

## SPECIAL ARTICLE

# Aeroallergens in Clinical Practice of Allergy in India- ARIA Asia Pacific Workshop Report

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**SUMMARY** Allergic diseases such as bronchial asthma, allergic rhinitis and atopic dermatitis are dramatically increasing all over the world including developing countries like India. Today, more than 30% of the population is known to suffer from one or other allergic ailment. Major causative agents implicated are pollen grains, fungal spores, dust mites, insect debris, animal epithelia, etc. Several aerobiological studies have been conducted in different parts of the country to ascertain aerial concentration and seasonality of pollen grains and fungi. Recently, an "All India Coordinated Project on Aeroallergens and Human Health" was undertaken by us to discover the quantitative and qualitative prevalence of aerosols at 18 different centers in the country. Allergenicity important airborne pollen identified by clinico-immunologic evaluation are *Alnus*, *Amaranthus*, *Argemone*, *Brassica*, *Cannabis*, *Cassia*, *Cedrus*, *Chenopodium*, *Cocos*, *Holoptelia*, *Mallotus*, *Morus*, *Parthenium*, *Prosopis juliflora*, *Quercus*, *Ricinus communis*, and grasses such as *Cenchrus*, *Cynodon*, *Imperata*, *Pennisetum* etc. Cross-reactivity of the IgE antibodies is a common phenomenon among various pollen allergens. *Ricinus communis* pollen a commonly growing weed/shrub in India, cross-reacts with latex (*Hevea brasiliensis*), *Mercurialis annua* and also with seeds of *Ricinus communis* – all belonging to family Euphorbiaceae but geographically distantly located. *Areca catechu* cross-reacts with other members of Arecaceae such as *Phoenix sylvestris*, *Cocos nucifera* and *Borassus flabelifer* while pollen of *Holoptelia integrifolia* from India cross reacts with pollen of *Parietaria judaica* from Mediterranean Europe, both of which are members of family Urticaceae. Several reports on pollen and fruit syndrome have been analyzed. Experiments conducted by us revealed that pollutants (NO<sub>2</sub> and SO<sub>2</sub>) not only affect pollen morphology but also changes its allergenic potency.

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Respiratory allergy is prevalent among all populations with increasing trend all over the world. However, development of civilization often at the expense of the natural environment by pollution or biopollution stimulates the appearance of new health problems, besides increase in allergic diseases. The gravity of situation can be perceived by looking at the epidemiological studies carried out in different countries.<sup>1-4</sup> The number of people suffering from allergy reaches to 20-30% of population and pollinosis alone occurs in about 10-15% of the world inhabi-

tants. A survey conducted in Finland indicated a prevalence of 14% allergic rhinitis and 2.5% of asthma.<sup>1</sup> Asthma among Greek population is reported to be as high as 9%.<sup>2</sup> In Australia, 27% of children had wheeze.<sup>3</sup> Recent survey carried out in India shows that 20-30% of population suffer from

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allergic rhinitis and that 15% of them suffer from asthma alone.<sup>4,5</sup>

Irrespective of the type of allergic symptoms, allergies are chronic disease seriously affecting the quality of life and may even sometime be fatal. Therefore, fighting with them may demand a change of lifestyle or even profession maintaining allergen avoidance, long term pharmacotherapy and even immunotherapy.

Aeroallergens such as pollen grains, molds, dust mite and insects play a major role in the pathogenesis of respiratory allergy, particularly asthma and rhinitis. Pollen grains are well studied from across the world and are important aeroallergens and cause of pollinosis. Therefore, it is essential to have the knowledge of locally prevalent aeroallergens for diagnosis and therapy of allergic patients. Knowledge about allergens has progressed, especially with recent molecular and immunological understanding of the allergic mechanisms. Structure and function of allergens have been identified. These researches have provided explanations about the relationship between allergic sensitization, allergen exposure and clinical observations such as cross-reactive or cross-allergenic properties. We have tried to briefly analyze the qualitative and quantitative prevalence of pollen and fungal allergens from India and their clinical implications in the brief review.

## Sources of aeroallergens

### *Pollen allergens*

The transport of pollen grains by wind or by the insects, from floral anther to recipient stigma is the critical reproductive event among higher plants. The dispersion of replicate units in massive abundance assures the success of wind pollination as well as its human health effects including asthma, rhinitis, atopic dermatitis, etc. Pollen prevalence (grains per cubic meter) at any point reflects (plant) source strength and location as well as the dynamics of the intervening environment conditions such as climatic factors, pollution and degree of exposure. The presence of pollen, profile of species, concentration, etc., depends on various climatic factors such as temperature, humidity, wind direction, sunshine, substrate,

precipitation and other seasonal factors. Because of change in the climatic conditions, the study of variations in the diurnal and seasonal prevalence becomes very important.<sup>6</sup>

### *Fungal allergens*

Fungi possess highly evolved mechanism of spore liberation due to which the spores remain suspended in the air for a varying duration, *i.e.* few hours to several days. Fungi and fungal particles can clearly induce an allergic response in susceptible individuals. Typical symptoms include wheezing, cough, rhinorrhea, itchy nose, sore throat, sinus congestion, etc.<sup>7,8</sup> The development of allergies to fungi follows the same biological phenomenon as allergies to other environmental allergens. Dead fungi are able to produce symptoms just as well as live fungi.<sup>9</sup> Hayward and coworkers reported a separation and characterization of antibodies to "molds" in human sera and the role of human precipitins to common fungal antigens in allergic reaction, which was later proved by Pepys.<sup>10,11</sup>

### **Monitoring airborne allergens**

Monitoring of airborne biological particles is carried out by various gravimetric, impaction, and filtration sampling devices.<sup>12-14</sup> In addition, new immunochemical techniques are also used for detecting allergenic pollen and fungal spores and also for measuring of the size of allergen-carrying particles.

Knowledge about diurnal, seasonal and annual fluctuations in air-borne pollen and fungi in any geographical area is essential for diagnosis and treatment of allergy. Aerobiological sampling is therefore carried out to achieve this objective through various sampling devices being currently used to monitor quality and quantity of bioallergens. The isolation and identification of aeroallergens is divided broadly in to two phases: (i) collection of air-borne pollen and (ii) sample analysis.<sup>15</sup>

### **Airborne pollen in different parts of India**

Airborne pollen and their concentration vary in the different seasons depending upon the flowering seasons and climatic factors which are quite variable from one part of the country to other. Recently,

an All India Coordinated Project on Aeroallergens and Human Health sponsored by the Ministry of Environment and Forests, Government of India, was successfully completed by Singh and his colleagues.<sup>4</sup> Important pollen and fungal allergens from 18 different places have been identified, quantified and characterized for their allergenic properties. Important tree, grass, and weed pollen of allergenic significance of different parts of the country are summarized in Table 1.

This provides the most scientific and up-to-date information on aeroallergens in India. Altogether, 43 types of pollen have been recorded from Northern India. The dominant types are: *Holoptelea*, Poaceae, Asteraceae, *Artemisia*, *Eucalyptus*, *Casuarina*, *Morus* and *Putranjiva*. Other important contributors in the air are *Cassia*, *Xanthium*, *Quercus*, *Pinus* and *Cedrus*.<sup>4,16</sup>

In an aerobiological survey from Delhi, ninety-four pollen types were recorded and the major contributors include *Morus*, *Cannabis*, Cheno-

pod/Amaranth, *Prosopis*, *Artemisia*, and *Eucalyptus*.<sup>17</sup> A significant reduction in pollen concentration was observed in subsequent years (Fig 1). The concentration of *Morus*, *Cannabis*, *Prosopis*, and *Artemisia* pollen decreased considerably (Figs. 2-3). It is suggested that the reduction in pollen concentration from 1990 to 1997 in Delhi is due to massive clearing of vegetation for developmental activities of the city.

From Central India, surveys carried out revealed that the dominant pollen types are from the Poaceae, Asteraceae, Apocynaceae, *Rosa*, *Ricinus*, *Ailanthus*, *Holoptelea*, *Cyperus*, *Cicer*, *Argemone*, *Cocos nucifera* and *Hibiscus*.<sup>4,16</sup>

In West Bengal, 59 types pollen were revealed from air and their maximum concentration was recorded in May. Important dominant types are *Trema orientalis*, Asteraceae and Chenopodiaceae, *Pongamia*, *Areca catechu*, *Xanthium* and *Cocos*. At Gauhati, Poaceae, *Cheno/Amaranth*, Asteraceae, *Putranjiva*, *Mangifera* and *Eucalyptus*, are the dominant types of pollen.<sup>4,16</sup>

**Table 1** Common allergenic plants of different seasons in India

	Spring (Feb–April)	Autumn (Sept–Oct)	Winter (Nov–Jan)
<b>Trees</b>	<i>Ailanthus excelsa</i> <i>Bauhinia variegata</i> <i>Casuarina equisetifolia</i> <i>Holoptelea integrifolia</i> <i>Mallotus philippensis</i> <i>Prosopis juliflora</i> <i>Putranjiva roxburghii</i> <i>Quercus incana</i>	<i>Anogeissus pendula</i> <i>Carica papaya</i> <i>Cedrus deodara</i> <i>Cocos nucifera</i> <i>Eucalyptus</i> spp. <i>Mallotus philippensis</i> <i>Phoenix sylvestris</i> <i>Prosopis juliflora</i> <i>Quercus incana</i>	<i>Cassia siamea</i> <i>Cedrus deodara</i> <i>Mallotus philippensis</i> <i>Salvadora persica</i> <i>Quercus incana</i>
<b>Weeds</b>	<i>Cannabis sativa</i> <i>Chenopodium murale</i> <i>Parthenium hysterophorus</i> <i>Plantago major</i> <i>Suaeda fruticosa</i>	<i>Amaranthus spinosus</i> <i>Artemisia scoparia</i> <i>Cassia occidentalis</i> <i>Ricinus communis</i> <i>Xanthium strumarium</i>	<i>Ageratum conyzoides</i> <i>Argemone mexicana</i> <i>Asphodelous tenuifolius</i> <i>Chenopodium album</i> <i>Ricinus communis</i>
<b>Grasses</b>	<i>Cynodon dactylon</i> <i>Dicanthium annulatum</i> <i>Imperata cylindrica</i> <i>Paspalum distichum</i> <i>Poa annua</i> <i>Polypogon monspeliensis</i>	<i>Bothriochloa pertusa</i> <i>Cenchrus ciliaris</i> <i>Hetropogon contortus</i> <i>Pennisetum typhoides</i> <i>Sorghum vulgare</i>	<i>Cynodon dactylon</i> <i>Eragrostis tenella</i> <i>Phalaris minor</i> <i>Poa annua</i>

From Southern India, studies carried out revealed that *Casuarina*, *Parthenium*, *Spathodia*, *Cheno/Amaranth*, *Cocos*, *Eucalyptus*, *Poaceae*, *Peltophorum* and *Cyperaceae* are dominant pollen types.<sup>4,16</sup> Pollen calendars are very useful for clinicians as well as allergic patients to establish chronological correlation between the concentration of pollen in air and seasonal allergic symptoms. The Centre for Biochemical Technology (Council for Scientific and Industrial Research) had published a book on pollen calendars of 12 different states in India,<sup>18</sup> which provides important pollen season for grass, weeds, and trees prevalent in India.

### Clinically important pollen allergens

Based on clinico-immunological evaluation of pollen antigens, important allergenic pollen in India have been identified. The work on pollen allergy was initiated in the 1950's by Shivpuri in Delhi. Subsequently, Kasliwal and his colleagues reported important pollen allergens of Jaipur.<sup>19</sup> Shivpuri and Parkash<sup>20</sup> observed *Prosopis juliflora* as a major cause of pollinosis with 12% patients showing a positive skin reaction. Later, important pollen allergens were identified for Delhi by Shivpuri and his colleagues.<sup>21</sup> They were: *Ageratum*, *Ailanthus*, *Amaranthus*, *Anogeissus pendula*, *Artemisia*, *Cassia siamea*, *Cenchrus*, *Chenopodium*, *Cynodon*, *Ipomoea fistulosa*, *Paspalum distichum* and *Poa annua*.<sup>21</sup> We recorded positive skin reactions in 16.9% patients to *Pinus roxburghii* from the foothills of Himalayas.<sup>22</sup>

Pollen causing allergy are quite variable in different ecozones which makes it very important to identify pollinosis causing species from every region, and prepare extracts from them for diagnosis and immunotherapy for the benefit of allergy sufferers.

From Northern India, important allergens identified are: *Prosopis juliflora*, *Ricinus communis*, *Morus*, *Mallotus*, *Alnus*, *Quercus*, *Cedrus*, *Argemone*, *Amaranthus*, *Chenopodium*, *Holoptelea*, and grasses. From Central India the important pollen allergens are: *Argemone*, *Brassica*, *Cannabis*, *Asphodelus*, *Parthenium*, *Cassia*, *Azadirachta*, grasses, *Alnus*, *Betula*, *Malotus*, *Trewia nudiflora*. From Eastern India, allergenically significant pollen types were found as: *Lantana*, *Cucurbita maxima*,

*Cassia fistula*, *Cocos nucifera* and *Calophyllum inophyllum*. Recent studies based on clinical and immunologic parameters reported *Phoenix*, *Ricinus communis* and *Aegle marmelos* as causative agents of allergy in this region.<sup>4</sup>

From South India *Cassia*, *Ageratum*, *Salvadora*, *Ricinus*, *Albizia lebbek* and *Artemisia scoparia* have been reported as important aeroallergens.<sup>23,24</sup> Subbarao *et al.*<sup>25</sup> recorded allergenicity to *Parthenium hysterophorus* pollen extracts in 34% of allergic rhinitis and 12% bronchial asthma patients from Bangalore. Agashe and Soucenadin<sup>26</sup> recorded high skin reactivity to *Casuarina equisetifolia* in patients from Bangalore.

Clinical studies undertaken by us recently at various medical centres under the All India Coordinated Project (AICP) on Aeroallergens and Human Health<sup>4</sup> sponsored by the Ministry of Environment and Forest, revealed important allergenic pollen for various regions in India. Thirty-five pollen antigens

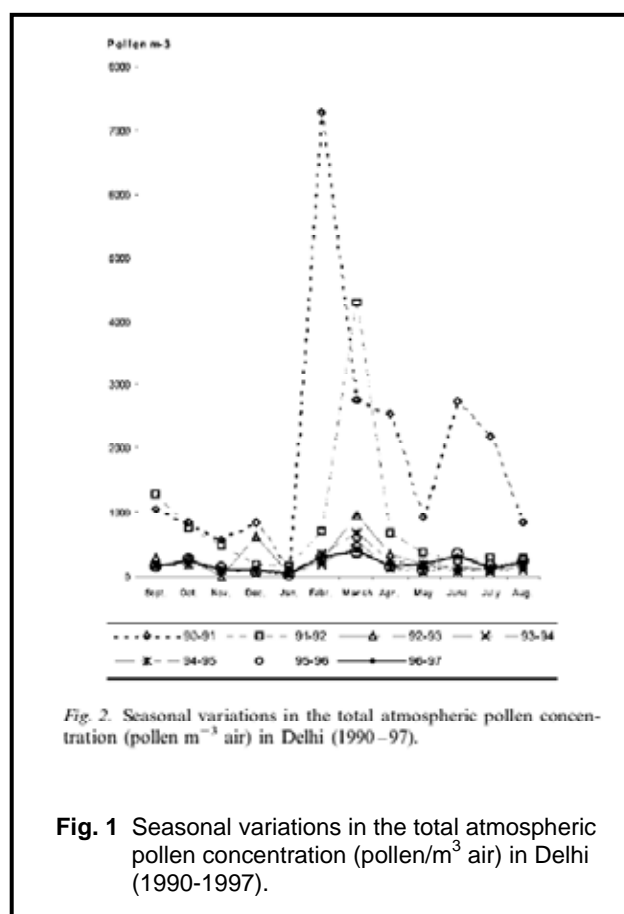


Fig. 2. Seasonal variations in the total atmospheric pollen concentration (pollen m<sup>-3</sup> air) in Delhi (1990-97).

Fig. 1 Seasonal variations in the total atmospheric pollen concentration (pollen/m<sup>3</sup> air) in Delhi (1990-1997).

were tested on atopic population. At Chandigarh, skin sensitivity was highest against *Rumex acetosa* and *Ailanthus excelsa* (17.6%), followed by *Trewia nudiflora* (9.7%), *Argemone mexicana* (9.5 %), and *Cedrus deodara* (9.3%). In Delhi, 12.6% of the atopic population was positive to *Amaranthus spinosus*, 8.5% to *Populus deltoides* and 7.5% to *Dodonea*

*viscosa* and *Bauhinia vareigata*. In Kolkata, 28.8% of the patients were sensitive against *Solanum sysimbrifolium*, 21.1% to *Crotalaria juncea* and 18.2% each to *Ricinus communis* and *Ipomea fistulosa*. In Trivandrum, maximum skin reactivity was recorded to *Mallotus phillipensis* (12.1%), followed by *Prosopis juliflora* (6.3%). For the first time,

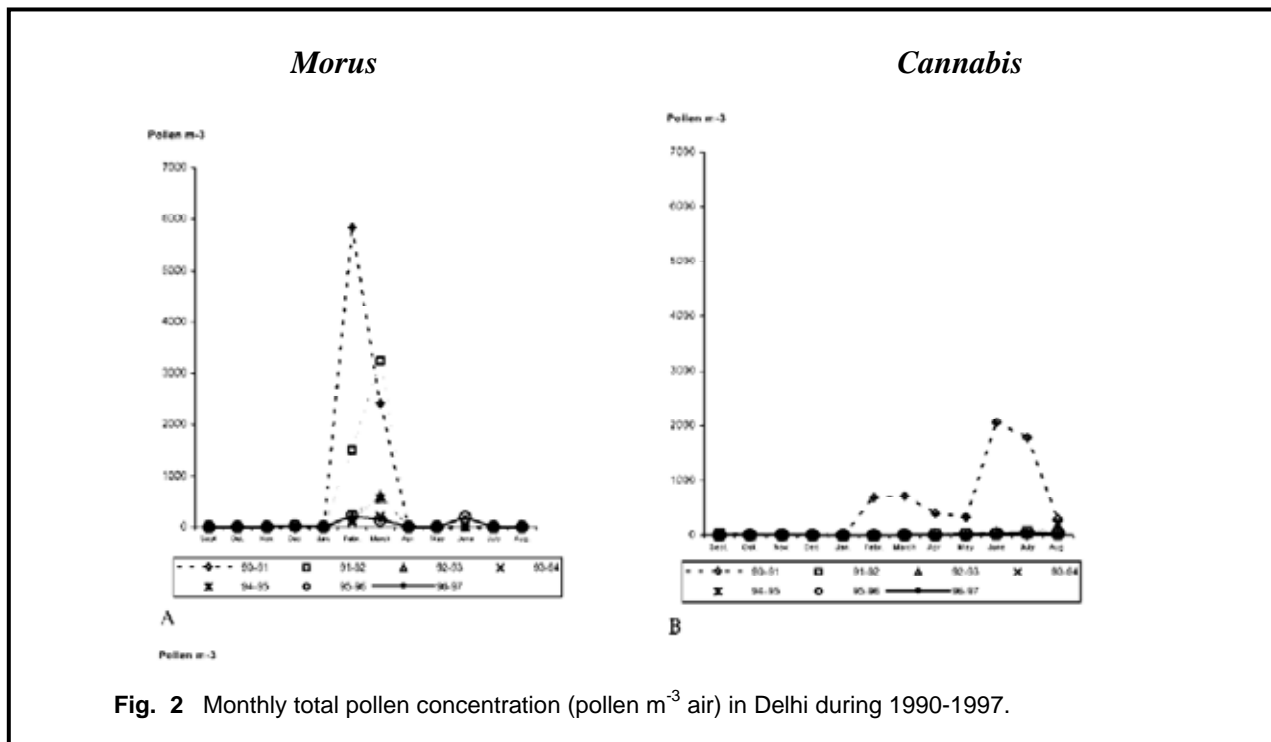


Fig. 2 Monthly total pollen concentration (pollen m<sup>-3</sup> air) in Delhi during 1990-1997.

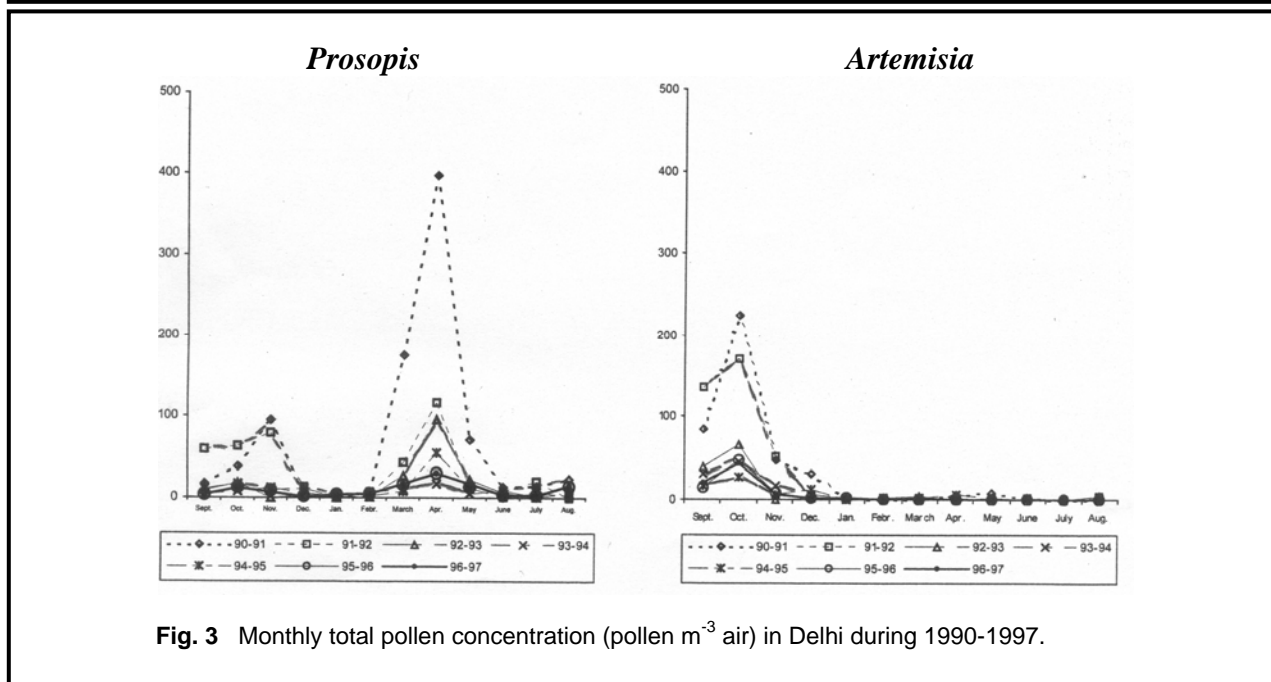


Fig. 3 Monthly total pollen concentration (pollen m<sup>-3</sup> air) in Delhi during 1990-1997.

*Cedrus deodara* (Pinaceae) pollen has been recognized as a new allergen from India in the patients from the Himalayan region, where *Cedrus deodara* occurs naturally.<sup>27</sup>

Major allergens vary from place to place. It is important for clinicians to select only those pollen antigens for skin testing which are prevalent in a particular area in which the patient resides.

### Airborne fungal allergens

Fungi are ubiquitous in nature and are reported to be prevalent from different parts of the world, both in outdoor and indoor environments. Airborne surveys of fungal allergens have been reported from different parts of India.

### Outdoor allergens

In India, many reports provide information of prevalence of fungi in ambient air.<sup>28-33</sup> *Alternaria* is reported as the dominant fungal type from Delhi. A survey conducted for culturable and non-culturable fungi reported 98 fungal forms with *Cladosporium* contributing 25-40% of total airborne fungi followed by *Ustilago* (smuts) (24%), *Aspergillus flavus* (10-13%), *Alternaria* (11%) and *A. niger* (8%).<sup>32</sup> *Basidiomycetes* contributed 7-13% at different sites.<sup>30,32</sup> Dominant forms reported from Visakhapatnam and Gulberga are *Cladosporium*, *Aspergillus*, *Nigrospora*, *Alternaria*, *Curvularia*, basidiospores, ascospores, *Helminthosporium* and *Periconia*.<sup>33,34</sup> From Mysore, Ramalingam reported high concentrations of *Cladosporium* spp., smuts and *Epicoccum*.

Studies carried out in Gaya, Gauhati and Kolkata revealed that *Cladosporium*, *Alternaria*, *Aspergillus*, *Penicillium*, *Curvularia*, *Helminthosporium*, *Aureobasidium*, *Neurospora*, *Mucor* and *Nigrospora* are the major types reported, recorded from Eastern India.<sup>4</sup>

### Indoor allergens

The spectrum of indoor airborne "mold" spores, such as in homes, offices, and other work places, differ from place to place due to the influx of spores from outdoor air through ventilation and air

exchanges. Hence, it is difficult to arrive at any significant conclusion on the role of the indoor "mold" spore in the allergic response. Again, it is not always the quantity but allergenicity of the "mold", which determines the overall development of clinical allergy. Sampling methods used to evaluate indoor environments include air sampling for spores, measurement of allergens, and determination of microbial generated volatile organic compounds, ergosterols, glucans, and mycotoxins, as well as environmental conditions that lead to fungal contamination.

At Visakhapatnam, a total of 8,909 and 9,327 cfu/m<sup>3</sup> were recorded from inside and outside, respectively, with 47 types identified. The dominant fungal types were *Cladosporium*, *Penicillium nigricans*, *Aspergillus versicolor*, and *Aspergillus oryzae*.<sup>4</sup>

While in Solan and Shimla sampling conducted in a wet house revealed *Penicillium* as the most dominant types contributing 30.7% followed by *Aspergillus* spp. (15.4%), and *Alternaria* spp. (10.5%). In the same place sampling conducted in a mud house revealed *Aspergillus* spp. at 35.1% as the most dominant contributor followed by *Penicillium* (26.9%). The other dominant types were *Alternaria*, *Cladosporium*, *Curvularia* and *Fusarium*.<sup>4</sup>

In West Bengal (Kolkata), the volumetric assessment of airborne culturable and non-culturable fungal spores showed higher frequencies of *Aspergillus/Penicillium*, *Cladosporium*, *Alternaria*, and smut spores by Burkard Sampler whereas Andersen Sampler showed the prevalence of *Aspergillus niger*, *Aspergillus flavus* and *Cladosporium cladosporioides* in large rural indoor cattle shed.<sup>35</sup>

In Delhi, an indoor survey of fungi in the homes of asthmatic/allergic children<sup>36</sup> revealed highest fungal load in the month of January while the lowest in June in indoors. A high viable "mold" concentration was observed in the homes of asthmatic children in Delhi. The predominant fungal types observed were *Aspergillus niger*, *A. flavus*, *A. fumigatus*, *A. nidulans*, *Alternaria* spp., *Cladosporium* spp., *Penicillium* spp., *Rhizopus* spp., and *Curvularia* spp., etc. The houses in Delhi contain rich and varied concentration of fungi, almost parallel to what is encountered just the outside air.

Besides the outdoor environment, indoor, work environments are also greatly influenced by fungi especially occupational sites employing organic raw materials, e.g. granary, poultry, flour mills, bakery, sugar factory, etc. Survey conducted at working environments by Singh and his students in bakery, poultry, sugar factory and libraries in Delhi revealed, *Aspergilli-Penicilli* and smut spores as significant contributors in indoor air.<sup>32</sup>

### **Poultry sheds**

The AICP study<sup>4</sup> revealed a total of 17 fungal forms were reported from Guwahati out of which *Cladosporium herbarum* was the most dominant followed by *Aspergillus schari* and *Penicillium* spp. In Gwalior, 21 fungal types were reported from the poultry. The most dominant being *Aspergillus niger* (24.6%) followed by *Cladosporium* spp. (22.3%), *Penicillium* spp. (10.7%), *Aspergillus flavus* (9.1 %), and *Botrytis*, *Fusarium*, *Aspergillus glaucus*, *Aspergillus fumigatus* and *Curvularia* were the other dominant species. While in Bangalore the *Aspergillus* spp. (531 cfu/m<sup>3</sup>) were the most dominant contributors of the environment followed by *Penicillium* spp. (301 cfu/m<sup>3</sup>) and *Cladosporium* spp. (169 cfu/m<sup>3</sup>). *Mucor* and *Rhizopus* were amongst the other dominant types. A total of 14,164 and 12,837 colonies were recorded inside and outside, respectively, from a poultry farm in Vishakhapatnam. A total of 54 fungal types were reported out of which majority belonged to *Aspergillus* and *Penicillium* groups. The other dominant fungi recorded were *Cladosporium*, *Penicillium nigricans*, *Trichoderma*, etc.

### **Garbage dump**

A total of 11,040 and 10,630 cfu/m<sup>3</sup> were recorded in Vishakhapatnam from inside and outside, respectively. The dominant fungal types were *Aspergillus niger*, *Cladosporium*, *Aspergillus versicolor*, *Aspergillus fumigatus*, *Mucor*, etc.<sup>4</sup>

### **Jaggery godown**

A total of 12,855 and 10,570 cfu/m<sup>3</sup> were recorded in Vishakhapatnam from inside and outside, respectively. The dominant fungal types were *Aspergillus niger*, *Cladosporium*, *Aspergillus versicolor*, *Penicillium brefeldianum*, *Curvularia*, etc .

### **Library**

A survey conducted in a library in Gwalior, *Cladosporium* spp. (30.3%) inside and (38.2%) outside was reported as the most dominant fungal type followed by *Aspergillus niger* (20.5%) inside and (15.2%) outside. Other dominant typed includes *A. teneus* and *Fusarium* spp. Another survey conducted in Bangalore City library also showed *Cladosporium* spp. (51.6%) as dominated fungal flora.<sup>4</sup>

### **Dairy farm**

A total of 9,000 cfu/m<sup>3</sup>, 8,500 cfu/m<sup>3</sup>, 940 cfu/m<sup>3</sup>, 10,110 cfu/m<sup>3</sup>, were recorded from reception, processing area, packaging area, cold storage and outside air, respectively, in Vishakhapatnam. The dominant fungal types were *Aspergillus niger*, *Cladosporium*, *Curvularia*, *Aspergillus nigricans* in reception; *Aspergillus niger*, *Cladosporium*, *P. nigricans* in processing and packaging areas; *Aspergillus niger* and *Cladosporium* in outside air. Very few colonies were recorded in the cold storage.

Several epidemiological studies have correlated symptoms of allergic patients to fungal spores concentration in their houses.<sup>37-40</sup> Epidemiological surveys conducted by Singh and coworkers<sup>41</sup> revealed 40% workers having respiratory problems in bakery, 59% in poultry, 40.5% in granary and 42.5% in sugar industry. The prevalence is 4-5 times higher in Delhi than what was estimated about 3-4 decades ago for general population.<sup>42</sup>

### **Cross-reactive allergens in clinical allergy practice**

Allergy is the result of binding between the epitopes on the proteins with the IgE. Because of evolution, certain proteins have remained conserved from the different sources. It is known that allergic patients are frequently co-sensitized against different allergen sources. Progress made in the field of allergen characterization by molecular biological techniques has now revealed that sensitization against different allergen sources can be explained as cross-reactivity of IgE antibodies with structurally and immunologically related components present in these allergen sources.<sup>43,44</sup> The similarities among allergens may facilitate allergy diagnosis in clinical practice by using a few representative cross-reactive al-

lergens to determine the patient's IgE reactivity profile.<sup>45,46</sup>

### **Cross reactive pollen allergens**

Studies carried out across the globe suggest cross-reactivity among different plants. *Lolium perenne* has been found to be cross-reactive with *Acacia*, pineapple, *Olea europaea*, *Dactylis glomerata*, *Ligustrum vulgare*, *Cynodon dactylon* and *Pinus radiata*.<sup>47-52</sup> *Platanus acerifolia* has been found to cross-react with *Corylus avellana*, *Prunus persica*, *Malus domestica*, *Arachis hypogaea*, *Zea mays*, *Cicer arietinum*, *Lactuca virosa*, *Musa* spp., and *Apium* spp.<sup>53,54</sup> Pollen from Japanese cypress (*Chamaecyparis obtusa*) cross reacts with Japanese cedar (*Cryptomeria japonica*) contributing to prolonged symptoms after the cedar pollen season in March and the following cypress pollen season in April.<sup>55</sup>

*Ricinus communis*, commonly grown in India for its oil and abundantly present in waste land, cross-reacts with *Hevea brasiliensis*, *Mercurialis annua*, *Olea europaea*, *Betula*, *Zygophyllum fabago*, *Putranjiva roxburghii* and *Ricinus* (seed).<sup>56-59</sup>

*Areca catechu* cross-reacts with *Phoenix sylvestris*, *Cocos nucifera*, *Borassus flabelifer*, as reported from India.<sup>54</sup> *Cynodon dactylon* (common grass) cross-reacts with *Pennisetum clandestinum*, *Stenotaphrum secundatum*, *Eragrostis*, *Brassica napus*, *Olea europaea*, *Ligustrum vulgare*, and *Lolium perenne*.<sup>47,61-65</sup>

*Holoptelea integrifolia* and *Parietaria judaica* belonging to the family Urticaceae are geographically distantly located. *H. integrifolia* is an important pollen allergen of India cross reacts with *P. judaica*, on the other hand, is a very dominant pollen allergen of the Mediterranean region. *H. integrifolia* and *P. judaica* pollens share cross-reactive as well as unique epitopes.<sup>66</sup>

### **Clinically important fungal allergens**

Fungal allergens are major causative agents of atopic disorders. The major problem in diagnosis is lack of standardized and well-characterized fungal extracts. Immunochemical and molecular characterization of fungal allergens has been hampered by the lack of pure proteins and to inherent variation among

fungal proteins and in their poor yield. The advents of molecular cloning technology and the development of phage display technology for cloning genes have facilitated the isolation of more relevant recombinant allergens.<sup>67</sup> The knowledge of the primary, secondary and tertiary structures of these allergens, the immunodominant regions of these proteins and their interactions with T and B- cell epitopes, results in better understanding of the molecular mechanism of allergy and may open new frontiers of immunological intervention to treat patients.<sup>68,69</sup> Some of the major fungal types characterized on molecular basis are discussed below. These protein fractions were purified using techniques like lectin affinity chromatography, gel filtration, electroelution and high-pressure liquid chromatography and characterization was carried out by immunoblot, ELISA and/or protease assays.

Many fungal allergens have been recently characterized in India. They are *Aspergillus ochraceus*, *Fomes*, *Ganoderma*, *Epicoccum*, *Fusarium*, *Aspergillus flavus* and some others. Further, under the All India coordinated project funded by Ministry of Environment and Forests, many new fungal allergens have been characterized such as *Paecilomyces*, *Uromyces*, *Ustilgo tritici*. These are described below for their protein characteristics.<sup>4</sup>

#### ***Aspergillus clavatus***

Thirteen bands could be detected in the antigenic extract of *A. clavatus*, which lied in between molecular weight range of 11.5-176 kDa. A 20 kDa protein was most prominent. Only 8 proteins were detected on IEF. All were in the acidic pI range (2.1-6.7).

#### ***Helminthosporium***

Nineteen protein fractions were detected in the molecular weight range of 12.2-138 kDa. Only 7 fractions were detected on IEF. Their pIs were acidic from 3.9-5.09. The pI 3.9 proteins were predominant.

#### ***Sphacelotheca eruenta***

Only 6 proteins were identified in the crude extract with molecular weights ranging from 12.2-128 kDa. The 12.2 and 21 kDa bands were predominant among all the proteins.



### *Sporitrichum pruinosum*

A total of 20 protein fractions could be detected in SDS-PAGE. Their molecular weights ranged from 12.5-128 kDa.

### *Ustilago triticii*

Antigenic extract was fractionated on SDS-PAGE and only 5 proteins were detected with molecular weight range of 14.2-172 kDa. On IEF, 6 proteins were detected with the pI range of 4.1-6.7.

### *Ustilago cynodontis*

Only 2 proteins were apparent on SDS-PAGE. Their molecular weights were 17 and 170 kDa. The 17 kDa band was more prominent. Eight protein fractions were detected on IEF. All of them were in the pI range of 3.5-6.7.

### Pollen-fruit syndrome

The existence of an association between sensitivity to different pollen and sensitivity to diverse edible vegetables has been described by various authors (Table 2). Some studies described a relationship between birch pollinosis and sensitization to hazelnut, apple, carrot, potato, kiwi and other vegetables or fruits.<sup>40,43,70,71</sup> Heiss *et al.*<sup>70</sup> reported association between mugwort pollinosis and sensitization to celery, carrot, spices, nuts, mustard and *Leguminosae* vegetables. Enberg *et al.*<sup>72</sup> have reported association between ragweed pollinosis and hypersen-

sitivity to *Cucurbitaceae* vegetables or fruits (e.g., water-melon, melon, cucumber and banana). Some studies have shown association between grass pollinosis and sensitization to tomato, potato, green-pea, peanut, water-melon, melon, apple, orange and kiwi.<sup>73</sup> The association between pollinosis and edible vegetable/fruit sensitization may be due to the presence of lectins in edible vegetables/fruits, presence of IgE to carbohydrates of the glycoproteins (cross-reactive carbohydrate determinants); existence of common allergens between pollens and edible vegetables/fruits. Up to now three allergens have been identified as responsible for cross-reactivity in these associations: profilin, a 14 kDa protein that regulates actin; Bet v 1, the 18 kD birch pollen allergen; and a 60-69 kD allergen.<sup>43,74</sup> It is important to study in depth these associated sensitizations and the common allergens responsible for them in order to improve diagnostic methods and treatment of the allergic syndromes.

### Pollen-pollution and allergy

Exposure to air pollution increases airway responsiveness to aeroallergens in atopic subjects. People who live in urban areas tend to be more affected by pollen-induced respiratory allergy than those from rural areas. The air pollutants could modify the antigenic properties by adhering to the surface of airborne allergenic agents. Factors such as type of air pollutant, plant species, nutrient balance, climatic factors, degree of airway sensitization and hyperresponsiveness of exposed subjects' influence this interaction. The airway mucosal damage and the

**Table 2** Examples of cross-reacting tree pollen allergens with different foods reported by various workers

Plants	Foods	Evaluation method
<b>Ambrosia spp. (Ragweed)</b>	Melon, banana	RAST
<b>Grass</b>	Swiss chard Tomato, peanut	RAST, nasal provocation test, RAST inhibition, skin test
<b>Birch</b>	Tomato, melon, water-melon, carrot, potato <i>Rosaceae</i> , hazelnuts Apple, cherry, peach, pear	Immunoblot, Immunoassay (IgE)
<b>Birch/mugwort</b>	Celery, carrot	SPT, RAST
<b>Grass and birch</b>	Kiwi fruit	
<b>Artemisia</b>	<i>Rosaceae</i> (peach, apple, chestnut)	

impaired mucociliary clearance induced by air pollution may facilitate the penetration and the access of inhaled allergens to the cells of the immune system thereby promoting airway sensitization.<sup>75</sup> Therefore, an enhanced immunoglobulin E-mediated response to aeroallergens and enhanced airway inflammation favored by air pollution could account for the increasing prevalence of allergic respiratory diseases in urban areas. Studies carried out by our group suggest that gases like SO<sub>2</sub> and NO<sub>2</sub> affects pollen grains, and these pollutants can modify the morphology of their carrying agents and alter the allergenic potential. Soluble protein content is altered significantly in experimental exposed pollen.<sup>76</sup> In addition, by inducing airway inflammation, which increases airway epithelial permeability, pollutants overcome the mucosal barrier and so "prime" allergen-induced responses. Lastly, air pollutants such as diesel exhaust particulates can also facilitate the immunoglobulin-E response that leads to pollinosis symptoms in atopic individuals.

### Allergen avoidance

Effective allergen avoidance reduces exposure to allergens, which in turn can lead to reduced allergic as well as asthma symptoms and consequently reduces the requirement for medications. The following common precautions assist in allergen avoidance: 1) avoid going outdoors on days when pollen are present in high concentrations in air, 2) close all windows in evening when pollen generally settles down to minimize their concentration, 3) air conditioning decreases indoor pollen counts, 4) do not plant too many trees and shrubs around your house, 5) take a bath after coming indoors and wear fresh clothes, 6) eliminate weeds and grasses in your house garden, and 7) electronic/electrostatic precipitator can be installed.

### Future priorities

The relentless increase in the prevalence of allergic diseases in the last century in various countries, their low prevalence in some populations living "indigenous" or "rural" lifestyles, point to the powerful and fundamental role of the environment in driving both expression of disease and its symptom severity. There is an urgent need to further understand the complexity of the interactions of lifestyle and environment on factors governing susceptibility and

protection as it relates to the induction and expression of allergic diseases. All the clinically relevant pollen have yet not been identified and characterized from the country. As allergen avoidance is the measure of choice for the treatment of allergies and asthma in particular, all the possible allergens are required to be studied at the molecular level. Relationship of the allergens with pathogenesis of the respiratory allergies and the increase in the prevalence are important questions, which need to be studied in detail. Molecular studies with reference to the cross-reactive allergens are scarce from India but important for the proper diagnosis and treatment of the allergy.

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