Introduction

The burden of allergic respiratory diseases in India has seen an upward spiral since the last few decades. A variety of factors have been blamed for the growing prevalence of allergy, namely rapid urbanisation, indoor and outdoor pollution, climatic changes, lifestyle modifications, dietary preferences and others. However, there exists a huge gap between genuine allergy and perceived allergy which can only be narrowed by careful clinico-diagnostic correlation, of which allergic history is a component of paramount importance. This chapter attempts to give the reader a meaningful insight into two of the most common allergic disorders of the respiratory system, namely allergic rhinitis and asthma.

Aetiopathogenesis

Both allergic rhinitis and asthma are chronic inflammatory diseases affecting the airways of the upper and lower respiratory tract. On exposure to allergen(s), T-helper (Th) lymphocytes are sensitized and activated, some of which migrate to the bone marrow to stimulate production and recruitment of mast cell precursors, eosinophils and basophils to the site of inflammation. An inflammatory cascade is set up, leading to outpouring of a cellular inflammatory exudate via several mediators, namely histamine and leukotrienes, Th, cytokines (Interleukins 4 & 5) and other chemokines which further propagate the inflammatory reaction by local as well as systemic synthesis of IgE. In addition to upper respiratory tract inflammation in patients of allergic rhinitis, selective recruitment of the same inflammatory cells in the lower respiratory tract can occur due to upregulation of cellular adhesion molecules by previous episodes of subclinical inflammation, leading to the subsequent development of bronchial hyperresponsiveness, fuelling the dual relationship between asthma and allergic rhinitis (the "one airway, one disease" concept).

Predisposing Factors

| Host factors                  | Environment factors                        |
|------------------------------|-------------------------------------------|
| Age : Young age              | Aeroallergens                             |
| Socio-economic status        | Food allergens                            |
| Genetic : Familial, gene polymorphisms affecting AHR | Occupational exposure                     |
| Atopy                        | Infections (Hygiene hypothesis)           |
|                              | Tobacco smoke                             |
|                              | Pollution - Indoor & Outdoor              |
|                              | Diet                                      |
|                              | Drugs (Aspirin, etc)                      |

Clinical Features

Allergic rhinitis: Allergic rhinitis often presents in childhood. Symptoms may be seasonal or perennial. The ARIA classification stratifies allergic rhinitis as intermittent (< 4 days/week or 4 weeks) and persistent (> 4 days/week and 4 weeks) and as mild or moderate-severe based on the absence or presence of one or more features which include sleep disturbances, impairment of daily activities, sport, leisure, abnormal performance at work or school and troublesome symptoms.

Clinical features include sneezing, rhinorrhea, nasal pruritus, nasal congestion, a sore red enlarged nose,
pain and tenderness over the paranasal sinuses, sore throat, headache, cough and post-nasal drip, throat. Examination of the eyes is not to be missed and may reveal ocular itching and congestion, catarrh, lacrimation and keratoconjunctivitis. Prominent signs in children include the allergic salute (children using the palms to thrust the nose superiorly to temporarily relieve nasal itching and open blocked nasal passages), allergic shiners (discolouration of the orbito-palpebral grooves beneath the lower eyelids), allergic facies (gaping expression, mouth breathing, allergic shiners and dental malocclusion), Dennie's line (a wrinkle beneath the lower eyelids) and a geographic tongue (pale bald sharply demarcated patches on the tongue).

**Bronchial asthma**: Asthma is twice as common in male children as compared to females, however this gender difference disappears as age advances and in adults it occurs with nearly equal frequency in both sexes. Patients tend to have a strong family and/or atopic history. Symptoms may be perennial or seasonal and often exhibit diurnal variation. The patient may present with episodes of wheezing, cough, breathlessness or chest tightness particularly at night or early in the morning. Chest examination may reveal an audible wheeze which is usually prominent during expiration.

Acute severe asthma may present with profound respiratory distress with increased activity of the accessory muscles, difficulty in speaking, intercostal retraction, tachycardia and pulsus paradoxus. The chest may be silent if the degree of airflow obstruction is severe during an attack. Examination of the upper respiratory tract is not to be missed and may reveal nasal turbinate hypertrophy, septal deviation, polypi, sinus tenderness and even oro-pharyngeal candidiasis due to frequent doses of inhaled corticosteroids.

Dermatological examination may reveal signs of atopic dermatitis or eczema in patients with a strong history of atopy. Severity of asthma is currently based on the level of control based on presence or absence of the following parameters: daytime symptoms, need for reliever/rescue medication, limitation of activities, nocturnal symptoms or awakening and lung function as controlled (none of the features), partly controlled (any one of them) and uncontrolled (three or more features).

### Diagnosis of Respiratory allergy

The importance of clinical history coupled with physical examination in diagnosis of respiratory allergy cannot be over-emphasized. The objectives of history are not only to establish whether the patients suffers from respiratory allergy but also to ascertain factors which contribute to symptoms and elicit clues to the etiological allergens which may be confirmed by specific allergen tests. Eliciting a good allergic history may be a time consuming practice which often requires ample patience and diligence from the physician. History should include the following questions in addition to patient details and chief complaints:

- **Duration of current illness/symptoms** and also history of childhood symptoms as usually the onset of allergic symptoms dates back to childhood.
- **Frequency and severity of symptoms**, their impact on daily activities and work/school performance and treatment taken (including over the counter medications, home remedies or alternative therapies).
- **Occurrence** - Usually if the symptoms are seasonal then pollens are implicated as the most common allergens and if they are perennial then indoor allergens like house dust mites, animal dander, cockroaches or mould spores are the commonest allergens. However some seasonal allergens may cause perennial symptoms and a few perennial allergens may cause symptoms only during certain periods, so also a few patients may be polysensitized to both seasonal and perennial allergens. It is equally important to understand the timing and location of symptoms. In young children, if symptoms occur at playtime then pollens from grass, weeds or other plants near the playground tend to be implicated whereas if they occur at night then indoor allergens in the bedroom like ceiling moulds or soft toys may be implicated. Similarly, attacks occurring during the daytime at the workplace implicate an occupational allergen. Increased frequency and severity of symptoms during houesecleaning often points to house dust mites as the culprit allergen. The practising allergy specialist should correlate occurrence of symptoms with the local pollen calendar.
- **Precipitating factors** - These could be inhalants, ingestants (foods, drugs like aspirin, etc), contact irritants like soap, cosmetics or perfumes, insects, climatic change and even heat, cold and dampness.
- **Dietary habits** - Careful history of symptoms and their relation to intake of certain foods is often required to distinguish perceived allergy from actual food allergy.
- **Co-morbidities** - It is well known that allergic rhinitis and asthma are closely linked epidemiologically, immunologically as well as clinically. Up to 40% patients with rhinitis may have asthma and upto 80% of asthmatics may have nasal symptoms[1].

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Furthermore, the prevalence of asthma may be up to three fold higher in children who have suffered from allergic rhinitis\(^1\). Hence every patient of allergic rhinitis should be evaluated for asthma in the presence of episodic symptoms and vice versa. Atopic dermatitis and eczema are other diseases that may co-exist.

- **Family history** - Children not only inherit atopic tendencies from their parents but are also likely to develop the same allergic disorder. The predisposition of young children to develop atopy to environmental allergens is about 13% when neither parent is atopic, 30% if at least one parent or sibling is atopic and about 50% if both parents are atopic\(^6\).

- **Personal and environmental history** - Particularly important with exposure to tobacco smoke (including environmental tobacco smoke), food habits, occupation, etc.

### Allergy tests

These are of two types, namely:

- **In-vivo tests** - Skin prick tests, intradermal tests, patch tests, mucosal challenge (Nasal and bronchial provocation tests) and food challenge tests
- **In-vitro tests** - Estimation of serum allergen specific IgE by radio-allergoadsorbent test (RAST), ELISA and multi-allergen screening assay.

The skin prick test (SPT) is the most validated and widely practiced modality of allergy testing worldwide and is often used to confirm clinical sensitivity to a wide variety of allergens. It is based on the presence of specific IgE directed against the allergen(s) tested which manifests as the classical “wheal and flare response”. A positive test to a specific allergen is indicated by a response of at least 3 mm or more than the diluent control. In Indian patients only wheal dimensions are measured as flare (erythema) may not always be distinguishable due to the typical dark brown or wheatitis complexion. SPT’s are usually less sensitive than the intradermal tests but correlate better with the presence of clinical allergy for inhalant and food allergens, whereas intradermal tests are more useful for the evaluation of drug and venom allergies.

Though intradermal tests have been reported to demonstrate better sensitivity, they also carry higher incidence of false-positive reactions and anaphylaxis due to direct sensitization of mast cells in the dermis. They are not recommended for evaluation of food allergy. The number of skin tests and the allergens selected should be dictated by the patients history, environmental living conditions, occupation and activities\(^7\). Provocation tests with allergens are recommended only at institutional level and are mainly done for research purposes.

Diagnosis of allergic rhinitis: A confident diagnosis of allergic rhinitis can be made clinically. Additional tests include imaging of the nose and paranasal sinuses, analysis of nasal secretions, rhinoscopy and rhinomanometry.

Diagnosis of bronchial asthma\(^8\): Asthma diagnosis is based on the presence of characteristic symptoms coupled with assessment of lung function by spirometry and peak expiratory flow, demonstration of airway hyperresponsiveness and the exclusion of underlying lung parenchymal or interstitial disease by chest imaging. Spirometry provides objective confirmation of diagnosis, information regarding the severity of airflow obstruction, bronchodilator reversibility and variability and also serves to assess response to treatment. However a normal spirometry does not exclude diagnosis of asthma in a patient with asthma-like symptoms. Peak flow monitoring is a valuable tool to assist the physician in the diagnosis of asthma in patients who are poor perceivers of asthma symptoms, in monitoring variability and also in identify occupational causes.

Measurements of airway hyper-responsiveness like direct or indirect bronchoprovocation challenge tests are not recommended in routine practice and are only useful in patients with asthma-like symptoms and normal spirometry or peak flow. A positive methacholine challenge test is consistent with airway hyper-responsiveness and therefore with asthma but may also be seen in other inflammatory disorders of the airways like COPD, bronchiectasis and allergic rhinitis whereas a negative test excludes the diagnosis of asthma with a high degree of accuracy. Other non-invasive tests like sputum cell counts, exhaled breath condensates and fractional concentration of exhaled nitric oxide may be used as surrogate measures of airway inflammation but are not routinely recommended. It is particularly important to exclude common mimics of asthma like COPD, allergic rhinitis (which may often coexist) and gastro-oesophageal reflux.

### Treatment

The treatment of respiratory allergy requires a multi-disciplinary approach with focus on several issues, namely
1. **Lifestyle & Environmental modifications**: Drugs, diet, exposure to precipitating factors like tobacco smoke, indoor allergens, etc.

2. **Treatment of allergic rhinitis**: Treatment of allergic rhinitis includes allergen and irritant avoidance and pharacomological therapy with anti-histamines (oral and intranasal H1 blockers), intranasal corticosteroids, intranasal mast cell stabilisers (cromones) or leukotriene modifiers (montelukast) or a combination of these. Persistent rhinorrhoea is often relieved by intranasal ipratropium[10]. Decongestants may be used if nasal blockade is severe. Nasal or sinus wash with saline removes pollen and other aeroallergens and also clears excess mucus. If allergic conjunctivitis co-exists, therapy with oral or topical anti-histamines, montelukast or cromones is often beneficial.

3. **Treatment of asthma**: The treatment of asthma focuses on achieving a level of control that is acceptable to both the patient and the physician, the components of which include patient education, avoidance of trigger factors, monitoring of symptoms and lung function and maximal optimization of pharmacological treatment[10]. Inhaled corticosteroids are the mainstay of therapy for asthma. Other drugs which may be used include long and short acting bronchodilators (inhaled or oral), systemic corticosteroids, phosphodiesterase inhibitors and leukotriene modifiers. Of particular importance is the difference between controller and reliever medications and directions to the patient regarding their use. Management of asthma exacerbations should be directed at relief of symptoms and respiratory failure, reversal of airflow obstruction and prevention of future exacerbations. Comorbidities are an important cause of poor asthma control and should be looked for and treated aggressively.

4. **Allergen specific measures**

   a.) **Allergen avoidance and reduction**: Certain allergens (e.g. food) can be avoided altogether. Others like house dust mites and mold spores can be reduced to a satisfactory level by a variety of control measures.

   b). **Allergen specific immunotherapy**: Allergen specific immunotherapy is indicated in patients of allergic rhinitis/rhinocconjunctivitis and bronchial asthma with history of symptoms after natural exposure to the allergen and demonstrable of specific allergy against the offending allergen(s) by history, skin tests and / or RAST or ELISA. Allergen immunotherapy induces a shift of the immune response from Th2 to Th1 type, manifested by a reduction in Interleukins 4 & 5 and increase in interferon-gamma. The Th1 immune response is associated with upregulation of cell-mediated immunity which is protective against the development of allergy and asthma by downregulating release of inflammatory mediators, airway hyperresponsiveness and specific IgE levels coupled with an increase in specific IgG levels (blocking antibodies). It is particularly useful in patients aged between 12-45 years with severe symptoms affecting their quality of life performance at work or school or causing sleep disturbances.

   The ideal candidates of immunotherapy are patients who either failed to avoid allergen exposure inspite of all efforts or had no response to allergen avoidance or had poor response to other forms of pharmacotherapy. Various forms of immunotherapy are available, the most common and validated being subcutaneous immunotherapy (SCIT) for which the category of evidence for clinical efficacy is I-A in asthma and I-B in allergic rhinitis. The patients selected should assure long-term compliance for immunotherapy. Allergen immunotherapy is usually administered for a period of 3 to 5 years; its total duration and the decision to discontinue it should be individualised and are usually dictated by patient response.

   Contraindications for immunotherapy include malignancy, coronary artery disease, recent myocardial infarction or arrhythmia, severe psychological disorder, severely compromised lung function, severe reactions to previous immunotherapy or patients on beta-blockers. Guidelines for the practice of allergen testing and immunotherapy in India have been published[11] and are being revised subsequently. Certified training courses are being conducted on a yearly basis by the V. P. Chest institute, Delhi since the last three decades.

5. **Other medications**: The anti-IgE monoclonal antibody Omalizumab has shown significant efficacy in bronchial asthma[10]. It is currently approved for use for two allergic diseases, namely moderate to severe persistent asthma in patients with an elevated total serum IgE and a positive skin test or in vitro reactivity to a perennial aeroallergen and inadequate symptom control with inhaled corticosteroids and chronic idiopathic urticaria. A few studies have investigated its use in patients with seasonal allergic rhinitis to ragweed, birch and grass pollens and have found significant improvement in symptoms and reduction in medication use amongst these patients[12-14].

6. **Surgical or other interventions** like nasal or sinus surgery for rhinitis and thermoplasty for asthma.
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