic rhinitis may include nasal saline irrigation and antibiotics. If an anatomic abnormality exists such as a deviated septum or nasal valve collapse, surgical inter-vention may be indicated.

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