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Rhinitis: A Practical and Comprehensive Approach to Assessment and Therapy

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EXECUTIVE SUMMARY

Rhinitis: An Executive Summary of a Practical and Comprehensive Approach to Assessment and Therapy

Peter Small, MD, Saul Frenkiel, MD, Allan Becker, MD, Pierre Boisvert, MD, Jacques Bouchard, MD, Stuart Carr, MD, Don Cockcroft, MD, Judah Denburg, MD, Martin Desrosiers, MD, Richard Gall, MD, Qutayba Hamid, MD, Jacques Hébert, MD, Amin Javer, MD, Paul Keith, MD, Harold Kim, MD, François Lavigne, MD, Catherine Lemière, MD, Emad Massoud, MD, Keith Payton, MD, Bob Schellenberg, MD, Gordon Sussman, MD, David Tannenbaum, MD, Wade Watson, MD, Ian Witterick, MD, and Erin Wright, MD, The Canadian Rhinitis Working Group

ABSTRACT

Rhinitis is a common disease entity, found in up to 40% of the population. Allergic rhinitis is also common in the population, and some studies indicate that its incidence is on the rise.

Since the last Canadian recommendations in 1994, considerable progress has been made in understanding the underlying inflammatory process involved in the clinical presentation of rhinitis. As well, new treatment modalities have evolved and are now available to practicing physicians.

It has also been established that rhinitis, as a presenting feature, may represent more than a local event and may herald a full-scale airway process. For these reasons, representatives of the related specialties of otolaryngology, allergy and clinical immunology, respirology, and family medicine and basic science researchers were brought together to discuss their viewpoints and develop a Canadian consensus on the concepts of etiology and treatment of rhinitis. This work provides an update of combined airway disease and provides a concise guide of the current modalities for treating nasal inflammation.

SOMMAIRE

La rhinite est une affection fréquente, documentée chez près de 40% de la population. La rhinite allergique en particulier est fréquente dans la population et certaines études semblent indiquer une augmentation de son incidence.

Depuis les dernières recommandations canadiennes en 1994, nous avons fait des progrès considérables dans la compréhension des processus inflammatoires impliqués dans la présentation clinique de la rhinite. De plus, de nouvelles modalités thérapeutiques sont maintenant disponibles.

Il est aussi établi que la rhinite peut être plus qu'un événement localisé et représenter en fait un processus affectant toutes les voies respiratoires. C'est pour toutes ces raisons que nous avons réuni des représentants des spécialités connexes que sont

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l'oto-rhino-laryngologie, l'immunologie clinique et aller-gologie, la pneumologie, la médecine de famille et des chercheurs fondamentalistes pour discuter de leurs perspec-tives respectives et de développer un consensus canadien sur l'étiologie et le traitement de la rhinite. Ce papier présente donc une mise-à-jour sur l'atteinte globale des voies respira-toires et offre un guide concis sur les modalités actuelles utilisées dans le traitement de l'inflammation nasale.

Key words: *allergic rhinitis, rhinitis, upper airway*

*T*his document provides Canadian health care professionals with an updated set of recom-mendations for the assessment and treatment of rhinitis. The document was created through a col-laborative process including representatives of the related specialties of otolaryngology, allergy and clinical immunology, respirology, family medicine, and basic science.

Anatomy and Physiology of the Respiratory Tract

The nose is a remarkable organ that performs vital func-tions under adverse conditions. The nasal valve, for example, regulates nasal airflow and resistance, where-as the nasal turbinates help create a thermally efficient energy exchange. These structures are supported by an intricate and specialized vasculature. Furthermore, the nose has powerful filtering properties thanks to both the vibrissae and the mucous blanket.

There are many similarities and differences between the upper and lower respiratory tracts. Rhinitis and asthma frequently coexist, and there is a growing body of research at the cellular level that supports the concept of a combined airway inflammatory disease.

Cellular Biology of Airway Disease

The hallmark of rhinitis is the infiltration of large numbers of inflammatory cells, including mast cells, CD4-positive T cells, B cells, macrophages, and eosinophils. In most types of rhinitis—and allergic dis-ease in particular—the T cells are predominantly T helper (Th)2 in nature and release cytokines (eg, inter-leukin [IL]-3, IL-4, IL-5, and IL-13) that promote immunoglobulin E (IgE) production by plasma cells.

Table 1. Symptom Classification

Class	Severity/Duration
I	Mild/intermittent
II	Moderate/intermittent
	Moderate-severe/intermittent
	Severe/intermittent
	Mild/persistent
III	Moderate/persistent
IV	Moderate-severe/persistent
	Severe/persistent

The mediators and cytokines released during the early phase trigger an inflammatory response over the next 48 hours. Inflammation can be a vicious cycle, with mediators and cytokines activating and releasing more mediators, perpetuating the inflammatory response.

Classification of Rhinitis

The document provides an explanation of classifica-tion systems for rhinitis both by etiology (eg, IgE medi-ated, autonomic, infectious, idiopathic) and by severi-ty and duration.

The severity/duration system has four classifica-tions, as shown in Table 1.

Patient Evaluation

Rhinitis is often a long-standing condition; many patients fail to raise this concern with routine physi-cian visits. It is always a good idea to "screen" for rhinitis with selected questions, particularly among asthmatic patients, up to 95% of whom suffer from associated rhinitis.

An appropriate history and physical examination remain the cornerstone of establishing the diagnosis. The most common presenting complaint for patients with rhinitis is nasal congestion or blockage. An eval-uation of the patient's home and work or school envi-ronment is recommended to help determine relevant allergens and irritants. Patients should be asked about their current or recent medication use; there are sever-al medications known to provoke rhinitis as a side effect. Patients should also be questioned about comorbidities in the respiratory tract (eg, asthma, oti-

tis media, sinusitis, common colds). Any previous medical treatment (and its effects, or lack thereof) should also be documented.

Complete physical examination involves assessment of outward signs (ie, persistent mouth breathing, frequent sniffling) and internal abnormalities (eg, structural abnormalities) by rhinoscopy. Referral to an otolaryngologist is recommended if nasal polyps or other structural pathology is suspected.

A complete physical examination in suspected rhinitis should also involve the nose, ears, sinuses, posterior oropharynx, chest, skin, and lymph nodes.

Diagnostic Tests

Diagnostic tests are usually necessary to confirm etiology of rhinitis. Skin testing is the primary diagnostic method for the confirmation of environmental allergens for allergic rhinitis. Serum-specific IgE can be measured as an alternative to skin tests. Diagnostic imaging may be needed to assess structural abnormalities and the paranasal sinuses.

Therapy: Nonsurgical

The full document provides a comprehensive, evidence-based assessment of the various modalities used to treat rhinitis.

In addition to patient education, avoidance of specific allergens or irritants, pharmacotherapy, and immunotherapy represent the cornerstones of treatment.

Patients may require a combination of treatments, depending on the symptom class and their response to therapy.

Oral antihistamines are recommended as a cornerstone of allergic rhinitis treatment for the relief of sneezing, itching (eyes, nose, and throat), and rhinorrhea. Newer, nonsedating compounds should be used in most instances, particularly for those whose occupations require mental alertness and/or manual dexterity.

Whereas antihistamines are generally used for milder symptoms, intranasal corticosteroids are used to treat moderate to severe intermittent symptoms or mild persistent rhinitis alone or in combination with antihistamines. Through their anti-inflammatory effects, intranasal corticosteroids are highly effective in reducing nasal stuffiness and blockage.
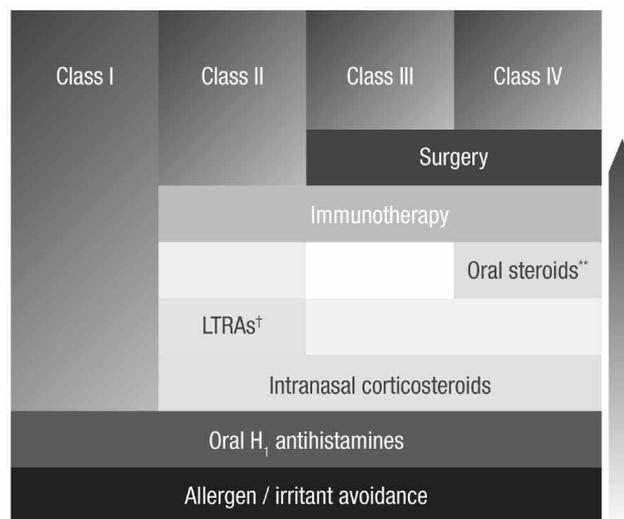
LTRAs: leukotriene receptor antagonists
* Step up if there is no response or incomplete response to treatment, regardless of class
† LRTAs may be used in class III and IV, but there is less supporting evidence
** Oral steroids may be considered for class II (severe intermittent), but there is little supporting evidence

Figure 1. Treatment of allergic rhinitis by symptom class.

Antileukotrienes have been shown to be particularly useful for nasal congestion in rhinitis, when taken either alone or in combination with antihistamines.

Figure 1 illustrates how the different types of therapies typically fit into a treatment strategy for allergic rhinitis, based on both the classification system presented in Table 1 and the response to therapy.

Importantly, allergic rhinitis is not a local disease; the entire respiratory tract is involved even in the absence of clinical asthma. Using the concept of a combined airway inflammatory disease, therapy should be directed both locally and systemically to correct clinical symptoms that may be predominant in one organ but are often detected in other areas concurrently.

Therapy: Surgical

Surgical therapy may be helpful in the management of rhinitis or chronic sinus disease refractory to medical treatment.

Numerous surgical procedures have been designed to reduce the size of the inferior turbinates or remove a portion or even the entire inferior turbinate. Surgical options address the bone, the mucosa, the submucosa, or a combination thereof. Most procedures can be performed under local anaesthesia in an office or outpatient setting.
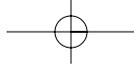
Conclusion

Although the authors recognize that each patient presents with a unique set of characteristics that may influence diagnosis and treatment decisions (eg, concomitant illness, polypharmacy, etc.), this guideline attempts to use general principles applicable to the majority of patients with rhinitis.
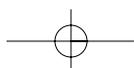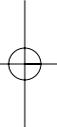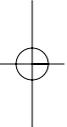
ARTICLE

Rhinitis: A Practical and Comprehensive Approach to Assessment and Therapy

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It has also been established that rhinitis, as a presenting feature, may represent more than a local event and may herald a full-scale airway process. For these reasons, representatives of the related specialties of otolaryngology, allergy and clinical immunology, respirology, and family medicine and basic science researchers were brought together to discuss their viewpoints and develop a Canadian consensus on the concepts of etiology and treatment of rhinitis. This work provides an update of combined airway disease and provides a concise guide of the current modalities for treating nasal inflammation.

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Address reprint requests to: Dr. Peter Small, Department of Clinical Immunology and Allergy, Jewish General Hospital, 3755 ch. Cote-Ste-Catherine, Montreal, QC H3T 1E2; e-mail: psmall@mtd.jgh.mcgill.ca.

l'oto-rhino-laryngologie, l'immunologie clinique et aller-gologie, la pneumologie, la médecine de famille et des chercheurs fondamentalistes pour discuter de leurs perspec-tives respectives et de développer un consensus canadien sur l'étiologie et le traitement de la rhinite. Ce papier présente donc une mise-à-jour sur l'atteinte globale des voies respira-toires et offre un guide concis sur les modalités actuelles utilisées dans le traitement de l'inflammation nasale.

Key words: *allergic rhinitis, rhinitis, upper airway*

*T*his article represents the end of a process that began with a gathering of the Canadian Rhinitis Working Group, which met recently to discuss the common symptoms of rhinitis. The motivation for this initiative was to update information that has emerged since 1994, when the first practical guide for Canadian physicians was published, entitled "Assessing and Treating Rhinitis."[1]

This Canadian update follows the joint efforts of the American Academy of Allergy, Asthma and Immunology and its European counterpart, which in 2001 published a report of their workshop entitled "Allergic Rhinitis and Its Impact on Asthma."[2]

Rhinitis is a common disease entity, found in up to 40% of the population.[3] Allergic rhinitis is also com-mon in the population, and some studies indicate that its incidence is on the rise.[4–6]

Unfortunately, there is a persistent belief that rhini-tis represents a symptom rather than a distinct disease. As the entranceway to the respiratory tract, inflamma-tory pathology within the nose may imply a more widespread disease process. Inflammation within the nasal chambers may be due to a local process or asso-ciated with systemic abnormalities.

What is most important is the fact that since 1994, considerable progress has been made in understanding the underlying inflammatory process involved in the clinical presentation of rhinitis. As well, new treatment modalities have evolved and are now available to prac-ticing physicians.

It has also been established that rhinitis, as a pre-senting feature, may represent more than a local event and may herald a full-scale airway process. For these reasons, representatives of the related specialties of otolaryngology, allergy and clinical immunology, respirology, and family medicine and basic science researchers were brought together to discuss their

viewpoints and develop a Canadian consensus on the concepts of etiology and treatment of rhinitis. This work provides an update of combined airway disease and provides a concise guide of the current modalities for treating nasal inflammation.

Anatomy and Physiology of the Respiratory Tract

The nose is a remarkable organ that performs vital functions under adverse conditions. The following sec-tion describes the various parts of the nasal structure and briefly outlines their function.

Nose

Nasal Valve

The external nasal cartilages, upper lateral cartilage, and cartilaginous septum combine to create a flow-limiting segment of the nasal airway called the nasal valve.[7] When nasal airflow exceeds a certain limit, the nasal ala collapses, preventing further airflow through that side of the nose. The nasal valve generates approximately 50% of the total resistance of the respiratory tract.[7]

Nasal Cycle

In approximately 80% of the population, the nose undergoes an alternating cycle (average 2–6 hours) of relative vasoconstriction and vasodilatation of the nasal lining, which provides for preferential respira-tion through one side at any given time while resting the opposite side.[8,9]

Turbinates

The lateral nasal wall has three scroll-like projections on each side called turbinates or conchae. These bony structures serve to add an element of turbulence to air traveling through the nose and help create a thermally efficient energy exchange.[10]

Vasculature

The nasal vasculature includes a unique pattern of resistance vessels, which divide into two parallel flow patterns consisting of a typical capillary bed near the mucosal surface, which then direct blood flow into venous sinusoids prior to emptying into the venous plexus and venule (Figure 1).[11,12] The venous sinusoids give the turbinates their pseudoerectile properties, which, in turn, permits the creation of the nasal cycle.
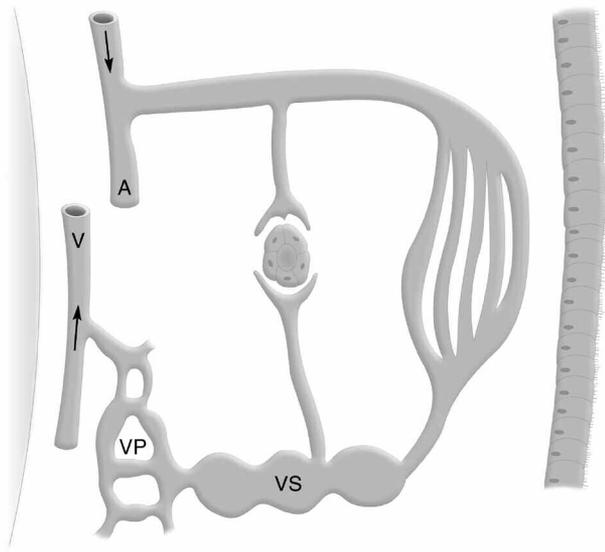
Figure 1. Illustration of the unique elements of the nasal microvasculature. Blood flows into the nasal mucosa via arterioles (A). After supplying the mucous glands and subepithelial capillaries, the blood flows into the venous sinusoids (VS), which are the capacitance vessels that give the nasal mucosa its pseudoerectile properties. Outflow is then via the venous plexus (VP) and venules (V). This pattern of blood flow is most common over the inferior turbinates (IT). Some authors have described the existence of arteriovenous anastomoses that can provide direct flow to the venous sinusoids, bypassing the capillary system.

In general, the reverse process occurs on expiration through the nose, with extraction of heat and humidity from the air being expired.

Vibrissae

Large particles are filtered from the inspired air by the nasal hairs (vibrissae) present in the nasal vestibule.

Mucous Blanket

Particles that are not trapped or filtered by the vibrissae are likely to be entrapped by the mucous blanket covering the nasal mucosa. The cilia are able to move freely in the sol phase and thus propel the gel phase with its trapped particles towards the sinus ostia or nasopharynx.[11]

This mucociliary clearance mechanism is tremendously effective in removing particles greater than 4 μm in size (nearly 100%) and preventing deposition in the lower respiratory tract.[13] Within the mucus are some important proteins, such as immunoglobulin (Ig)A, which is secreted into the mucous blanket and provides protection against microorganisms and other foreign antigens. Lysosomes and other nonspecific defense proteins and enzymes are also found in the mucous blanket.

Disruption of the mucociliary clearance mechanism can occur as a result of infection, which can destroy parts of the epithelium, or by environmental irritants such as cigarette smoke, which alters and renders less functional the mucous blanket, with its sol and gel layers.

Paranasal Sinuses

Anatomy

The paranasal sinuses consist of four air-filled cavities on each side of the nose. They take their pneumatization from the lateral wall of the nose and drain into the nose along its lateral wall.

The epithelium lining the paranasal sinuses is contiguous with—and similar to—that of the nose, the primary difference being that sinuses have a thinner, less vascular epithelium containing fewer mucus-producing cells.

Physiology

The physiologic role of the paranasal sinuses is less clear than that of the nose. The theoretical roles include lightening of the skull, warming and humidifying inspired air, and provision of resonance for speech, but there is considerable debate on this topic, with no clear consensus.

Lower Airway: Comparative Approach

Similarities with the Upper Respiratory Tract

The most obvious similarity between the upper and lower respiratory tract is the presence of a pseudostratified, ciliated epithelium with goblet cells. Additionally, the submucosa of both the upper and lower respiratory tracts includes a collection of blood vessels, mucous glands, supporting cells, inflammatory cells, and nerves. In both upper and lower respiratory systems, the mucus helps warm and humidify the incoming air, as well as aiding in filtration and defense.

In terms of innervation, both upper and lower tracts receive parasympathetic innervation, which results in stimulation of secretions. In the lower airway, this innervation also stimulates bronchoconstriction. In both upper and lower respiratory tracts, there is a lack of direct sympathetic innervation.

Both the upper and lower respiratory tracts contain inflammatory cells in their respective submucosae. In inflammatory situations, there is a significant prominence of T cells, as well as eosinophils and intercellular messengers, including cytokines.

In other words, the upper and lower airways represent a continuum in many respects.

Differences between the Upper and Lower Respiratory Tracts

The nasal mucosa has the previously mentioned distinct vascular supply overlying the turbinates, which provides pseudoerectile properties. Conversely, the nose does not have the smooth muscle present in the submucosa, with its attendant ability to alter the calibre of the air passage.

In the nose, the vascular supply does carry some sympathetic innervation that controls and reduces blood flow via α-adrenergic receptors. Conversely, the lower respiratory tract contains receptors that respond to β-adrenergic agents with bronchodilation.

Relationship between the Upper and Lower Airway

Rhinitis and asthma frequently coexist,[14–21] and there is a growing body of research at the cellular level that supports the concept of a combined airway inflammatory disease.[22,23] There is evidence that immune responses within the airway are paralleled by similar immunoinflammatory events in peripheral blood and bone marrow. Indeed, the systemic nature of the inflammatory response is also confirmed by the finding that allergen provocation of the upper airway induces not only local changes but findings in the lower airway, peripheral blood, and bone marrow.

Similar systemic inflammation occurs when challenging only the lower airway, further suggesting the systemic nature of allergic disease. This supports the hypothesis that there is communication between bone marrow, peripheral blood, and airway tissue compartments, which contributes to the allergic inflammatory process.[24] Evidence at the cellular level confirmed these observations.[22,23]

These studies and others like them provide strong evidence that allergic airway inflammation is a total airway disease. The recent literature is ripe with reviews championing this hypothesis.[25–27] The clinical significance is that treating the entire airway should be considered to achieve the maximum effect.

Cellular Biology of Airway Disease

Although a complete explanation of the cellular biology of airway disease is beyond the scope of "a practice guideline," it is nevertheless important to understand the basics of the immunoinflammatory cascade. This process not only helps describe the processes leading to rhinitis in particular, it also shows how airway disease shares some similar mechanisms in the upper and lower tracts. The hallmark of rhinitis is the infiltration of large numbers of inflammatory cells. These cell types include mast cells, CD4-positive T cells, B cells, macrophages, and eosinophils. These cells, except eosinophils, can also be found in normal nasal mucosa.

T cells are immunoregulatory cells that differentiate from T helper (Th)0 into Th1 and Th2 subsets.

In most types of rhinitis—and allergic disease in particular—the T cells are predominantly Th2 in nature and release the cytokines interleukin (IL)-3, IL-4, IL-5, and IL-13, among others that promote IgE production by plasma cells (both locally and systemically).

Other effects of cytokines include recruitment and promotion of survival of inflammatory cells. Th1-type cells regulate inflammation and produce other sets of cytokines, including interferon-γ, which is involved primarily in cell-mediated immunity to viral, bacterial, and other infections.

A change in the balance between Th1 and Th2 responses is critical to the development of the inflammatory response (Figure 2). Some of the cytokines are more important than others in the early stage of airway disease, whereas some are more important in the chronic stage.

In allergic disease, there is more expression of Th2 cytokines, particularly IL-4. However, in many cases of nonallergic rhinitis, the immune response is also Th2.
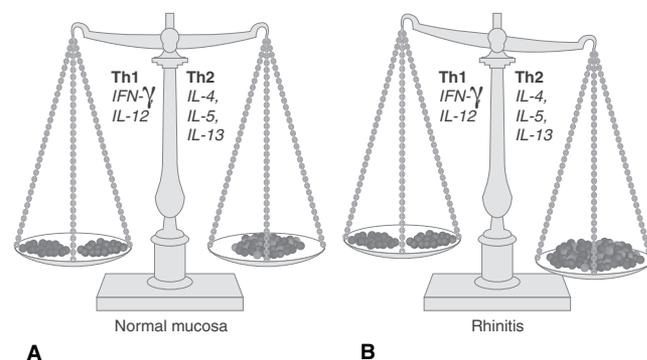
Figure 2. *A,* The normal mucosa has a balance of regulating T helper (Th)1-type cells (eg, interferon [IFN]-γ, interleukin [IL]-12) and inflammatory Th2-type cells (eg, IL-4, IL-5, IL-13). *B,* In rhinitis, the normal balance of Th1- and Th2-type cells is skewed towards the Th2 type. Airway inflammation is the result.

Upon allergen exposure, the inflammatory cells and their progenitors begin to differentiate in the bone marrow and to migrate through the vasculature. Within minutes, there is cross-linking of IgE on mast cells and basophils. This triggers degranulation and release of preformed mediators, such as histamine and tryptase. There is rapid de novo generation of cysteinyl-leukotrienes and prostaglandin D_2. Also released is preformed IL-4, which is important in shifting the T-cell response to Th2, with further production of IL-4, IL-5, and IL-13. Nitric oxide can also be detected.

The mediators and cytokines released during the early phase trigger an inflammatory response over the next 48 hours (late response). The effects lead to up-regulation of vascular cell adhesion molecule and E-selectin expression. These promote adherence of circulating cells to endothelial cells. Chemokines produced by epithelial cells—including eotaxin, RANTES, and MCP4—attract cells from the blood to the nose. IL-5 is an important cytokine in attracting eosinophils. As a result, the lamina propria of the mucosa is infiltrated with many eosinophils, as well as neutrophils, basophils, CD4-positive (Th2) lymphocytes, and macrophages. These cells, in turn, activate and release more mediators, and further inflammation occurs.

Classification of Rhinitis

Over the years, numerous classification systems for allergic and nonallergic rhinitis have been proposed. This has led to an increasing amount of confusion on the topic. Developing a common set of definitions and terms enables physicians across large geographic areas to discuss and treat similar patients in similar ways. The hope is that this will lead to an agreeable set of guidelines, which will better serve the patient population.

Strictly speaking, rhinitis refers to inflammation of the mucosa of the nasal cavity. The term *rhinitis* is increasingly being supplanted by the term *rhinosinusitis*. Rhinosinusitis is defined as an inflammatory disease involving the nasal mucosa and extending to the paranasal sinuses. The inference is that the intranasal and intrasinus mucosa are in a continuum, with each ostium representing the critical points at which obstruction could occur, as they affect mucociliary outflow from each respective sinus.

Although this terminology is more predominant when referring to infectious rhinitis, there is a movement to label all rhinitis as rhinosinusitis. For the purposes of these guidelines, we continue to refer to the term *rhinitis* when not discussing infectious rhinosinusitis.

Rhinobronchitis or rhinoasthma or rhinitis in asthma is defined as inflammatory disease involving the nasal mucosa and extending to the lower airway. Various authors have suggested various names to denote the close relationship between rhinitis and asthma, including "allergic rhinobronchitis," "chronic allergic inflammatory airway syndrome," and "the united airways."[25] The members of this panel decided that although they endorse the concept of a combined airway inflammatory disease, little could be gained by endorsing a specific name or term. There have also been few therapeutic trials looking at treatments of these combined disorders. Although studies have looked at the treatment of asthma affecting rhinitis or treatment of rhinitis affecting asthma, few studies have looked at treatments of patients with both conditions.

Etiology

The mechanism of airway inflammation can be quite variable. In the past, the classification system of upper airway inflammation has commonly been broken down simply into allergic and nonallergic rhinitis.[28] Although, initially, this broad classification system may have been adequate, current knowledge and research allow us to more accurately classify rhinitis into allergic, autonomic, infectious, and idiopathic (unknown) etiologies (Table 1). As time passes and more research is done, it is likely that the following classification system will require further revision.

IgE Mediated (Allergic)

Allergic rhinitis is an inflammatory disease involving the nasal mucosa, characterized by IgE-mediated inflammation with eosinophilic infiltration with a predominantly (T cell) Th2 cytokine profile. This category can be subdivided into intermittent or persistent allergic rhinitis, depending on symptom duration.

The understanding that the inflammation associated with allergic asthma has mechanisms similar to those of allergic rhinitis has prompted the movement towards treating the allergic airway as one entity.

Autonomic (Vasomotor Rhinitis)

The autonomic nervous system, through its control of sympathetic and parasympathetic nerve fibres to the

Table 1. Etiologic Classification of Rhinitis

IgE-mediated (allergic)
    Intermittent
    Persistent

Autonomic
    Drug-induced (rhinitis medicamentosa)
    Hypothyroidism
    Hormonal
    Emotional
    Physical (eg, temperature related)
    Foods (smells, taste)
    Irritative
    Exercise
    Recumbency
    NARES
    Pregnancy?

Infectious

Idiopathic

Ig = immunoglobulin; NARES = Non-Allergic Rhinitis with Eosinophilia Syndrome.

nose and paranasal structures, is responsible for many types of rhinitis. The different types of autonomic causes are shown in Table 1. Together these causes represent a very common type of clinical presentation. Although pregnancy has historically been considered a cause of autonomic rhinitis, a recent study found no difference in the incidence of rhinitis between pregnant and nonpregnant women.[29]

Infectious

Rhinitis can also have an infectious etiology, whether it be viral, bacterial, or fungal. Viral infection, the most common, is usually precipitated by a sinus or related infection but may be associated with colds and influenza.

Idiopathic

In the event that an etiology cannot be determined for the rhinitis symptoms, a diagnosis of idiopathic rhinitis may be made.

Differential Diagnosis

A number of other conditions can cause symptoms of rhinitis (Table 2), including granulomatous diseases such as sarcoidosis and Wegener's granulomatosis.

Rhinitis symptoms can also be caused by atrophy of blood vessels and seromucinous glands, which result in abnormally wide and open nasal cavities.

A foreign body in the nasal cavity should also be considered as a possible cause of rhinitis symptoms, particularly in children.

Anatomic abnormalities, such as a septal deviation, can also lead to symptoms mimicking those of rhinitis.

Finally, the presence of a defect in the floor of the brain cavity can lead to leakage of cerebrospinal fluid (CSF) into the nasal cavity. This rare, but very serious, condition may cause symptoms like those of rhinitis. The key symptom of CSF rhinorrhea is clear, watery discharge, usually from only one nostril. One should be aware of this possibility in patients who have undergone recent head trauma.

Symptom Classification

In addition to etiologic considerations, the classification of rhinitis takes into account the duration and severity of symptoms. The symptoms of rhinitis include nasal rhinorrhea, sneezing, itching, and nasal obstruction. Associated with this are non-nasal symptoms, including those related to the eyes (watery discharge, burning, and itching), sinuses (facial pain, headache, and drainage), and lungs (cough, wheeze, and shortness of breath).

Symptom Duration

Rhinitis is said to be of an intermittent nature when the total duration of the episode of inflammation is less than 6 weeks. Many previous classification systems referred to intermittent disease as "seasonal allergic rhinitis." Conversely, persistent disease is characterized by symptoms that continue to occur throughout the year.

Symptom Severity

Symptoms can be classified as mild, moderate, moderate-severe, and severe. Mild symptoms are usually intermittent; patients are generally able to perform normal activities (including work or school) and sleep normally, with only minor disruption.

Table 2. Rhinitis: Differential Diagnosis

Granulomatous diseases
Atrophic rhinitis
Presence of foreign body
Anatomic abnormality
CSF rhinorrhea

CSF = cerebrospinal fluid.

Moderate symptoms are also usually intermittent but interfere significantly in the normal performance of activity (including work or school duties) and normal sleep. If these symptoms are persistent, they are classified as moderate to severe.

Symptoms are classified as severe if they are persistent and the patient is unable to perform normal work or to sleep normally.

Putting the two elements (duration and severity) together, a new classification system is now presented. Those with mild, intermittent symptoms fall into class I. Those with moderate to severe intermittent symptoms—as well as those with mild, persistent symptoms—are said to be in class II. Those with moderate persistent symptoms fall into class III, whereas those with moderate to severe or severe persistent symptoms are in class IV (Table 3).

Patient Evaluation

For the evaluation of patients with suspected rhinitis, appropriate history and physical examination remain the cornerstone of establishing the diagnosis; selected ancillary tests may also be required (discussed in more detail in the following section).

Because allergic rhinitis is often a long-standing condition, many patients fail to raise this concern with routine physician visits. It is always a good idea to "screen" for rhinitis with selected questions. This is especially important for asthmatic patients, up to 95% of whom have been found in some studies to suffer from associated rhinitis.[18–22]

History

Symptoms

The most common presenting complaint for patients with rhinitis is nasal congestion or blockage, which may be either intermittent (often seasonal) or persistent (Table 4). It is important to document the duration of congestion and any associated symptoms and whether they have been increasing or stable over time.

Several historical features increase the likelihood of an allergic cause for nasal congestion, including nasal itch, rhinorrhea, sneezing, eye involvement, seasonality of symptoms, and sensitivity to irritants or triggers.

Table 3. Symptom Classification

Class	Severity/Duration
I	Mild/intermittent
II	Moderate/intermittent
	Moderate-severe/intermittent
	Severe/intermittent
	Mild/persistent
III	Moderate/persistent
IV	Moderate-severe/persistent
	Severe/persistent

Family History

Allergic disease can have a genetic component. An inquiry into the allergic history of immediate family members (parents and siblings) may provide additional information.

Environment

An evaluation of the patient's home and work or school environments is recommended. This may help determine relevant allergens and irritants to which the patient may be exposed and may identify potential targets for intervention. The history should focus on common and potentially relevant allergens, such as the presence of furred animals (and their reservoirs), textile flooring, and upholstery.

Exposure to known irritants, such as tobacco smoke or other noxious substances at home or work, is critical, and it is always valuable to identify whether the home environment is overly dry or humid.

Medication History

Patients should be asked about their current or recent medication use. Several medications are known to provoke rhinitis as a side effect. Use of α- and β-blockers, acetylsalicylic acid (ASA), nonsteroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme (ACE) inhibitors, oral contraceptives, and hormone therapy can all lead to symptoms of rhinitis. Furthermore, the recreational use of cocaine is typically associated with rhinitis symptoms.

An investigation of medication use may also uncover overuse of topical decongestants. Overuse of these agents can lead to rhinitis medicamentosa, a rebound nasal congestion that will typically resolve within a week of discontinuation of these agents.

Table 4. Elements of Complete History for Suspected Rhinitis

Personal history
    Nasal itch
    Rhinorrhea
    Sneezing
    Eye involvement
    Seasonality
    Triggers
    Irritants
Family history
    Allergy
    Asthma
    Smell disturbance (hyposmia or anosmia)
Environmental history
    Animals
    Flooring
    Upholstery
    Tobacco exposure
    Other noxious irritants
    Humidity
Medication history
Quality of life
    Rhinitis-specific questionnaire
Comorbidities
    Asthma
    Mouth breathing
    Snoring
    Sinus involvement
    Otitis media
    Polyps
    Conjunctivitis
    Atopic dermatitis
Response to prior treatment
    Decongestants
    Antihistamines
    Topical eyedrops
    Intranasal steroids
    Immunotherapy
    Prednisone
    Antileukotrienes
Hormonal abnormalities
    Pregnancy

Quality of Life

The history should include an assessment of the severity of the condition and its impact on quality of life. Recent studies have shown that patients with rhinitis often report a poorer quality of life than patients with asthma, and this underscores the importance of an adequate evaluation.

Comorbidities

History should include questions regarding the presence of comorbidities such as breathing difficulties (ie, asthma, mouth breathing, snoring, sleep apnea), sinus involvement (look for headache or facial pain, persistent cough, purulent nasal secretions, bad breath, or frequent throat clearing), otitis media (particularly in children), nasal polyps, or sinus surgery. The history should also document the frequency and duration of "colds"; patients may attribute persistent nasal symptoms to a "constant cold."

Response to Treatment

Most patients try at least some over-the-counter medication before being seen by their physician; response to such treatment can offer important clues to the diagnosis.

Most patients with rhinitis will enjoy at least transient improvement with oral or topical decongestants.

Many patients report improvement with antihistamines, although a beneficial response to first-generation products does not imply an allergic etiology. Most older antihistamines have anticholinergic properties, which decrease rhinorrhea, along with sedative effects, which may improve sleep quality regardless of whether the inflammation is allergic (the presence of allergy). On the other hand, a clear improvement in symptoms with newer, highly specific second-generation antihistamines is a very strong suggestion of underlying allergy. A past beneficial response to topical intranasal corticosteroids is a favourable sign and would suggest that such treatment would continue to be helpful in the future but does not alone indicate the presence of underlying allergy.

Physical Examination

The physical examination is an integral part of rhinitis assessment (Table 5).

Outward Signs

Outward signs include persistent mouth breathing, rubbing at the nose or an obvious transverse nasal crease, infraorbital pooling of venous blood reflecting long-standing congestion, and frequent sniffling or throat clearing. Examination of the external nose may

Table 5. Elements of a Complete Physical Examination for Suspected Rhinitis

Outward signs
    Mouth breathing
    Rubbing the nose
    Transverse nasal crease
    Infraorbital blood pooling/venous stasis
    Frequent sniffling
    Throat clearing

Nose
    Mucosal swelling, erosions, bleeding
    Septal crusting, perforation, spurs, or significant
      deviation
    Polyps
    Secretions
    Odour
    Inspiratory and expiratory nasal airflow

Ears
    Usually normal
    Pneumatic otoscope to assess for eustachian tube
      dysfunction
    Valsalva's maneuver to assess for middle ear impedance

Sinuses
    Palpation of the sinuses for tenderness
    Maxillary tooth sensitivity

Posterior oropharynx
    Postnasal drainage
    Lymphoid hyperplasia ("cobblestoning")
    Tonsillar hypertrophy

Chest and skin
    Atopic disease
    Wheezing

reveal an obvious structural abnormality (ie, septal deviation).

Close inspection may reveal Dennie-Morgan lines, which are extra skin folds of the lower eyelids from tissue edema. As well, injection or swelling of the conjunctiva may be seen, along with "cobblestoning" or lymphoid hyperplasia of the tarsal conjunctival surface.

Nasal Examination

A rhinoscopic examination by whatever method is mandatory for proper diagnosis. For primary care physicians without access to a nasal endoscope, examination with an open-style otoscope and speculum is sufficient for viewing of the anterior and middle nasal cavity. The nasal mucosa should be examined for uni-

lateral or bilateral swelling. Modest unilateral turbinate swelling is likely a reflection of the normal nasal cycle and is not a concern on its own. Hypertrophy of the inferior turbinate can be reduced with local decongestants to allow for a more complete inspection of the intranasal chamber.

In allergic disease, the mucosal surface classically appears pale and boggy, whereas the tissues are more likely to appear red or "beefy" in vasomotor rhinitis. That being said, there is some overlap in appearance between allergic and vasomotor diseases.

In atrophic disease, there may be little apparent mucosal swelling; the nasal cavity is usually roomy despite complaints of severe nasal congestion. The mucosal surface should be carefully assessed for erosions or frank bleeding, and the septum must be evaluated for crusting, perforation, septal spurs, or significant deviation. If direct examination proves too difficult because of marked mucosal swelling, or if nasal polyps are suspected, the nose should be reexamined after application of topical decongestants.

Nasal polyps have a classic "peeled grape" appearance, with a translucent body descending from a narrow stalk superiorly. They usually protrude from the middle meatus, although the middle turbinate may also occasionally undergo polypoid degeneration. Severe swelling of the middle turbinate is often mistaken for nasal polyposis, but polyps are insensate and do not readily shrink with topical decongestant sprays.

Referral to an otolaryngologist is recommended if nasal polyps or other structural pathology is suspected, particularly in children. These findings can be easily confirmed by nasal endoscopy. Evidence of chronic sinusitis may be apparent on a computed tomographic scan.

Secretions may be minimal or profuse and are traditionally clear and thin with allergic disease. Many patients with recurrent nasal polyps have very thick rubbery nasal mucus. Purulent drainage from under the middle turbinate is suggestive of sinusitis. Excessive nasal crusting may be seen in atrophic rhinitis (entire nose) and septal perforation (at the site of perforation).

A foul nasal odour may be a suggestion of anaerobic colonization of the paranasal sinuses but can also be noted with atrophic rhinitis. A nasal foreign body must always be considered in young children with a foul odour, especially if associated with unilateral

obstruction or purulent discharge. Halitosis is also common with persistent mouth breathing.

Ear Examination

Inspection of the tympanic membranes is important, and although these are usually normal, they may be retracted, reflecting negative pressure in the middle ear, or there may be scarring from previous perforations or surgical drainage. A pneumatic otoscope can be used to assess for eustachian tube dysfunction, although the presence of middle ear effusion would also suggest this diagnosis.

Valsalva's maneuver (increasing the pressure in the nasal cavity by attempting to blow out the nose while holding it shut) can also be used to uncover middle ear impedance.

Sinus Examination

Application of direct pressure under the orbital ridge and over the ethmoid and maxillary sinuses may reveal tenderness, although this also does not indicate sinusitis on its own. Transillumination of the sinuses has proven unreliable and difficult to reproduce and is no longer routinely recommended. Tapping the maxillary teeth with a tongue depressor may also reveal sensitivity, which may be a sign of sinus involvement.

Other Examinations

Examine the posterior oropharynx for postnasal drainage, lymphoid hyperplasia ("cobblestoning"), and tonsillar hypertrophy. Assessment for enlarged cervical or pre- and postauricular lymph nodes may also be useful.

As always, careful examination of the chest and skin is important in assessing potentially atopic individuals for signs of concurrent asthma (eg, wheezing) or dermatitis.

Diagnostic Tests in Rhinitis

Although the history and physical examination of the patient may lead to the clinical diagnosis of rhinitis, further diagnostic tests are usually necessary for the correct identification of etiologic factors. The most commonly used tests are shown in Table 6.

Skin testing is the primary diagnostic method for the confirmation of environmental allergens for allergic rhinitis. Serum-specific IgE can be measured as an alternative to skin tests. Diagnostic imaging may be needed to assess structural abnormalities and the paranasal sinuses.

Skin Tests

Skinprick tests remain the primary diagnostic tool for identifying specific allergic triggers of rhinitis. Skin tests have distinct advantages over in vitro tests such as radioallergosorbent tests (RASTs) in that they are more cost-effective and the results are immediately available to the physician and patient.

Methods of Testing

Evaluation of the wheal-and-flare skin reaction following introduction of the allergen into the skin by the prick or puncture technique is the most sensitive method for the detection of allergen-specific IgE.

Table 6. Diagnostic Tests for Allergic Rhinitis

Test	Comments
Prick or puncture skin test	Most sensitive test for presence of skin test allergen-specific IgE; cost-effective
Serum-specific IgE (eg, RAST)	Reasonable alternative for those in whom skin testing cannot be performed; drugs and skin disease do not affect results
Nasal allergen challenge	Particularly useful for occupational rhinitis
Acoustic rhinometry	Quantifies degree of nasal obstruction
Sweat chloride	Rule out polyps caused by cystic fibrosis
Antineutrophil cytoplasmic afterantibody (ANCA)	Useful if considering vasculitis
Routine radiograph	May reveal anatomic abnormalities but can be misleading
CT/MRI	Useful in assessing anatomic changes, particularly in more complicated sinus disease

CT = computed tomography; Ig = immunoglobulin; MRI = magnetic resonance imaging; RAST = radioallergosorbent test.

Intradermal tests have poor reproducibility and carry a risk of systemic reactions.[24] Skin-prick tests should not be used as a screening tool for allergies in an asymptomatic individual. Intradermal tests may increase the sensitivity of detecting an allergen as the cause of symptoms, but false-positive results occur, and there may be poor correlation with symptoms.

The most clinically useful skin-test allergens in Canada include pollens appropriate to the specific geographic area, animal danders, moulds, and house dust mite.

Interpretation

To avoid over- or under interpretation, skin tests should be performed using appropriate positive and negative controls under the supervision of qualified physicians. False-negative tests may occur in patients who are receiving medications such as antihistamines, tricyclic antidepressants, and other psychotropics. Topical corticosteroids may have some effect on skin test results, but oral corticosteroids generally do not.[24]

The results of skin tests can change over time and should be repeated if indicated. The size of the skin tests does not correlate with symptoms. Testing should be tailored to the age of the patients. Careful interpretation of the test results in light of symptoms must be made for children less than 3 years of age.

Serum-Specific IgE

In vitro serum-specific IgE levels offer a reasonable alternative to skin testing. RASTs and similar serologic techniques provide an in vitro measure of a patient's specific IgE directed against a particular allergen. Several techniques are available, but the capRAST appears to be the most popular.

Serum-specific IgE may be useful for patients unable to have optimal skin tests performed; drugs and skin disease do not affect RAST results.

Other Tests

Other tests that may be useful in some patients include total serum IgE, mucociliary tests (sweat chloride or assessment of mucociliary clearance—more popular in Europe), nasal challenge with allergen (for occupational rhinitis), acoustic rhinometry, antineutrophil cytoplasmic antibody (if considering vasculitis), and nasal secretions (for eosinophils and cytokines).

Diagnostic Imaging

Imaging studies for sinus disease should be performed only after a poor response to adequate treatment of rhinitis or in the evaluation of specific symptoms of sinusitis. Any image studies must be correlated with clinical evidence of disease.

CT scans are useful in assessing anatomic changes, including the ostiomeatal complex, and bony changes. Soft tissue changes as seen on a radiograph may be misleading and should be interpreted in conjunction with clinical findings.[30]

Magnetic resonance imaging can be useful to evaluate more complicated sinus disease.[31]

Therapy: Nonsurgical

In assessing the utility of various nonsurgical therapies for airway disease, these recommendations apply standard level-of-evidence criteria. Level I evidence is extracted from meta-analyses of several randomized, controlled clinical trials (RCTs); level II evidence comes from individual RCTs or a small number of RCTs; level III evidence is taken from noncontrolled clinical trials; and level IV is expert opinion (Table 7).

Patients with rhinitis benefit from a customized approach to management. The use of guidelines for the management of seasonal allergic rhinitis has been shown to be effective; in a 2003 study, patients with seasonal allergic rhinitis presented a significant improvement by comparison with those receiving a nonstandardized treatment.[32]

In addition to patient education and avoidance of specific allergens or irritants, pharmacotherapy and immunotherapy represent the cornerstones of treatment. Surgery can also play a role in management. Patients may require a combination of treatments,

Table 7. Categories of Evidence for Interventions in Rhinitis

Grade of Evidence	*Criteria*
I	Meta-analysis of several RCTs
II	Individual RCTs or a small number of RCTs
III	Noncontrolled clinical trials
IV	Expert opinion

RCT = randomized controlled trial.

depending on the symptom class and their response to therapy. Figure 3 illustrates how the different types of therapies typically fit into a treatment strategy for allergic rhinitis, based on both the classification system presented in the section on classification of rhinitis and the response to therapy.

It is important that the correct type of rhinitis be determined before specific treatment is prescribed. The most significant benefits and side effects of available treatments are discussed. The product monographs for each drug should be reviewed for detailed prescribing information and reviews of side effects.

Patient Education

Managing Expectations

Educating the patient is important because of the recurrent or chronic nature of most types of rhinitis. Allergic and nonallergic rhinitis both may persist for years, and nonallergic rhinitis may be particularly difficult to treat.

Allergen Avoidance

Although pollens and outdoor moulds may be difficult to avoid, patients who have seasonal symptoms owing to these allergens should keep their home, car, and work environments as closed or filtered of allergens as possible, particularly during the early-morning pollinating hours. Activities, such as jogging or gardening

LTRAs: leukotriene receptor antagonists
* Step up if there is no response or incomplete response to treatment, regardless of class
† LRTAs may be used in class III and IV, but there is less supporting evidence
** Oral steroids may be considered for class II (severe intermittent), but there is little supporting evidence

Figure 3. Treatment of allergic rhinitis by symptom class.

at this time, should be avoided (level IV). Air conditioning can reduce the amount of pollen exposure (level III).[33]

Dust mites are a major perennial source of allergen in our increasingly airtight North American homes. House dust mites live in carpets, mattresses, bedding, pillows, and upholstered furniture and thrive when ambient conditions are warm and humid. Encasing mattresses and pillows in impermeable covers will minimize conditions for mite growth (level II).[34] Commercial mattress covers (polyurethane coating inside cotton or microfibre) may be more comfortable to sleep on if air permeable. The use of small vaporizers in bedrooms or other rooms by allergic patients should be discouraged because the increased humidity can facilitate mite growth.[35]

Mite growth can be inhibited by keeping the temperature low (less than 18°C or 65°F) and the relative humidity below 50% (ideally 30–50%). Mites can be destroyed in blankets and bedding by washing them once a week in hot water (above 54°C or 130°F) (level III).[36] Direct measures to reduce mite growth are much more successful than vacuuming, which may disturb mite antigen and cause transient increases in symptoms owing to increased exposure.[37] Commercial acaricides using tannic acid or benzoate are being assessed or have been released for use. They require repeated use.

Mould spores are ubiquitous indoors, even in winter. Patients with mould allergy should search their home for sources of mould growth. Damp areas should be kept cool and dry, if possible (level IV). Other areas of high humidity, such as bathrooms, central humidification units, and window wells, should be inspected for mould and cleaned regularly. Dead leaves should be removed from around the home.

Cat and dog allergens remain ubiquitous perennial triggers for allergic rhinitis. At the present time, no consensus has been reached with respect to the role of animals in the prevention of allergy.[38–43] Some studies have found that sensitization to cat is a risk factor for asthma in childhood and adulthood, whereas others have found no such correlation.[44] Others have commented that the question is not whether there is an animal in the house but rather the presence of animals in the community.[45]

Patients who are allergic to cats may experience symptoms within minutes of entering a room containing a cat. Although removal of the animal from the home usually results in a significant reduction of

symptoms within 4 to 6 months (level III),[44] most pet owners are unwilling to part with their pets. Recent evidence suggests that washing a cat weekly can reduce the allergen load in the home[45,46] and, when combined with restricting the cat outside the bedroom and the use of HEPA (high-efficiency particulate air) filters, may result in decreased symptoms (level III).[42]

Converting a dog from an indoor pet to an outdoor pet is usually helpful in reducing symptoms in the dog-allergic patient (level IV).

A role for animals in the prevention of allergy in children was recently explored,[38] but a clear consensus has not evolved at this time.

Other perennial allergens, such as cockroach allergen found in urban dwellings, may cause symptoms of allergic rhinitis. Skin-test or RAST evidence of cockroach sensitivity should be sought if suspected. Cockroach exposure can be reduced by commercial means (level IV).

Limiting Exposure to Irritants

The importance of eliminating tobacco smoke from the home environment of children and adults with all types of rhinitis cannot be overemphasized (level IV). The effect of passive smoke on the nose has been demonstrated in olfactory studies. Children exposed to passive smoke have difficulty identifying odours in comparison with children raised in relatively smoke-free environments.[47]

Avoidance of irritants, such as strong perfumes, spicy foods, alcohol, and, occasionally, air conditioning, can be helpful (level IV).

Patients with nasal polyps and asthma should be aware of the risk of acute severe bronchospasm with ASA and NSAIDs. Over-the-counter preparations often unexpectedly contain ASA. Susceptible patients may find wearing a medical alert bracelet with this information invaluable. Cyclooxygenase 2 inhibitors are less likely to cause a problem, but there are case reports of individual reactions.

Pharmacotherapy

The goal of treatment in rhinitis is relief of symptoms. Pharmacotherapy includes the use of antihistamines, antileukotrienes, decongestants, and corticosteroids, both topical and systemic. These agents are shown in Table 8.

Antihistamines

Antihistamines have been recommended as a cornerstone of allergic rhinitis treatment for many years and are readily available as over-the-counter preparations or by prescription. They are subdivided into older,

Table 8. Pharmacologic Treatments for Allergic Rhinitis

Agents	Potential Benefits
Oral H_1 antihistamines	Reduction in sneezing, rhinorrhea, itching (eyes, nose, throat) Some impact on concomitant asthma
Intranasal corticosteroids	Reduction in mucosal swelling and secretions Reduction in nasal symptom score, nasal obstruction May reduce lower airway symptoms, decrease hospital admissions for asthma Improve course of infectious rhinosinusitis
Leukotriene receptor antagonists	Positive impact on concomitant asthma Reduction in sneezing, rhinorrhea, itchy eyes, nose and throat congestion
Intranasal H_1 antihistamine	Reduction in nasal itching, sneezing, and rhinorrhea
Intranasal ipratropium bromide	Reduction in watery rhinorrhea
Cromoglycate	Reduction in sneezing, rhinorrhea, nasal itching
Decongestants	Acute reduction in mucosal swelling
Topical nasal lubricants	Reduction in sensation of nasal congestion Relief from intranasal crusting (atrophic rhinitis)

generally more sedating compounds (ie, diphenhydramine, chlorpheniramine) and newer, nonsedating agents (ie, desloratadine, fexofenadine, loratadine). Although sedative effects may be desirable in a limited number of patients with insomnia, these agents typically do not improve sleep quality. Nonsedating drugs should be used in most instances, particularly for those whose occupations require mental alertness and/or manual dexterity (level II).[48]

H$_1$-receptor antihistamines provide maximum benefit if taken regularly at the time of maximal symptoms or before exposure to an allergen.[49] These agents effectively reduce sneezing, itching (eyes, nose, and throat), and rhinorrhea when used on a short- or long-term basis.

Patients with both allergic nasal and ocular symptoms may benefit from a combination of an antihistamine and an intranasal corticosteroid, particularly at the height of a pollen season (level II).

Treatment with newer antihistamines has also been shown to have some impact on asthma, with or without the concomitant administration of an inhaled corticosteroid (level II).[50–53] In high-risk children with atopic dermatitis already sensitized to inhalant allergens, the early use of antihistamines may delay or prevent the onset of asthma.[54]

Intranasal Corticosteroids

Intranasal corticosteroids have represented a significant advance in the treatment of rhinitis of many etiologies. These medications have allowed many patients to achieve control of their rhinitis symptoms with enhanced compliance, particularly using once-a-day dosing schedules. Whereas the antihistamines are generally used for milder symptoms, intranasal corticosteroids are used to treat moderate to severe intermittent symptoms or mild persistent rhinitis alone or in combination with antihistamines.

Many clinical investigators agree that the main clinical benefits of intranasal corticosteroids are due to their ability to reduce nasal mucosal inflammation. Multiple anti-inflammatory actions have been demonstrated. Intranasal corticosteroids effectively reduce mucosal swelling and secretions by decreasing the number of basophils, mast cells, eosinophils, and neutrophils, as well as the amounts of mediators in the nasal mucosa and nasal secretions.[24] They can inhibit both early and late responses[55,56] to inhaled antigen and decrease nonspecific hyperreactivity of the nasal mucosa during the early response to nasal provocation with antigen.

Owing to their mechanisms of action, compared with the antihistamines and antileukotrienes, intranasal corticosteroids are superior in reducing nasal symptom score and nasal blockage (level I).[57–59] They can also reduce nasal obstruction owing to nasal polyps and may prolong the time to their recurrence following surgical removal. Furthermore, there is evidence that treatment of allergic rhinitis with intranasal corticosteroids in patients with asthma may reduce lower airway symptoms (level II)[60] and decrease hospital admissions for asthma (level III).[61]

In infectious sinusitis, intranasal corticosteroids have been shown to reduce symptoms, accelerate recovery, and increase time to recurrence when combined with antibiotics compared with antibiotics alone (level I).[62–65] Although these agents are not indicated for the relief of ocular symptoms, there is some evidence that they are efficacious in this regard as well.[66,67]

Various preparations are available, including intranasal beclomethasone, flunisolide, budesonide, triamcinolone, fluticasone, and mometasone.

Proper application of the spray is needed for an optimal clinical response. The patient should be counseled on proper use of the device.

The most common side effects of intranasal corticosteroids, nasal irritation and stinging, can usually be prevented by aiming the spray slightly away from the nasal septum.

In terms of safety, intranasal corticosteroids are rapidly degraded enzymatically in the nasal mucosa to less active metabolites. The systemic absorption varies between the different agents, in part owing to the degree of hepatic first-pass inactivation of the particular agent.[68]

Suppression of the hypothalamic-pituitary-adrenal axis has not been a significant clinical problem with intranasal corticosteroids. Childhood growth has been affected after 1 year of treatment with twice-daily intranasal beclomethasone,[69] but longer studies are lacking. It is possible that catch-up growth may occur later, as with inhaled steroids.[70] Intranasal mometasone[71] and fluticasone[72] have not demonstrated growth suppression compared with placebo. Intranasal steroids have a benefit in asthma, and 50% of patients with rhinitis have asthma.

Antileukotrienes

Antileukotrienes (montelukast, zafirlukast) are a relatively new class of compounds. For intermittent rhini-

tis, they have been shown to be particularly useful for nasal congestion when taken either alone or in combination with antihistamines (level II).[59,73] Their efficacy compared with antihistamines was shown to be approximately equivalent overall, with some differences in their effects on individual symptoms and inflammatory indices. Studies evaluating combination therapy with antileukotrienes and antihistamines have not yet clarified whether the combination is more effective than either agent alone.[59,73]

As monotherapy, antileukotrienes have been shown to be inferior to intranasal corticosteroids for nasal symptoms (level II).[59,74] In combination with antihistamines, antileukotrienes have demonstrated efficacy that is similar to monotherapy with intranasal corticosteroids in one study of short duration,[75] whereas in other studies of longer duration, the intranasal steroid produced better results in nighttime and nasal symptoms.[59,76]

Antileukotrienes have been shown to be anti-inflammatory in rhinitis. In a 2-week trial in seasonal rhinitis, there was a significant decrease ($p \leq .001$) in blood eosinophil numbers in the montelukast group compared with the placebo group but not in the loratadine group.[77]

There was less nasal mucosal eosinophilic infiltration with montelukast compared with loratadine in a seasonal allergic rhinitis study, but intranasal steroid was superior to both in preventing the rise in nasal mucosal eosinophils.[59] Furthermore, antileukotrienes have been shown to have a greater benefit for asthma than H_1 antihistamines, particularly for exercise-induced symptoms.[78]

A preliminary report on the utility of antileukotriene agents in nasal polyposis was favourable, but further study is required (level III).[79] Studies have also shown a benefit of antileukotrienes on rhinitis in patients being treated for asthma (level II).[80]

As an oral agent, compliance is excellent and is particularly attractive for many patients with concomitant rhinitis and asthma.

In terms of safety, zafirlukast has been reported to be associated with rare cases of hepatic failure. Montelukast has not been associated with hepatic failure.[81]

Decongestants

Both topical and systemic decongestant medications are available to produce vasoconstriction and decrease edema of the nasal mucosa in allergic and nonallergic rhinitis. Topically applied nasal decongestant sprays can be effective for the acute relief of nasal congestion and the facilitation of intranasal drainage of purulent secretions associated with bacterial sinusitis.

Oral decongestants, such as pseudoephedrine, can reduce symptoms of nasal congestion and may be used in combination with antihistamines. Side effects such as insomnia, headache, irritability, nightmares, and palpitations may limit their long-term use. They are contraindicated in patients with uncontrolled hypertension, severe coronary artery disease, and concomitant use of monoamine oxidase inhibitors.

Oral Steroids

Patients with severe allergic or nonallergic rhinitis that are not controlled with the use of oral antihistamines, decongestants, and intranasal corticosteroids often respond to oral prednisone.

Other Agents

Disodium cromoglycate (cromolyn) is available for ocular, nasal, and intrapulmonary use. Although cromolyn can be effective in reducing sneezing, rhinorrhea, and nasal itching, it is not as effective as intranasal corticosteroids.

Levocabastine is an H_1 antagonist available as a topical nasal spray for allergic rhinitis and as topical eyedrops for allergic conjunctivitis. When applied intranasally, it can reduce nasal itching, sneezing, and rhinorrhea.[82]

Nasal ipratropium bromide is a useful anticholinergic medication for decreasing watery rhinorrhea[83,84] but has little effect on nasal congestion.

Topical nasal lubricants (ie, saline) may be useful to reduce the sensation of nasal congestion and provide relief from intranasal crusting in patients with atrophic rhinitis.

Immunotherapy

Immunotherapy has been available as a treatment for allergic rhinitis for decades. The administration of allergen extracts by injection can significantly reduce the nasal symptoms of allergic rhinitis, as well as the need for concomitant medications. It is only useful for allergic rhinitis and has no role in the management of the various types of nonallergic rhinitis.

Immunotherapy injections are effective for allergic rhinitis caused by pollens and dust mites and have limited usefulness in treating mould and animal dander

allergies. There are multiple mechanisms of action, but, primarily, immunotherapy has a modulating effect on allergen-specific T cells, with a shift towards Th1 cytokine expression.[85]

Clinical observation over 12 to 18 months remains the only reliable method of determining the therapeutic success of immunotherapy.

Immunotherapy is usually administered in aqueous extract on a perennial basis with a weekly incremental buildup in dosage usually over 6 to 8 months, followed by maintenance injections of the tolerated maximum dose every 3 to 4 weeks. If successful, this treatment regimen is normally carried on for 3 to 5 years, and then consideration is given to stopping. Preseasonal injections on an annual basis can also be effective.

Immunotherapy should be reserved for patients with allergic rhinitis for whom optimal avoidance measures and pharmacotherapy are insufficient to control their symptoms. Patients receiving immunotherapy must be educated about the need for regular visits to their physician for injections. All immunotherapy injections should be administered in a medical facility where personnel, equipment, and medications are available to treat an anaphylactic reaction to an injection. All patients should be advised to report any systemic symptoms of anaphylaxis following an injection. Any anaphylactic reaction should be treated immediately with appropriate resuscitative therapy, including epinephrine, and the indications for continuing with the immunotherapy should be carefully reviewed.

Patients with significant cardiac disease are not good candidates for immunotherapy. Coexisting therapy with β-blockers is also a contraindication because they make it difficult to treat anaphylaxis should it occur. ACE inhibitor use is a relative contraindication.

Other directions in immunotherapy have included a sublingual-swallow technique.[86] The efficacy of a high allergen dose (50–100 times the cumulative dose of subcutaneous immunotherapy) has been documented in double-blind, placebo-controlled studies. Recombinant allergens,[87] T-cell peptide vaccines,[88] and Th1 immunostimulants (cytosine-phosphate-guaonosine oligodeoxynucleotides) are also being studied.[89]

Anti-IgE

Both intravenous and subcutaneous administration of IgE has been shown to be effective in seasonal allergic rhinitis and asthma.[90–98] At the time of writing, one such agent, omalizumab, had just been approved for use in Canada for asthma. Clinical experience with this agent has not been extensive enough to date to form a consensus opinion.

Intravenous Gammaglobulin

Sinusitis is often the presenting feature of common variable immunodeficiency. We now have effective ways to treat such individuals. Intravenous immunoglobulin can be administered to prevent recurrent infection. Approximately 5% of chronic rhinosinusitis patients seen in specialist clinics have humoral immune deficiency.[99]

Therapy in the Era of Combined Airway Inflammatory Disease

Allergic rhinitis is not a local disease; the entire respiratory tract is involved even in the absence of clinical asthma. Using the concept of a combined airway inflammatory disease, therapy should be directed both locally and systemically to correct clinical symptoms that may be predominant in one organ but are often detected in other areas concurrently.

Corticosteroids work both locally and systemically by suppressing cytokine formation, correcting the imbalance of the Th2 bias, and affecting bone marrow inflammatory cell differentiation and migration.

Immunotherapy also shifts the response from Th2 to a more Th1-dominant pattern. This effect may be long-lasting (for up to 3 years after stopping shots). Drugs that primarily antagonize mediators, such as antihistamines and antileukotrienes, are also effective in controlling inflammation in both the upper and lower airways. These changes are not uniform, with predominant clinical efficacy more pronounced in either the upper or lower airway.[100]

Few studies to date have assessed therapies for combined airways inflammatory disease. A recent study of rhinitis and asthma compared the effects of inhaled steroids with or without intranasal steroids. In this 6-week study of seasonal rhinitis and asthma, the greatest benefit was seen in those patients treated with both intranasal and inhaled steroids.[101]

The current literature shows that modulating the inflammatory cascade in allergic rhinitis leads to improvements in concomitant asthma.[60,61] In the primary care setting, prompt recognition, diagnosis, and treatment of rhinitis may be the first step in addressing allergic inflammation throughout the airway.

Pregnancy Issues

Allergic rhinitis is common in women during the child-bearing years. The condition may worsen during pregnancy, which may result in a need for pharmacotherapy. Because most medications can cross the placenta, there is a fear among patients and physicians of fetal malformations owing to medications. During pregnancy, the benefit to risk ratio needs to be considered before recommending any medical therapy.

Although no medication may be guaranteed safe in pregnancy, some have fewer problems than others. It is always important to review allergen avoidance.

The US Food and Drug Administration classifies drugs into five categories as to their safety during pregnancy. The medications in the first three categories are described below.

Category A drugs are those with which studies in pregnant women show no adverse effects during pregnancy.

Category B drugs either have studies in animals that have shown adverse effects on the fetus at doses many times higher than the usual human dose, but human studies show no adverse effects on the fetus, or studies in animals that show no adverse effects on the fetus, but human studies have not been done. Because the studies in humans cannot rule out the possibility of harm, these drugs should be used during pregnancy only if clearly needed. Included in category B are sodium cromoglycate, ipratropium, loratadine, cetirizine, montelukast, and zafirlukast. The latter two, the antileukotriene receptor antagonists, have some benefit in rhinitis, but their use in pregnancy is generally restricted to poorly controlled asthma.

Category C drugs are those that have been associated with adverse effects on the fetus in animal studies, but there are no controlled studies in women, or drugs for which no studies in women or animals are available. Drugs in this category should be given only if the potential benefit justifies the risk to the fetus. Included in this category are intranasal steroids and some antihistamines, such as fexofenadine.

Anticholinergic agents may pass through the placenta. Although they have not been associated with any teratogenicity, their use during pregnancy is not recommended because of the lack of clinical studies. With the cromones, no teratogenic effect has been identified in humans or animals. Intranasal cromolyn can be used as a first-line medication for allergic rhinitis in pregnancy.[102]

The first-generation antihistamines may also be considered for allergic rhinitis in pregnancy.[102] Chlorpheniramine and diphenhydramine can be recommended if antihistamines are required because of their longer-term safety record. The patient should be warned, however, of the sedation that may occur with these medications. One prospective study suggested that cetirizine and hydroxizine are not associated with an increased teratogenic risk,[103] but the first-generation antihistamines are still favoured over newer antihistamines during pregnancy.

There are no epidemiologic pregnancy studies with the intranasal corticosteroids. Fluticasone nasal spray was, however, studied in pregnancy-associated rhinitis in a randomized controlled study of 53 women.[104] There were no documented fetal anomalies or cortisol suppression in the fluticasone group. Although in animal studies, corticosteroids have been found to be teratogenic, there have been no such reports in humans. If an intranasal corticosteroid is required during pregnancy, beclomethasone nasal spray is considered the first-line treatment because of its longer safety record.[102]

Specific-allergen immunotherapy is felt to be safe and effective during pregnancy if it is given at a maintenance dose.[105,106] It is not, however, recommended to start or increase the immunotherapy dose during pregnancy because of the risk of anaphylaxis on the fetus. There is no evidence that treating pregnant women will prevent allergies in their offspring.[107]

Therapy: Surgical

Surgical therapy may be helpful in the management of rhinitis or chronic sinus disease refractory to medical treatment. The normal function of the sinus mucosa depends on proper ventilation and drainage; structural deformities that compromise these functions or contribute significantly to nasal obstruction should be corrected. However, endoscopic sinus surgery (ESS) for sinus disease is generally not considered as a treatment of rhinitis in itself. Following ESS, patients often comment on an improved sensation of nasal airflow, but this is not a reason to offer this surgery to the patient with allergic or nonallergic rhinitis alone.

Nasal obstruction caused by an obvious anatomic problem, such as a deviated nasal septum, should be corrected. Historically, one of the surgical options

(vidian neurectomy) attempted to address the parasympathetic nervous supply to the nose to relieve nasal obstructive symptoms (particularly rhinorrhea). This is a difficult procedure to perform, with a high risk of collateral damage (ie, to the optic nerve, etc.) and is rarely performed today. The most common procedures performed to help nasal obstructive symptoms in patients with rhinitis are those directed at the inferior turbinates (Table 9).[108]

Turbinate-Related Procedures

The inferior turbinate, particularly the anterior end, contributes to the nasal valve, the most resistive segment of the upper airway. Numerous surgical procedures have been designed to reduce the size of the inferior turbinates or remove a portion or even the entire inferior turbinate. Surgical options address the bone, the mucosa, the submucosa, or a combination thereof. Most procedures can be performed under local anesthesia in an office or outpatient setting.

Types of Interventions

The most common surface mucosal procedure is cryotherapy, in which a cryoprobe is placed along the medial surface of the anterior end of the inferior turbinate for various periods of time ranging from seconds to a minute or more. The temperature of the probe tip drops to approximately −70°C to accomplish the therapeutic objective of reducing turbinate tissue bulk. There is ample evidence in the literature supporting the efficacy of this procedure.[109–115] The mechanism of how cryotherapy works is unknown but is hypothesized to include tissue destruction with vessel thrombosis and creation of scar tissue, which prevent the venous sinusoids in the turbinate mucosa from engorging.

Submucosal cauterization is performed by placing a needle into the submucosal tissues of the inferior turbinate and applying an electrical current for various periods of time, usually until there is blanching of the mucosa itself. The mechanism of how cauterization works is likely similar to cryotherapy but using heat

Table 9. Turbinate Reduction Procedures for Allergic Rhinitis

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Cryotherapy
Cauterization
Laser therapy
Radiofrequency ablation

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rather than cold. Submucosal cauterization is an easy and well-tolerated procedure to reduce turbinate tissue and has been shown to improve nasal breathing, at least in the short term.[116–121] Both cryotherapy and submucosal cauterization may need to be repeated more than once to maintain benefit. In addition, both techniques can cause significant nasal crusting for a week or more following the procedure, which can be effectively dealt with by saline nasal rinses and lubrication.

Similarly, laser therapy's mechanism of benefit is similar to cryotherapy and submucosal cauterization. There have been a number of reports of success using various types of lasers,[122–127] all of which have the same goal: vaporization and/or excision of mucosa, submucosa, and, sometimes, bone. The results of one study showed that laser surgery was effective in 87% of patients in the short term.[125] In the long term, the short-term results persisted in 81% of cases treated for sneezing, 78% for nasal discharge, and 76% for nasal obstruction.

Radiofrequency ablation is a newer technique with a goal similar to the above-mentioned therapies. Mechanically, the technique is most similar to that of cauterization; the radiofrequency probe is inserted submucosally into the inferior turbinate and turned on for various periods of time. The radiofrequency generated heats up the tissue to ablate it and effectively shrinks the inferior turbinate. Although there is evidence showing the effectiveness of this intervention,[128–131] the probes used are expensive and not covered by provincially funded health care plans.

Inferior turbinoplasty is a procedure usually performed under general anesthesia and is designed to remove bone and some of the submucosal tissue. An incision is made along the anterior end of the inferior turbinate, lifting mucosa off the underlying turbinate bone, resecting some of the bone, and then laying the mucosa back down.[132] More recently, a microdébriding tool to remove submucosal tissue was introduced to perform the surgery less invasively, with use of a small incision and camera-guided instrumentation.

Turbinate resection involves partial or, rarely, full removal of the inferior turbinate.[133] Full removal raises the risk of atrophic rhinitis. More common is the removal of the anterior end of the inferior turbinate, to reduce the amount of tissue in the nasal valve area. There is always concern over the potential for significant epistaxis within the first week postresection even when only a portion of the inferior turbinate is

removed, prompting many surgeons to leave nasal packing in for several days following the procedure.

Most studies analyzing the various turbinate procedures are retrospective in nature, and there are few, if any, well-controlled randomized studies comparing one or more therapies together in the treatment of allergic or nonallergic rhinitis. It is impossible to recommend a single modality for all patients. The evidence supporting the efficacy of these procedures remains debatable, and properly conducted randomized controlled trials are required to establish whether there is long-term patient benefit from these commonly performed operations.[134]

Surgery for Severe Rhinitis

A small subgroup exists of patients with severe mucosal edema, extending to polypoid turbinate development. In the most exaggerated state, these individuals may exhibit diffuse polyposis within the nose and sinus cavities. The classic example of such a disease state is the ASA triad. When mucosal disease or polyp formation contributes to sinus outflow obstruction or, more specifically, ostiomeatal complex disease, an endoscopic sinus procedure may be considered. The purpose of surgical intervention in these cases would be to reestablish ostial patency and promote mucociliary clearance from the sinus chambers.

Conclusion

The goal of this guideline is to provide a one-stop reference tool for clinicians treating patients with allergic rhinitis, a very common disease entity. Several members of the Canadian Rhinitis Working Group have collaborated on each of the sections to produce these consensus guidelines.

Although we recognize that each patient presents with a unique set of characteristics that may influence diagnosis and treatment decisions (eg, concomitant illness, polypharmacy, etc.), this guideline attempts to use general principles applicable to the majority of patients with rhinitis.

In the intervening decade since the last Canadian rhinitis guidelines, our understanding of the disease and its treatment has evolved considerably. As these guidelines describe, rhinitis is a condition that is highly prevalent, with easily identifiable symptoms and widely available diagnostic testing methods.

Furthermore, there are effective therapies available to treat patients with rhinitis to reduce the impact of symptoms and improve their quality of life. The classification system presented provides clinicians with a straightforward means of planning a treatment strategy, which is discussed in the section on surgical therapy.

Although the new agents that have been introduced since 1994 have been incorporated into the treatment recommendations, we acknowledge that with the ever-changing pharmacologic landscape, some of the observations in this document may be out of date.

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