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**Research Paper**

# Basic Allergology and Allergies in India

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***ABSTRACT:*** *Between 1997 and 2011 food allergies in children have increased approximately 50 percent and now affect 1 in 13 children in the United States. Prevalence of food allergies in first world countries is steadily approaching 10%. Despite this increasing burden on the healthcare system worldwide, inadequate diagnoses and lack of treatment of allergies are common occurrences. This review serves as an elementary guide to allergies, their action mechanism, and treatments. The later part of this article is concerned with certain specific allergens and the allergic reactions they cause. 40-50% of Indian cases of paediatric asthma as severe or uncontrolled- which, on its own, is a strong argument for the fact that more research with focus on region-specific data, as well as affordable and effective medication, and condemnation of stigma regarding chronic illness are imperative for better diagnosis, treatment, and prevention of allergies. Through this review we aim to spread awareness regarding allergies in general, as well as some specific allergens, their effects, and how they are presently being treated. This information, if appropriately used, can help design more effective solutions and eventually make millions of lives better.*

***KEYWORDS: allergy, IgE response, glycoproteins, antibodies, anaphylaxis***

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## I. INTRODUCTION

Allergens are foreign proteins that induce immunoglobulin (IgE) responses, i.e., production of glycoprotein molecules by the white blood cells in order to destroy particular antigens. Such reactions are commonly termed as allergies. Allergies vary greatly in their nature of response, clinical presentation, causal allergen, time elapsed between exposure to antigen and onset of reaction, etc. For example, a wasp sting can cause generalised hives within 10-15 minutes, whereas rashes from poison ivy may take several hours to appear. Rapid onset of the disease greatly simplifies the process of identification of the causal allergen [1].

Allergic responses are characterised by the production of IgE antibodies but can also include other isotypes such as IgG, IgA, IgG4 as well as T cells. Respiratory symptoms such as sneezing, and in severe cases anaphylaxis, are caused by delivery of allergen to the nose on particles that carry several other molecules in addition to the protein allergen. These molecules are capable of altering the reaction[2]. For instance, the dose of exposure to mite or grass pollen and the prevalence of IgE responses are directly proportional, whereas the highest levels of exposure to cat allergen are associated with a lower prevalence of IgE responses. It is interesting to note that the animal sources that are most clearly associated with decreased responses at high allergen dose are derived from animals from which humans evolved more recently (~65 million years ago).[1] [3].

Of these respiratory allergens, those found indoors generally lead to development of asthma due to the chronic nature of exposure, some of the most common ones being fungi, dust mites, cockroaches, and certain mammals. Children who grow up in households with pet cats exhibit a positive correlation between degree of exposure to allergens and the frequency, severity, and exacerbation of bronchitis-like symptoms [4]. The occurrence and severity of asthma cases have increased vastly over the past 50 years due to the more sedentary lifestyles and warm, highly furnished homes with inadequate ventilation in most parts of the world. Studies report that perennial asthma is associated with sensitization to specific indoor allergens, rather than generalised IgE hyperreactivity- exemplified by the frequency of sensitization to allergens from German cockroach being commonly associated with asthma among low income populations living in houses containing high concentrations of cockroach allergens. Presence of cockroach allergen in the bedroom, floorboards, and bed dust of such houses is associated with increased asthma morbidity and more number of days when asthma symptoms are aggravated. Furthermore, age at the time of exposure to allergens is another factor that affects sensitization and the manifestation of symptoms [5]. For instance, Evidence demonstrates that exposure to cockroach antigen

causes exacerbation of asthma in specifically sensitised adults, but such evidence is less consistent for children, even with the same level of sensitisation. Taking another example, evidence suggests that chronic exposure to ETS (environmental tobacco smoke), which contains carcinogens in addition to eye and respiratory irritants, is responsible for decreased peak flow in preschool-age children. However, evidence suggesting a similar effect in older adolescents and adults is limited [6].

Some allergens that definitively cause an increase in airway reactivity and unscheduled medical visits include dog allergens, fungi (specifically penicillium), dampness and brief high level exposure to nitrogen dioxide (produced by gas stoves and space heaters). Allergens that are supported by limited evidence as to causing the above mentioned effects include domestic birds, non-occupational formaldehyde (its largest source being cigarette smoke), and certain fragrances. Although the nose is still recognized as the primary route for sensitization to inhalant allergens, there is increasing evidence supporting the skin and mouth as important sites for the generation of IgE antibody responses [7].

Despite the exorbitant detriment allergies have conclusively caused on patients' quality of life– including illness related school absences, hospitalisation, economic stresses–there is currently no cure for allergies. Patients can only rely on accurate labelling of food items, cosmetics etc. to avoid reactions. Hence, contamination is a major issue which can be dealt with through the development of more rapid, standardised and accurate detection methods. Along with detection, detailed analyses and quantification of the allergenic compounds prove crucial in diagnosis and treatment plans, as well as management of production processes in various industries. For example, determination of food allergens is primarily based on detection of either proteins or nucleic acids, using such techniques as immunoblotting, enzyme-linked immunosorbent assay (ELISA), and chromatography most often coupled with MS or MS/MS [8] [9]. PCR is the technique based on nucleic acid determination. Generally, a combination of different methods is applied for allergen analysis [10]. The understanding of different types of Allergens present and the kind of allergies they cause is extremely important. Also, we explore a few allergens that have existed in India since a long time.

## II. THE TYPES OF ALLERGENS AND THEIR EFFECTS

### II.1 2S ALBUMIN STORAGE PROTEINS

They have been reported as major food allergens in seeds of some of the most common plant-derived allergens, namely peanut, soybean, nuts, sesame, and buckwheat. They are deposited in protein bodies of developing seeds and are utilised by the plant as a source of amino acids and carbon skeletons during germination and seedling growth. Sensitization to 2S albumin occurs directly via the gastrointestinal tract [11]. The high stability of their intrinsic protein structure enables them to withstand, to some extent, the harsh conditions present in the gastrointestinal tract (pH<7, denaturing effects of surfactants secreted by intestinal epithelium, and proteolysis by digestive enzymes) cross the gut mucosal barrier and elicit an allergic response. Presence of disulphide bonds contributes to their stability in acidic medium and retention of their three-dimensional structure despite thermal processing [12].

### II.2 NSLTPS (NON SPECIFIC LIPID TRANSFER PROTEINS)

They are highly stable plant defence proteins. They have a conserved molecular structure with a characteristic globular shape and are made up of α-helices with short loops. Their stability is attributed to the 4 disulphide bonds and hydrophobic cavities present in the structure, and therefore ns LTPSs are resistant to heat and proteolytic digestion [13] [14]. They are commonly found in members of the Rosaceae family, such as walnuts, hazelnuts, and peanuts, and are a major source of plant-food allergies in the Mediterranean region. In fact, they are the most frequent cause of food allergy and anaphylaxis in Italy. One such nsLTP, Pru p3, is found in peach and apple. Sensitization to Pru p 3 is attributed as a risk factor for severe and possibly life-threatening allergic reactions in central Europe. Additionally, nsLTP has also been reported as a major allergen in Chinese cases of mugwort-pollen related allergies [15].

### II.3 LEGUMINS,

These like 2S Albumin, are storage proteins that are found as allergens in high amounts in various varieties of seeds, such as Ara h 3 in peanut, Jug r 1 in walnut, glycinin in soybean, Cor a 9 in hazelnut, and Pru du 8 in almond. Their molecular structure comprises of a β-barrel and an α-helix. Proteases in the seeds cleave alpha-peptide bonds, dividing them into acidic and basic chains with different isoelectric points, resulting in the formation of hexamers. Highly conserved disulphide bonds are present between these chains, stabilising the molecule. Coming to their allergenicity, several reports have highlighted the positive relation between legumin sensitization and chronic respiratory disease (CRD). Additionally, co-sensitization with legumin, 2S Albumin, and another storage protein-vicilin- has proved useful in predicting buckwheat allergy. Sensitization to Cor a 9 has a high positive correlation with severe allergic symptoms in the Netherlands [16].

## III. TYPES OF ALLERGIES:

### III.1 CONTACT DERMATITIS

It is an inflammatory skin disease with mainly 2 causal routes- toxic effects of metal ions causing direct chemical skin damage, or T-cell responses induced by small reactive chemicals, called contact allergens. The first route leads to irritant contact dermatitis, which is a non-specific skin response that does not involve immune responses, does not require prior sensitization to the substance, and elicits similar reactions in most individuals. It is manifested in the form of either acute or chronic skin lesions, caused by exposure to chemical agents (alkaline and acid solutions, organic solvents), physical agents (UV radiation, x-rays), food stuffs, plants, and airborne irritants (irritating dusts or fumes). Effects of acute irritant CD can become chronic upon prolonged exposure to the toxin, gradually degrading the protective skin barrier. Contrastingly, the second pathway leads to allergic contact dermatitis, which is a delayed hypersensitivity response. It manifests as skin lesions, which are induced by sensitization through consistent exposure to an allergen, followed by an immune response mediated by T-cells. Irritant contact dermatitis is more prevalent than allergic contact dermatitis. Patch testing- which checks and proves delayed hypersensitivity reactions-is a widely accepted and practiced method of distinguishing between irritant and allergic CD [16].

### III.2 ALLERGIC ASTHMA

It is defined as airway inflammation and common asthma symptoms like shortness of breath, wheezing, etc. caused by sensitization to airborne allergens. It is the most common phenotype of asthma, with an estimated 80% of childhood asthma cases and 50% of adult asthma cases believed to be allergic in nature. It is more common in males than in females. The onset of this disease is seen most often in childhood, and is usually accompanied by other comorbidities like allergic rhinitis and atopic dermatitis (eczema). Patients that show early-onset asthma (exhibition of symptoms before the age of 12) have significantly more allergen sensitization and allergic symptoms as compared to those with late-onset asthma. Allergic asthma is prevalent in patients that have a family history of asthma. The main criteria for diagnosis are physician-diagnosed atopic dermatitis, parental history of asthma, and sensitization to an aeroallergen. Its treatment includes environmental intervention (for eg. decreasing cockroach and dust mite allergen exposure by using impermeable bedding), immunotherapy, administration of corticosteroids, and treatment with biologics that target the underlying disease pathway [17].

### III.3 ANAPHYLAXIS

It has been described by the "International Consensus on (ICON) Anaphylaxis as a "serious, generalised or systemic, allergic or hypersensitivity reaction that can be life-threatening or fatal". It has a rapid onset, characterised by airway, breathing, and circulatory problems. Presently available data regarding the immunological mechanisms involved in anaphylaxis is limited, owing to its lethal nature. This data has been obtained primarily through induction of anaphylaxis in volunteers through hymenoptera sting, and collection of samples from patients presenting for emergency management of anaphylaxis. According to these data, anaphylaxis results from activation of inflammatory pathways, which are the result of mast cell and/or basophil degranulation. This process is mediated via T cells, T helper cell 2 cytokines, B-cell production of IgE, and subsequent crosslinking of the high affinity IgE receptor on mast cells and basophils by IgE-antigen complexes. Some non-IgE dependent pathways that can trigger degranulation are IgG immune complexes, complement products, neuropeptides, opiates, and radiocontrast media. Apart from the obvious method of preventing exposure to the allergen and accurate labelling, injectable epinephrine (adrenaline), commonly sold under the brand name 'EpiPen' is widely agreed upon as the first line therapy for anaphylaxis. It helps decrease the allergic reaction by relaxing the muscles in the airways to make breathing easier, alongwith muscles in the stomach, intestines, and bladder, and reversing the rapid decrease in blood pressure [18]

## IV. ALLERGENS IN INDIA:

### IV.1. COMMON IVY

Common ivy (Hedera helix) is a strong irritant native to Europe, but is cultivated in colder parts of India as well. Despite there being consistent reports of contact dermatitis caused by this plant since the 1890s, a deficit in commercial patch test material has led to the distribution of these cases being unknown. Common ivy's allergenicity is primarily caused due to the presence of falcarinol and didehydro-falcarinol, two moderate polyacetylenic sensitizers, which are highly reactive alkylating agents towards thiol groups in proteins and form antigenic complexes. Studies have deciphered the unlikelihood of non-professional persons interacting with common ivy and self-diagnosis of mild cases as the reasons for fewer reports of skin allergy symptoms in lay people as compared to gardening professionals [19] [20] [21].

### IV.2 EPICOCCUM

The generally humid climate of most regions in India is conducive for fungal growth. *Epicoccum* is amongst the 3 fungal genera, the other 2 being *Aspergillus* and *Rhizopus*, whose role in causing respiratory allergy in the Indian population has been studied in detail. A major allergen from the species *Epicoccum purpurascens* is a glycoprotein named Epi p 1, which manifests its allergenicity through detachment of epithelial cells from the lung lining. The active protease content of fungal extracts can influence the onset as well as severity of allergic airway disease, such as allergic rhinitis and asthma. Biological activity of such proteases permits them to bypass the airway mechanisms which otherwise inhibit allergic response to inhaled antigens. Such molecules can even facilitate the contact of non-proteolytic allergens with the immune system. The enzymatically inactive form of such proteases may be investigated for potential use in immunotherapy [22].

### IV.3 AMERICAN COCKRAOACH

The detrimental effect of poor sanitation system, which are so commonly found in rural areas as well as crowded slums in urban areas of India, is not just limited to transmission of hygiene-related diseases like typhoid and dysentery, but also contributes to insect allergies. Allergens from *Periplaneta americana*, the most commonly found species of cockroach in India, are a triggering factor for atopic asthma. Purified form of Per a 10, which is the major allergen from this insect, exhibits strong IgE reactivity and uncontrolled production of lymphocytes within 80% of cockroach-sensitized patients. The intrinsic enzymatic nature of Per a 10 is responsible for initiating allergic reaction at the mucosal surface by increasing the permeability of lung epithelium [23].

## V. CONCLUSION

Allergies represent one of the major medical emergencies that where it is important to understand the root cause. The more we understand the details and origin of each of the different allergens it will be easier to design therapies and find a cure for the diseases. Sometimes these allergies can be life threatening and have caused major havoc. Conditions like asthma have become common nowadays, but the reason behind them can be numerous.

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