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A review on diagnosis and treatment of allergic rhinitis

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Abstract
Rhinitis is one of the most common chronic conditions for which medical care is sought. Allergic rhinitis is an Ige-mediated disorder of the nose caused by the interaction of airborne allergens with specific Ige type antibodies on the surface of mast cells. The Ige-allergen interaction leads to the mast cell releasing and synthesizing a number of chemical which then cause the surrounding tissues to become inflamed. Typical symptoms which are initiated include rhino rhea, nasal itching, sneezing and nasal congestion, although extra nasal symptoms such as allergic conjunctivitis, itchy ears and palate, and asthma are commonly associated as well. It is usually a long-standing condition that often goes undetected in the primary-care setting. A thorough history, physical examination and allergen skin testing are important for establishing the diagnosis of allergic rhinitis. Second-generation oral antihistamines and intranasal corticosteroids are the mainstay of treatment. Allergen immunotherapy is an effective immune-modulating treatment that should be recommended if pharmacologic therapy for allergic rhinitis is not effective or is not tolerated, or if chosen by the patient.

Keywords: Allergens, allergic rhinitis, antihistamine, corticosteroids, histamine, immunology, inflammation, pollen

1. Introduction
Rhinitis is broadly defined as inflammation of the nasal mucosa. It is a common disorder that affects up to 40% of the population [1]. Allergic rhinitis is the most common type of chronic rhinitis, affecting 10–20% of the population, and evidence suggests that the prevalence of the disorder is increasing [2]. Severe allergic rhinitis has been associated with significant impairments in quality of life, sleep and work performance [2]. Allergens of importance include seasonal pollens and molds, as well as perennial indoor allergens, such as dust mites, pets, pests, and some molds. The frequency of sensitization to inhalant allergens is increasing and is now more than 40% in many populations in the united states and Europe [3-4]. The prevalence of allergic rhinitis in the united states is approximately 15% on the basis of physician diagnoses [6] and as high as 30% on the basis of self-reported nasal symptoms [4].

2. Pathophysiology of allergic rhinitis
2.1. Sensitization to allergens
Antigen presenting cells (APCS), such as dendritic cells in the mucosal surface, process allergens and present some peptides from allergens on the major histocompatibility complex (MHC) class ii molecule [11]. this MHC class ii molecule and antigen complex take a role as the legend of t-cell receptors on naive $cd4^+$ t cells, which result in differentiation of naive $cd4^+$ t cells to allergen-specific th2 cell. Activated th2 cells secret several cytokines, which induce isotype switching of b cells to produce specific Ige and proliferation of eosinophils, mast cells and neutrophils (fig. 1) [10]. produced antigen-specific Ige binds to high-affinity Ige receptors on mast cells or basophiles.

2.2. Early and late reactions
When AR patients are exposed to allergens, allergic reactions develop in 2 different patterns according to time sequence. One is the early reaction, in which sneezing and rhino rhea develops in 30 minutes and disappears. The other is the late reaction, which shows nasal obstruction approximately 6 hours after exposure to allergens and subsides slowly. The early reaction is the response of mast cells to offending allergens (type I hypersensitivity). Stimulated mast cells induce nasal symptoms by secreting chemical mediators such as histamine, prostaglandins and leukotrienes.[12]in contrast to the early reaction, eosinophil chemotaxis is the main mechanism in the late reaction, which is caused by chemical mediators produced in the early reaction.

Several inflammatory cells, eosinophils, mast cells and t cells migrate to nasal mucosa, break up and remodel normal nasal tissue, [13] and these processes result in nasal obstruction which is the main symptom of AR patients.

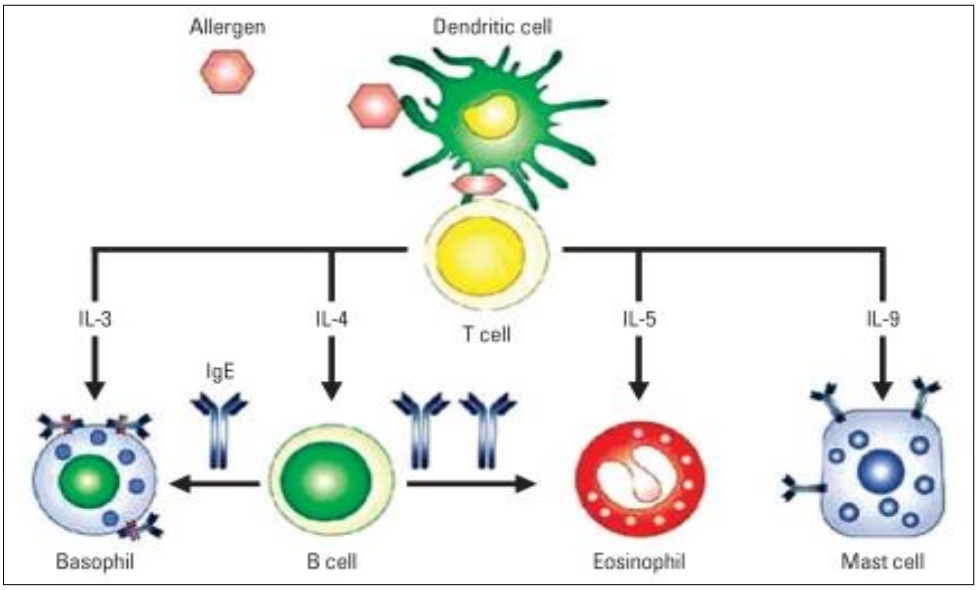

Fig 1: allergen-induced sensitization and inflammation [10].

2.3. Neurogenic inflammation

When respiratory epithelium is destroyed and nerve endings are exposed by cytotoxic proteins from eosinophils, sensory nerve fibers are excited by nonspecific stimuli and stimulate both sensory afferent and surrounding efferent fibers, the so called retrograde axonal reflex. This makes the sensory nerve fibers secrete neuropeptides such as substance p and neurokinin a, which induce contraction of smooth muscles, mucous secretion of goblet cells and plasma exudation from capillaries. This process is called neurogenic inflammation [14].

2.4. Non-specific hyper responsiveness

Non-specific hyper responsiveness is one of the clinical characteristics of allergic inflammation. Due to eosinophilic infiltration and destruction of nasal mucosa, the mucosa becomes hyperactive to normal stimuli and causes nasal symptoms such as sneezing, rhino rhea, nasal itching and obstruction [15]. This is a non-immune reaction that is not related to Ige. Hypersensitivity to non-specific stimuli such as tobacco or cold and dry air as well as specific allergens increases in AR patients.

2.5. Relationship between AR and Asthma - one airway, one disease

The prevalence of asthma in AR patients has been reported to be from 10% up to 40%. Several clinical studies have revealed that although AR patients do not have asthma, they can have eosinophilic infiltration in bronchial mucosa [16, 17]. Madonini *et al.* 18 have indicated that AR patients with positivity to pollens have bronchial hyper responsiveness during the pollen season. Corren *et al.* [19] have demonstrated that allergen stimulation to nasal mucosa in AR patients induces bronchial hyper responsiveness. With cumulative of evidence for structural analog [20, 21] and the similarity of allergic inflammatory cells, inflammatory mediators and cytokines between upper and lower airways, the "one airway, one disease" concept has been introduced. This means that since AR and asthma are not separate disease entity, concurrent asthma in AR patients and concurrent AR in asthmatic patients should be indentified and both upper and lower airway allergy should be treated simultaneously.

3. Diagnosis of allergic rhinitis by pharmacists

The diagnosis of allergic rhinitis is often made clinically on the basis of characteristic symptoms and a good response to empirical treatment with an antihistamine or nasal glucocorticoid. Historically, diagnosis of allergic rhinitis has been made by primary healthcare practitioners. However, pharmacists are now being encouraged to make the primary diagnosis of allergic rhinitis and establish a management and therapy plan [7].

3.1. Taking a history from the patient

When questioning the patient, pharmacists should listen for indicators that can lead to the diagnosis of allergic rhinitis, for example:

- Recurrence at a particular time of year or day, or variability of symptoms, suggesting worsening on exposure to the relevant allergen;
- Involvement of the eyes (itching, watering, redness, puffiness); or
- Predominance of itch as a symptom, which can also involve the pharynx and ears.
- Allergic rhinitis is more likely if there is a past or family history of allergic disease, but can also occur as the first manifestation of allergy in a previously unaffected person.

3.2. Seasonal considerations

Patients may be allergic to trees, plants and fungi that use the wind to disperse their pollen or spores.[8] While high amounts of pollen and fungal spores are released during warmer days compared to colder ones, house dust mite allergens are present all year round. However, these tend to be higher indoors during winter when windows are shut and the humid, centrally heated atmosphere is optimum for their reproduction [9].

3.3. Triggers of non-allergic rhinitis

1. Cold air.
2. Changes in climate (such as temperature, humidity, and barometric pressure).
3. Strong smells (such as perfume, cooking smells, flowers, and chemical odors).
4. Environmental tobacco smoke.
5. Changes in sexual hormone levels.
6. Pollutants and chemicals (e.g., volatile organics).
7. Exercise.
8. Alcohol ingestion.

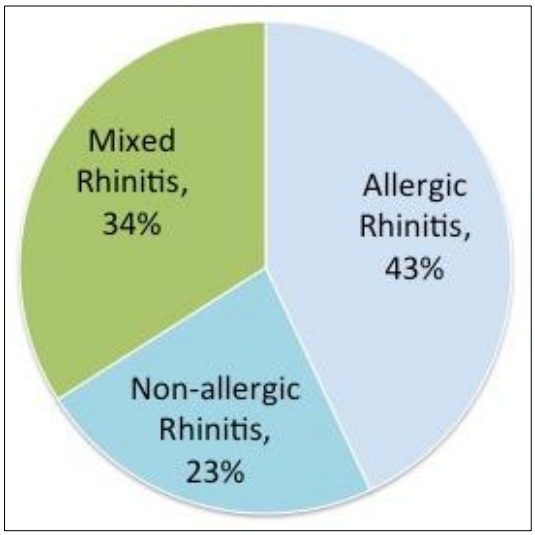

Fig 2: relative incidence of allergic rhinitis, non-allergic rhinitis, and mixed rhinitis

4. Treatment

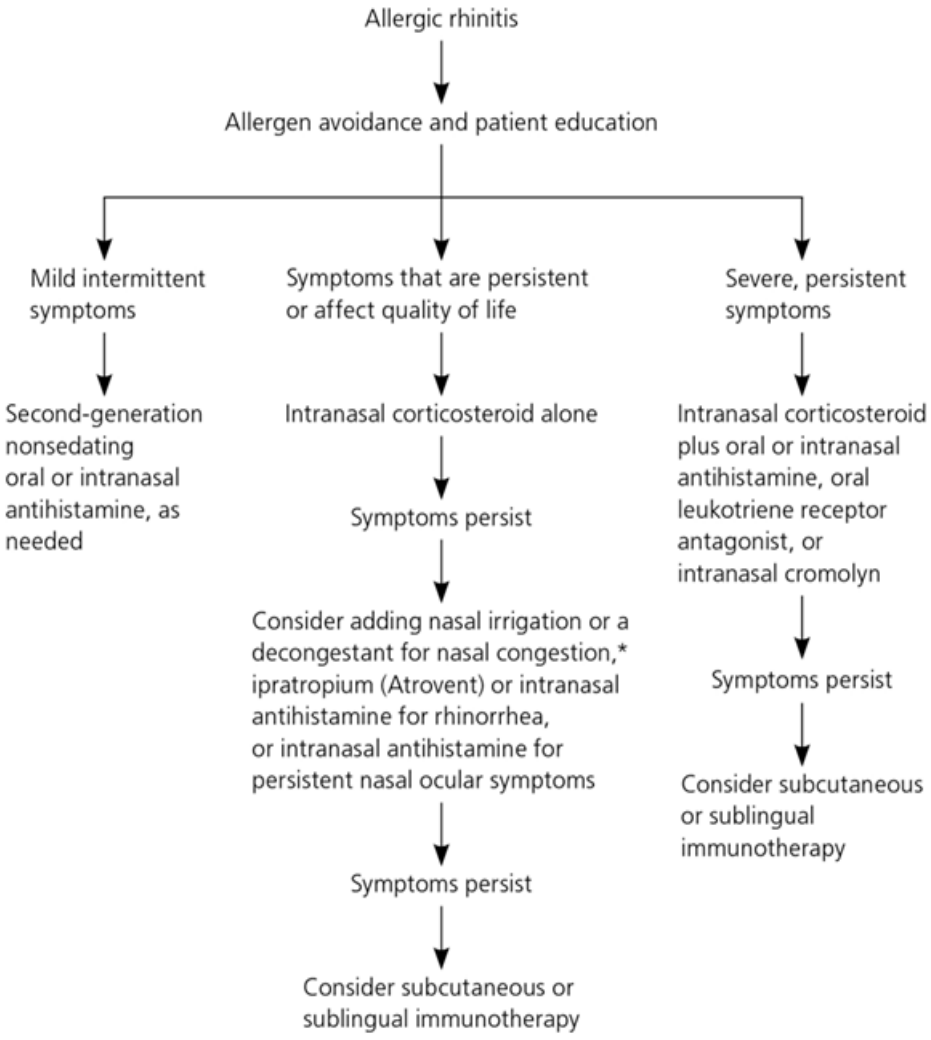

Fig 3: Use of nasal decongestants for longer than three days is not recommended because of possible rebound congestion

4.1. Allergen avoidance
The first-line treatment of allergic rhinitis involves the avoidance of relevant allergens (e.g., house dust mites, moulds, pets, pollens) and irritants (e.g., tobacco smoke). Patients allergic to house dust mites should be instructed to use allergen-impermeable covers for bedding and to keep the relative humidity in the home below 50% (to inhibit mite growth). Pollen and outdoor mould exposure can be reduced by keeping windows closed, using window screen filters, using an air conditioner, and limiting the amount of time spent outdoors during peak pollen seasons. For patients allergic to animal dander, removal of the animal from the home is recommended and usually results in a significant reduction in symptoms within 4–6 months. These avoidance strategies can effectively improve the symptoms of allergic rhinitis, and patients should be advised to use a combination of measures for optimal results Patients may be allergic to trees, plants and fungi that use the wind [1].

4.2. Intranasal corticosteroids
Intranasal corticosteroids are the mainstay of treatment of allergic rhinitis. They act by decreasing the influx of inflammatory cells and inhibiting the release of cytokines, thereby reducing inflammation of the nasal mucosa [22]. their onset of action is 30 minutes, although peak effect may take several hours to days, with maximum effectiveness usually noted after two to four weeks of use [9]. One randomized controlled trial (RCT) looking at quality-of-life measures compared the antihistamine loratadine (Claritin) with the nasal corticosteroid fluticasone (flonase) in 88 adults over a four-week period [13]. The study's results showed that symptom scores were comparable, but quality-of-life scores were superior in the nasal corticosteroid group.

4.3. Antihistamines
The second-generation oral anti-histamines (e.g., desloratadine [aerius], fexofenadine [Allegra], loratadine [Claritin], cetirizine [reactine]) are the first-line pharmacological treatments recommended for all patients with allergic rhinitis. Recently, two new second-generation antihistamines-bilastine (blexten) and rupatadine (rupall)-have been introduced in Canada. The second-generation oral anti-histamines have been found to effectively reduce sneezing, itching and rhino rhea when taken regularly at the time of maximal symptoms or before exposure to an allergen. Although the older (first-generation) sedating antihistamines (e.g., diphenhydramine, chlorpheniramine) are also effective in relieving symptoms, they have been shown to negatively impact cognition and functioning and, therefore, they are not routinely recommended for the treatment of allergic rhinitis [1, 25].

4.4. Combination intranasal corticosteroid and antihistamine nasal spray
If intranasal corticosteroids are not effective, a combination corticosteroid/antihistamine spray can be tried. Combination fluticasone propionate/azelastine hydrochloride (dymista) is now available in Canada. This combination spray has been shown to be more effective than the individual components with a safety profile similar to intranasal corticosteroids [26, 27].

4.5. Decongestants
Oral and intranasal decongestants improve nasal congestion associated with allergic rhinitis by acting on adrenergic receptors, which causes vasoconstriction in the nasal mucosa, decreasing inflammation [28-30]. The most common decongestants are phenylephrine, Oxymetazoline (Afrin), and pseudoephedrine. The abuse potential for pseudoephedrine should be weighed against its benefits.

4.6. Cromolyn sodium
Cromolyn sodium has been shown to prevent the onset of allergic rhinitis symptoms in multiple placebo-controlled trials. It is extremely safe but requires regular use and is not as effective as other medications for acute symptoms. Direct comparison studies have shown that Cromolyn is not as effective as intranasal corticosteroids [31, 32].

4.7. Herbal treatments
According to Sushrut Sanhita, medicated smokes (Dhooma) which contain pungent (Katu) and bitter (Tikta) containing herbs such as mustard, Rasanjan (made up of daru haldi), Nagarmotha, Pathaa, Tejovati (Tamalpatra), Katfal can be used for treatment. Some Tailas (oils) that contain Kutki, Vacha (Vekhand), mustard, Saindhav, Chitrak, Pippali, Pillli Mul, copper sulfate, daru Halad can be used. Base oil for this preparation is sesame oil (til oil). This oil is kept in mouth (kaval) for some time and then excretion from nose will occur. Oil for nasal instillation (Nasya) can be made using 5 types of salts useful to treat vatic Pratishyaya. These include Saindhav, samudra, bida, Audbhida, Samvarchana.

5. Abbreviations
Th2: T helper 2
Il: Interleukin
Ige: Immunoglobulin e
Lar: Local allergic rhinitis
Ace: Angiotensin-converting enzyme
Asa: Acetylsalicylic acid
Nsaids: Non-steroidal anti-inflammatory drugs

6. Conclusions
Allergic and non-allergic rhinitis detrimentally affects the quality of life in a significant portion of the population. The co-morbidities associated with rhinitis can have a further negative impact on patients' wellbeing. Treatment of rhinitis requires that underlying triggers be identified and if at all possible modified. A step-wise approach using pharmacologic and non-pharmacologic therapies can then be implemented, typically with a satisfactory outcome for patients and physicians alike.

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