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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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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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-

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