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# Diagnosis and Management of Rhinitis: Parameter Documents of the Joint Task Force on Practice Parameters in Allergy, Asthma, and Immunology

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Official Publication of the American College of Allergy, Asthma & Immunology

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These parameters were developed by the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology, representing the American Academy of Allergy, Asthma and Immunology (AAAAI), the American College of Allergy, Asthma and Immunology (ACAAI) and the Joint Council on Allergy, Asthma and Immunology.

*These parameters were developed with Dr. Nicklas in his private capacity and not in his capacity as a medical officer with the Food and Drug Administration. No official support or endorsement by the Food and Drug Administration is intended or should be inferred.

The American Academy of Allergy, Asthma and Immunology (AAAAI) and the American College of Allergy, Asthma and Immunology (ACAAI) have jointly accepted responsibility for establishing the statements in documents of these parameters. Because these documents incorporated the efforts of many participants, no single individual, including those who served on the Joint Task Force, is authorized to provided an official interpretation of these practice parameters by the AAAAI or ACAAI. Any request for information about or an interpretation of these practice parameters by the AAAAI or ACAAI should be directed to the Executive Offices of the AAAAI, ACAAI and the Joint Council on Allergy, Asthma and Immunology.

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# Diagnosis and Management of Rhinitis: Complete Guidelines of the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology

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This document contains complete guidelines for diagnosis and management of rhinitis developed by the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology, representing the American Academy of Allergy, Asthma and Immunology, the American College of Allergy, Asthma and Immunology and the Joint Council on Allergy, Asthma and Immunology. The guidelines are comprehensive and begin with statements on clinical characteristics and diagnosis of different forms of rhinitis (allergic, non-allergic, occupational rhinitis, hormonal rhinitis [pregnancy and hypothyroidism], drug-induced rhinitis, rhinitis from food ingestion), and other conditions that may be confused with rhinitis. Recommendations on patient evaluation discuss appropriate use of history, physical examination, and diagnostic testing, as well as unproven or inappropriate techniques that should not be used. Parameters on management include use of environmental control measures, pharmacologic therapy including recently introduced therapies and allergen immunotherapy. Because of the risks to patients and society from sedation and performance impairment caused by first generation antihistamines, second generation antihistamines that reduce or eliminate these side effects should usually be considered before first generation antihistamines for the treatment of allergic rhinitis. The document emphasizes the importance of rhinitis management for comorbid conditions (asthma, sinusitis, otitis media). Guidelines are also presented on special considerations in patients subsets (children, the elderly, pregnancy, athletes and patients with rhinitis medicamentosa); and when consultation with an allergist-immunologist should be considered.

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The Joint Task Force has made an intense effort to appropriately acknowledge all contributors to this parameter. If any contributors are inadvertently excluded, the Task Force will insure that appropriate recognition of such contributions is subsequently made.

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## INTRODUCTION

Rhinitis may be caused by allergic, non-allergic, infectious, hormonal, occupational and other factors. All too often, important causes of rhinitis go unrecognized by both physicians and patients. This leads to suboptimal control of the disease.

Rhinitis is a significant cause of widespread morbidity. Although sometimes mistakenly viewed as a trivial disease, symptoms of rhinitis may significantly impact the patient's quality of life, by causing fatigue, headache, cognitive impairment and other systemic symptoms. Appropriate management of rhinitis may be an important component in effective management of co-existing or complicating respiratory conditions, such as asthma, sinusitis, or chronic otitis media. The cost of treating rhinitis and indirect costs related to loss of workplace productivity resulting from the disease are substantial. The estimated cost of allergic rhinitis based on direct and indirect costs is 2.7 billion dollars for the year 1995, exclusive of costs for associated medical problems such as sinusitis and asthma. Allergic rhinitis, the most common form of rhinitis, affects 20 to 40 million people in the United States annually, including 10% to 30% of adults and up to 40% of children.

This document reviews clinically relevant information about pathogenesis and provides guidelines about diagnosis and management of rhinitis syndromes. Throughout the document, summary statements that articulate key points precede supporting text and relevant citations of evidence-based publications.

## DEFINITION OF RHINITIS

**1. Rhinitis is defined as inflammation of the membranes lining the nose, and is characterized by nasal congestion, rhinorrhea, sneezing, itching of the nose and/or postnasal drainage.**

Rhinitis can be defined as a heterogeneous disorder characterized by one or more of the following nasal symptoms: sneezing, itching, rhinorrhea, and/or nasal congestion. Rhinitis frequently is accompanied by symptoms involving the eyes, ears, and throat. Post-nasal drainage may also be present frequently.

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## DIFFERENTIAL DIAGNOSIS OF RHINITIS

**2. Rhinitis should be classified by etiology as allergic or nonallergic.**

Allergic rhinitis is a very common cause of rhinitis. However, since approximately 50% of patients with rhinitis do not have allergic rhinitis, other potential causes must also be ruled out.[1–3] The following outline lists different forms of allergic and non-allergic rhinitis, and conditions that may mimic rhinitis.

I. Allergic rhinitis
   - A. Seasonal
   - B. Perennial
   - C. Episodic
   - D. Occupational (may also be non-allergic)

II. Non-allergic rhinitis
   - A. Infectious
     1. Acute
     2. Chronic
   - B. NARES syndrome (Nonallergic rhinitis with eosinophilia syndrome)
   - C. Perennial nonallergic rhinitis (Vasomotor rhinitis)
   - D. Other rhinitis syndromes
     1. Ciliary dyskinesia syndrome
     2. Atrophic rhinitis
     3. Hormonally-induced
        - A. Hypothyroidism
        - B. Pregnancy
        - C. Oral contraceptives
        - D. Menstrual cycle
     4. Exercise
     5. Drug-Induced
        - A. Rhinitis medicamentosa
        - B. Oral contraceptives
        - C. Anti-hypertensive therapy
        - D. Aspirin
        - E. Nonsteroidal anti-inflammatory drugs
     6. Reflex-Induced
        - A. Gustatory rhinitis
        - B. Chemical or irritant-induced
        - C. Posture reflexes
        - D. Nasal cycle
        - E. Emotional factors
     7. Occupational (may be allergic)

III. Conditions that may mimic symptoms of rhinitis
   - A. Structural/mechanical factors
     1. Deviated septum/septal wall anomalies
     2. Hypertrophic turbinates
     3. Adenoidal hypertrophy
     4. Foreign bodies
     5. Nasal tumors
        - A. Benign
        - B. Malignant
     6. Choanal atresia
   - B. Inflammatory/immunologic
     1. Wegener's granulomatosis
     2. Sarcoidosis
     3. Midline granuloma
     4. Systemic lupus erythematosus
     5. Sjogren's syndrome
     6. Nasal polyposis
   - C. Cerebrospinal fluid rhinorrhea

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3. Sibbald B, Rink E. Epidemiology of seasonal and perennial rhinitis: clinical presentation and medical history. Thorax 1991;46:895–901.


### Allergic Rhinitis

**3. Allergic rhinitis affects 20 to 40 million people in the United States annually, including 10% to 30% of adults and up to 40% of children.**

4. **The severity of allergic rhinitis ranges from mild to seriously debilitating.**
5. **The cost of treating allergic rhinitis and indirect costs related to loss of workplace productivity resulting from the disease are substantial. The estimated cost of allergic rhinitis based on direct and indirect costs is 2.7 billion dollars for the year 1995, exclusive of costs for associated medical problems such as sinusitis and asthma. Rhinitis is also a significant cause of lost school days.**
6. **Risk factors for allergic rhinitis include: (1) family history of atopy; (2) serum IgE > 100 IU/mL before age 6; (3) higher socioeconomic class; (4) exposure to indoor allergens such as animals and dust mites; (5) presence of a positive allergy skin prick test.**

Rhinitis is reported to be a very frequent disease, although data regarding the true prevalence of rhinitis are difficult to interpret. Most population surveys rely upon physician-diagnosed rhinitis for their data, and this may give rise to a much lower reporting of rhinitis. Some population studies have been done with questionnaires administered to the subjects followed in many cases by telephone interviews to try to make a specific diagnosis of rhinitis. These studies may reflect a more accurate prevalence of rhinitis but probably still underreport this disease.[1–7]

Most epidemiologic studies have been directed towards seasonal allergic rhinitis, or hay fever, since this symptom complex with its reproducible seasonality is somewhat easier to identify in population surveys. Perennial allergic rhinitis is more difficult to identify because its symptom complex may overlap with chronic sinusitis, recurrent upper respiratory infections, and vasomotor rhinitis.

The prevalence of rhinitis in various epidemiologic studies ranges from 3% to 19%. Studies suggest that seasonal allergic rhinitis (hay fever) is found in approximately 10% to 20% of the population.[2,8–10] One study showed a prevalence of physician-diagnosed allergic rhinitis in 42% of 6-year-old children.[3] Overall, allergic rhinitis affects 20 to 40 million individuals in the United States annually.[11,12]

In childhood, males with allergic rhinitis outnumber females, but the gender ratio becomes approximately equal in adults and may even favor females. Surveys of medical students have resulted in a higher prevalence of rhinitis, but this may be related to the survey technique.[1,6,8]

Allergic rhinitis develops before age 20 in 80% of cases. Studies have shown that the frequency of allergic rhinitis increases with age until adulthood and that positive immediate hypersensitivity skin tests are significant risk factors for the development of new symptoms of seasonal allergic rhinitis.[1,8,13] There is a greater chance of a child developing allergic rhinitis if both parents have a history of atopy, than if only one parent is atopic. Children in families with a bilateral family history of allergy generally develop symptoms before puberty; those with a unilateral family history tend to develop their symptoms later in life or not at all.[5,10]

There tends to be an increased prevalence of allergic rhinitis in higher socioeconomic classes, in non-whites, in some polluted urban areas, and in individuals with a family history of allergy. Allergic rhinitis is more likely in first-born children. Studies in children in the first years of life have shown that the risk of rhinitis was higher in those youngsters with early introduction of foods or formula, heavy maternal cigarette smoking in the first year of life, exposure to indoor allergens such as animals and dust mite, higher serum IgE levels (>100 IU/mL before age 6), and parental allergic disorders.[3]

Seasonal allergic rhinitis is apparently becoming more common. One study showed that the prevalence of hay fever increased from 4% to 8% in the 10 years from 1971 to 1981.[14] In another study, atopic skin test reactivity increased from 39% to 50% in during an 8-year period of evaluation.[15]

The impact on society is tremendous.[16] The severity of allergic rhinitis ranges from mild to seriously debilitating. The cost of treating allergic rhinitis and indirect costs related to loss of workplace productivity resulting from the disease are substantial. The estimated cost of allergic rhinitis based on direct and indirect costs is 2.7 billion dollars for the year 1995, exclusive of costs for associated medical problems such as sinusitis and asthma. The total direct and indirect cost estimates for allergic rhinitis have been reported to be $5.3 billion for 1996. This figure included the higher indirect costs associated with increased loss of productivity, which, in turn, was related to extensive over-the-counter antihistamine use. Such treatment can cause drowsiness and impair cognitive and motor function (see summary statement #34).

Rhinitis is also a significant cause of lost school attendance, resulting in more than 2 million absent school days in the US annually. In children, there is evidence that symptoms of allergic rhinitis can impair cognitive functioning, which can be further impaired by the use of first generation antihistamines.[17]

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**7. The symptoms of allergic rhinitis result from a complex allergen-driven mucosal inflammation resulting from an interplay between resident and infiltrating inflammatory cells, and a number of inflammatory mediators and cytokines. Sensory nerve activation, plasma leakage and congestion of venous sinusoids also contribute.**

The nasal mucosa is designed to humidify and clean inspired air. The actions of epithelium, vessels, glands, and nerves are carefully orchestrated to perform these functions.[1] Dysfunction of any of these structures may contribute to the symptoms of allergic and nonallergic rhinitis.[2]

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**8. Allergic rhinitis may be characterized by early and late phase responses. Each type of response is characterized by sneezing, congestion and rhinorrhea, but congestion predominates in the latter.**

Atopic subjects inherit the tendency to develop IgE-mast cell-$TH_2$ lymphocyte immune responses. Exposure to low concentrations of dust mite fecal proteins, cockroach, cat, dog and other danders, pollen grains, or other allergens for prolonged periods of time leads to the presentation of the allergen by antigen presenting cells (APC) to CD4+ lymphocytes that release IL3, IL4, IL5, GM-CSF and other cytokines. These promote IgE production against these allergens by plasma cells, mast cell proliferation and infiltration of airway mucosa, and eosinophilia.

*Early or immediate allergic response.* With continued allergen exposure, increasing numbers of IgE-coated mast cells move into the epithelium, recognize the mucosally-deposited allergen, and degranulate.[1] Mast cell products include preformed mediators such as histamine, tryptase (a mast cell specific marker), chymase (in "connective tissue" mast cells only), kininogenase (generates bradykinin), heparin, and other enzymes. Newly formed mediators include prostaglandin $D_2$ and the cysteinyl-leukotrienes $LTC_4$, $LTD_4$, and $LTE_4$. These mediators stimulate vessels to leak and produce edema plus watery rhinorrhea; stimulate glands to exocytose their mucoglycoconjugates and antimicrobial substances; and dilate arteriole-venule anastomoses to cause sinusoidal filling and occlusion of nasal air passages. Sensory nerves are stimulated that convey the sensations of nasal itch and congestion, and initiate systemic reflexes such as sneezing paroxysms. Release of these mast cell mediators and induction of these reactions occur within minutes of allergen exposure, and are termed the early or immediate allergic response.[2] While most subjects experience sneezing and copious rhinorrhea after allergen exposure, some subjects have sensations of nasal congestion as their predominant symptom.

*Late phase response.* The mast cells mediators, including the cytokines, are thought to act upon post-capillary endothelial cells to promote VCAM and E-selectin expression that permits circulating leukocytes to stick to the endothelial cells. Chemoattractants, such as IL-5 for eosinophils, promote the infiltration of the superficial lamina propria of the mucosa with some neutrophils and basophils, many eosinophils, and, at later time points, T lymphocytes and macrophages.[3,4] Over the course of 4 to 8 hours, these cells become activated and release their mediators, which in turn activate many of the proinflammatory reactions of the immediate response. This late occurring inflammatory reaction is termed the "late phase response". While this reaction may be clinically similar to the immediate reaction, congestion tends to predominate.[5] Eosinophil products such as major basic protein, eosinophil cationic protein, hypochlorate, leukotrienes and others are thought to damage the epithelium and other cells, an inflammatory response that promotes the tissue damage of chronic allergic reactions.

$TH_2$ lymphocytes are thought to play a critical role in promoting the allergic response by releasing their combination of IL3, IL4, IL5, and other cytokines that promote IgE production, eosinophil chemoattraction and survival in tissues, and mast cell recruitment.[6] Cytokines released from $TH_2$ lymphocytes, mast cells, eosinophils, basophils and epithelial cells may circulate to the hypothalamus and promote the fatigue, malaise, irritabil-

ity, and neurocognitive deficits that commonly afflict those suffering from allergic rhinitis. Glucocorticoids are effective at reducing the release of these cytokines during late phase responses.[7]

*Priming response.* When allergen challenges are given repeatedly, the amount of allergen required to induce an immediate response decreases.[8] This "priming" effect is thought to be due to the influx of inflammatory cells during ongoing, prolonged allergen exposure and repeated late phase responses. This response is clinically important, since exposure to one allergen (eg, early spring tree pollen) may promote the more exaggerated later responses to another allergen (eg, late spring grass pollen). This priming effect demonstrates the importance of knowing the full spectrum of allergens to which a patient responds, the seasons of their allergic responses, and highlights the need to initiate effective anti-inflammatory therapies before pollen seasons and allergen exposures so that the inflammatory allergic phase will not occur.

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## Seasonal and Perennial Allergic Rhinitis

**9. Symptoms of allergic rhinitis may occur only during specific seasons, may be perennial without seasonal exacerbation, perennial with seasonal exacerbation, or may occur sporadically after specific exposures.**

**10. Seasonal allergic rhinitis is caused by an IgE-mediated reaction to seasonal aeroallergens. Typical seasonal aeroallergens are pollens and molds. The length of seasonal exposure to these allergens is dependent on geographic location.**

**11. Perennial allergic rhinitis is caused by an IgE-mediated reaction to perennial environmental aeroallergens. These may include dust mites, molds, animal allergens, or certain occupational allergens, as well as pollen in areas where pollen is prevalent perennially.**

**12. Allergic rhinitis often coexists with allergic conjunctivitis.**

Symptoms of allergic rhinitis may include paroxysms of sneezing, nasal pruritus (itching) and congestion, clear rhinorrhea and palatal itching. In severe cases, mucous membranes of the eyes, eustachian tube, middle ear and paranasal sinuses may be involved. This produces conjunctival irritation (itchy, watery eyes), redness and tearing, ear fullness and popping, itchy throat, and pressure over the cheeks and forehead. Malaise, weakness and fatigue may be present. The coincidence of other allergic syndromes such as atopic eczema or asthma, and a positive family history of atopy, point toward an allergic etiology. Around 20% of cases are accompanied by symptoms of asthma.[1]

When all the typical rhinitis symptoms are not expressed, the diagnosis is more difficult to make. Chronic nasal obstruction alone may be the major symptom of perennial rhinitis due to ongoing inflammation and late-phase allergic reactions.[2] Distinct temporal patterns of symptom production may aid diagnosis. Symptoms of rhinitis which occur whenever the patient is exposed to a furry pet suggest IgE-mediated sensitivity to that pet. Patients who are exquisitely sensitive to animal proteins may develop symptoms of rhinitis and asthma when entering a house or laboratory even though the animal is no longer present. Exposure to airborne allergens in the workplace may produce symptoms only at work with symptom-free periods away from work. Seasonal and perennial forms of allergic rhinitis often coexist in the same individual. Symptoms may be chronic and persistent and patients may present with secondary complaints of mouth-breathing, snoring, or symptoms of sinusitis.[3]

Seasonal allergic rhinitis symptoms typically appear during a defined season in which aeroallergens are abundant in the outdoor air. Familiarity with the pollinating season of the major trees, grasses and weeds of the locale makes the syndrome easier to diagnose.[4,5] Certain outdoor mold spores also display seasonal variation, with highest levels in the summer and fall months.[6] Tree (eg, birch, oak, maple, mountain cedar), grass, and weed (eg, ragweed) pollens, and fungi ("molds": Alternaria, Aspergillus, Cladosporium) are common seasonal allergens. Priming effects, increases in sensory nerve irritability, and mucosal infiltration by activated eosinophils, mast cells, and $TH_2$ lymphocytes have been identified. Hyperresponsiveness to irritant triggers such as tobacco smoke, noxious odors, changes in temperature, and exercise may persist beyond the actual pollen season.

In studies of allergic seasonal rhinitis, a correlation between the daily pol-

len count and overall daily symptom score and medication score has been found. The symptoms on any particular day will be influenced by exposure on that day but also on previous days due to the priming phenomenon. As a consequence, at the end of the pollen season, it is usual to observe a decline in symptoms which is slower than that of the pollen counts themselves.[7] Individual sensitivity will also influence the intensity of symptoms. In highly sensitive individuals, many symptoms occur with pollen counts of 15 to 75 pollen grains/$m^3$ per 24 hours, whereas in the less sensitive, 4 to 10 times this exposure may be necessary to provoke equivalent symptoms.[8] The levels of pollen counts that cause symptoms may vary with an individual's degree of sensitivity and with different pollens.[9]

In perennial allergic rhinitis the responsible allergens are present in the environment throughout the year, and are usually indoor. Chronic exposure to dust mites (*Dermatophagoides pteronyussinus, D. farinae*), cockroach, perennial molds, cat, dog and other danders leads to persistent tissue edema and infiltration with eosinophils, mast cells, $TH_2$ lymphocytes, and macrophages.[10] Chronic allergen exposure with unremitting recruitment of inflammatory cells often requires corticosteroids for control. In some subjects, nasal congestion and mucus production (post-nasal drip) symptoms predominate, and sneezing and watery rhinorrhea may be minimal.

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## Non-Allergic Rhinitis

**13. Nonallergic rhinitis is characterized by sporadic or persistent perennial symptoms of rhinitis that do not result from IgE-mediated immunopathologic events. Examples of nonallergic rhinitis are infectious rhinitis, hormonal rhinitis, vasomotor rhinitis, nonallergic rhinitis with eosinophilia syndrome (NARES), certain types of occupational rhinitis, and gustatory and drug-induced rhinitis.**

The differential diagnosis of nonallergic rhinitis is extensive.[1] The mechanisms in each are poorly understood. Nonallergic rhinitis with inflammatory cells present in the mucosa can be classified by inflammatory cell type.

Nonallergic rhinitis with eosinophilia syndrome (NARES) is characterized by nasal congestion and prominent nasal eosinophilia. (see summary statement #15) The mechanism of the eosinophil infiltration is not known. Eosinophilia is also prominent when nasal polyps are present, but again the mechanism of eosinophil recruitment is not known. Subjects with aspirin sensitivity have nasal eosinophilia. Aspirin and other nonsteroidal antiinflammatory drugs (NSAIDs) block cyclooxygenase activity, and shunt arachidonic acid to the 5-lipoxygenase pathway that increases production of the potent proinflammatory cysteinyl leukotrienes ($LTC_4$, $LTD_4$, and $LTE_4$).[2]

Neutrophilic infiltrates usually indicate the presence of bacterial rhinosinusitis, especially when humoral immunodeficiency or ciliary dysmotility are present. $LTB_4$, IL8, bacterial products, and complement fragments may contribute to their recruitment and activation. Neutrophilic infiltrates may also be present in rhinoviral and other viral rhinitis syndromes. Early in rhinovirus infections there is an increase in vascular permeability that is likely due to bradykinin. Later, there may be an increase in glandular secretion, particularly of locally synthesized secretory IgA.

There are several causes of nonallergic rhinitis without inflammation/inflammatory cells. Endocrine changes of hypothyroid and hyperthyroid disease, and pregnancy can lead to unremitting nasal congestion. Damage to sympathetic nerves, as in Horner's syndrome, can ablate sympathetic vasoconstrictor tone and lead to unopposed vasodilatory parasympathetic reflexes and chronic nasal congestion. Overuse of topical-adrenergic agonists/nasal decongestants also leads to chronic nasal congestion ("rhinitis medicamentosa").

*Vasomotor rhinitis* is unrelated to allergy, infection, structural lesions, systemic disease, or drug abuse. (see summary statement #16) Although the term vasomotor implies increased neural efferent traffic to the blood vessels supplying the nasal mucosa, this has never been proven. Subjects with vasomotor rhinitis fall into two general groups: "runners" who have "wet" rhinorrhea, and "dry" subjects with predominant symptoms of nasal congestion and blockage to airflow, and

minimal rhinorrhea. These reactions can be provoked by nonspecific irritant stimuli such as cold dry air, perfumes, paint fumes, and cigarette smoke. Subjects with predominantly rhinorrhea (sometimes referred to as cholinergic rhinitis) appear to have enhanced cholinergic glandular secretory activity, since atropine effectively reduces their secretions.[3] Subjects with predominantly nasal congestion and blockage may have nociceptive neurons that have heightened sensitivity to innocuous stimuli.

Emotional factors such as stress and sexual arousal are known to have an effect on the nose, probably due to autonomic stimulation.[4]

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## Infectious Rhinitis

**14. Infectious rhinitis may be acute or chronic. Acute infectious rhinitis is usually due to one of a large number of viruses, but secondary bacterial infection with sinus involvement is a common complication. Symptoms of chronic infectious rhinosinusitis include mucopurulent nasal discharge, facial pain and pressure, olfactory disturbance, and post-nasal drainage with cough.**

Acute rhinitis is usually associated with a viral upper respiratory infection, but may follow trauma.[1] Symptoms of acute viral rhinitis include rhinorrhea, nasal obstruction, and fever. Initially, viral rhinitis is characterized by clear, watery rhinorrhea that is accompanied by sneezing and nasal obstruction. Edema of the nasal mucosa produces occlusion of the sinus ostia with resulting facial pain or of the eustachian tube with resulting ear fullness. The nasal drainage may become cellular and cloudy due to the presence of organisms, white blood cells and desquamated epithelium. Responsible viruses include rhinoviruses, respiratory syncytial virus, parainfluenza, influenza and adenoviruses. Unless there is bacterial superinfection, the condition is self-limiting and usually resolves within 7 to 10 days. Acute bacterial rhinitis may occur de novo or may follow viral rhinitis. Nasal obstruction, cloudy drainage, vestibular crusting and facial pain occur. Not all patients report fever. Bacteria frequently recovered from nasal or sinus cultures include *Streptococcus pneumoniae,* group-A beta-hemolytic *Streptococci* and *Hemophilus influenzae.*[2] In patients with immunodeficiency, HIV positivity, or acquired immunodeficiency syndrome (AIDS), mycobacterial, fungal, and other opportunistic organisms may be involved.

The symptoms of allergic rhinitis are frequently confused with infectious rhinitis when patients complain of a constant cold. Purulent nasal drainage may be present in either infectious or non-infectious rhinitis. Symptoms persisting longer than two weeks should prompt a search for causes other than infection. Foreign body rhinitis should be considered in the differential diagnosis, especially in children. Symptoms may be acute or chronic, unilateral or bilateral, and the nasal discharge may be blood-stained or foul-smelling.

Exacerbations of rhinitis symptoms with predominant clear rhinorrhea in patients with a known history of allergic rhinitis may prove to be a diagnostic difficulty. The distinction between active infection and allergy should be made. When the history or physical examination is not diagnostic, a nasal smear may be obtained to aid in differentiation.

There is controversy about whether chronic infectious rhinitis (diagnosed after 8 to 12 weeks of symptoms) can exist in the absence of chronic sinusitis. Symptoms of chronic infectious rhinosinusitis can include nasal congestion, predominantly purulent nasal discharge, facial pain, and pressure, olfactory disturbances and post-nasal drainage with cough.[3]

Allergy, mucociliary disturbance and immune deficiency may predispose certain individuals to the development of chronic infection.[4,5] Mucociliary abnormalities may be congenital, as in primary ciliary dyskinesia,[6] Young's syndrome,[7] or cystic fibrosis, or secondary to infection. Similarly, immune deficiency may be congenital or acquired.

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## Non-Allergic Rhinitis Without Eosinophilia

**15. Nonallergic, noninfectious rhinitis, generally termed vasomotor rhinitis, comprises a heterogeneous group of patients with**

**chronic nasal symptoms that are not immunologic or infectious in origin and usually not associated with nasal eosinophilia. Most of these patients develop rhinitis in response to environmental conditions, such as cold air, high humidity, strong odors and inhaled irritants.**

The term vasomotor rhinitis has been used loosely to describe patients with perennial rhinitis whose symptoms are intensified by changes in temperature or relative humidity, alcohol, odors such as bleach, perfume or solvents, bright lights or hot spicy foods, and irritants such as tobacco smoke, dusts and automotive emission fumes. This disorder is not due to allergy or infection, nor is it associated with nasal eosinophilia. The symptoms are variable, consisting mainly of nasal obstruction and increased secretion. Sneezing and pruritus are less common. Although the term vasomotor implies increased neural efferent traffic to the blood vessels supplying the nasal mucosa, this has never been proven. Some investigators prefer to use the descriptive term "nonallergic" or "idiopathic" rhinitis that does not imply known pathophysiology.

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## Non-allergic Rhinitis with Eosinophilia Syndrome

**16. The nonallergic rhinitis with eosinophilia syndrome (NARES) is characterized by nasal eosinophils in patients who have perennial symptoms and occasionally loss of sense of smell. These patients lack evidence of allergic disease as demonstrated by lack of clinically significant positive skin tests and/or specific IgE antibodies in the serum.**

In the NARES syndrome, individuals experience perennial symptoms of sneezing paroxysms, profuse watery rhinorrhea and nasal pruritus and occasional loss of smell.[1,2] Patients are typically middle-aged and have a characteristic perennial course but with paroxysmal episodes. Nasal smears reveal eosinophils during symptomatic periods. Patients lack evidence of allergic disease as determined by skin testing or by serum levels of IgE antibody to specific allergens. It is difficult to assess the prevalence of this syndrome in the general population. The etiology of the syndrome is obscure, but may be an early stage of aspirin sensitivity.[3]

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## Occupational Rhinitis

**17. Occupational rhinitis refers to rhinitis arising in response to airborne substances in the workplace, which may be mediated by allergic or nonallergic factors, eg, laboratory animal antigen, grain, wood dusts, and chemicals. It often coexists with occupational asthma.**

Occupational rhinitis may be defined as sneezing, nasal discharge and/or congestion caused by exposure to an airborne agent present in the workplace. Triggering substances may be irritants, such as tobacco smoke, cold air, formaldehyde, hair sprays, or chemicals acting apparently through non-immunologic mechanisms. Alternatively, occupational exposure may involve IgE-mediated reactions triggered by allergens such as laboratory animals (rats, mice, guinea pigs, etc.), animal products, grain (bakers and agricultural workers), coffee beans, wood dusts (particularly hard woods such as mahogany, western red cedar, iroko), latex, chemicals (eg, acid anhydrides, platinum salts, glues), mites, mold spores, pollen, psyllium, enzymes, and a litany of other substances. This disorder frequently coexists with occupational asthma. Occupational rhinitis may precede development of occupational asthma.

Symptoms may occur acutely at work after intermittent exposure or more chronically at work after continuous exposure. Occupational rhinitis should be suspected in patients with nasal symptoms which are temporally related to exposure at work and which improve away from the workplace. For occupational allergens, skin testing may confirm sensitivity, if appropriate reagents are available. The most specific diagnostic test for occupational rhinitis is a challenge with the suspected agent, either naturally in the workplace setting or in a medical setting. Optimally, in addition to symptom scores, such a challenge could include pre-challenge and post-challenge measures of nasal airway resistance using anterior rhinomanometry.

The optimal management of occupational rhinitis is avoidance of the occupational trigger, either by modifying the workplace, use of filtering masks, or removing the patient from the adverse exposure. If this is impossible, pharmacologic therapy as discussed in earlier sections should be instituted, recognizing that chronic use of medication will probably be required for adequate relief and prevention of symptoms. Strategies to prevent or reduce symptoms may include the daily use of anti-inflammatory intranasal corticosteroids or the administration of antihistamines and/or intranasal cromolyn immediately prior to allergen exposure. It is also important to institute avoidance measure for non-occupational allergens that may contribute to rhinitis symptoms.

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### Hormonal Rhinitis

**18. Causes of hormonal rhinitis include pregnancy and hypothyroidism. Although symptoms of rhinitis, in particular nasal congestion, may occur during pregnancy, most notably from the second month to term, these symptoms usually disappear rapidly after delivery. Other causes of rhinitis such as allergic rhinitis, infectious rhinitis and rhinitis medicamentosa are also common during pregnancy.**

Pregnancy,[1] puberty, the use of oral contraceptives, hypothyroidism,[2] or conjugated estrogens can be associated with nasal obstruction and/or hypersecretion. Evidence linking thyroid disease directly with nasal pathology is limited.[2] Increased nasal secretion in hypothyroidism has been reported on an anecdotal basis. The frequency of rhinitis symptoms was unclear. Symptoms of hypothyroidism such as lethargy, constipation, and cold intolerance, should be sought. No clear data exist which indicate that thyroid replacement treatment alone leads to resolution of an associated rhinitis.

During pregnancy, rhinitis symptoms, especially congestion, often develop during the second month and persist to term, but usually disappear shortly after delivery.[2] These symptoms are likely related to hormone-induced intranasal vascular engorgement and mucosal hypersecretion.[3] However, non-hormonal causes of rhinitis such as allergic rhinitis, vasomotor rhinitis, rhinitis medicamentosa and sinusitis are more common causes of rhinitis in pregnancy.

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### Drug-Induced Rhinitis

**19. Drug-induced rhinitis may be caused by a number of medications, including ACE (angiotensin-converting enzyme) inhibitors, reserpine, guanethidine, phentolamine, methyldopa and prazosin, as well as beta blockers, chlorpromazine, aspirin, other NSAIDs (non-steroidal anti-inflammatory drugs) and oral contraceptives. Rhinitis medicamentosa commonly refers to the over-use of nasally inhaled vasoconstrictor (decongestant) agents such as the OTC (over-the-counter) products, oxymetazoline or phenylephrine. Repeated use of cocaine may also produce rhinitis.**

Medications may induce symptoms of nasal congestion and/or rhinorrhea.[1] Antihypertensive medications are most frequently incriminated. Reserpine was thought to be the major cause of nasal obstruction, but guanethidine, phentolamine, methyldopa, ACE inhibitors (angiotensin-converting enzyme) and prazosin (alpha receptor antagonist) have been implicated. Other antihypertensive drugs from varied pharmacologic classes have been documented to have similar side effects. Oral contraceptives, chlorpromazine and beta blockers have also been implicated.[2] Aspirin and non-steroidal anti-inflammatory agents (NSAIDs) may produce rhinorrhea. The rhinorrhea may be isolated, or part of a complex involving hyperplastic rhinosinusitis, nasal polyposis and asthma. Drugs of abuse, such as cocaine, should also be considered potential causes of rhinitis. Nasal irritation and inflammation may produce a rhinitis picture before the end-stage effects, such as nasal septal perforation, occur.[3]

The repetitive use of topical alpha-adrenergic nasal decongestant sprays for more than 5 to 7 days may induce rebound nasal congestion upon withdrawal. These agents include over the counter products containing oxymetazoline or phenylephrine. Also, patients may develop tachyphylaxis, due to the need for more frequent doses to provide adequate decongestion. Prolonged usage may lead to a hypertrophy of the nasal mucosa termed "rhinitis medicamentosa". The nasal mucosa is often beefy-red, appears inflamed, and shows areas of punctate bleeding and scant mucus. This condition may be caused by down regulation of the nasal mucosal alpha-adrenergic receptors. Similar consequences may occur with prolonged use of other vasoconstrictor agents such as cocaine.

Management of rhinitis medicamentosa is discussed in text for summary statement #48.

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### Rhinitis from Food Ingestion

**20. Rhinitis may occur after ingestion of foods or alcoholic products. This may be due to vagally mediated mechanisms, nasal vasodilation, food allergy and/or other undefined mechanisms. Food allergy is a rare cause of rhinitis without associated gastrointestinal, dermatologic or systemic manifestations.**

Foods can provoke rhinitis symptoms by a variety of different mechanisms.[1,2] Ingested food allergens rarely produce isolated IgE mediated rhinitis without involvement of other organ systems. Urticarial rash, facial or lip swelling, or bronchospasm, strongly suggest an IgE mediated reaction.[3] Symptoms which promptly follow eating foods or food additives may suggest a causal etiology, but this may or may not be IgE-mediated. In adults, food skin tests may be appropriate in occasional cases if a careful history suggests food-related rhinitis symptoms, particularly if rhinitis symptoms are associated with other systemic symptoms. Although a variety of opinions have been expressed in the literature,[1-10] there is little or no credible data available to justify routine performance of food skin tests in the evaluation of rhinitis in adults. In the evaluation of rhinitis in children where the history may be more difficult to interpret and food allergy is more common, there is greater justification to consider performance of limited food skin testing. Beer, wine and other alcoholic drinks may produce symptoms by nasal vasodilation. The syndrome of copious watery rhinorrhea occurring immediately after ingestion of foods, particularly hot and spicy foods, has been termed "gustatory rhinitis" and is vagally mediated.[10]

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## Other Conditions that May Be Confused with Rhinitis

**21. Signs and symptoms suggestive of rhinitis can be produced by other conditions including: nasal septal deviation, tumors, adenoidal hypertrophy, hypertrophy of the nasal turbinates.**

Nasal obstruction may be caused by congenital or acquired anatomic abnormalities, which may mimic symptoms of rhinitis. Reduced air flow through the nasal passages in infants may be due to congenital choanal atresia. The most common acquired anatomic cause of nasal obstruction in infants and children is adenoidal hypertrophy.

Nasal septal deviation, and nasal turbinate or adenoidal hypertrophy many block flow of nasal secretions, leading to rhinorrhea or postnasal drip, as well as causing nasal blockage.

Although comparatively rare, both benign and malignant tumors may cause rhinitis symptoms.[1] Lesions may occlude the nasal airway, often unilaterally and invariably. Rapidly growing nasal malignancies may cause nasal obstruction early in the disease. Lesions arising in the maxillary sinus present intranasally in the late stages of the disease, after the tumor has penetrated the medial wall of the antrum. Bleeding may occur, as well as hyposmia or anosmia, pain and otalgia. Prolonged occupational exposure to chemicals such as nickel, wood or leather dusts, chromate, formaldehyde and chlorophenol, have been associated with hypertrophic rhinosinusitis, metaplasia and carcinoma. Refractory clear rhinorrhea may be due to CSF leak even in the absence of trauma or recent surgery.

Nasal mastocytosis presents with symptoms of rhinorrhea and nasal congestion without pruritus.[2] Patients with nasal mastocytosis display an especially pale mucosa, which contains increased numbers of mast cells, and few eosinophils. Skin tests and other tests for IgE-mediated disease are negative.

Primary atrophic rhinitis occurs in elderly patients who report nasal congestion and a constant bad smell (ozena) in the nose.[3] This persistent condition is characterized by progressive atrophy of the nasal mucosa and underlying bone of the conchae.[4] Thick crusts form that produce the characteristic foul odor. The nasal cavities are enlarged and squamous metaplasia of the surface epithelium is detectable. Patients report associated headaches and chronic sinusitis. The syndrome should be separated from secondary atrophic rhinitis, developing as a direct result of chronic granulomatous nasal infections, chronic sinusitis, radical nasal surgery, trauma and irradiation. The incidence of atrophic rhinitis in developed countries has declined, but the disease is still prevalent in Eastern Europe, Greece, Egypt, India, and China. The etiology of primary atrophic rhinitis has not yet been established. Theories include infection with *Klebsiella ozaenae*[5] and other bacteria. Despite the sensation of congestion, rhinomanometric studies have shown no evidence of increased resistance to airflow.

Systemic immunologic and non-immunologic diseases may affect the nose. In uremia and diabetes, ischemia may cause an anterior rhinitis. Others include Wegener's granulomatosis, sarcoidosis, relapsing polychondritis and midline granuloma.[6] In certain syndromes, the systemic symptoms may be absent or undetected when patients present with nasal complaints. Infections such as tuberculosis, syphilis, leprosy, sporotricosis, blastomycosis, histoplasmosis, and coccidiomycosis also may cause granulomatous nasal lesions. These are usually ulcerative, and crust formation may lead to nasal obstruction or bleeding. Rhinoscleroma is a rare chronic granulomatous disease associated with the bacterium *Klebsiella rhinoscleromatis*. Rhinoscleroma is endermic to Eastern Europe and Central America, but is now increasing in incidence in the US. Symptoms include purulent nasal discharge, crusting and nodule formation producing nasal obstruction.


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### Nasal Polyps

**22. Nasal polyps may occur in conjunction with chronic rhinitis or sinusitis and may contribute significantly to the patient's symptoms. Nasal polyps should always be considered in the differential diagnosis of patients who present with invariant nasal congestion and its sequelae. Allergy as a cause of nasal polyps has not been established but nasal polyps may occur in conjunction with allergic rhinitis.**

Nasal polyps present as invariable nasal obstruction and may occur in association with chronic allergic rhinitis or sinusitis. They may occur in association with cystic fibrosis in children[1] and adults,[2] asthma and as part of aspirin idiosyncracy[3] (acetylsalicylic acid sensitivity, sinusitis and asthma), but they most commonly occur alone. Allergy does not appear to predispose to polyp formation, but mast cell reactions and eosinophil activation with subsequent inflammation seem to be important and may explain why corticosteroids are therapeutically effective. Between 10% and 15% of patients with allergic rhinitis also have nasal polyps.[4]


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## EVALUATION OF RHINITIS

### History

**23. Full evaluation of the patient with rhinitis should include a determination of the pattern, chronicity, and seasonality of symptoms (or lack thereof), response to medications, presence of coexisting conditions, occupational exposure, a detailed environmental history and identification of precipitating factors.**

A careful history will usually suggest the diagnosis of rhinitis (Table 1). A thorough general medical history should be followed by questions specific to rhinological symptoms, including information on environmental and occupational factors and family history. Allergic rhinitis can occur at any age, including infancy, and the physician should note the onset of symptoms. Most patients with allergic rhinitis develop their symptoms prior to the age of 20 years.[1,2] The frequency of symptoms should be noted and whether they are daily, episodic, seasonal or perennial. The duration and severity of the symptoms should also be mentioned, and whether the severity has increased, decreased, or remained the same over a period of time.

Presentation of allergic rhinitis may vary considerably. Some patients present primarily with symptoms of sneezing and rhinorrhea whereas others present with nasal blockage with little or no itching or sneezing.

Symptoms may be perennial, with or without seasonal exacerbations. In evaluating the patient, it is important to obtain a detailed account of when and where the symptoms arise. Common seasonal allergens include tree, grass and weed pollens, and airborne molds. In seasonal allergic rhinitis, there is a distinct relation between timing of pollen release at various geographic locations and the appearance of symptoms.

It is important to ask about the association of acute symptoms with exposure to specific allergens such as mites during house cleaning, episodic exposures to animals or mold spores, which are present in increased amounts during harvesting, mowing, or leaf raking. Perennial allergens, such as dust mites, cockroaches, pet danders and mold spores can cause chronic symptoms.

Frequently, unsuspected occupational allergens can stimulate an IgE-mediated response, and inquiries should be made about this and poten-

Table 1. Important Historical Points in the Evaluation of Rhinitis

- Symptoms: magnitude, duration, timing in relation to exposure (ie, early and/or late-phase allergic reactions), effects on daily living
- Triggers/seasonality
- Environment, including home, job and school or day care for children
- History of other allergic symptoms (eg, asthma, conjunctivitis, eczema)
- Past medical history, including trauma
- Feeding history in young children
- Past treatment experience
- Current treatment
- Family history, including allergic diseases
- Review of systems

tial exposures to irritants in the workplace. (see Summary Statement #17)

Consistent obstruction on the same side suggests a polyp, foreign body, structural problem, or rarely, a tumor. Hyposmia and anosmia are most often associated with nasal polyps or severe disease. Symptoms related to blockage of the airways include: frequent sore throats, dryness of the mouth and oropharynx, a nasal quality to the voice and snoring. An allergic salute may be characterized by an upward or sideways thrust of the palm of the hand against the tip of the nose when watery rhinorrhea and itching are significant, resulting in a transverse crease in the skin of the lower third of the external nose. If sneezing is present, it often occurs in paroxysms.

The allergens, irritants and weather conditions that precipitate or aggravate symptoms should be detailed. Perennial symptoms more commonly occur when there are indoor pets, dust mites or mold spores present throughout the year. Moisture favors the growth of mites and molds. Mattresses, pillows, upholstered furniture, curtains and carpets are frequent sources of dust mites. House plants and stored paper goods favor mold growth. There is a direct relationship between the amount of pollen exposure and severity of symptoms.[3] As the season progresses, there is a gradual increase in severity of symptoms in relation to the pollen count due to immunologic enhancement of sensitivity or "priming."[4] Certain foods can induce rhinitis symptoms as has been confirmed by double blind challenges.[5] Irritants can potentiate the symptoms of allergic rhinitis. Emotional upsets can also exacerbate rhinitis symptoms. In an allergic individual, an upper respiratory infection can either mimic allergies or worsen or prolong the effects of allergies or other non-specific irritants.[6,7] Hormonal factors or medications/drugs, such as antihypertensives or cocaine, can be responsible for a persistent rhinitis. A positive family history makes it more likely that an allergy will develop,[8] but the pattern of inheritance seems to be polygenic and a negative family history by no means rules out the diagnosis of allergic rhinitis. The level of response to previous medication trials is also important to assess. For example, a favorable response to antihistamines would support a diagnosis of allergy, while such a response to intranasal corticosteroids could support any of a number of diagnoses, including rhinitis due to allergy, or the NARES syndrome.

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### Taking History of Impact on Quality of Life

**24. Symptoms of rhinitis may significantly impact the patient's quality of life, by causing fatigue, headache, cognitive impairment and other systemic symptoms. An assessment of the degree to which these symptoms interfere with the patient's ability to function should be made.**

The "individuals subjective assessment of his/her physical, physiologic and social well being"[1] is the cornerstone of evaluating the effect of the various therapies provided by physicians. In rhinitis, it is not only the clinical outcome—relief of sneezing, itching, rhinorrhea or congestion—or the effect on measures of nasal patency studies which define success of treatment, but also it is the functional impact of the treatment on the patients daily life which defines successful treatment. Diseases have a variety of impacts on patients in addition to making them feel ill. They also interfere in a variety of ways with carrying out ones day to day responsibilities. In patients with rhinitis, loss of sleep and concomitant fatigue, headache, poor concentration, repeated nose blowing, itchy watery eyes and general irritability all impact negatively on their ability to carry out physical, social and work/school responsibilities effectively.

There are several surveys which have been used to measure the out-

comes of treatment on a variety of diseases. The Medical Outcomes Study Short Form Healthy Survey (SF-36) has been used to measure the outcomes on specific functions such as physical and role functioning and on emotional well being. On the other hand specific rhinitis questionnaires, such as the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ), have been validated in the measurement of the effects of treatment of nasal disease on important parameters of every day living.[2,3]

Another look at the Rhinoconjunctivitis Quality of Life Questionnaire reveals that a questionnaire specifically designed for 12 to 17-year old patients is necessary to determine significant quality of life impacts of different therapies for this age group.[4]

Another quality of life study evaluated the impact of the relief of rhinorrhea on moods and daily activities in patients with non-allergic rhinitis. This study revealed that patients treated with topical ipratropium had substantially greater improvement in mood than those on placebo.[5]

Finally, one must note that numerous studies have demonstrated that better health outcomes occurred in patients who adhere to treatment recommendations as compared to those who are not compliant with recommended drug regimens.[6] This fact is worrisome in evaluating the results of clinical drug trials which require patients to be compliant with drug administration and do not make allowances for the non-compliant patient.

Allergic rhinitis, particularly when perennial, can cause restrictions on the physical, psychological, and social well-being of patients. In one study that used the SF-36 questionnaire to evaluate the quality of life in patients with perennial allergic rhinitis, values for patients with moderate to severe perennial allergic rhinitis were significantly different from those for healthy subjects for 8 of 9 variables.[7] Indeed, patients with allergic rhinitis had decreased physical and social functioning, energy, mental health, and general health perception. They had increased physical and emotional limitations and experience of pain.

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## Physical Examination

**25. An examination of the nose should be performed in patients with a history of rhinitis. This should include examination of the nasal passageways, secretions, turbinates, septum, and determination of whether nasal polyps are present.**

Examination of the nose is indicated in all cases of rhinitis (Table 2). This is accomplished with a nasal speculum with appropriate lighting, otoscope with nasal adapter, rigid Hopkins rod or flexible nasopharyngoscope.[1] Use of the latter procedure may be limited in the pediatric population. If it is used, the middle meatus should also be examined, if possible, to evaluate bony or mucosal crowding with obstruction of the sinus ostia. The presence of mucopurulent material in this region is suggestive of sinusitis. "Cobblestoning" of the pharynx with lymphoid tissue may be seen. A nasal speculum should be inserted gently, since the septum may be tender. Elevating the end of the nose with the other hand provides a better view of the nasal passage.

On physical examination, the patient with rhinitis may appear quite uncomfortable and distressed with mouth breathing. On nasal examination, the typical mucosa of the allergic patient appears pale and swollen, with a bluish-gray appearance when the mucosal edema is severe. Occasionally, the mucosa can be hyperemic. The mucosa is usually reddened in acute infections and with overuse of topical medications. Mucosal appearance may not distinguish between allergic and non-allergic rhinitis, because non-allergic rhinitis may also present with mucosal pallor, edema or hyperemia.

The quantity and quality of nasal secretions should be noted. With allergic rhinitis, there may be watery mucus on the epithelial surface or on the floor of the nasal passage. With abnormal mucociliary clearance or total nasal obstruction, thick secretions can be seen pooling in the floor of the nose.

An examination of the nasal cavity may identify polyps, tumors, foreign bodies, or septal deflections. Unlike the nasal turbinates with which they are often confused, polyps appear glistening, mobile, and opaque and are insensitive to touch.[3] Nasal polyps may be differentiated from severely edematous mucosa by applying a small amount of a topical vasoconstrictor such as phenylephrine to the mucosa, and reexamining the mucosa 5 to 10 minutes later. Nasal polyps will not shrink in size after topical vasoconstrictor has been applied, unlike edematous mucosa. Crusting on an inflamed mucosa may suggest atrophic rhinitis or a systemic disease such as sarcoidosis. The presence of a septal perforation should raise the possibility of cocaine abuse, previous surgery or,

Table 2. Elements of Physical Examination and Procedures to Consider in Patients With Rhinitis

- General observations: facial pallor, "allergic shiners", mouth breathing, and nasal crease, evidence of systemic disease (e.g. nail clubbing).
- Growth percentiles for children.
- Eyes: evidence for conjunctivitis, Dennie-Morgan lines (accentuated lines or folds below the margin of the inferior eyelid).
- Nose: presence or absence of external deformity, nasal mucosal swelling, nasal polyps, deviated septum, septal perforation, discharge (noting color and consistency), blood. Consider examining the nasopharynx using indirect mirror visualization or fiberoptic endoscope
- Ears: Consider pneumatic otoscopy to look for abnormalities of tympanic membranes, including abnormal mobility patterns, retraction, air-fluid levels, bubbles behind tympanic membrane; consider tympanometry to confirm the presence or absence of effusion and middle ear under- or over-pressures.
- Mouth: Observe for malocclusion or high arched palate associated with chronic mouth breathing, tonsilar hypertrophy, lymphoid "streaking" in the oropharynx, pharyngeal postnasal discharge, halitosis, and pain upon mouth occlusion suggestive of temporomandibular joint syndrome.
- Neck: Lymphadenopathy, thyroid enlargement.
- Chest: Signs of asthma.
- Skin: Eczema, skin dryness, dermographism.
- Other relevant organ systems.

again, systemic granulomatous diseases.

In allergic rhinitis associated with conjunctivitis, the palpebral conjunctivae may be injected with watery discharge and puffiness of the eyelids. Subconjunctival edema may be present. With chronic or severe acute allergic rhinitis, a transverse crease is often seen across the bridge of the nose, particularly in children, as a result of rubbing of the nose to relieve nasal obstruction and itching. The characteristic gesture in which the patient elevates the tip of the nose with the palm of the hand to relieve itching and obstruction has acquired the name "the allergic salute." Allergic "shiners" (infraorbital dark skin discoloration),[3] and facial pallor may be present. The eyes and periorbital region also should be examined for evidence of Dennie-Morgan lines (accentuated lines or folds below the margin of the inferior eyelid) and cataracts, particularly if atopic dermatitis is present.

With prolonged nasal obstruction and constant mouth breathing in childhood, an individual may have elevation of the upper lip, an overbite (dental malocclusion) and a high arched palate.[4] The tympanic membranes should be examined for evidence of associated middle-ear disease, including middle-ear effusion and tympanic membrane retraction or immobility.[5] This may provide evidence of allergen-induced Eustachian tube dysfunction.[6] The examination should also focus on the possible involvement of the sinuses. Evidence of associated allergic diseases, such as asthma and atopic dermatitis, should be sought. Examination of the lungs may reveal wheezing or a persistent cough, since there are often accompanying symptoms and signs of asthma when allergic rhinitis is present.[7] In the evaluation of patients with rhinitis it may be necessary to rule out involvement of any other relevant organ system.

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### Testing for Specific IgE

**26. The demonstration of specific IgE antibodies to known allergens by skin testing or in-vitro tests (as delineated in the "Parameters for Diagnostic Testing"[1]) is of particular importance in determining whether the patient has allergic rhinitis and for identifying specific allergens for which avoidance measures and/or allergen immunotherapy are warranted.**

A careful history is the most important step toward the diagnosis of allergic disease. Skin testing to allergens is indicated to provide evidence of an allergic basis for the patient's symptoms, to confirm suspected causes of the patient's symptoms, or to assess the degree of sensitivity to a specific allergen. The simplicity, ease and rapidity of performance, low cost, and high sensitivity of these tests makes them favorable for use in patients with rhinitis. Quality control measures and proper performance of skin testing are vital to produce accurate and reproducible results. The number of skin tests that are necessary may vary depending on the age, potential allergen exposures, and area of the country. To properly interpret skin tests or in vitro tests for specific IgE, it is essential to know which aeroallergens are present locally, are clinically important and have allergenic cross-reactivity with botanically related species (see "Practice Parameter for Allergy Diagnostic Testing").

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## Special Diagnostic Techniques

27. **In selected cases, special techniques such as fiberoptic nasal endoscopy and/or rhinomanometry may be useful in evaluating patients presenting with rhinitis symptoms. These tests may require special expertise for appropriate administration and interpretation. Patients with nasal disease require appropriate examination for associated diseases, such as sinusitis and otitis media.**

History and routine physical examination are usually sufficient for a definitive diagnosis of rhinitis. Patients with upper airway complaints may initially report symptoms suggestive of rhinitis. When symptoms or physical findings are atypical, complications or other conditions are suspected, or when symptoms do not respond appropriately to therapy, endoscopy may be indicated. Traditional examination of the nasal cavity consists of inspection with a nasal speculum following mucosal decongestion; mirrors are used for examination of the nasopharynx and larynx. Unfortunately, it is not possible to view many of the important recessed structures of the upper airway by these methods. A more complete upper airway examination can easily be performed endoscopically, using either the rigid Hopkins instruments or the flexible fiberoptic endoscope. Radiologic imaging techniques, such as plain films, computed tomography (CT), and magnetic resonance imaging (MRI) have limited use in the evaluation of patients with uncomplicated rhinitis which responds well to therapy.

**Upper Airway Endoscopy.** Upper airway endoscopy (rhinolaryngoscopy) is the most useful diagnostic procedure in an evaluation for anatomic factors causing upper airway symptoms. Endoscopy provides a clear view of the nasal cavity and allows for detailed examination of the middle meatus, superior meatus, sphenoethmoidal recess, and posterior nasopharynx, as well as structures of the oropharynx and larynx.[1,2] The procedure is usually performed in the office following decongestion and topical anesthesia. Some children may require sedation. Analysis of videotaped fiberoptic upper airway endoscopy has also been used as a research technique to measure cross sectional area of the nasal cavity.[3]

**Imaging Techniques.** The primary goals of radiologic imaging of the upper airway are to provide an accurate reproduction of the regional anatomy and to establish the presence and extent of anatomic disease. This information may assist in planning medical therapy and provide an anatomic guide to facilitate subsequent surgical treatment.[3]

*Standard radiographs.* Although standard radiographs have traditionally been the most frequently used radiologic modality for evaluating disease of the upper airway and paranasal sinuses, they are not indicated in the evaluation of patients with uncomplicated rhinitis. The Caldwell (anterior-posterior) and Waters views best demonstrate the frontal and maxillary sinuses. The lateral view is the best choice for visualization of the sphenoid sinus. These projections are not useful for demonstration of structures of the nasal cavity, and are of limited use in demonstration of structures of the nasopharynx, oropharynx, and larynx. Lateral views are sometimes used for evaluation of the soft tissues of the nasopharynx, adenoids, oropharynx, and larynx, but are generally not needed when endoscopy is available.

*Computed tomography and magnetic resonance imaging.* Computerized tomographic scanning (CT) and magnetic resonance imaging (MRI) using coronal sections for imaging of sinuses frequently identify turbinate congestion, concha bullosa, polyps and septal deviation as causes of nasal airway obstruction. Although CT and MRI have been used to validate acoustic rhinometry (see below) as a method, they are expensive and may not correlate well with functional obstruction.

High resolution computed tomography can demonstrate disease that is not shown on routine x-ray films. It can also delineate pathologic variations and demonstrate anatomic structures inaccessible by physical examination or endoscopy. Because of its superb contrast resolution, CT is an excellent method for examining the complex anatomy of the upper airway, particularly the ostiomeatal complex. The capability of CT to display bone, soft tissue, and air facilitates accurate definition of regional anatomy of the nose and paranasal sinuses. The main indications for the CT are chronic sinusitis not responding to appropriate medical therapy, acute recurrent sinusitis, abnormal diagnostic nasal endoscopic examination and persistent facial pain.[4] In some centers, a limited CT study including only 4 to 5 views can be performed as a cost effective alternative to sinus radiographs.

Magnetic resonance imaging (MRI) provides better imaging of soft tissue than CT, but it is less suited to imaging the bony anatomy of this region. Because bone and air yield similar signal intensities on MRI, precise definition of the ostiomeatal air passages and their bony perimeter is difficult. Furthermore, in the patient with extensive inflammatory disease, the signal intensity of this pathologic process is indistinguishable from the appearance of the normal mucosa in the edematous phase of the nasal cycle. These factors limit the MRI evaluation of underlying anatomy in a patient with upper airway disease. MRI is useful, however, in evaluation of upper airway malignancies.

**Aerodynamic methods for estimation of nasal airway obstruction.** Resistance to air flow through the nose

(or conductance, the inverse of resistance) may be measured by rhinomanometry. Rhinomanometry objectively measures functional obstruction to airflow in the upper airway, although the technique has not been fully standardized. Subjective perception of nasal stuffiness may correlate only loosely with measured nasal airway resistance,[5] but rhinomanometry may be used in the assessment of the severity of symptoms. In addition, rhinomanometry may provide objective information on results of therapeutic interventions. The objective information obtained from rhinomanometry may be particularly important when it is suspected that occupational exposure results in nasal symptoms including nasal congestion. Rhinomanometry is not a substitute for careful endoscopy of the nose because significant pathology in the nose can occur with nasal airway resistance values in the normal range.

Rhinomanometry may be used to assess the severity of anatomical abnormalities that are causing airway obstruction in the nose, including nasal valve abnormalities, septal deviation, and polyposis. This application requires measurements before and after treatment with a potent intranasal decongestant agent.

Other indications for rhinomanometry include the evaluation of patients with obstructive sleep apnea.[6]

**Acoustic Rhinometry.** Acoustic rhinometry depends on reflection of acoustic signals from structures in the nasal cavity.[7–9] It is currently not a technique used in the routine evaluation of patients with rhinitis. It produces an image that represents variations in the cross sectional dimensions of the nasal cavity and closely approximates nasal cavity volume and minimal cross sectional area. It also allows identification of the distance of the minimal cross section area of the nasal cavity from the naris. Changes in nasal geometry measured by acoustic rhinometry during histamine challenge testing have been documented[10,11] and the results of parallel determinations by acoustic rhinometry and rhinomanometry are comparable.[11] However, nasal airway resistance cannot be easily computed from the acoustic rhinometry data.

**Nasal Provocation Testing.** Identification of sensitivity of the nose to a particular aeroallergen can be usually based on a history of symptoms of allergic rhinitis provoked by exposure to the allergen and confirmed by skin testing. Nasal provocation testing with allergen is unnecessary unless more stringent criteria are needed to incriminate the suspected allergen. For example, nasal provocation testing with allergen may be required for confirmation of sensitivity to allergens in the workplace. Testing of sensitivity to allergens requires that responses to incremental doses of allergens are assessed.[12] Single dose allergen provocation measures nasal reactivity to allergens, not sensitivity. Since nasal reactions to instillation of placebo materials may occur, response to diluent must be measured before provocation with allergens.

Nasal sensitivity/hyperresponsiveness to histamine and methacholine has been found in allergic rhinitis[13–15] and vasomotor rhinitis.[16] Although this may be a marker for these diseases, the clinical utility of nasal provocation testing with histamine or methacholine may be limited to trials of the efficacy of drugs and allergen immunotherapy on nasal irritability, because of a considerable overlap between allergic and nonallergic patients in their sensitivity to these agents.

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## Nasal Cytology

**28. Nasal cytology may aid in differentiating allergic rhinitis and**

**NARES from other forms of rhinitis, eg, vasomotor, infectious rhinitis, if the correct procedure is followed and the appropriate stains are utilized.**

Visualization of large numbers of eosinophils may be helpful in narrowing the differential diagnosis between allergic rhinitis and non-allergic rhinitis with eosinophilia from other types of rhinitis. The presence of neutrophils may support a diagnosis of infectious rhinosinusitis, but secretion neutrophilia is not uncommon in apparently normal subjects.[1] There is lack of expert consensus about whether nasal cytology should be routinely performed in the evaluation of rhinitis.

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## Total Serum IgE, Blood Eosinophil Counts

**29. Neither total serum IgE nor total circulating eosinophil counts are routinely indicated in the diagnosis of rhinitis.**

Serum total IgE has been measured in individuals with a variety of disease conditions.[1] It has often been used as a screening test for allergy. Adults and children with allergic rhinitis and asthma tend to have more elevated total serum total IgE levels.[2] In spite of its wide use, however, it is neither very sensitive nor very specific. There is considerable overlap in total IgE levels between atopic and nonatopic individuals, making the test results difficult to interpret in many instances.[3–7] In general, between 35% to 50% of individuals with allergic rhinitis have normal total IgE levels, while as many as 20% of nonatopic individuals have elevated total IgE levels. In one study of 244 individuals with allergic rhinitis, the specificity and sensitivity of total serum IgE determinations using a cutoff level of 200 IU/mL were 85% and 50% respectively.[8] A similar result was also observed in a study with pediatric patients.[9] Although significant elevations (greater than 50 IU/mL in infants or greater than 200 IU/mL in older children and adults) may correlate with the presence of atopy, a variety of nonatopic conditions can also be associated with these elevated levels of serum total IgE.[1] Recently, there have been several investigations done to evaluate the association respiratory symptoms with serum total IgE and skin-test reactivity.[10–12] The overall results of these studies revealed a poor correlation, especially with allergic rhinitis. Although serum IgE levels may have the advantage of providing some index of overall allergy and can identify the individuals who are least "allergic," they have the disadvantage of measuring all types of IgE, not all of which appear relevant to the respiratory symptoms and skin-test reactivity. Hence, there is still no convincing evidence to support the routine use of total serum IgE measurement in patients suspected of having allergic rhinitis and other related atopic diseases.

The routine measurement of total circulating eosinophil counts in the diagnosis of allergy is subject to similar limitations as for serum total IgE.[13]

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## Unproven or Inappropriate Diagnostic Techniques

**30. Cytotoxicity testing, provocative and neutralization testing carried out by either intracutaneous or subcutaneous injection or sublingual administration, and measurement of specific and non-specific IgG4 are controversial, unproven and/or not appropriate for diagnostic use in evaluation of rhinitis.**

Those techniques summarized below are considered controversial or unproven because they have not been subjected to validation by accepted standards of scientific evaluation or are

not appropriate for diagnostic use in IgE-mediated disease. The techniques are cytotoxicity testing, provocative and neutralization testing carried out by either intracutaneous or subcutaneous injection or sublingually and measurement of specific and nonspecific IgG4.

*I. Cytotoxicology Testing*

Leukocytotoxic testing is based on the claim that the addition of specific allergen in vitro to whole blood or to serum leukocyte suspensions will result in reduction in white blood cell count or death of the leukocytes. In 1960, Bryan and Bryan[1] published the first of a series of articles describing the method. Hence, this has also been called Bryan's Test. The test is performed by removing the buffy coat from whole blood and the cells are then added to a mixture containing sterile distilled water and serum. The suspension is then applied to a microscope slide containing dried antigen within a ring of petrolatum jelly. A control slide is used containing a mixture of the patient's cells, serum and water. The slides are examined at intervals up to 2 hours for any changes in the appearance of the leukocytes or a decrease in motility. These changes are claimed to be the consequence of an allergic reaction, and the test is used for diagnosis of both food and inhalant allergy.

The test has never been proven effective by controlled studies nor has a scientific basis for its use been demonstrated. The results of numerous published control trials indicate that the procedure is not effective for diagnosis of food or inhalant allergy. In serum-leukocyte preparations from patients sensitive to a variety of specific allergens, there are no consistent differences between leukocytes exposed to allergens to which the patients are clinically sensitive and those exposed to allergens to which the patients are not sensitive.[2,3] In a controlled study of the cytotoxic effect of specific allergens on white cells and plasma suspensions, tests did not correlate with atopic reactions to foods or with other untoward reactions to foods (headache, diarrhea, fatigue), and the test was dependent on subjective interpretation and inconsistent end results when repetitive results were performed on the same patient. In a double-blind controlled study,[4] a similar cytotoxic test afforded no reliable help in establishing the diagnosis of food allergy because positive cytotoxic effects were frequently obtained to foods that produced no clinical symptoms, and negative cytotoxic reactions were obtained to foods that did produce clinical symptoms.

The test is not performed under standardized conditions and the interpretation of changes is entirely subjective. Leukocytotoxic changes in IgE-mediated hypersensitivity have not been confirmed. Therefore, there is no proof that cytotoxic testing is a valid technique for diagnosing inhalant allergy and a number of controlled trials have indicated that this test is ineffective for diagnostic purposes.[5]

*II. Provocation–Neutralization testing (Intracutaneous or subcutaneous)*

Intracutaneous or subcutaneous provocation neutralization testing is claimed to be a method of diagnosing allergic disease.[6] In this technique, an intracutaneous or subcutaneous injection of antigen is administered in increasing concentrations to elicit symptoms that correspond to the patient's complaints. As soon as symptoms appear, weaker dilutions of the same antigen are injected at intervals until a dose is found that relieves the provoked symptoms. The patient is observed for 10 minutes after each dilution and all symptoms are recorded. The symptoms can take many forms including drowsiness, chills and muscle pain. Thus, there are 2 phases to the process, provocation and neutralization. A modification of the provocative intracutaneous test to diagnose inhalant allergy was developed using wheal size. However, the principle of provoking and neutralizing symptoms remained the basis for the procedure. One double-blind study of 61 atopic subjects was unable to confirm and reproduce the validity of results from subcutaneous provocative-neutralization testing.[7] A study of symptoms, chest auscultation and peak expiratory flow rates in 20 asthmatic children after provocation skin testing found no correlation of these measurements with skin tests.[8] No attempts at scientific establishment of the possible mechanisms involved have been published. Moreover, from what is known about IgE-mediated reactions, there is no immunologic basis for a therapeutic response to a neutralizing dose of allergenic extract. Therefore, there is no rationale or immunologic basis for subcutaneous or intracutaneous provocation and neutralization testing to be used as a method for the diagnosis of allergic disease in patients with rhinitis.[9]

*III. Provocation–Neutralization Testing (Sublingual)*

Sublingual antigen administration has been advocated as a technique for the diagnosis of food induced respiratory symptoms.[8] The method consists of placing drops of an allergenic extract in various dilutions under the tongue of the patient and waiting 10 minutes for the appearance of symptoms and any symptom is interpreted as a positive test. When the symptoms occur, a neutralizing dose is administered which is usually drops of a more dilute solution of the same extract. Symptoms are expected to disappear in approximately the same temporal sequence in which they appeared. Two separate controlled studies carried out by the Food Allergy Committee of the American College of Allergy, Asthma and Immunology revealed that sublingual provocative testing did not discriminate between placebo controls and allergenic extracts.[10,11] Another study evaluated this technique with 5 physicians, all of whom had been using this method of testing for at least 7 years.[12] The technique was performed according to a double-blind protocol and there was no distinction of reactions between placebo and active extracts. Another study obtained similar negative results.[13] Therefore, there are no controlled clinical studies indicating that sublingual antigen administration

has diagnostic efficacy for human atopic disease. Moreover, there are no known immunologic mechanisms that can account for the neutralizing effects of dilute solutions of allergenic extracts.

*IV. Specific and Non-Specific IgG4*

Measurement of nonspecific and specific IgG4 has been advocated as a diagnostic test for clinical allergy. Because of controversial and inconclusive scientific evidence,[14-18] the measurement of IgG4 should not be part of the diagnosis of patients with allergic nasal disease.[19]

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## MANAGEMENT OF RHINITIS

### Environmental Control Measures

**31. Avoidance of inciting factors, eg, allergens, irritants, medications, is fundamental to the management of rhinitis. Triggers should be identified and avoidance measures instituted.**

*General Considerations*

There are five major categories of IgE-dependent triggers for allergic rhinitis: pollens, molds, house dust mites, animals and insect allergens. In patients sensitive to multiple allergens, it is important to institute avoidance measures for all relevant allergens. This may improve tolerance to unavoidable exposure to aeroallergens, eg, pollens. Although sensitive immunochemical techniques permit direct quantitation of actual changes in allergen level, the effectiveness of environmental control procedures is judged primarily by patient symptoms and medication scores.[1,2]

*Clinical Science*

*Pollens.* Pollen triggering allergic rhinitis is principally derived from wind-pollinated (anemophilus) trees, grasses and weeds though insect-pollinated (entemophilus) plants may produce symptoms if encountered at close range. Pollen allergens are quickly eluted from pollen grains on contact with ocular or respiratory mucosa. Similar allergens may be found on fragments derived from other portions of the plant. Pollen allergens, possibly eluted from pollen grains and passively borne on plant debris and soil particles, can be found on air sampling even when pollen grains are no longer being recovered. Pollens responsible for symptoms vary widely with locale, climate and introduced plantings. In temperate regions of North America, tree pollen generally predominates in early to mid-spring, grasses in late spring and early summer, and weeds from late summer until early fall. The dose of pollen allergen necessary to elicit symptoms exhibits considerable variability depending on level of allergic sensitization and degree of extant allergic nasal mucosal inflammation ("priming"). Reducing pollen exposure is important in the effective management of allergic rhinitis.

Windows and doors must be kept closed and air conditioning used, if necessary, on indoor cycle (closed vents) to keep the home or vehicle comfortable.[3] Indoor pollen levels are increased by window or attic fans. Though remaining entirely indoors is impractical, it is helpful to reduce outdoor exposure during periods of high pollen counts. Activities involving extended time out-of-doors, such as camping trips, may need to be avoided during offending pollen seasons. In general, limiting outdoor activity on sunny, windy days with low humidity is also advisable whereas such activities may be well-tolerated following a gentle, sustained rain. Because the in-

terplay of different weather factors (eg, wind currents, sunshine, rain, humidity) is complex, it is not possible to reliably predict levels of outdoor aeroallergens from the influence of a single weather factor.[4] A shower or bath following outdoor activity removes pollen from the hair and skin and avoids contamination of bedding. In highly sensitive patients whose symptoms are triggered by very low pollen levels, effective allergen avoidance may necessitate severely curtailing outdoor activity. Medications and allergen immunotherapy are required in such patients.

*Molds.* Molds or fungi are ubiquitous and important allergens. These saprophytic organisms exist in great numbers outdoors but also may heavily contaminate indoor environments. Most mold allergens are encountered through inhalation of spores although fragments of hyphal elements may also contribute. Though displaying a poorly defined summer-early autumn seasonal pattern in the northern US, mold spores are recovered on outdoor air sampling year-round in the southern US except during periods of snow cover. Outdoor molds grow on both viable and decaying vegetation, and are strongly influenced by local vegetation. Abundant mold is also found in soil and is released when the earth is disturbed by plowing, excavation, etc. Harvesting activities are also associated with increased mold counts. Mold spore levels are affected by temperature, wind, rain and humidity. Some fungi require the action of water droplets for spore release. High levels of these spores appear during rainy weather and with dew formation at night. "Wet weather" molds include Fusarium, Phoma and Cephalosporium. Other common allergenic molds, such as Alternaria and Cladosporium, are released by wind as humidity falls. Rain or high humidity lowers "dry release" mold spore counts, but counts rise rapidly when the rainy period ends.[4]

Like pollens, avoidance of outdoor molds consists of remaining in a closed environment as much as practical. Air conditioning on indoor cycle is helpful[4] though air conditioning units may be heavily contaminated with mold. Mold exposure is increased by walking in uncut fields and may reach very high levels with activities such as mowing or threshing. Working with compost, silage or dry soil commonly triggers symptoms in mold sensitive patients as does raking leaves. The latter activities may also involve exposure to resuspended pollens and insect debris. Face masks are recommended for such outdoor activities though their value is limited by entrainment of air around the edges of the mask. Also, they offer no protection for the eyes.

Many factors influence the amount of indoor mold, including age and construction of the dwelling, presence of a basement or crawl space, type of heating system, and use of humidifiers and air conditioning. Damp homes, basements, cold outside walls and window moldings provide favorable conditions for mold growth as do sinks, shower stalls, non-refrigerated vegetable storage areas and garbage pails. Fungicides to kill and retard mold growth, such as Clorox® or Lysol®, should be used in these locations. Mold spores also are present in carpeting, bedding and upholstered furniture and are reduced by dust mite avoidance measures. Console humidifiers and cool mist vaporizers may be reservoirs for mold and are best avoided by mold sensitive patients. If employed, such equipment must be kept scrupulously clean. If the home is constructed over a crawl space, a plastic vapor barrier over exposed soil and keeping foundation vents open will reduce moisture and mold. If a basement is damp or tends to flood, carpeting and furnishing the basement should be avoided, a dehumidifier employed at all times and any standing water evacuated as quickly as possible. Chemical and physical measures to control indoor mold will usually fail if relative humidity and condensation are not reduced.

*House dust mites.* The fecal residue of dust mites, belonging to the genus *Dermatophagoides,* is the major source of allergen in house dust. Their principal food source is exfoliated human skin scale. Consequently, mites exist in reservoirs of skin scale: bedding, fabric covered furniture, soft toys and carpeting.[1] Aside from availability of food, the major factors influencing mite growth are temperature and humidity. To replicate, a relative humidity of 50% or greater (absolute humidity of >8 g/kg) is required.[5] Recent changes in home construction and housecleaning methods including more energy-efficient buildings with reduced ventilation and increased humidity, wall-to-wall carpeting, wider use of furnished basements, central heat, and use of cool water detergents for laundering bedding all favor dust mite growth.

Vigorous measures are required to reduce dust mite allergen. Ordinary vacuuming and dusting have little effect.[6] To achieve effective reduction in mite allergen, the bedroom and main living areas (eg, family room) should be simply furnished without carpets. Whenever feasible, mite-sensitive patients should avoid vacuuming or making beds. If vacuuming is required, use a vacuum cleaner with an efficient double filtration system. Patients who do their own cleaning should wear a face mask while cleaning and for 10 to 15 minutes afterward. Better still, housecleaning should be carried out while the patient is not at home. There is no evidence that electrostatic purifiers and conflicting evidence that HEPA air purifiers reduce symptoms in dust mite allergy.[7,8] At most, such filters are of modest benefit.[9] Likewise, cleaning heating ducts is of no demonstrated value. On the other hand, air conditioning reduces mite numbers by lowering indoor humidity. Humidifier use should be minimized.

All mattresses, box springs and pillows in the patient's bedroom must be encased in zippered, allergen-proof encasings. Vinyl encasings are effective, but cloth encasings with semi-permeable plastic backing are more comfortable and durable. If a mattress is old, replacement should be considered but even new "hypoallergenic" mattresses

and pillows must be encased since mite colonization occurs within weeks. Bedclothes should be washed in hot water (greater than 130 degrees F) at least every 2 weeks to remove mite allergen and kill mite ova. Quilts and comforters should be avoided or covered with an allergen-proof duvet. Stuffed toys that cannot be washed should be eliminated or replaced with a washable toy. Avoid storing items under beds.

Mites may be abundant in fabric covered furniture and presently, no effective means exist in the US for eliminating mites in upholstered furniture. Plastic, leather or wood furniture is best. When fabric upholstered furniture cannot be avoided, a 3% tannic acid solution can be used to denature mite and other allergens on these furnishings. This solution does not kill mites, however, so mite allergen reaccumulates rapidly and requires retreatment.[1]

Since thorough vacuuming removes only surface dirt and mite allergen, carpeting is best removed from the bedroom and replaced with smooth finish wood, tile or vinyl flooring.[6] If this is impractical, one may consider treating carpets with Acarosan®, a special carpet treatment containing benzyl benzoate.[10] However, the effects of treatment do not appear to be maintained for long periods and are not dramatic.[11] If Acarosan® is used, it should be repeatedly brushed into the carpet over 12 hours followed by careful vacuuming to remove all powder. Efficacy of allergen removal and need for re-treatment can be ascertained with a kit (Acarex®) that measures guanine, a fecal excretion product of dust mites, in house dust. Carpeting installed over a concrete slab is a particularly potent source of mite allergen and is best avoided, if possible. Acarosan® and other treatments may not control mite allergen in carpets that are damp from seepage or condensation.[12]

*Animal allergens.* Because of the popularity of indoor pets, cats, dogs and other domestic animals are important causes of allergic rhinitis. All warm-blooded animals, including birds, potentially are capable of sensitizing susceptible allergic patients. Positive skin test reactivity to cat and dog is found in 1/4 to 1/3 of allergic individuals, and animal allergens are a significant occupational hazard for workers exposed to mice, rats, guinea pigs, etc. Farm workers may develop sensitivities to farm animals. In inner city areas, rodent urine may be an important source of animal allergen. Though furs processed for use in clothing are no longer allergenic, feather products retain significant allergenicity. Because allergen-bearing particles of animal origin are generally quite small and low density, they remain suspended in air for extended periods and disseminate widely in homes and other facilities. Symptoms of allergic rhinoconjunctivitis may occur within minutes of entering a contaminated area.

The major antigen in cat allergen, *Fel d* I is found on cat skin/dander and in saliva and urine. Cat albumin is also allergenic but a less frequent cause of sensitivity than *Fel d* I. *Fel d* I and albumin are common to all breeds of cats. Cat allergen has been identified in homes and other locations where cats were never present and occasionally may reach concentrations found in homes where cats are kept.[2] This is presumed to be passive contamination from cat allergen borne on clothing. Such contamination may be an unsuspected cause of symptoms in sensitive individuals.[13]

Allergy to dogs, though common, appears less frequent than cat allergy. The major dog allergen, *Can f* I, is found in dog skin/dander and saliva and is present in varying amounts in all breeds tested. Still, many dog-sensitive patients claim to respond differently to various breeds of dogs or even specific dogs of a single breed. Like cat allergen, *Can f* has been found in rooms in which dogs were never present.[2,13] Analysis of the location of this allergen suggests passive transport on clothing. Levels may be sufficient to elicit symptoms in sensitized patients.[13]

Avoidance clearly remains the most effective way of dealing with animal sensitivity. If the pet producing symptoms is in the home, the patient and family should be counseled to consider removing the animal to avoid possible progression of symptoms. A "trial" removal of a pet for a few days or even weeks may be of little value or, worse, misleading since, in the case of cat allergen, an average of 20 weeks (and in some cases much longer) is required for allergen levels to reach levels found in homes without cats. This decrease can be accelerated by removing carpeting and discarding upholstered furniture, but this is generally impractical. Steam cleaning of carpets and upholstered furniture following removal of the animal seems to have little advantage over routine vacuuming with a double filter vacuum system. If despite vigorous counseling the patient and/or family refuses to remove the pet, confining the animal to an uncarpeted room (other than the bedroom) with a HEPA or electrostatic air purifier may reduce airborne allergen in the remainder of the home by 90%.[13] Some[14,15] but not all[16] studies have demonstrated reduced airborne cat allergen by washing the animal on a weekly basis. Whether frequent bathing of dogs reduces airborne dog allergen is uncertain. Litter boxes should be eliminated whenever feasible or placed in an area unconnected to the air supply for the rest of the home. If not removed, caged pets (birds, rodents, guinea pigs, etc.) also should be kept in an uncarpeted area of the home and remote from the patient's bedroom.

*Insect allergens.* Allergic rhinoconjunctivitis and asthma have been reported with exposure to debris of numerous insects including cockroaches, crickets, caddis flies, house flies, midges and moths. Because of their prevalence and indoor living habits, cockroaches are a significant cause of respiratory allergy, especially in inner city populations. Up to 60% of dust-sensitive patients from urban areas react to cockroach allergens. The major cockroach allergens, *Bla g* I and *Bla g* II, are found on the insect's body and its feces. Cockroach allergen is most abundant in kitchen floor dust and may

reach high levels in poorly maintained homes and apartments. Eliminating cockroaches requires careful sanitation such as not allowing food to stand open or remain on unwashed dishes, promptly wiping up food spills and storing garbage in tightly closed containers. Use of "roach traps" has been advocated since these permit removal of the allergen-containing bodies of the insects. If the infestation is heavy, however, repeated applications of insecticide by a professional exterminator or changing homes may be required.

*Miscellaneous and non-allergic factors.* A host of other environmental factors may incite or worsen rhinitis. Agents producing occupational asthma by IgE-dependent mechanisms commonly trigger nasal and ocular symptoms. Because asthma may be more debilitating, occupational rhinoconjunctivitis is often ignored. Measures to control occupational asthma usually reduce occupational rhinitis and will not be discussed further. Rhinitis has also been attributed to irritants eg, tobacco smoke, formaldehyde, perfume and other strong odors, and newspaper ink. Some persons display increased "sensitivity" to environmental tobacco smoke.[17] The headache, nasal and chest symptoms do not appear to involve IgE. Avoidance of passive tobacco smoke is mandatory for such patients. The capacity of formaldehyde to cause stinging and burning of the eyes and nose, lacrimation, and decreased nasal mucous flow is well-established.[18] This appears to be irritant effect since even prolonged, high-level formaldehyde exposure only rarely results in IgE to formaldehyde-protein conjugates and this does not correlate with clinical symptoms.[18,19] Since respiratory symptoms generally occur at concentrations well above those at which the odor of formaldehyde is detectable, it is unlikely that formaldehyde would be an unsuspected cause of rhinitis. Perfume and newsprint are claimed to elicit symptoms in some rhinitis sufferers. The mechanism is uncertain but felt to be irritant.[20] If troublesome, avoidance is indicated.

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## Pharmacologic Therapy

**32. Pharmacologic management should be considered in relation to the etiology and pathophysiology of the condition. If it is possible to anticipate the onset of symptoms, eg, seasonal rhinitis or rhinitis triggered by sporadic exposure, initiating prophylactic use of medications may lessen the impact of such exposure on the patient.**

*Antihistamines*

33. **Oral antihistamines are effective in reducing symptoms of itching, sneezing, and rhinorrhea, and are first line therapy for treatment of allergic rhinitis. However, oral antihistamines have little objective effect on nasal congestion. Antihistamines reduce symptoms of allergic conjunctivitis, which are often associated with allergic rhinitis.**

*Issues with sedation/performance impairment*

34. **Sedation and performance impairment are undesirable and potentially dangerous side effects of first generation antihistamines. Consequently, second generation antihistamines that are associated with less risk or no risk for these side effects should usually be considered before sedating antihistamines for the treatment of allergic rhinitis, and are even mandated in some segments of the transportation industry. Studies have demonstrated that many patients may not perceive performance impairment that is associated with first generation (classical) antihistamines. In the majority of states, patients taking sedating antihistamines are legally considered "under the influence of drugs."**

*Adverse cardiac effects of some second generation antihistamines*

35. **Some older non-sedating antihistamines such as astemizole and terfenadine (the latter withdrawn from the US market in 1998) may cause prolongation of the QTc interval that may lead to the ventricular arrhythmia torsade de pointes especially with overdose, administration with certain concomitant medications (eg, some macrolide antibiotics, azole anti-fungal agents), and in the presence of severe liver disease.**

Although many chemical mediators of inflammation play a role in producing the various symptoms and signs of allergic rhinitis, there is strong evidence that histamine is a mediator of major importance in this disorder. Once released from mast cells and basophils, histamine dilates blood vessels, increases vessel permeability, and stimulates sensory nerve endings and reflexes through the parasympathetic system that cause glandular secretion. Histamine given intranasally can reproduce all the symptoms of allergic rhinitis (sneezing, pruritus, rhinorrhea, blockage),[1] and therefore, $H_1$ histamine receptor antagonists (ie, $H_1$ antihistamines) are generally effective in controlling many of the symptoms of allergic rhinitis. Antihistamines are less efficacious (if at all) in other forms of rhinitis (eg, vasomotor, infectious), thereby making it important to establish a correct diagnosis before initiating therapy.

A major limitation of the use of the first generation (classical) antihistamines has been sedation. However, second generation antihistamines have been developed that in recommended doses significantly reduce or eliminate this problem. The availability of these second generation antihistamines has greatly improved the usefulness of antihistamines as pharmacotherapeutic agents since patients who otherwise would avoid antihistamine therapy due to sedation, can now utilize them and obtain significant benefit.

*Mechanism/pharmacokinetics.* Both first and second generation $H_1$ antihistamines are pharmacologic antagonists of histamine at the $H_1$-receptor site and act by competitively binding to the $H_1$ receptor, thus blocking the $H_1$ response. Certain $H_1$-receptor antagonists have metabolites that are active and as relevant, or even more relevant, than their parent compound (eg, loratadine, terfenadine, astemizole, hydroxyzine).[2] In addition to being antagonists of histamine, some of the second generation antihistamines may inhibit release of mast cell and basophil inflammatory mediators resulting in anti-allergic and anti-inflammatory effects. Some of this action may be due to the ability of some, but not all, antihistamines to prevent release of histamine after antigen challenge.[3]

Oral antihistamines are readily absorbed, with peak serum concentrations usually occurring within 2 to 3 hours after a dose. The metabolism of all first generation and several second generation antihistamines is via the hepatic cytochrome P450 system. Clearance rates of $H_1$ antagonists are quite variable (2 hours to 10 days) but generally, serum elimination half-lives are shorter in children than in adults, longer in the elderly, but in all ages serum half-lives are less than their duration of bioactivity. In studies of the ability of antihistamines to suppress histamine- or antigen-induced wheal and flare reactions, peak suppression by antihistamines usually occurs 5 to 7 hours after an oral dose. Histamine suppressive effects can persist for up to 24 to 36 hours and longer (eg, hydroxyzine, cetrizine), even when serum concentrations of the parent compound have declined to their lowest limit of detection, probably secondary to the presence of active metabolites and/or high tissue drug concentrations.[2] Astemizole is unique in that it binds to peripheral $H_1$-receptor sites with far greater affinity than do other $H_1$-receptor antagonists. As a result, a single dose of astemizole produces serum and tissue levels that persist for days to weeks, with skin test suppression noted to last up to at least 6 weeks.[4]

*Clinical efficacy.* Oral antihistamines are capable of decreasing all the symptoms of allergic rhinitis (especially sneezing, itching, and nasal discharge) but are least effective in relieving nasal blockage. Numerous first generation antihistamines are available over-the-counter or by prescription. All first generation antihistamines belong to one of 6 different chemical classes based on their specific side chain substitution. There generally is little difference in clinical efficacy amongst these classes, although chlorpheniramine (alkylamine class) and hydroxyzine (piperazine class) have

been found to be more effective in certain studies when compared to other first generation antihistamines.[5]

*Adverse Effects.* Many patients with significant allergy symptoms would rather tolerate their symptoms than use an antihistamine for relief because of the associated sedation, performance impairment and other adverse effects. This phenomenon has great inter-patient variability. Some patients will be completely free of drowsiness, whereas others are heavily sedated even after a small dose. After continued use of antihistamines, it has been reported that some individuals may develop tolerance to sedation or performance impairment effects from these agents, but other studies report little or no reduction in these side effects.[6]

Many patients deny sedation with the use of first generation antihistamines but an increasing body of information suggests that CNS impairment can exist even when sedation is not reported.[7] The major objective parameters used to detect CNS effects with antihistamines are reduced sleep latency (greater sleepiness) and performance impairment. Measurements used to assess performance impairment include reaction time, visual-motor coordination, arithmetical exercises, memory, learning, and driving tests (eg, ability to avoid obstacles and drive in a straight line). Using these measurements, first generation antihistamines have been clearly associated with CNS depression and impairment, and these effects can be independent of any subjective complaints by the patient. First generation antihistamines have been demonstrated to impair children's learning and academic performance.[8,9] First generation antihistamines also may cause driving impairment and fatal automobile accidents.[10–14] One large epidemiologic study has demonstrated that drivers responsible for fatal automobile accidents were 1.5 more likely to be taken first-generation antihistamines than drivers killed but not responsible for accidents.[15] In the majority of states, patients taking sedating antihistamines are legally considered "under the influence of drugs."[16] Workers taking first generation antihistamines have decreased work performance and productivity and are also more likely to be involved in occupational accidents, a risk greater than that attributable to narcotics and sedative hypnotics.[17–20] Other CNS active substances such as alcohol, sedatives, hypnotics and anti-depressants may potentiate the performance impairment from antihistamines. Similar effects on performance and sleep latency have not been observed with the standard doses of available "non-sedating" second-generation antihistamines described below. Consequently, second generation antihistamines that are associated with less risk or no risk for these side effects should usually be considered before sedating antihistamines for the treatment of allergic rhinitis, and are even mandated in some segments of the transportation industry.

Adverse effects other than drowsiness can occur with first generation antihistamines, and are related mainly to the peripheral and central cholinergic nervous system; antiserotonin and anti-bradykinin effects may also be important. Peripheral anticholinergic effects including dry mouth, dry eyes, and urinary retention are not uncommon; tachycardia, impotence, worsening of glaucoma, and headache also rarely occur. Central effects in addition to somnolence may include coma, seizures, dyskinesia and behavioral changes. An atropine-like "psychosis" can result from overdose.

*Second-Generation Antihistamines.* Second generation $H_1$-receptor antagonists are relatively lipophobic, have a large molecular size, and possess an electrostatic charge, all of which contribute to poor penetration of the CNS, thereby decreasing or eliminating sedation. Other advantages of these second generation antihistamines include preferential binding to peripheral $H_1$-receptors over central ones and the feature of possessing minimal antiserotonin, anticholinergic and alpha-adrenergic blocking activity.[21]

The present list of available second generation antihistamines includes astemizole, loratadine, cetirizine, and fexofenadine; terfenadine marketing in the US ceased in 1998 (Table 3). These agents have proven effective in decreasing symptoms of sneezing, itching, and nasal discharge, and the ocular symptoms of allergic conjunctivitis often associated with allergic rhinitis. Although they possess an improved safety profile, most evaluations show, however, that this new class of antihistamines is no more effective than the first generation $H_1$-receptor antagonists.[22]

Pharmaceutical manufacturers recommend the following adult doses to provide optimal efficacy with minimal likelihood of causing sedation or other adverse effects: astemizole, 10 mg QD; cetirizine, 5 to 10 mg QD; fexofenadine, 60 mg BID; and loratadine 10 mg QD. Cetirizine, fexofenadine and loratadine have serum half-lives and duration of histamine-induced wheal and flare suppression in the range of 8 to 24 hours. Astemizole has an initial half-life of 7 to 9 days, and a

Table 3. Second Generation Oral Antihistamines

| Agent | Usual adult dosing* | Available with decongestant | Reduce dose with liver disease? | Reduce dose with renal impairment? | Pregnancy category |
|---|---|---|---|---|---|
| Astemizole* (Hismanal®) | 10 mg QD | No | Avoid | No change | C |
| Cetirizine (Zyrtec®) | 5–10 mg QD | No | 5 mg QD | 5 mg QD | B |
| Fexofenadine (Allegra®) | 60 mg PO BID | Yes | 60 mg QD | No change | C |
| Loratadine (Claritin®) | 10 mg PO QD | Yes | Start at 10 mg QOD | Start at 10 mg QOD | B |

* For pediatric dosing, see Table 6.

terminal half-life of 19 days, accounting for its ability to suppress skin test responses for a month or longer in many subjects.

Although comparison trials of second generation agents are limited in number, overall clinical efficacy and patient acceptance appear similar among the different non-sedating or less sedating preparations. Astemizole does have a longer time for peak onset of symptom relief making it less useful as a prn medication.[23] When comparing antihistamine therapy with intranasal corticosteroids, both first and second generation oral antihistamines are less potent in improving allergic rhinitis symptoms, although, they provide more relief of ocular symptoms. Intranasal cromolyn and intranasal antihistamines provide comparable control of allergic rhinitis. Therefore, while antihistamine therapy is useful in the treatment of mild to moderate allergic rhinoconjunctivitis, patients with more severe disease will usually require an intranasal corticosteroid or combination regimen.[24]

Administration of standard doses of some second generation antihistamines (astemizole, fexofenadine, loratadine) result in no greater incidence of sedation than that seen with placebo. Therefore, these preparations have been termed "nonsedating." However, some nonsedating agents have been reported to cause sedation or CNS dysfunction at higher than usual doses (eg, with loratadine), or at recommended doses in certain individuals.[25] The incidence of sedation with the second generation antihistamine cetrizine at a standard adult dose of 10 mg is higher than with placebo, although it is significantly less sedating than most first generation antihistamines.

Non-sedating antihistamines have not been shown to potentiate the CNS effects of alcohol or diazepam. Astemizole has the additional property of appetite stimulation in certain patients resulting in unwanted weight gain. Previous concerns about the potential adverse effects of antihistamines in patients with asthma have not been substantiated with the second generation antihistamines. In fact, some other non-sedating antihistamines appear to have some mild anti-asthma effects[26] (see "Summary Statement #47").

Astemizole (and the no longer marketed terfenadine) can rarely produce serious cardiovascular effects if used in doses that exceed the manufacturer's recommendations. Patients with hepatic dysfunction, hypokalemia, hypocalcemia, congenital QT syndrome, or who are using certain concomitant medications that interfere with the metabolism of astemizole (or terfenadine), are also at risk.[27] The cardiovascular events seen include ventricular tachyarrhythmias (particularly torsades de pointes but also ventricular tachycardia, and ventricular fibrillation or flutter), cardiac arrest, sudden near death and death. The serious rhythm changes that occur are likely due to prolongation of the QT interval as a direct effect of elevated tissue levels of the parent compound of these second generation antihistamines, and, because of this prolongation, place the patient at risk for a ventricular arrhythmia. Cetirizine, fexofenadine, and loratadine have not been shown to be associated with QT interval changes or rhythm disturbances.[28] Astemizole should not be prescribed at greater than the recommended dose, or with concomitant medications that could inhibit astemizole metabolism by the cytochrome P450 3A4 isoenzyme system of the liver. Drugs that should be avoided or approached with caution include azole anti-fungals (fluconazole, itraconazole, miconazole), some macrolides (eg, erythromycin, clarithromycin) and ciprofloxacin. Patients using astemizole (or existing supplies of terfenadine) should inform all physicians that they are taking these agents when other medications are prescribed. Physicians should avoid giving these antihistamines to alcoholic patients or anyone suspected of significant liver disease. The dose of the antihistamines should always be decreased to the lowest dose that controls the symptoms.

*Combined therapy with first and second generation antihistamines.* In a strategy intended to reduce costs of antihistamine therapy while avoiding daytime sedation and performance impairment, it has been advocated that one may dose a non-sedating second generation antihistamine (that would otherwise be dosed twice daily) only once daily in the morning, followed by a first generation (and cheaper) antihistamine in the evening. The rationale for this strategy assumes that daytime sedation and performance impairment will be avoided if a first generation antihistamine is administered only at bedtime. However, studies have demonstrated that first generation antihistamines dosed only at bedtime may cause significant daytime sedation, decreased alertness and performance impairment,[29–34] in part because antihistamines and their metabolites have prolonged plasma half-lives and their end-organ effects persist even longer than plasma levels of the parent antihistamine agent. Consequently, an "AM/PM" dosing regimen combining a second generation agent in the AM with first generation agent in the PM is an ineffective strategy for avoiding daytime sedation and performance impairment from antihistamine treatment.

*General principles of antihistamine therapy.* There are certain general principles of antihistamine use that should be followed when treating patients with allergic rhinitis. Since neither first nor second generation oral antihistamines are very effective in relieving nasal blockage, a decongestant agent (eg, pseudoephedrine, phenylpropanolamine) or a topical nasal corticosteroid may need to be added to oral antihistamine therapy. Many combination antihistamine-decongestant formulations are available in a fixed dose preparation which allow the patient the ease and convenience of taking just one tablet. The drawbacks of these combination agents are: (1) certain patients are unable to tolerate the fixed dose of the decongestant (eg, cause stimulation), and (2) the dose of one ingredient cannot be adjusted, if necessary, without changing the dose of the second ingredient which may not need to be changed. For these reasons, using a separate antihistamine and sep-

arate decongestant can have the advantage of permitting one medication to be titrated independently of the other.

Patients need to be educated that for optimal results, antihistamines should be administered either prophylactically (2 to 5 hours before allergen exposure) or on a regular basis if needed chronically. Although antihistamines are effective on a PRN basis, they work best when taking them in a maintenance fashion.

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*Intranasal Antihistamines*

**36. Intranasal antihistamines are effective for treatment of allergic rhinitis. These agents are appropriate for use as first-line treatment for allergic rhinitis, and in contrast to most oral antihistamines, may help reduce nasal congestion. However, patients may perceive them as having a bitter taste and because significant systemic absorption may occur, they may be associated with resultant sedation in some patients.**

Intranasal antihistamines have been approved for the treatment of the symptoms of seasonal allergic rhinitis such as rhinorrhea, sneezing and nasal pruritus. These agents are appropriate for use as first line treatment for the symptoms of allergic rhinitis, or as part of combination therapy with nasal corticosteroids or oral antihistamines.

Astelin (azelastine hydrochloride) is the first intranasal antihistamine preparation approved for use in the US.[1–3] It is formulated as a 0.1% aqueous solution in a metered spray delivery device. Recommended dosing is 2 sprays in each nostril BID for patients ≥12 years. An onset of action has been demonstrated within 3 hours versus placebo. Several studies have demonstrated efficacy that is at least equal to oral antihistamines. In clinical trials, 19.7% of patients complain of bitter taste, and 11.5% report somnolence.[4] In addition, azelastine nasal has been reported to reduce nasal congestion.[1–3]

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*Oral and Nasal Decongestants*

**37. Oral decongestants, such as pseudoephedrine or phenylpropanolamine, can effectively reduce nasal congestion produced by rhinitis, but can cause insomnia, loss of appetite or excessive nervousness. In addition, these agents should be used with caution in patients with certain conditions, eg, arrhythmias, angina pectoris, some patients with hypertension and hyperthyroidism. Topical sympathomimetics can be useful for short-term (eg, 2 to 3 days) therapy for nasal congestion associated with rhinitis.**

Oral alpha-adrenergic agents, such as pseudoephedrine, phenylephrine and phenyl-propanolamine, cause nasal vasoconstriction. These oral preparations are useful in the management of vasomotor rhinitis and relief of nasal congestion due to upper respiratory infections. In addition, studies have demonstrated that the efficacy of these drugs in combination with antihistamines in the management of allergic rhinitis is superior to the efficacy of either drug alone.[1] These combinations have also been shown to be useful for eosinophilic nonallergic rhinitis and in some individuals with nasal hyperreactivity with diffuse rhinorrhea or post nasal discharge.[2]

Some patients may experience systemic side effects from oral alpha-adrenergic agents which include elevated blood pressure, palpitations, loss of appetite, tremor and sleep disturbance.[2] Pseudoephedrine is less likely to cause elevated blood pressure than phenylpropanolamine.[3,4] Oral alpha-adrenergic agonists should be used with caution in patients with certain conditions, eg, arrhythmia, coronary heart disease, hypertension, hyperthyroidism, glaucoma, diabetes, and urinary dysfunction.

Topically applied sympathomimetic decongestant alpha-adrenergic agonists can be catecholamines such as phenylephrine or imidazoline agents such as oxymetazoline or xylometazoline. These medications cause nasal vasoconstriction and decreased nasal edema, decreased edema but have no effect on the antigen provoked nasal response.[2] Also, alpha-adrenergic vasoconstrictors reduce nasal obstruction but do not alter itching, sneezing or nasal secretion. Topical decongestants can decrease nasal airway resistance and nasal blood flow[5,6] but usually do not cause systemic sympathomimetic reactions.

Topical sympathomimetics can lead to rebound nasal congestion (rhinitis medicamentosa) with rhinitis medicamentosa which usually occurs after 5 to 10 days of treatment.[7] This can occur due to downregulation of alpha adrenoreceptors which makes them less sensitive to endogenously released noradrenalin and exogenously applied vasoconstrictors. Topical sympathomimetics can be useful for short-term (eg, 2 to 3 days) therapy for nasal congestion associated with acute bacterial or viral infections, allergic rhinitis, and eustachion tube dysfunction.[2]

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*Nasal Corticosteroids*

**38. Nasally inhaled corticosteroids are the most effective medication class in controlling symptoms of allergic rhinitis. They are particularly useful for treatment of more severe allergic rhinitis and may be useful in some other forms of rhinitis. Except for intranasal dexamethasone, these agents are generally not associated with significant systemic side effects in adults. Although local side effects are minimal if the patient is carefully instructed in the use of this class of drugs, nasal irritation and bleeding may occur, and nasal septal perforations are rarely reported. Intranasal corticosteroids should be considered before initiating treatment with systemic corticosteroids for the treatment of severe rhinitis.**

*Oral and Parenteral Corticosteroids*

**39. A short (3 to 7 day) course of oral corticosteroids may be appropriate for the treatment of very severe or intractable nasal symptoms or to treat significant nasal polyposis. However, the use of parenteral corticosteroids, particularly if administered recurrently, is discouraged because of greater potential for long-term corticosteroid side effects.**

The main mechanism by which corticosteroids relieve the symptoms of allergic rhinitis is through their anti-inflammatory activity.[1] The concept of delivering steroids topically to the nasal airway was developed in order to minimize potential steroid side effects of using systemic corticosteroids. Nasal steroids are variously available in propellant metered dose inhalers and/or aqueous suspensions or glycol solutions (Table 4).

Nasal steroids are effective in controlling the four major symptoms of allergic rhinitis, including sneezing, itching, rhinorrhea and nasal blockage. In clinical trials nasal steroids are more efficacious than nasal cromolyn sodium,[2] or oral antihistamines.[3–5] However, one study has reported that at least 50% of patients need to take both nasal corticosteroids and oral antihistamines to adequately control symptoms of seasonal allergic rhinitis.[6] Nasal steroids have also been shown to be effective in the treatment of certain types of non allergic rhinitis, especially NARES.[7] Because a patent nasal airway is necessary for optimal intranasal delivery of nasal steroids, a topical decongestant spray may be necessary for several days when nasal steroids are introduced.

The most common side effects encountered using nasal steroids are due to local irritation. This may present with burning or stinging and is more commonly associated with glycol-containing solutions.

Nasal bleeding is also seen with use of intranasal steroids. This is usually apparent as blood-tinged blown secretions but nasal septal perforation has also been rarely reported with long-term use of intranasal steroids.[8] This may occur secondary to local septal trauma from the spray in combination with the vasoconstrictor activity of the steroid. The use of aqueous preparations, longer extension applicators, and lower velocity sprays should help reduce local trauma to the nasal septum. Patients should always direct the spray away from the nasal septum to prevent the repetitive direct application to the septum. The nasal septum should be periodically examined to assure that there are no mucosal erosions that may precede development of nasal septal perforations that are rarely associated with intranasal corticosteroids. Nasal biopsies in subjects with perennial allergic rhinitis suggest no signs of tissue atrophy or change after five years of therapy.[9] The judicious use of nasal steroids in children is indicated with frequent re-evaluation of the patient to assess further need for nasal steroid use.

Current studies in adults suggest minimal systemic side effects with administration of nasal steroids in recommended doses (except dexamethasone which is capable of producing minor systemic steroid effects). Studies of new steroid preparations even in relatively high doses demonstrate no sys-

Table 4. Nasal Corticosteroid Sprays

| Agent | Trade Name(s) | Dose Per Inhalation | Base Initial Adult Dosage* |
|---|---|---|---|
| Beclomethasone dipropionate | Beconase®<br>Beconase AQ®<br>Vancenase Pockethaler® | 42 μg | 1–2 sprays per nostril 2×/day |
| | Vancenase AQ Double Strength® | 84 μg | 1–2 sprays per nostril 1×/day |
| Budesonide | Rhinocort® | 32 μg | 2 sprays per nostril 2×/day or 4 sprays per nostril 1×/day |
| Flunisolide | Nasarel®<br>Nasalide® | 25 μg | 2 sprays per nostril 2×/day |
| Fluticasone propionate | Flonase® | 50 μg | 2 sprays per nostril 1×/day or 1 spray per nostril 2×/day |
| Mometasone | Nasonex(AQ)® | 50 μg | 2 sprays per nostril 1×/day |
| Triamcinolone acetonide | Nasacort®<br>Nasacort AQ® | 55 μg | 2 sprays per nostril 1×/day |
| Dexamethasone sodium phosphate | Dexacort® | 84 μg | 2 sprays per nostril 2–3×/day |

temic steroid effect on hypothalamic-pituitary-adrenal axis as assessed by morning cortisol concentrations, cosyntropin stimulation and 24-hour urinary-free cortisol excretion.[10] Despite the not uncommon occurrence of candida in the oropharynx in association with the use of inhaled steroids for asthma, candida overgrowth seems uncommon with intranasal steroid administration.

There have been reports of a possible association between the development of posterior subcapsular cataracts and the use of intranasal or inhaled steroids,[11] but this association has not been confirmed by other studies.[12] Concomitant use of systemic steroids in some subjects receiving intranasal steroids confounds interpretation of studies that attempt to address the question of this possible association. Studies of newer intranasal steroids in prospective trials over 24 weeks of treatment have not demonstrated the development of lenticular changes consistent with posterior subcapsular cataracts.[13] Based upon available studies, patients receiving standard doses of nasal steroids are not at increased risk for glaucoma.[14] Although steroids as a class of drugs are not thought to be teratogenic in humans, safety during pregnancy has not been established and benefit/risk ratio should be carefully considered. (See section on Rhinitis and Pregnancy under Summary Statement #48) In children, concerns about possible adverse effects on growth raise special considerations (see section on treatment of children under Summary Statement #48).

Although systemic steroids are not appropriate for chronic rhinitis therapy, short courses of systemic steroids may be very effective in severe cases that are unresponsive to other modalities of treatment, and especially those cases associated with polyposis. When systemic steroids are necessary, it is preferable to administer short (5 to 7 day) bursts of short-acting oral steroids such as prednisone or methylprednisolone. At doses equivalent to 40 mg/day of prednisone in adults, adrenal suppression is avoided. Depot injections of steroids may be effective for rhinitis symptoms but may be associated with prolonged adrenal suppression and lack the flexibility of oral dosing. Consequently, parenteral corticosteroid administration (particularly if recurrent) is discouraged because of greater potential for long-term corticosteroid side effects.

Intraturbinate injection of corticosteroids is not recommended for treatment of rhinitis because the potential benefits do not outweigh the potentially serious side effects of cavernous vein thrombosis and blindness,[15] and alternatives such as nasal and oral steroids are available.

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*Intranasal Cromolyn*

**40. Intranasal cromolyn sodium is effective in some patients in controlling symptoms of allergic rhinitis and is associated with minimal side effects.**

A 4% solution of cromolyn sodium, USP, was introduced into the US in 1983 as Nasalcrom for topical intranasal treatment of allergic rhinitis. Cromolyn sodium has been shown to inhibit the degranulation of sensitized mast cells thereby preventing the release of mediators of the allergic response and of inflammation. Thus, it prevents the allergic event rather than alleviate the symptoms once the reaction has begun.[1–6] The protective effect of cromolyn against nasal antigen challenge persists for 4 to 8 hours after insufflation.[7]

Cromolyn sodium nasal spray is administered as a metered aerosol via a pump spray. Each spray contains approximately 5.2 mg of cromolyn so-

dium, and the starting dose is 1 spray in each nostril every 4 hours when the patient is awake until relief is evident; effect is normally noted within 4 to 7 days. Severe or perennial cases may require 2 weeks or more for maximum effect. Thereafter, the treatment is continued at whatever maintenance dose is effective for the remainder of the expected season or period of exposure. Since a patent nasal airway is a prerequisite, a decongestant may be necessary for a few days. The presence of obstructing nasal polyps calls for the use of measures other than cromolyn sodium.

Cromolyn sodium has no intrinsic antihistamine effect. Although reported to be most effective in patients with a high preseasonal serum IgE level, it can be of benefit in both seasonal and perennial allergic rhinitis. The protective effect of cromolyn sodium in preventing both the acute and late-phase allergic reaction is noteworthy, especially in treating individuals with predictable periods of exposure (eg, veterinarians). Pretreatment with cromolyn sodium before an allergen exposure will result in considerable diminution or ablation of the nasal allergic response. Patients who are given nasal cromolyn sodium must be instructed to use it before an anticipated allergen exposure and to use it on a regular basis during the season or period of exposure normally associated with allergic symptoms. In controlled studies, cromolyn is generally less effective than intranasal corticosteroids.

Cromolyn appears to be useful for the treatment of allergic rhinitis and because of its safety profile it should be considered in very young children and pregnancy.

Patient selection is critical. Its use should be begun as early in an allergy season as possible. The rationale for early therapy is prevention of mediator release from mast cells rather than treatment of the pathologic sequelae of such release. Because it is immediately effective (provided that the nasal passages are patent), it can be administered just before exposure in patients with allergic rhinitis caused by occupational allergens or animal danders, or in those who anticipate a limited allergen exposure. When patients with high serum IgE levels and strongly positive skin test reactions are begun on cromolyn prior to or early in their season, they are most likely to benefit. Patients who are already highly symptomatic may require the addition of an antihistamine-decongestant combination during the first few days of cromolyn treatment.

Side effects are usually minor, including sneezing (10%), nasal stinging or burning (4% to 5%), nasal irritation (less than 3%), and epistaxis (less than 1%). No septal perforations or nasal crusting have been reported with the use of nasal cromolyn sodium. Teratogenicity of cromolyn sodium has not been demonstrated in animal studies, and nasal cromolyn sodium appears to be one of the safest preparations for use by the pregnant or pediatric patient with nasal allergy. Therefore, an advantage is its favorable safety profile.

There is no evidence that intranasal cromolyn will benefit patients with (1) vasomotor rhinitis; (2) NARES syndrome (nonallergic rhinitis with eosinophilia); or (3) with nasal polyposis.[8,9]

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*Intranasal Anti-Cholinergics*

**41. Intranasal anticholinergics may effectively reduce rhinorrhea but have no effect on other nasal symptoms. Although side effects are minimal, dryness of the nasal membranes may occur.**

Increased cholinergic hyperreactivity has been documented in nonallergic and allergic patients as well as in patients with recent upper respiratory tract infections.[1–4] A significant proportion of histamine- and antigen-induced secretion also appears to be cholinergically-mediated as well.[5,6] In addition to increased glandular secretion, parasympathetic stimulation also causes some vasodilation, particularly sinusoidal engorgement, which may contribute to nasal congestion.

Ipratropium bromide, oxitropium bromide, tiotropium bromide and glycopyrrolate are quaternary structured ammonium muscarinic receptor antagonists which are poorly absorbed across biological membranes. Ipratropium bromide, which has been most extensively studied in rhinitic patients, is poorly absorbed into the systemic circulation from the nasal mucosa; less than 20% of an 84 mcg per nostril dose is absorbed from the nasal mucosa of normal volunteers, induced-cold patients or perennial rhinitis patients.[7]

Controlled clinical trials have demonstrated that a quaternary agent such as intranasal fluorocarbon-propelled ipratropium bromide, does not alter physiologic nasal functions (eg, sense of smell, ciliary beat frequency, muco-

cilliary clearance, or the air conditioning capacity of the nose).[8,9]

Ipratropium bromide has been the most extensively studied intranasal anticholinergic agent. As a quaternary amine that minimally crosses the nasal and gastrointestinal membrane and the blood-brain barrier, ipratropium bromide exerts its effect locally on the nasal mucosa resulting in a reduction of the systemic anticholinergic effects (eg, neurologic, ophthalmic, cardiovascular, and gastrointestinal effects) that are seen with tertiary anticholinergic amines. Both a chlorofluorocarbon based nasal formulation (Atrovent MDI) developed in Europe and a new aqueous formulation (Atrovent Nasal Spray) developed in the United States are available for use.

The MDI formulation resulted in a relatively high incidence of nasal adverse events (dryness, bleeding, irritation and congestion) which may have been related to the concomitant administration of a fluorocarbon (a physical drying agent) with ipratropium bromide (a pharmacological drying agent). This has limited the clinical use of this formulation to those vasomotor patients with refractory rhinorrhea.[10]

Atrovent Nasal Spray sold in the U.S.A. is an isotonic aqueous solution with a pH of 4.7 that is compatible with nasal mucosa. It is available in two strengths, Atrovent (ipratropium bromide) Nasal Spray 0.03% for the symptomatic relief of rhinorrhea associated with allergic and nonallergic perennial rhinitis and Atrovent Nasal Spray 0.06%, for the symptomatic relief of rhinorrhea associated with the common cold.

The most frequently reported adverse events from ipratropium bromide nasal spray 0.03% compared to saline vehicle were mild, transient episodes of epistaxis (9% versus 5%) and nasal dryness (5% versus 1%). The dose of ipratropium bromide nasal spray 0.03% is 2 sprays (42 mcg) per nostril 2 or 3 times daily (total daily dose 168 to 252 mcg).

Ipratropium bromide has been demonstrated to be effective in reducing rhinorrhea in adults and children with perennial allergic and non-allergic rhinitis. Consequently, Atrovent (ipratropium bromide) Nasal Spray 0.03% alone or in combination with an antihistamine or a nasal steroid is indicated for treatment of rhinorrhea associated with allergic and nonallergic perennial rhinitis.[10–15] Ipratropium bromide is also useful in reducing rhinorrhea associated with eating, "gustatory rhinitis."[16]

Rhinorrhea associated with the common cold is due in part, to parasympathetic stimulation. Treatment with an anticholinergic agent such as ipratropium bromide (Atrovent nasal 0.06%) provides relief of rhinorrhea associated with the common cold.[17–21]

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*Oral Anti-Leukotriene Agents*

**42. Although there is evidence that oral anti-leukotriene agents may be of value in treatment of allergic rhinitis, their role in therapy for this condition needs to be defined by further study.**

Data suggest that some oral anti-leukotriene agents are beneficial in allergic rhinitis. In one study, montelukast 10 mg QD (a cysteinyl leukotriene antagonist) provided significant improvement in symptoms of seasonal rhinoconjunctivitis. The potential role of anti-leukotriene agents in treatment of allergic rhinitis needs to be defined by further study.

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**Allergen Immunotherapy**

**43. Allergen immunotherapy may be highly effective in controlling symptoms of allergic rhinitis. Patients with allergic rhinitis should be considered candidates for immunotherapy based on the severity of their symptoms, failure of other treatment modalities, presence of comorbid conditions, and of preventing worsening or possibly the development of comorbid conditions. Selection of the patient's immunotherapy extract should be based on a correlation between the presence of specific IgE antibodies (demonstrated by allergy skin testing or in vitro testing) and the patient's history. (See parameters on immunotherapy and on diagnostic testing).**

Individuals are appropriate candidates for immunotherapy if their rhinitis is allergic in origin, due to allergens for which potent extracts are available, and the exposure to those allergens is significant and unavoidable. Also, the symptom complex should be severe enough to warrant the time, expense and relative risk of immunotherapy. Other factors such as age, duration of illness, progression of illness, concurrent illnesses, concurrent medications, response to pharmacotherapy and patient acceptance should be considered by the physician in the decision to recommend allergen immunotherapy. With rare exceptions, immunotherapy is inappropriate in preschool children and senior citizens. Immunotherapy may be appropriate for those individuals with yearly recurrent seasonal symptoms, perennial symptoms due to allergic factors and/or significant progression of symptoms. Immunotherapy is generally unnecessary for the treatment of an individual with sensitivity to only a single seasonal allergen when the seasonal exposure to that allergen is relatively short. Severe pulmonary and cardiovascular disease may be a relative contraindication, as is the concurrent use of beta blockers. Initiation of immunotherapy during pregnancy is to be avoided but continuation of effective maintenance immunotherapy during pregnancy is advisable.

A most important shortcoming is the lack of available standardized allergenic extracts for all clinically important allergens. Ideally, patients should be treated with only potent standardized extracts, but this is not yet possible. Since standardized potent extracts are not available for all clinically important allergens, nonstandardized but potent extracts are used commonly in clinical practice. In the future, once a standardized potent extract becomes available for any given allergen, it should be utilized and the nonstandardized extract abandoned. It is unacceptable to routinely treat patients with allergenic extracts that are not potent.

It is common clinical practice to treat patients with more than one allergen. Often these allergens are combined into a single mixture for administration. When this is done, it is important to insure that the components are compatible and that the potency of each individual allergen is not diminished by the presence of the other components because of a chemical interaction or excessive dilution. Once immunotherapy is begun, every attempt should be made to administer the highest possible tolerated dose. Immunotherapy is most effective when a "high dose" is used. It should be recognized that while safe, immunotherapy is not totally without risk. Immunotherapy should only be administered by professionals familiar with the procedure, in a setting where they are prepared to deal with anaphylaxis. Patients should wait at least 20 minutes in such a setting since most cases of anaphylaxis from immunotherapy occur in this time frame. Periodic assessments of efficacy should be made. In general, if after one year the patient has not improved, then immunotherapy should be discontinued. In those patients benefiting from immunotherapy, treatment should not be indefinite. Generally three to five years of treatment will be appropriate for most patients. There will be individual variability.

The above discussion pertains to the use of immunotherapy for the treatment of allergic rhinitis only. Many patients have both allergic rhinitis and asthma. The presence of concomitant asthma may be the determining factor in whether or not a specific patient is a good candidate for immunotherapy. Presence of a comorbid condition such as asthma that may benefit from immunotherapy may be an additional indication for considering immunotherapy. However, severe, unstable asthma may be associated with increased risk for reactions and possibly mortality from immunotherapy. Consequently, asthma should be well controlled when immunotherapy doses are given.

In summary, immunotherapy is a unique and effective treatment modality for allergic rhinitis. The increasing costs associated with excellent drug therapy for allergic rhinitis place this form of therapy in a position of relative

cost-effectiveness as well. The proper selection of patients and treatment allergens is key to the appropriate and successful use of this therapy. The ongoing supervision of a trained allergist is necessary. Both physician and patient should have a clear understanding of the therapeutic goals.

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## Surgical Approaches for Co-Morbid Conditions

**44. Although there is no surgical treatment for allergic rhinitis per se, surgery may be indicated in the management of co-morbid conditions, eg, nasal obstruction from severe nasal septal deviation or recurrent refractory sinusitis.**

There is no surgical treatment for allergic rhinitis. Surgery, however, plays a role in the management of nasal obstruction and in the management of problems that are sequelae of rhinitis. In these situations, surgical consultation should be considered.

Sixty percent of patients with perennial allergic rhinitis have x-ray evidence of sinus disease, which may significantly contribute to the patients symptoms. (See "Practice Parameter on Sinusitis"). Patients with coexisting sinusitis will often require antibiotics and some will require surgical intervention. Even though they seldom occur, complications of sinusitis may lead to permanent loss of vision or be life threatening. Complications can be classified as local, orbital and intracranial or combinations of these three types.

Allergic rhinitis causes swelling of the nasal mucosa. The effect of swelling on nasal function depends on the structure of the nasal cavity. For example a person with allergic rhinitis and an anterior septal deviation will become more obstructed compared to one without the septal deviation. Structural improvements in the airway may also permit greater access for topical medications. Whether cauterization, cryosurgery or laser reduction of turbinates helps the patient with allergic rhinitis by inducing submucosal fibrosis is unproven. Turbinate surgery in patients without allergic rhinitis provides mixed clinical results and has poor correlation with rhinomanometric changes.

In summary, although there is no specific surgical treatment for allergic rhinitis, surgery may be indicated for co-morbid conditions eg, severe nasal septal deviation or recurrent refractory sinusitis. Some patients with rhinitis benefit optimally from a dual approach which includes both medical management as well as surgery to improve nasal obstruction or aid in the management of concomitant sinusitis.

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## Important Considerations in Management

**45. Management of rhinitis should be individualized, based on the spectrum and severity of symptoms, with consideration of cost effectiveness and utilization of both step-up and step-down approaches. More severe rhinitis may require multiple therapeutic interventions, including: (1) use of multiple medications, (2) evaluation for possible complications, and (3) instruction in and/or modifications of the medication or immunotherapy program. Similar to other chronic diseases, appropriate follow-up of patients with allergic rhinitis on a periodic basis is recommended.**

## Education of Patients and Caregivers

**46. Education of the patient and/or the patient's caregiver in the regard to the management of rhinitis is essential. Such education maximizes compliance and the possibility of optimizing treatment outcomes.**

After initiation of therapy, appropriate follow-up for patients with rhinitis is essential. This optimizes the chances that a patient will benefit from the broad array of therapeutic approaches available, and that possible complications from rhinitis or its treatment are identified and addressed. At these visits, education and compliance are critical elements.

Maximum therapeutic responses require patients who are compliant with recommendations. Patient compliance with physicians' recommendations for therapy is more likely in patients who understand their disease, the various available treatment options, and the likelihood of success of each possible treatment. This demands that the patient establishes a relationship of trust with, and confidence in their physi-

cian. It is important to educate both the patient and relevant family members regarding the nature of the disease and available treatments. This should include general information regarding the symptoms, causes and mechanisms of rhinitis. In addition, education about means of avoidance, immunotherapy, and drug therapy must be provided. It is vital that patients understand the potential side effects of therapy, especially drug side effects, in order to insure that patients do not abruptly discontinue beneficial therapy but rather communicate adverse events to their physician so they can deal with them in a manner best for the patient. It is also important to provide education to patients about complications of rhinitis including sinusitis, and otitis media, and about comorbid conditions such as nasal polyps. They should be aware of how such complications are recognized and how they are treated. Patients need to be aware of the potential negative impact of rhinitis on quality of life and potential benefits of complying with therapeutic recommendations. Patients must also have realistic expectations for the results of therapy and should understand that complete cures do not usually occur in treatment of any chronic disease, including rhinitis.

Compliance is enhanced when: (1) a fewer number of daily doses is required; (2) the patient schedules when doses are to be taken and selects an appropriate reminder mechanism, such as mealtimes, daily rituals, etc; (3) there is a good doctor-patient relationship with a high level of physician trust; (4) the patient has written instructions to follow; (5) rhinitis medication is taken with the same dosing frequency as other medications; (6) there is a well designed reminder chart for times of dosing interval.[1–5]

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## Importance of Rhinitis Management for Concomitant Asthma, Sinusitis, and Otitis Media

**47. Appropriate management of rhinitis may be an important component in effective management of co-existing or complicating respiratory conditions, such as asthma, sinusitis, or chronic otitis media. Data suggest that failure to reduce inflammation in the upper airway may lead to suboptimal results in asthma treatment.**

Rhinitis and asthma frequently coexist in patients, and there is evidence that rhinitis is a risk factor for asthma. Mechanisms that connect upper and lower airway dysfunction are under investigation but include a nasal bronchial reflex, mouth breathing caused by nasal obstruction, and pulmonary aspiration of nasal contents.[1] In a study of patients with a history of allergic rhinitis symptoms that preceded or coincided with exacerbations of asthma, controlled allergen challenge to the nasal airways without delivery to the lungs significantly increased bronchial reactivity, suggesting that the nasal allergic response alters bronchial responsiveness.[2] Nasal obstruction has been shown to lead to increased pulmonary function decrements caused by exercise induced bronchospasm, presumably caused by mouth breathing that fails to warm and humidify air as efficiently as does nasal breathing.[3]

There is clinical evidence that treatment of rhinitis can improve the status of co-existing asthma. Nasal beclomethasone has been shown to prevent a seasonal increase in bronchial hyperresponsiveness in patients with allergic rhinitis and asthma.[4] Although systemic absorption of nasal corticosteroids is minimal, the unlikely possibility has been raised that systemic absorption of corticosteroids administered intranasally may have a direct effect on the lungs. However, in a large placebo-controlled study of patients with asthma and allergic rhinitis, nasal cromolyn (an agent that has negligible systemic absorption) as well as intranasal steroids cause a significant reduction in asthma symptoms.[5] Although very high doses of some antihistamines have been required to achieve a modest bronchodilator effect in some studies, conventional doses of cetirizine, loratadine and oral decongestants have been reported to improve asthma symptoms and pulmonary function in patients with concomitant allergic rhinitis in placebo controlled trials.[6,7] Consequently, optimal control of asthma may require effective control of concomitant rhinitis.

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## Special Considerations in Children, the Elderly, Pregnancy, Athletes, and Patients with Rhinitis Medicamentosa

**48. Special diagnostic and therapeutic considerations are warranted in selected patient subsets, including in children, the elderly, pregnancy women, athletes, and in those with rhinitis medicamentosa.**

*Rhinitis in Children*

**Disorders and prevalence.** Rhinitis in children shares most of the pathophysiologic, clinical, diagnostic, and therapeutic characteristics observed in adults; however, the existence of some differences justify discussion.[1,2]

Viral-induced rhinitis, which may occur in the neonatal period, becomes more common later in infancy with increasing exposure of the infant to other children, averaging about 6 episodes per year in children between 2 to 6 years of age. The progression of viral to secondary bacterial rhinitis will prolong infection and symptoms from several days to weeks unless shortened by appropriate antibiotics. Staphylococcal aureus infection secondary to other primary rhinitis disorders, including allergic rhinitis, may manifest as impetigo of the anterior nares with characteristic crusting and irritation. Secondary bacterial rhinitis occurs with or without sinusitis in children with antibody, complement, and leukocyte deficiency disorders, hyper-IgE syndrome, structural defects (cleft palate, osteopetrosis) and cystic fibrosis, and may also occur in normal children. Sinusitis is common in perennial allergic rhinitis in childhood, occurring in half of children referred to specialists. Purulent rhinorrhea, especially if unilateral, persistent, bloody, or fetorous may indicate an intranasal foreign body.[3]

Chronic bacterial infectious rhinitis (distinct from coexisting sinusitis and pharyngitis) has been poorly documented, but probably does occur in children in unusual cases. Characteristics include nasal obstruction and purulent anterior and post-nasal discharge with erythematous turbinates and neutrophilic and bacterial infiltration of the nares. Primary bacterial rhinitis, though uncommon, may occur in the newborn due to congenital syphilis with characteristic rhinorrhea followed by ulceration. Localized bacterial rhinitis may also occur in during β-hemolytic Streptococcal infections, particularly scarlet fever (50% prevalence), diphtheria, yaws, gonorrhea, tuberculosis, typhus, and scleroma.[3]

Nasal symptoms, particularly congestion and rhinorrhea, are common in infants and children with pharyngonasal reflux resulting from prematurity, neuromuscular disease, dysautonomia, velopharyngeal incoordination, or cleft palate. Those affected experience frequent choking, apneic spells, recurrent pneumonia (due to concomitant gastroesophageal reflux and/or tracheal aspiration), and aspiration of formula leading to secondary chemical/infectious rhinitis. Increasing age and thickened feedings improve the pharyngonasal reflux.[3]

A critical period appears to exist early in infancy in which the genetically programmed atopic-prone or high-risk infant is at greater risk to become sensitized when exposed to both food and aeroallergens. Food sensitization in infancy manifests as food allergy, atopic dermatitis, urticaria/angioedema, and anaphylaxis which typically develops in infancy and early childhood. Sneezing, nasal congestion, rhinorrhea, and ocular symptoms occur in about 30% of children during a food allergic reaction. These upper respiratory symptoms rarely occur in the absence of gastrointestinal, dermatologic, or systemic manifestations. Although upper respiratory symptoms in infancy and early childhood are frequently attributed to foods, many studies have consistently failed to demonstrate foods as a trigger for chronic rhinitis.[4] On the other hand, aeroallergen sensitization which may begin in infancy manifests typically in allergic rhinitis and atopic asthma beginning after the toddler years.[5] The natural history of atopic disease characteristically begins with atopic dermatitis, food allergy, and food sensitization in infancy and early childhood followed by allergic rhinitis, atopic asthma, and aeroallergen sensitization after early childhood. In the general population, up to 10% of children and about 20% of adolescents manifest allergic rhinitis. Studies suggest that allergic rhinitis tends not to remit during childhood.[6] Atopic-prone infants and young children compared to their non-risk cohorts appear to experience more otitis media and upper respiratory infections which probably derives from subtle immunologic differences rather than specific-IgE causes, since sensitization is often not present yet. The child and adolescent with allergic rhinitis manifests symptoms indistinguishable from that seen in the adult, except for a greater frequency of the allergic salute and eye rubbing.

Non-allergic, non-infectious rhinitis with eosinophils (NARES) occurs extremely infrequently in childhood and probably accounts for less than 2% of children with nasal eosinophilia. Antihistamines/decongestants may provide adequate relief in some, but others may require topical or oral corticosteroids to control symptoms.[7]

Nasal obstruction from structural defects or adenoidal hypertrophy are often seen in children with rhinitis. Nasal polyps are rare in childhood, usually occurring only in adults. Conditions associated with nasal polyps in childhood include cystic fibrosis, ciliary dyskinesia, chronic infections as seen in immunologic deficiency states, and occasionally allergic rhinitis, while aspirin intolerance may be responsible in adolescents.

**Diagnosis in children.** The evaluation of children with chronic rhinitis demands a systematic approach. Accurate diagnosis rests with careful historical data collection and physical examination supplemented by appropriate laboratory studies. The history should include information pertaining to (1)

the onset of symptoms (infancy vs childhood, post viral upper respiratory infection, trauma, or acquisition of a new pet or home), (2) frequency (daily, seasonal, episodic, or unremitting), duration (weeks, months, or years), severity (annoying, disabling, interfering with sleep, or leading to emotional disturbance), symptoms (sneezing, anterior or posterior rhinorrhea, obstruction, or anosmia), character (watery, mucoid, or purulent) and color (clear, yellow, green) of the secretions, precipitating factors (allergens, irritants, climatic conditions), associated factors (atopic disorders, drugs, infections), and previous response to medication/treatment (efficacy and side effects).[8,9] The child with allergic rhinitis often manifests characteristic facial features and mannerisms including the "allergic salute," the allergic crease, Dennie-Morgan's lines (accentuated lines or folds below the margin of the inferior eyelid), and infraorbital dark circles or "allergic shiners."

The physical exam of children with rhinitis complaints should include, in addition to the nasal exam described below, the ears (evaluating for infection, fluid, and eustachian tube dysfunction, with additional use of a pneumatic otoscope or impedance tympanometer), the eyes (visualizing the palpebral infraorbital area for Dennie-Morgan's lines, the conjunctiva for infection, and the lids for blepharitis), the nasal pharynx for tonsillar and adenoid hypertrophy, and the chest for asthma or bronchitis. Class II malocclusions due to chronic mouth breathing may also be present. The nasal exam should describe the position of the septum, appearance of the turbinates, quality and quantity of secretions, and the presence of any abnormal growths. Should obstructing inferior turbinates be present in older children, topical vasoconstriction can be instilled to permit better visualization. Rhinopharyngoscopy may be necessary to evaluate structural defects in the child with recalcitrant rhinitis or suspected abnormality.

The laboratory work-up for children with rhinitis is similar to adults and includes the determination of specific-IgE by skin test or sensitive in vitro testing when directed by history and symptoms of allergic rhinitis. Other tests may also be indicated on an individual basis, including: (1) nasal cytology; and (2) specific diagnostic tests such as quantitative immunoglobulins, complement studies, leukocyte assays, ciliary function and morphology, and sweat test when disorders such as immunodeficiency, ciliary dyskinesia, and cystic fibrosis are suspected. As in adults, CT scans of the sinuses are more sensitive than standard radiographs for detecting sinus disease in children. Nonetheless, a single Water's view may be helpful in diagnosing sinusitis in children, with mucosal thickening >6 mm, opacification, or air fluid levels strongly suggestive of infection. A lateral nasal pharynx x-ray may help to exclude adenoid hypertrophy in those children with clinical history and physical exam consistent with mouth breathing, snoring, sleep apneic episodes, and nasal obstruction.

Techniques for skin testing are similar in children as for adults, except that reactions may be smaller in infancy and early childhood due to lower levels of specific-IgE and reduced skin reactivity particularly in infants. A multi-head puncture device may be useful in uncooperative infants and young children. Topically-applied EMLA® cream (lidocaine, prilocaine) has been advanced as a possible means of reducing the discomfort associated with skin testing in children. Total serum IgE levels are not sensitive enough (only about 50%) for routine clinical diagnosis of allergic rhinitis.

The cellular pattern derived from the nasal smear or tissue may help to differentiate eosinophilic from non-eosinophilic conditions. Eosinophil predominance suggests allergic rhinitis, aspirin sensitivity, or NARES. The degree of nasal eosinophilia is related to the severity of the condition. Basophilic cells, either basophilic leukocytes or mast cells, are common in pediatric allergic rhinitis and NARES. Levels of nasal eosinophils and basophilic cells correlate highly with each other from ages 4 months to 7 years. Nasal eosinophils in nasal scrapings possess a sensitivity, specificity, and positive predictive value of about 90% for aeroallergen sensitization in high-risk children.[9] (Also see Summary Statement #28)

Nasal allergen challenge in children is reserved for research purposes.

**Therapeutic approach in children.** The therapeutic approach to rhinitis in children is based on principles used in adults, generally differing only in specifics and dosages. Understanding the child's suffering and discomfort represents the cornerstone of therapy. The clinician must function as an advocate for the infant and child who may be unable to express the extent of their rhinitis problem.

Allergen avoidance as described in an earlier section represents the primary treatment of allergic rhinitis and is especially relevant in early infancy and childhood in which allergen sensitization first occurs. Early effective allergen avoidance measures may function during secondary prevention to down-regulate IgE production and turn off allergic sensitization, if instituted early enough in life. Controlled studies are proceeding to determine whether the early treatment of the atopic child with allergen avoidance, anti-inflammatory allergic medication, or immunotherapy will modify the natural history of allergic rhinitis and asthma.

Regurgitant rhinitis in infants should be treated with thickened and upright feedings, avoiding lying with a bottle, discontinuing formula feeding by 1 year, and prone resting at 30° following feeding.

Nasal saline washes may be tolerated by the older child and adolescent. For the younger child and infant, commercial saline sprays followed by bulb syringe suctioning of the nares may be helpful in reducing the tenacity of secretions often seen in bacterial rhinitis.

Specific intervention for infectious rhinitis of childhood include appropriate antibiotics in childhood dosages for proven bacterial rhinitis/sinusitis (Table 5).

Surgery may be indicated for adenoid hypertrophy, nasal webs, pharmacologically resistant nasal polyps,

medically unresponsive sinusitis, and other structural defects. Correction of septal deviation should be delayed until late adolescent after cessation of nasal growth. Multidimensional therapy is necessary for immune deficiency disorders, cystic fibrosis, and ciliary dyskinesia.

Pharmacotherapy is usually required in the management of allergic rhinitis when supportive and avoidance measures are inadequate in controlling symptoms.

Oral antihistamines (Table 6) or nasal cromolyn remain the first-line pharmacologic treatments of childhood allergic rhinitis.

The second generation antihistamines astemizole, fexofenadine, and loratadine are labelled as non-sedating. The second-generation antihistamine cetririzine is significantly less sedating than its parent drug hydroxyzine. Not all of these second generation antihistamines have received approval by the US Food and Drug Administration (FDA) for use in young children. These agents should provide a greater benefit risk ratio than the first generation antihistamines, but generally do not provide any greater clinical effectiveness at ameliorating rhinitis symptoms.

Cromolyn nasal spray at dosages of 1 to 2 sprays TID to QID is effective in preventing allergic rhinitis and may be used in very young children. It is well tolerated but the frequency of needed administration may reduce its overall compliance and effectiveness.

Topical nasal corticosteroids in children as in adults represent the most effective pharmacologic therapy of allergic rhinitis with the capacity to control sneezing, pruritus, rhinorrhea, and congestion but not ocular symptoms. Extensive clinical and toxicologic studies have generally demonstrated that nasal corticosteroids have an excellent benefit/risk profile in long-term usage in children. In 1998, the FDA presented data that some nasal corticosteroids may have a temporary adverse effect on growth in children, but it is uncertain whether there may be a long term effect on ultimate attained height.

Table 5. Antibiotics and Pediatric Dosages in the Treatment of Bacterial Rhinosinusitis

| Antibiotic (generic name) | Usual Pediatric Dosage |
|---|---|
| First line therapy | |
| Amoxicillin | 20–50 mg/kg/24 hr divided TID |
| Trimethoprim(TMP)-sulfamethoxazole | Dosage based on TMP component: 10 mg/kg/24 hr divided BID |
| Penicillin and sulfisoxazole in combination but each prescribed separately | Penicillin (25–50 mg/kg/24 hr divided QID and sulfisoxazole (children >2 months of age = 150 mg/kg/24 hr divided QID) |
| Second line therapy | |
| Erythromycin ethylsuccinate 50 mg/kg/24 hr) and acetyl sulfisoxazole (150 mg/kg/24 hr) | Erythromycin (50 mg/kg/24 hr) and sulfisoxazole (150 mg/kg/24 hr) divided QID |
| Amoxicillin-clavulanic acid | Children <40 kg: 20–40 mg/kg/24 hr divided TID |
| Cefaclor | 40 mg/kg/24 hr divided TID |
| Cefixime | 8 mg/kg/24 hr divided QD or BID |
| Clarithromycin | 15 mg/kg/24 hr divided BID |

Table 6. Representative Oral Antihistamines and Their Pediatric Dosages

| $H_1$-antihistamine | Usual Pediatric Dosage |
|---|---|
| First generation | |
| Brompheniramine | 0.5 mg/kg/day in 4 divided doses (max. 6 mg/24 hr for ages 2–6 yr; 12 mg/24 hr for ages 6–12 yr) |
| Carbinoxamine | 0.8 mg/kg/24 hr in 4 divided doses |
| Chlorcyclizine | 1.5 mg/kg/24 hr in 2–3 divided doses |
| Chlorpheniramine | 0.35 mg/kg/24 hr in 4 divided doses; over 7 years may use up to 8 mg q 12 hr time release form |
| Clemastine | Children 6–12 yr: 0.5–1 mg BID |
| Cyproheptadine | 2–6 yr: 2 mg q 8–12 hr (max. 12 mg/24 hr); 7–14 yr: 4 mg q 8–12 hr (max. 16 mg/24 hr) |
| Diphenhydramine | 5 mg/kg/24 hr in 4 divided doses |
| Hydroxyzine | 2 mg/kg/24 hr in 3 divided doses or at bedtime if tolerated |
| Promethazine | 0.5 mg/kg/dose q 6–8 hr |
| Tripelennamine | 5 mg/kg/24 hr in 4 divided doses |
| Triprolidine hydrochloride | <6 yrs: 0.3–0.6 mg q 6–8 hr<br>>6 yrs: 1.25 mg q 6–8 hr |
| Second generation | |
| Astemizole (Hismanal®) | 6–12 yr: 5 mg/24 hr in single dose* |
| Cetirizine (Zyrtec®) (tablet and syrup) | ≥6 yr: 5–10 mg PO QD<br>2–5 yr: 2.5–5 mg in 24 hr (QD or BID) |
| Fexofenadine (Allegra®) | ≥12 yr: 60 mg PO BID |
| Loratadine (Claritin®) (tablet, syrup, RediTab™) | ≥6 yr: 10 mg PO QD<br>2–6 yr: 5 mg PO QD for <30 kg body weight* |
| Terfenadine† (Seldane®) | 3–6 yr: 15 mg BID†<br>7–12 yr: 30–60 mg BID† |

* As of August, 1998, not approved in the US for this age group. Information on pediatric dosages obtained from published medical literature or information supplied by pharmaceutical manufacturers about pediatric doses used in other countries.
† Withdrawn from US market in 1998.

It is also unclear whether all nasal corticosteroids may have such an effect. Because of this concern, nasal corticosteroids should be used in children at the lowest possible effective dose, the FDA recommends that height be monitored routinely, and other therapeutic approaches (environmental control, non-steroid pharmacologic agents, and if appropriate, allergen immunotherapy) should be used in conjunction with nasal corticosteroids so that nasal corticosteroid doses may be minimized.

Systemic corticosteroids are rarely needed for uncomplicated rhinitis in childhood. Rarely they may be necessary to control nasal polyps when topical corticosteroids prove ineffective. Topical vasoconstrictors are dangerous in infancy, due to the narrow margin between therapeutic and toxic dose which increases the risk for cardiovascular and CNS effects. Oral decongestants also should be used cautiously during childhood owing to their stimulatory effects. Indications for instituting immunotherapy (noted in an earlier section) should be considered.

Ipratropium nasal spray (Atrovent 0.03%) is approved for ages ≥6 years and may reduce rhinorrhea from allergic and non-allergic rhinitis, but has no effect on other nasal symptoms (summary statement #41).

The treatment of the child with allergic rhinitis should emphasize preventive, non-pharmacologic measures whenever possible before instituting medication to control the disorder.

*Rhinitis in the elderly.* Allergic rhinitis is an uncommon cause of perennial rhinitis in individuals over 65 years of age.[10] More commonly, rhinitis in the elderly is due to cholinergic hyperreactivity (associated with profuse watery rhinorrhea which may be aggravated after eating, "gustatory rhinitis"), alpha adrenergic hyperactivity (congestion associated with antihypertensive drug therapy) or sinusitis. The watery rhinorrhea syndrome frequently responds to intranasal ipratropium.[11] Discontinuation of an antihypertensive medication responsible for nasal congestion should be considered but may not always be feasible. Although alpha adrenergic agonists must be used with caution in hypertensive patients, recent data suggests that pseudoephedrine does not elevate the blood pressure in patients with well controlled hypertension.[12] Other side effects from decongestants that are of concern in the elderly include urinary retention in patients with prostatic hypertrophy and cardiac and CNS stimulation.[13]

In the elderly, certain adverse effects of medication for the treatment of allergic rhinitis may be more common or be of greater concern. The anticholinergic effects of the first generation antihistamines may cause bladder disturbances or problems with visual accommodation, and sedation may also be bothersome. Second generation antihistamines (eg, fexofenadine and loratadine), which do not cause significant anticholinergic effects, sedation, performance impairment or adverse cardiac effects[14] are better choices than sedating antihistamines for treatment of the elderly. Elderly patients may also be more likely to be treated with beta blockers, a relative contraindication for immunotherapy.[15]

*Pregnancy.* The most common causes of nasal symptoms during pregnancy are allergic rhinitis, sinusitis, rhinitis medicamentosa, and vasomotor rhinitis.[16] Sinusitis has been reported to be six times more common in pregnant than non-pregnant women.[17] Preexisting allergic rhinitis may worsen, improve or stay the same during pregnancy.[16] Progesterone and estrogen-induced glandular secretion[18] as well as nasal vascular pooling due to vasodilation and increased blood volume may account for worsening allergic rhinitis, increased sinusitis and vasomotor rhinitis during pregnancy. In contrast, increased serum free cortisol during pregnancy could improve allergic rhinitis.

Chlorpheniramine and tripelennamine have been the preferred antihistamines for use during pregnancy, and pseudoephedrine is the preferred decongestant.[19] Case control studies have linked first trimester use of oral decongestants with infant gastroschisis (a defect in the abdominal wall).[21,22] Therefore, oral decongestants should probably be avoided during the first trimester, if possible. For allergic rhinitis, nasal cromolyn is useful and may be considered first in view of its topical application and reassuring gestational human and animal data.[19] Intranasal beclomethasone may be used if nasal cromolyn does not provide adequate control of daily symptoms, or as an alternative to oral therapy, although there is no published experience on the use of intranasal beclomethasone during pregnancy. Intranasal beclomethasone may also be used to allow discontinuation of topical decongestants in patients with rhinitis medicamentosa. If nasal beclomethasone is used, it should be tapered to the lowest effective dose. Vasomotor rhinitis often is adequately controlled by intranasal saline instillation, exercise appropriate for pregnancy, and pseudoephedrine.[16] Appropriate antibiotics for use during pregnancy for the treatment of sinusitis include amoxicillin with or without clavulanate, erythromycin, and cephalosporins.[19]

Immunotherapy for allergic rhinitis may be continued during pregnancy, if it is providing benefit without causing systemic reactions.[19,20] Doses should not be increased and should be adjusted in order to minimize the chance of inducing a systemic reaction, which could be harmful to both mother and fetus. Benefit/risk considerations do not generally favor starting immunotherapy during pregnancy.[19]

*Athletes.* Physical exercise acts as a potent vasoconstrictor, gradually decreasing nasal resistance in proportion to increasing effort and pulse, owing to release of noradrenaline. In most athletes, physical exercise will increase nasal due to vasodilatation, with the effect frequently unobserved by the individual. In normal exercise situations, no rebound occurs and the vasoconstriction persists for about one hour. Athletes, especially long-distance runners, cyclists, or triathletes, may experience a rebound nasal congestion after the initial improvement in nasal patency which may affect peak performance.

Prescription of medication for the competitive athlete should be based on

two important principles: (1) no medication given to the athlete should be on any list of doping products and should be approved for use by the US Olympic Committee (USOC) and International Olympic committee (IOC) and (2) no medication should adversely affect the athlete's performance.

The USOC generally observes the International Olympic Committee list of banned and allowed drugs. Before a competitive athlete takes any medication prior to competition, it should be determined if it is allowed (Table 7). The USOC has a toll-free hotline (1-800-233-0393) to answer any questions a physician or athlete may have. Athletes and their physicians should be aware that all decongestants are banned with the exception of topical (nasal or ophthalmological) phenylephrine and imidazole preparations (ie, oxymetazoline and tetrahydrozoline).

Antihistamines are allowed by the USOC but may be banned by the international federation of certain sports. Substances allowed by the USOC for competitive athletes with asthma include: (1) inhaled beta-2-agonists, but only albuterol and terbutaline; (2) inhaled corticosteroids; and (3) theophyllines. Other allowed medications include (1) local anesthetics, (2) NSAIDs, (3) antacids, (4) antibiotics, antifungicides and antiviricides, (5) contraceptives, (6) ulcer medications, (7) anti-diarrheals, (8) guaifenesin expectorants, (9) codeine/dihydrocodeine/ and dextromethorphan antitussives, (10) laxatives, (11) anti-diabetics, and (12) certain pain and fever medications. Medications which are allowed by the USOC but may be banned by International Federations of certain sports include: (1) anti-anxiolytics, (2) antinauseants, (3) beta-blockers, and (4) sedatives/sleep aids. All physicians treating potential competitive athletes should have the USOC booklet of allowed and banned substances available for quick reference.

An adverse influence on physical performance may occur in the athlete with rhinitis treated with (1) first generation antihistamines which may have undesirable sedative and anticholinergic effects, or (2) immunotherapy, in which local discomfort of an extremity may rarely persist for several days after a subcutaneous injection.

Table 7. Rhinitis Medications/Substances Banned by the USOC and Considered Doping

| Class of substance | Agents |
|---|---|
| Vasoconstrictors<br>These agents may be found in many single or combination agent OTC and prescriptions used for allergy URIs, and cough, | Desoxyephredrine (oral or nasal)<br>Ephedrine (oral or nasal)<br>Ma Huang (herbal ephedrine)<br>Phenylephrine (oral)<br>Phenylpropanolamine (oral or nasal)<br>Propylhexedrine (oral or nasal)<br>Pseudoephedrine (oral or nasal) |
| Stimulants<br>Caffeine in any form leading to urinary levels of >12 mcg/mL | Equivalent to 6–8 cups of coffee, 4 vivarin tablets, or 8 No Doz tablets 2–3 hr before testing |
| Corticosteroids | The use of corticosteroids is banned except for topical use (ear, eye, and skin), inhalation therapy (allergic rhinitis and asthma), and local or intra-articular injections. Physicians prescribing topical, inhalational, and intraarticular corticosteroids must send written notification of the indication to the USOC (USOC Drug Control Program, Medical Notifications, One Olympic Plaza, Colorado Springs, CO 80909). Taking corticosteroids (prednisoine, methylprednisolone, cortisone) orally or intravenously is banned. |
| Narcotic analgesics | All narcotics except codeine and dihydrocodone |

After consideration of these issues, the optimal therapy for the athlete with symptomatic allergic rhinitis consists of aggressive allergen avoidance, a second generation $H_1$-antihistamine and a topical nasal corticosteroid. Intranasal cromolyn may be useful 30 minutes prior to commencing a competition likely to be associated with high allergen exposure. Immunotherapy may provide help for those athletes with seasonal allergic rhinitis not responding adequately to avoidance and medication.

**Rhinitis medicamentosa.** Rhinitis medicamentosa is a syndrome of rebound nasal congestion which follows the overuse of intranasal alpha-adrenergic decongestants or cocaine and occasionally even systemic decongestants.[23,24] Rhinitis medicamentosa may complicate a viral upper respiratory infection or be superimposed on any cause of chronic rhinitis. A presumptive diagnosis may be made in a patient with prominent nasal congestion who has used intranasal decongestants or cocaine on a daily basis for more than one week. Examination of the nose usually reveals a congested and reddened mucous membrane, but a pale, edematous mucosa may occasionally be observed. The mucosa in patients with rhinitis medicamentosa is characteristically unresponsive to further application of decongestants.[24]

Patients with rhinitis medicamentosa should receive intranasal corticosteroids and be advised to discontinue the topical decongestants as soon as clinical symptoms abate. Occasionally, a short course of oral corticosteroids (eg, prednisone 30 mg daily for 5 to 7 days) may be necessary in adults to allow for discontinuation of the topical decongestants. Underlying chronic rhinitis in patients with superimposed rhinitis medicamentosa must be appropriately evaluated and treated.[25]

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## Consultation with an Allergist-Immunologist

**49. There are a variety of circumstances in which the special expertise and training of an allergist-immunologist may offer benefits to a patient with rhinitis. Reasons for consultation for rhinitis with an allergist/immunologist include, but are not limited to:**

1. Clarification and identification of allergic or other triggers for the patient's rhinitis condition.
2. When management of rhinitis is unsatisfactory due to inadequate efficacy or adverse reactions from treatment.
3. When allergen immunotherapy may be a consideration.
4. When there is impairment of patient's performance because of rhinitis symptom manifestations or medication side effects, eg, patients involved in the transportation industry, athletes, students, etc.
5. When the patient's quality of life is significantly affected (eg, patient comfort and well-being, sleep disturbance, small, taste).
6. When complications of rhinitis develop, eg, sinusitis, otitis media, orofacial deformities.
7. In the presence of co-morbid conditions such as recurrent or chronic sinusitis, asthma or lower airway disease, otitis media, nasal polyps.
8. When patients require systemic corticosteroids to control their symptoms.
9. When the duration of rhinitis symptoms is greater than 3 months.
10. When there is a significant cost from use of multiple medications.
11. When education in allergen avoidance techniques is needed.

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