



# ALLERGIC RHINITIS

ALI HOSSEIN SAMADI MD.

ASSISTANT PROFESSOR OF INTERNAL  
MEDICINE(PULMONOLOGIST)

ARDABIL UNIVERSITY OF MEDICAL SCIENCE

## ■ DEFINITION

- Rhinitis is characterized by sneezing; rhinorrhea; obstruction of the nasal passages; conjunctival, nasal, and pharyngeal itching; and lacrimation and can be classified as allergic or non-allergic.
- A clinical history of rhinitis symptoms occurring in a temporal relationship to allergen exposure and documentation of sensitization to an environmental allergen are required for a diagnosis of allergic rhinitis.

## ■ DEFINITION

- Although commonly seasonal due to elicitation by airborne pollens, it can be perennial in an environment of chronic exposure to house dust mites, animal danders, or insect (cockroach) products.
- The overall prevalence in North America has increased in the past 20 years and is 10–30%, with the peak prevalence of >30% occurring in the fifth decade.

## ■ PREDISPOSING FACTORS AND ETIOLOGY

- Allergic rhinitis generally occurs in atopic individuals, often in association with atopic dermatitis, food allergy, urticaria, and/or asthma.
- Up to 50% of patients with allergic rhinitis manifest asthma, whereas 70–80% of individuals with asthma and 80% of individuals with chronic bilateral sinusitis experience allergic rhinitis.
- Female sex, particulate air pollution exposure, and maternal tobacco smoking increase the risk of developing allergic rhinitis over the life span.

## ■ PREDISPOSING FACTORS AND ETIOLOGY

- Trees, grasses, and weeds that depend on wind rather than insects for pollination produce sufficient quantities of pollen suitable for wide distribution by air currents to elicit seasonal allergic rhinitis.
- The dates of pollination of these species historically varied little from year to year in a particular locale, but may be quite different in another climate.

## ■ PREDISPOSING FACTORS AND ETIOLOGY

- Molds, which are widespread in nature because they occur in soil or decaying organic matter, propagate spores in a pattern that depends on climatic conditions.
- Perennial allergic rhinitis occurs in response to allergens that are present throughout the year, including animal dander, cockroach-derived proteins, mold spores, or dust mites such as *Dermatophagoides farina* and *Dermatophagoides pteronyssinus*.
- Dust mites are scavengers of human skin and excrete cysteine protease allergens in their feces. In up to 40% of patients with perennial rhinitis, no clear-cut allergen can be demonstrated as causative.

## ■ PATHOPHYSIOLOGY AND MANIFESTATIONS

- Episodic rhinorrhea, sneezing, obstruction of the nasal passages with lacrimation, and pruritus of the conjunctiva, nasal mucosa, and oropharynx are the hallmarks of allergic rhinitis.
- The nasal mucosa is pale and boggy, the conjunctiva congested and edematous, and **the pharynx generally unremarkable**.
- Swelling of the turbinates and mucous membranes with obstruction of the sinus ostia and Eustachian tubes precipitates secondary infections of the sinuses and middle ear, respectively.



## ■ PATHOPHYSIOLOGY AND MANIFESTATIONS

- A growing number of patients with seasonal allergic rhinitis demonstrate **pollen-associated food allergen syndrome** characterized by oropharyngeal pruritus and/or mild swelling following the ingestion of raw plant-based foods which contain cross-reacting pollen-related allergens.
- **Nasal polyps**, can increase obstructive symptoms with anosmia as a defining feature and can concurrently arise within the nasopharynx or sinuses.

## ■ PATHOPHYSIOLOGY AND MANIFESTATIONS

- ✓ Atopy is not a risk factor for nasal polyps, which instead may occur in the setting of cystic fibrosis, aspirin-exacerbated respiratory disease characterized by the triad of asthma, rhinosinusitis, and respiratory reactions to all cyclooxygenase-1 inhibitors, and in patients with chronic staphylococcal colonization, which produces superantigens leading to an intense TH2 inflammatory response.

## ■ PATHOPHYSIOLOGY AND MANIFESTATIONS

- The nose presents a large mucosal surface area through the folds of the turbinates and serves to adjust the temperature and moisture content of inhaled air and to **filter out particulate materials  $>10\text{ }\mu\text{m}$  in size** by impingement in a mucous blanket; ciliary action moves the entrapped particles toward the pharynx.
- Entrapment of pollen and digestion of the outer coat by mucosal enzymes such as lysozymes release protein allergens. The initial interaction occurs between the allergen and intraepithelial mast cells and then proceeds to involve deeper perivenular mast cells, both of which are sensitized with specific IgE.

## ■ PATHOPHYSIOLOGY AND MANIFESTATIONS

- During the symptomatic season when the mucosae are already swollen and hyperemic, there is enhanced adverse reactivity to the seasonal pollen as well as irritants such as tobacco smoke and fragrances.
- Biopsy specimens of nasal mucosa during seasonal rhinitis show submucosal edema with infiltration by eosinophils, along with some basophils and neutrophils.

## ■ PATHOPHYSIOLOGY AND MANIFESTATIONS

- In sensitive individuals, the introduction of allergen into the nose is associated with sneezing, nasal obstruction, and discharge, and the fluid contains histamine, PGD<sub>2</sub>, and leukotrienes.
- Thus the mast cells of the nasal mucosa and submucosa generate and release mediators through IgE-dependent reactions that are capable of producing tissue edema and eosinophilic infiltration.

## ■ DIAGNOSIS

- The diagnosis of seasonal allergic rhinitis depends largely on an accurate history of occurrence coincident with the pollination of the offending weeds, grasses, or trees.
- The continuous character of perennial allergic rhinitis due to contamination of the home or place of work makes historic analysis difficult, but there may be variability in symptoms that can be related to exposure to animal dander, dust mite and/or cockroach allergens, fungal spores, or work-related allergens such as latex.

## ■ DIAGNOSIS

- ✓ Patients with perennial rhinitis commonly develop the problem in adult life, and manifest nasal congestion and a postnasal discharge, often associated with thickening of the sinus membranes demonstrated by radiography.

## ■ DIAGNOSIS

- ✓ Perennial nonallergic rhinitis with eosinophilia syndrome (NARES) occurs in the middle decades of life and is characterized by nasal obstruction, anosmia, chronic sinusitis, and prominent eosinophilic nasal discharge in the absence of allergen sensitization.



## ■ DIAGNOSIS

- ✓ The term **vasomotor rhinitis or perennial nonallergic rhinitis** designates a condition of enhanced reactivity of the nasopharynx in which a symptom complex resembling perennial allergic rhinitis occurs with nonspecific stimuli, including **chemical odors, temperature and humidity variations**, and **position changes** but occurs without tissue eosinophilia or an allergic etiology.

## ■ DIAGNOSIS

- Other entities to be excluded are :
  - ✓ Structural abnormalities of the nasopharynx
  - ✓ Exposure to irritants
  - ✓ **Gustatory rhinitis** associated with cholinergic activation that occurs while eating or ingesting alcohol
  - ✓ Hypothyroidism
  - ✓ Upper respiratory tract infection
  - ✓ **Pregnancy** with prominent nasal mucosal edema
  - ✓ Prolonged topical use of  $\alpha$ -adrenergic agents in the form of nasal sprays (**rhinitis medicamentosa**) and

## ■ DIAGNOSIS

- ✓ Use of certain systemic agents such as  $\beta$ -adrenergic antagonists, ACE inhibitors, direct vasodilators (hydralazine),  $\alpha$ 1-adrenergic receptor antagonists, estrogens, progesterone, NSAIDs, gabapentin, phosphodiesterase-5 inhibitors, and psychotropics (Risperidone, chlorpromazine, amitriptyline).

## ■ DIAGNOSIS

- The nasal secretions of allergic patients are rich in eosinophils, and a modest peripheral eosinophilia can be observed.
- Total serum IgE is frequently elevated, but the demonstration of immunologic specificity for IgE is critical to an etiologic diagnosis.
- A skin test by the intracutaneous route (puncture or prick) with the allergens of interest provides a rapid and reliable approach to identifying allergen-specific IgE that has sensitized cutaneous mast cells.

## ■ DIAGNOSIS

- ✓ A positive intracutaneous skin test with 1:10– 1:20 weight/volume of extract has a high predictive value for the presence of allergy.
- ✓ An intradermal test with a 1:500–1:1000 dilution of 0.05 mL may follow if indicated by history when the intracutaneous test is negative, but while more sensitive, it is less reliable due to the reactivity of some asymptomatic individuals at the test dose.

## ■ DIAGNOSIS

- Newer methodology for detecting total IgE, including the development of enzyme-linked immunosorbent assays (**ELISA**) employing anti-IgE bound to either a solid-phase or a liquid-phase particle, provides rapid and cost-effective determinations.
- Measurements of specific anti-IgE in serum are obtained by its binding to an allergen and quantitation by subsequent uptake of labeled anti-IgE.
- As compared to the skin test, the assay of specific IgE in serum is less sensitive but has high specificity.

# TREATMENT

- Although **allergen avoidance** is the most cost-effective means of managing allergic rhinitis, only in the case of animal dander and possibly dust mites is it really feasible.
- Treatment with **pharmacologic agents** represents the standard approach to seasonal or perennial allergic rhinitis.
- **Oral long-acting H1 antihistamines** are effective for nasopharyngeal itching, sneezing, and watery rhinorrhea and for such ocular manifestations as itching, tearing, and erythema, but they are **less efficacious for the nasal congestion**.

# TREATMENT

- The older antihistamines are sedating, and they induce psychomotor impairment, including reduced eye-hand coordination and impaired automobile driving skills.
- Their anticholinergic (muscarinic) effects include visual disturbance, urinary retention, and constipation.



# TREATMENT

- ✓ Because the **newer H1 antihistamines** such as fexofenadine, loratadine, desloratadine, cetirizine, levocetirizine, olopatadine, bilastine, and azelastine are less lipophilic and more H1 selective, their ability to cross the blood-brain barrier is reduced, and thus **their sedating and anticholinergic side effects are minimized.**
- ✓ These newer antihistamines do not differ appreciably in efficacy for relief of rhinitis and/or sneezing.

# TREATMENT

- ✓ **Intranasal high-potency glucocorticoids** are the most potent drugs available for the relief of established rhinitis, seasonal or perennial, and are effective in relieving nasal congestion as well as ocular symptoms.
- ✓ Their most frequent side effect is **local irritation**, with **Candida overgrowth** being a rare occurrence.

# TREATMENT

- ✓ The currently available intranasal glucocorticoids—**beclomethasone, flunisolide, triamcinolone, budesonide, fluticasone propionate, fluticasone furoate, ciclesonide, and mometasone furoate**—are equally effective for nasal symptom relief, including nasal congestion; **these agents all achieve up to 70% overall symptom relief** with some variation in the time period for onset of benefit.

# TREATMENT

- ✓ **Azelastine nasal spray** may benefit individuals with nonallergic vasomotor rhinitis as well as additive benefit to intranasal steroids in allergic rhinitis, but it has an adverse effect of **dysgeusia (taste perversion)** in some patients.

# TREATMENT

- ✓ Alternative **nasal decongestants** include  $\alpha$ -adrenergic agents such as **phenylephrine** or **oxymetazoline**; however, the duration of their efficacy is limited because of rebound rhinitis (i.e., 7- to 14-day use can lead to **rhinitis medicamentosa**) and such systemic responses as **hypertension**.

# TREATMENT

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- Oral  $\alpha$ -adrenergic agonist decongestants containing pseudoephedrine are standard for the management of nasal congestion, generally in combination with an antihistamine.
- While oral antihistamines typically reduce nasal and ocular symptoms by about one-third, pseudoephedrine must be added to achieve a similar reduction in nasal congestion.
- These pseudoephedrine combination products can cause insomnia and are precluded from use in patients with narrow angle glaucoma, urinary retention, severe hypertension, marked coronary artery disease, or a first-trimester pregnancy.

# TREATMENT

- ✓ The **CysLT1 blocker montelukast** is approved for treatment of both seasonal and perennial rhinitis, and it reduces both nasal and ocular symptoms by about 20%.
- ✓ **Cromolyn sodium nasal spray** inhibits mast cell degranulation, and can be used prophylactically on a continuous basis during the season.
- ✓ **Topical ipratropium** is an anticholinergic agent effective in reducing rhinorrhea, including that of patients with perennial non-allergic symptoms, and it can be additionally efficacious when combined with intranasal glucocorticoids.

# TREATMENT

- ✓ For concomitant allergic conjunctivitis, **topical treatment with cromolyn sodium** is effective in treating mild allergic symptoms and **topical antihistamines such as olopatadine, azelastine, ketotifen, or epinastine** administered to the eye provide rapid relief of itching and redness and are more effective than oral antihistamines.



# TREATMENT

- **Immunotherapy** consists of repeated exposure to gradually increasing concentrations of the allergen(s) considered to be specifically responsible for the symptom complex.
- Two forms of immunotherapy, **subcutaneous** (SCIT) and **sublingual** (SLIT), are currently available.
- **The duration of SCIT is 3–5 years**, with discontinuation being based on minimal symptoms over two consecutive seasons of exposure to the allergen.

# TREATMENT

- SLIT is prepared as a tablet to be dissolved under the tongue at home after the first dose.
- The efficacy of SLIT is comparable to SCIT but only for the three allergens formulations available, dust mite, timothy/northern grasses and ragweed.

# TREATMENT

- ✓ Immunotherapy is contraindicated in patients with significant cardiovascular disease or unstable asthma and should be conducted with particular caution in any patient requiring  $\beta$ -adrenergic blocking therapy because of the difficulty in managing an anaphylactic complication.

# TREATMENT

- ✓ Systemic treatment with a **monoclonal antibody to IgE (omalizumab)** that blocks mast cell and basophil sensitization has efficacy for allergic rhinitis and can be used with immunotherapy to enhance safety and efficacy.
- ✓ However, current approval is only for treatment of patients with persistent allergic asthma not controlled by inhaled glucocorticoid therapy.

# TREATMENT

- A sequence for the management of allergic or perennial rhinitis based on an allergen-specific diagnosis and stepwise management as required for symptom control would include the following:
  - (1) Identification of the offending allergen(s) by history with confirmation of the presence of allergen-specific IgE by skin test and/or serum assay;
  - (2) Avoidance of the offending allergen
  - (3) Medical management in a stepwise fashion

## TREATMENT

- **Mild intermittent symptoms** of allergic rhinitis are treated with oral antihistamines, oral CysLT1 receptor antagonists, intranasal antihistamines, or intranasal cromolyn prophylaxis.

## TREATMENT

- **Moderate to more severe** allergic rhinitis is managed with intranasal glucocorticoids plus oral antihistamines, oral CysLT1 receptor antagonists, or antihistamine-decongestant combinations.

# TREATMENT

- Persistent or seasonal allergic rhinitis, rhinoconjunctivitis, or asthma which remains uncontrolled with maximal medical therapy merit consideration of allergen-specific immunotherapy.



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