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Vasomotor Rhinitis Is Not a Wastebasket Diagnosis

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Hypothesis: Vasomotor rhinitis is best conceptualized as a distinct entity in a continuum of chronic sinonasal disease.

BACKGROUND

The impact of chronic rhinitis on patients, health care systems, and resources is substantial, resulting in more than 25 million office visits per year and resulting in total indirect and direct costs of \$6 billion annually.^{1,2} It is estimated that more than 10% of the population has chronic or recurrent nasal obstruction or congestion, rhinorrhea, sneezing, and pruritus. Approximately half of these patients are classified as having allergic rhinitis and half as having nonallergic rhinitis, including vasomotor rhinitis.^{3,4} These forms of chronic, noninfectious rhinitis represent a spectrum of nasal disorders that are best categorized as a hyperreactivity of the nasal mucosa to a variety of stimuli.⁵ Allergic rhinitis is diagnosed when specific antigens can be identified and is often subclassified as seasonal or perennial allergic rhinitis.⁶ When specific antigens are not identifiable, chronic rhinitis is often classified as vasomotor or nonallergic. These nonallergic forms of chronic rhinitis can be further evaluated by nasal cytology. Nasal scrapings of the inferior turbinate can yield epithelial lining, and detailed analysis of different cell types can be made. Patients with nonallergic rhinitis and abundant eosinophils on nasal cytology have the so-called nonallergic rhi-

nititis with eosinophilia syndrome, which is sometimes associated with aspirin intolerance. Patients with nonallergic rhinitis and unremarkable nasal smear findings could have rhinitis medicamentosa, pregnancy, or hypothyroidism, but most are thought to have vasomotor rhinitis.

Most of the literature concerning vasomotor rhinitis and its relationship to the autonomic nervous system came from investigations 50 years ago.⁷⁻¹⁰ These authors discuss the role of the autonomic nervous system in maintaining sinonasal health through the regulation of vascularity and mucosal gland function, and they speculate that the autonomic nervous system regulates the reactivity of the nasal and sinus mucous membranes and glands. They note that the inferior turbinate in particular contains mucous and serous glands, vascular channels, and autonomic nervous system branches that constitute a delicately sensitive and reactive organ. Vasomotor rhinitis was thought to represent either hyperfunction of the parasympathetic nervous system in the nose and paranasal sinuses or an imbalance between the parasympathetic nervous system and sympathetic nervous system.

Does vasomotor rhinitis exist, and if so, what is its etiology? Is it a specific entity and part of a continuum of disease or is it a "wastebasket" diagnosis? This article hypothesizes the former.

PRO

Vasomotor rhinitis is characterized by nonspecific symptoms such as nasal obstruction, increased secretions, and an impaired sense of smell.¹¹ Ultrastructural evaluation of the respiratory nasal mucosa in patients with



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vasomotor rhinitis reveals a scarcity of eosinophils and plasma cells and the absence of immunologically stimulated or degranulated mast cells compared with perennial allergic rhinitis.¹² Vasomotor rhinitis is a noninfectious, nonallergic entity, experimentally suggested to be the result of autonomic imbalance with a relative dominance of the parasympathetic nervous system in the nasal mucosa.

The autonomic nervous supply to the nose regulates vascular tone and state of turbinate congestion. Parasympathetic fibers synapse in the sphenopalatine ganglion before innervating the nasal mucosa, whereas sympathetic fibers pass through the ganglion but do not synapse before distribution to the nasal vasculature. There is an intimate association between these autonomic nerves and the nasal mucosal vasculature.^{13,14} Baseline sympathetic tone provides constant α - and β -adrenergic receptor stimulation. Since there is a marked α predominance in nasal blood vessels, vasoconstriction generally prevails.

Parasympathetic tone can be adversely altered by medications, certain physiological states, and irritants. Formulations of estrogen are

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thought to inhibit acetylcholinesterase and potentiate cholinergic effect.¹³ Pregnancy induces a similar effect resulting in rhinitis of pregnancy. Inhalant irritants, such as tobacco smoke and industrial pollutants, induce parasympathetic activity in the nose. Even cold, dry air alone can provoke the release of these mediators.¹⁵ Trauma has been implicated in the development of vasomotor rhinitis through 2 possible mechanisms.¹¹ One is through direct stimulation of the parasympathetic nerve endings in the nasal mucosa, which is a result of the anatomic changes in the nasal tissues produced by the trauma.¹¹ Beekhuis,¹⁶ who reports vasomotor rhinitis in 10% of postrhinoplasty patients, believes that it is a result of autonomic changes in the turbinate tissue as a result of the surgical trauma. Local reflexes are thought to be disturbed by trauma, resulting in neuropeptide release and adverse tissue response.¹¹

It has been speculated that vasomotor rhinitis is due to either a hyperactive parasympathetic nervous system or an imbalance between it and the sympathetic nervous system. Krajina et al¹⁷ extirpated the superior cervical sympathetic ganglion in dogs and observed increased nasal obstruction and hypersecretion, supporting the contention that a relative parasympathetic dominance leads to rhinitis. A recent study at our institution demonstrates a significant relationship between vasomotor rhinitis and autonomic nervous system dysfunction.³ In this study, an autonomic nervous system testing laboratory was utilized to compare control subjects without rhinitis with patients with chronic vasomotor rhinitis. Significant differences were noted between these groups and indicate that patients with vasomotor rhinitis have a dysfunctional autonomic nervous system. This dysfunction appears to result in a hypoactive sympathetic nervous system relative to the parasympathetic nervous system, producing a critical imbalance. This research supports the hypothesis that vasomotor rhinitis is a distinct entity that may be more clearly defined through diagnostic testing of autonomic nervous system function.

CON

In the practical management of patients with chronic rhinitis, does knowledge of the precise cause really affect management? Perhaps if allergy plays a role, antihistamines and immunotherapy may be considered. Other than that, rhinitis is rhinitis and the specific cause is of little clinical significance. For these reasons, vasomotor rhinitis is often considered a "wastebasket" diagnosis by many clinicians. It is thought to be an idiopathic form of chronic rhinitis, and after an unrevealing investigation for allergy and infection, it is the default diagnosis or diagnosis of exclusion. There are a number of likely reasons for this. Vasomotor rhinitis is poorly defined and often underemphasized in the training of the modern otolaryngologist. A review of the literature demonstrates that most studies of vasomotor rhinitis have investigated treatments for the disorder. Diagnostic criteria for vasomotor rhinitis in these studies are variable and generally include any patient with chronic symptoms and negative allergy evaluation findings.^{18,19} Very few studies have investigated the pathophysiology of vasomotor rhinitis.

Furthermore, the clinical picture of vasomotor rhinitis exhibits wide variation.¹³ Patients generally complain of perennial nasal obstruction accompanied by profuse, watery discharge or by thick, scanty rhinorrhea. Most patients and physicians attribute these symptoms to "allergies." In fact, the diagnosis of vasomotor rhinitis is rarely assigned in the primary care setting. Headache and sneezing have both been associated with vasomotor rhinitis, but pruritus is not prominent. Symptoms seem to be exacerbated by nonspecific irritants such as strong odors or fumes and changes in weather and humidity. In comparing the symptoms of allergic rhinitis with those of vasomotor rhinitis, about 60% of both groups report problems with nonspecific airway irritants such as cigarette smoke and perfumes.²⁰ Nasal blockage occurs in both groups but is a more prominent symptom in vasomotor rhinitis. Patients with allergic rhinitis are more likely to experience eye irritation.²⁰ In the end, it can be dif-

ficult to differentiate between allergic and vasomotor rhinitis by symptoms alone.

The physical characteristics of the nasal mucosa in vasomotor rhinitis are not consistent and in fact vary notably from patient to patient. The turbinates are generally congested but may be erythematous or pale. Significant thick or thin discharge can be seen on the mucosa, or the mucosa may appear excessively dry. The inferior turbinate is thought to be the most notably affected but is also the most apparent on anterior rhinoscopy. Once again, differentiating between the various forms of chronic rhinitis by physical signs can be challenging.

Early work by Goldman⁹ in vasomotor rhinitis underlines the multiple vague factors thought to be associated with the vasomotor reaction. He divided vasomotor rhinitis into clinical categories including physical, emotional, and idiopathic. Physical hypersensitivity occurs from exposure to cold, dry air, sudden changes in temperature, and fatigue. Goldman also reported nasal reactions to emotional stimuli and identified stress as the primary offender. Idiopathic hypersensitivity was thought by Goldman to characterize the largest proportion of patients with vasomotor rhinitis. Goldman's classification of noninfectious rhinitis is simpler than others. He believed that there are 2 basic forms of perennial rhinitis—those mediated by IgE (perennial allergic rhinitis) and those that are not (vasomotor rhinitis). He viewed eosinophilia and mastocytosis as descriptive cytologic findings that were found in both allergic and vasomotor rhinitis.

In the end, the terms *vasomotor* and *nonallergic* rhinitis are used loosely in the literature. Some suggest that precise terminology is of little clinical significance and the labeling of these cases is purely academic.

BOTTOM LINE

It is the nature of medicine to attempt to precisely define and classify patients, especially as it relates to diagnosis. In textbooks, articles, and presentations, we are pushed to

define our patient population. Our patients with chronic rhinitis push us to explain to them what they are "allergic" or reacting to. The diagnosis of the allergic component of rhinitis is made by identifying the specific IgE antibodies associated with the symptoms that are clearly exacerbated on exposure to that antigen. A classic example of this is seasonal allergic rhinitis (hay fever). Since this entity is readily identified and the immunopathology is well defined, clinical studies limited to allergic rhinitis are more interpretable than those that include perennial rhinitis, especially when a major nonallergic component is apparent. It is therefore no surprise that a review of the literature yields many more articles studying allergic rhinitis than articles studying nonallergic rhinitis. Interestingly, little attempt is made in studies of allergic rhinitis to identify and exclude patients with other forms of rhinitis such as vasomotor rhinitis. That is, patients with positive allergy testing results are assumed to have only allergic rhinitis. In clinical practice, however, many patients are not readily categorized into one of the currently available diagnostic groups, which in any case are not necessarily clearly defined entities.⁵ In fact, it is likely that many of our patients' symptoms and physical findings are multifactorial in nature so that the patient who has the common symptoms of nasal obstruction and congestion, sneezing, burning, and drainage and who is found to have positive allergy test results will be categorized as having "allergic rhinitis" but may still have a combination of allergic and nonallergic rhinitis.^{8,21}

The true wastebasket diagnosis is "nonallergic rhinitis," since it includes rhinitis medicamentosa, rhinitis of pregnancy, nonallergic rhinitis with eosinophilia syndrome, and vasomotor rhinitis, to name a few. The fact is, after eliminating allergy as a possible cause, the diagnosis of nonallergic rhinitis is lazily offered unless obvious factors such as pregnancy or topical decongestant misuse are present, in which case the diagnosis is further specified. Further etiologic investigation in most cases of nonallergic rhinitis is unlikely because the practical importance of that investigation has yet to be established. But as research expands our understanding of the various causes of nonallergic rhinitis resulting in the introduction of effective treatments, we will strive to specifically identify the subtypes of nonallergic rhinitis. The term *nonallergic rhinitis* will go the way of the generic term *sinusitis*, now subclassified into specific diagnoses with specific diagnostic criteria and treatment options.

Chronic rhinitis may be alleviated by many nonpharmacologic, nonsurgical therapies including patient education, environmental control, nasal irrigation, and exercise. Pharmacological agents are the mainstay of treatment, and 5 main classes of agents are used in the prevention and control of symptoms of chronic rhinitis, including histamine₁ receptor antagonists, adrenergic drugs, anticholinergic drugs, sodium cromolyn, and topical corticosteroids.⁵ More recently, extraesophageal manifestations of reflux disease have been implicated in vasomotor rhinitis, and proton pump inhibitors are considered in the treatment of these patients.^{22,23} It is clear, however, that more evidence is necessary prior to the routine use of proton pump inhibitors in these patients. Multiple surgical procedures have been described for patients in whom medical therapy has failed. Most of these procedures are directed at the inferior turbinates despite the fact that most airflow does not proceed along the inferior aspect of the nasal cavity but toward the middle turbinate and middle meatus. Success seen in inferior turbinate surgery is likely the result of changes at the nasal valve. The surgeon must remember that the initiating pathologic condition persists following surgery and should be managed medically for long-term success.

Characterized by hyperreactivity of the nasal mucosa, chronic rhinitis can be classified either as seasonal or perennial allergic rhinitis (when antigens can be identified) or as nonallergic rhinitis (when antigens are not identifiable). While this simplistic classification is used by most clinicians, components of both

pathophysiological processes are potentially contributing to the patient's disease. Furthermore, nonallergic rhinitis likely represents a number of disorders that have been previously elucidated and perhaps even more that have yet to be fully understood. Vasomotor and nonallergic rhinitis should not be used interchangeably; rather, vasomotor rhinitis is a subtype of nonallergic rhinitis and is best conceptualized as a distinct entity in a continuum of chronic sinonasal disease.

Accepted for publication December 3, 2002.

The author wishes to acknowledge Robert J. Toohill, MD, for his insight in the preparation of the manuscript.

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Vasomotor Rhinitis Remains a True Clinical Problem

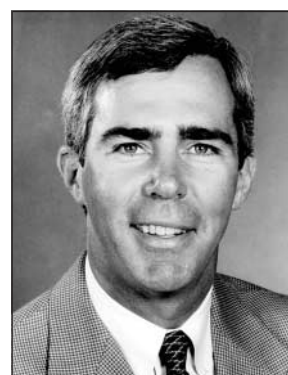
Of the many causes of chronic upper respiratory tract disorders, chronic nonallergic, noninfectious rhinitis remains one of the most elusive disorders without specific etiology. In his article, Dr Smith discusses the pros and cons of the etiology of vasomotor rhinitis as a part of a continuum of diseases of nasal hyperreactivity. His article enhances our knowledge of the subject, and he is to be congratulated for his efforts.

Inflammatory rhinitis is one of the most common upper respiratory tract disorders and is estimated to affect up to 20% of the adult population in the United States. It is now recognized to be a medical condition that substantially alters the quality of life and impairs both physical and cognitive functioning in adults. Costs for the care of these disorders amount up to \$1.9 billion per year.¹

It is well recognized that allergic rhinitis is an inflammatory disease secondary to mast cell degranulation, which may be either seasonal or perennial. When there are no identified specific allergens that provoke the mast cell degranulation, the diagnosis of "nonallergic" rhinitis is given. Vasomotor rhinitis is considered a subcategory of nonallergic rhinitis. Despite the advances in molecular biology, our current testing methodologies may still not be sensitive enough to detect the causes that produce the specific inflammatory reaction in these forms of rhinitis, or other causes may produce the symptoms.

Over the past number of years, there has been a dramatic increase in the knowledge of the inflammatory and infectious causes of rhinitis. Developments in molecular biology and clinical immunology have progressed to a marked degree, and pharmacology has progressed similarly. For example, comprehension of arachidonic acid breakdown of the cell wall and the effects of leukotrienes has fostered the development of leukotriene receptor antagonists such as zafirlukast and montelukast, which assist in the treatment of patients with rhinitis. Unfortunately, most of the diagnostic methods specifying the immunological and molecular biological changes are used in the research laboratory, but rarely in clinical practice.

From a clinical point of view, most of the patients whom the otolaryngologist encounters have a number of complaints relating to rhinitis. Nasal congestion and thick postnasal discharge (rhinorrhea) are prominent among other complaints of facial pressure and nasal obstruction. Classically, these patients respond to changes in temperature or humidity, irritants such as smoke or chemicals, and sometimes emotions. An appropriate history review will elucidate the tendency for allergic causes. However, for those patients without any suggestion of allergic diathesis, the suggested "wastebasket" diagnosis of nonallergic rhinitis or vasomotor rhinitis is usually given. Based on the inflammatory nature of rhinitis, most



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clinicians prescribe either anti-inflammatory medications or antihistamines to alleviate patients' symptoms of congestion and rhinorrhea. Several topical intranasal corticosteroids and the topical intranasal antihistamine azelastine are now recognized by the Food and Drug Administration to have an indication for treatment in nonallergic rhinitis.

Vasomotor rhinitis, as proposed by Dr Smith, may potentially be due to a hyperactive parasympathetic nervous system or a dysfunctional autonomic nervous system. However, in the practical management of these patients, he correctly queries whether knowledge of the cause really affects management.

The absence of an infectious or allergic cause based on the histopathologic examination of the nasal mucosa suggests an imbalance of the regulatory mechanisms of the nasal vasculature. The nasal blockage experienced by patients is mainly caused by vasodilation. Although