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Mini Review:

POLLEN ALLERGY IN SAUDI ARABIA

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Epidemiological studies in Saudi Arabia have revealed that between 10% - 20% children, age 7-12 years, suffer from bronchial asthma and even a higher percentage suffer from allergic rhinitis [1,2]. In majority of respiratory allergic diseases, extrinsic factors or allergens of varying natures are known to be involved. These can be classified as contactants, injectants, ingestants and inhalant allergens. Most common allergens belong to inhalant group [3] and may include a variety of agents such as house dust mites, storage mites, animal dander, hairs, saliva, faecal particles, feathers, cotton flock, plant fragments, fungal spores and pollen grains [4]. In this article, we will discuss pollen grains in relation to allergic diseases in Saudi Arabia.

Pollen grains, the structures housing the male gametes of plants, are known to induce allergic reactions in susceptible individuals [5-10]. Children who are allergic have an altered capacity to react to potential allergens or are said to be hypersensitive to them. Pollen grains have been implicated in several allergic diseases, including asthma, hay fever or allergic rhinitis, together with several eye, skin and other respiratory disorders [11,12]. Pollen grains from a large number of anemophilous (wind-pollinated) plants are carried by the wind. A characteristic feature of pollen sensitivity is its seasonal pattern of occurrence usually at the time when the pollen is most frequent in the atmosphere.

Pollen allergens contain proteins or glycoproteins. However, not all the proteins that are contained in winds-dispersed pollen grains give rise to sensitization in susceptible individuals. The atopen or molecule capable of sensitizing humans have a known size range of 10,000 – 40,000 daltons and tend to occur in the outer wall of the pollen grain rather than within the cytoplasm. This localization of allergenic proteins has been demonstrated by showing that they begin eluting from the pollen grain within minutes of being moistened. It has also been shown by immunofluorescent demonstration of known allergens, such as antigen E of ragweed and Group 1 antigen of rye grass.

Immunologic reactions to allergenic pollen protein are specific, yet the diversity of sensitization produced is not as broad as might be anticipated from the number of wind-disseminated pollens to which an allergic child is exposed. This relative restriction of sensitization reflects the occurrence of broad patterns of cross-reactivity among proteins derived from different, but taxonomically related, plants species.

Characterization of pollen allergens

Pollen allergens have been characterized for some grasses, weeds (particularly ragweed) and tree pollens [13,14]. For example, the characterised allergens from the short ragweed, *Ambrosia artemisiifolia* (elatior) were named antigens (Ag) as "E" (AgE) and "K" (AgK). According to WHO allergen nomenclature published by the International Union of Immunological Societies (IUIS) Sub-Committee (W.H.O. Bulletin 1986;64:767-70), these two antigens, based on criteria set forth, have been changed to *Amb a 1* and *Amb a* II, respectively. However, these are acidic proteins, comprising two sub-units, an α-chain of molecular weight 21,800 and a β–chain of 15,700 giving a total molecular weight of about 38,000. Amb a 1 (Antigen E) is present in four different forms which are immunologically similar to each other but differ in their isoelectric points. The allergens of grass pollen are equally complex and three groups of heat-stable glycoproteins are the principal allergens. The two principal groups of allergens called group 1 and II have molecular weight of 30,000 and 10,000 and each have several isoallergens differing in isoelectric point. However, several other groups of allergens have been characterized and given a new nomenclature [15,16]. For example, in grasses, *Lol p1* (Group II (Rye II), *Lol p III* (Group

III (Rye III), *Lol p IV* (HMBA (Group IV) and *Lol p x* (Cytochrome) c) from *Lolium perenne* (perennial rye grass); *Phl p V* (Ag25), *Phl p* VI (Ag19), *Phi p VII* (Ag30), and *Phl p VIII* (Ag 3) from *Phelum pratensis*; *Dac g 1* (Dg 1) from *Dactylis glomerata* (orchard or cocksfoot) and *Poa p X* (Cytochrome c) from *Poa pratensis* (Kentucky blue grass), have been characterized. In addition to pollen from grasses and weeds some tree pollens have also been characterized. The number of characterised allergen is increasing day by day.

Most pollen grains have a size (diameter) range 15-40 μm with the exception of some larger pollens such as Privet (*ligustrum* which is not wind-pollinated). The inhalation and deep penetration of pollen grains are dictated by the mode of breathing and the size of pollen grains. In normal nose breathing, the larger pollens are not inhaled deep into the respiratory system, while in mouth breathing (habitually or during exercise) even larger pollens can be inhaled deeper. Particles as large as pollen grains cannot reach the lungs in the inhaled aerosol. The nasal cavity filters them out by inducing a high degree of turbulence in the airflow.

Mechanism of allergic response

The reason why pollen causes asthma in some patients and rhinitis in others, is not clear. However, it is believed that rhinitis is induced by pollen grains when it makes contact with the upper respiratory tract including the nostrils, oral cavity, and eyes. Such patients will experience considerable irritation or itching, sneezing and redness of the eye or rhinorrea, etc. immediately after contact with pollen grains. When inhaled into the lower respiratory tract (to the uppermost ciliated portion of the tract), asthmatic symptoms may develop as a result of accumulation of fluid and secretions in the terminal bronchioles. As in atopic subjects, all allergic reactions are immune-bound with the production of specific IgE (also called re-aginic) antibodies, the reaction may be immediate (Type I, within seconds or minutes) or in non-atopic subject (cell-mediated reaction) be delayed (Type IV). However, the first or primary exposure results in sensitization (production of specific IgE antibodies) of susceptible individuals while the second or subsequent exposure to the same pollen grains, by reacting to specific antibodies already produced, causes the symptom(s).

Very little is known about the critical or threshold level of pollen grains or actual number of pollens required to bring about sensitization or allergic symptoms in sensitized individuals. However, estimation can be made on known figures for pollen concentrations and respiratory volumes. It is widely accepted that effective values should be expressed per cubic meter of air. One cubic meter of air roughly represents the volume of air an individual inspires during the course of an hour. Frankland and Davies in London noted that when grass pollen concentrations in a city atmosphere rose above 50 grains/ Rm^{-3}, all patients in the area who were clinically sensitive to grass pollen experienced symptoms, while the majority of other individuals remained unaffected. Thus, it is clear that the degree of reactivity depends upon the particular patient's degree of sensitivity. On the other hand, it appears that the estimation of critical levels depends upon the amount of active antigen contained in the allergenic particles and the solubility of the atopen in the moisture of the mucus blanket of the subject. Entry of inhaled pollen into the lungs is regulated in different ways, depending upon the size of the pollen grains and the diameter of the airways. From the trachea to the terminal bronchi, the airways divide into two equal branches about 19 times and their cross-sectional area is reduced from 13 mm^2 to 3 mm^2 with a consequent reduction in air flow rate from 150 $cm.s^{-1}$ to about 1.5 $cm.s^{-1}$ in the terminal bronchiole.

Identification of allergen

In order to consider any pollen as allergen, compliance with "Thommen's postulates" is desired. The postulates require that (i) the plant species concerned must be widely and abundantly distributed; (ii) the pollen grain must be sufficiently buoyant to become airborne; (iii) the pollen (or spore) must be produced in sufficiently large quantities; (iv) they must contain an excitant or toxins (antigen) or hay fever (rhinitis or asthma); and (v) in order that any type of pollen (or spore) is regarded as the causative agent in a particular case of hay fever or asthma, it must be shown that the patients display symptoms at a time or times, when the pollen grains concerned are present in larger quantities in the air. If these postulates are satisfied and a given kind of pollen is present in effective concentrations, susceptible individuals may become sensitized with formation of the relevant specific IgE antibody. Once the subjects have become sensitized, an even lower concentration of the pollen may produce the symptoms.

Therefore, not only is the correlation between the symptoms and the presence of pollen grains in the ambient environment of children is important in the diagnosis of allergic rhinitis or asthma, but the choice and selection of an appropriate allergen extract for the skin-prick test (SPT) or other diagnostic tests, such as bronchial provocation (BPT) or nasal provocation (NPT) tests, is also equally important. Both conditions of correlation and choice of antigen can be met when a detailed and thorough study of the airborne activities of varying species of pollen grains of a particular area [17] has been conducted outlining their identify, concentration, seasonal and circadian periodicities, or other values in relation to the disease.

Whereas the importance of the case history can hardly be over-emphasized, details regarding the time and place of occurrence of symptoms mean nothing unless they can be compared with reliable information on the geographic distribution and relative abundance of various kinds of allergenic pollen producing plants and particularly their usual seasons of pollination. A probable decision as to the possible causative pollen in each case is the logical basis of the selection of skin test profile to be used. There is no point in testing with the pollen of plants which do not grow within hundreds of miles of the patient's home and which pollinate at a time of year when he or she never has symptoms. In every case of pollen allergy, the patient's symptoms calendar, positive skin reactions and the pollen calendar of his or her locality must tell the same story. If not, then the pollen may not possibly be the offending agent and other allergenic agent(s) may be responsible for the patient's distress. Moreover, some researchers describe that skin reactions must not be regarded as infallible and suggest a repetition of tests and collection of more data on atmospheric pollen distribution before a difficult inhalant allergy problem is solved.

Problem of pollen allergy in Saudi Arabia

In Saudi Arabia, data on such airborne activities of pollen families have been obtained using continuous volumetric air samples from 9 different cities including Riyadh. However, both sites in Riyadh appeared to be micro-climatic environments with planting, trimming and irrigation occurring throughout the year. Consequently, both sites in Riyadh have shown pollen activities in the air beyond those expected from the flowering seasons [18]. However, there is a need to compare these data with the data from a non-microclimatic environment to assess the real risk of pollen exposure in the population of Riyadh in general and the allergic section of that population in particular. Furthermore, breakdown of the families to the generic or species level is required. This is because cross-reactivity among various species is not very clear except among some genera, including species of family Gramineae where grass pollen antigens show marked cross-reactivities. Nevertheless, Bermuda grass (*Cynodon dactylon*) pollen extract is almost independent in its allergenic reactivity in the skin-prick test, indicating little or no cross-reactivity with other members (grasses) of the same family. As there are published reports on the existence of species specific antigens in some allergens, the subject needs special attention while selecting antigens for IgE mediated SPT reactions in diagnosed allergic patients.
Comparison of pollen grains from various locations in Riyadh and other parts of Saudi Arabia also becomes important in order to determine the nature of these pollen. They may differ from place to place depending upon the distance from the sources in the area. The long term transportation of pollen grains is dictated by various factors. Despite their shape (most pollens are spherical or subspherical) at release, their fate is much the same, and most of them are deposited on the ground within a few meters. However, a variable portion, termed by Gregory in 1963, the "escape fraction" is able to diffuse upwards and travel longer distances before it is eventually deposited. As mentioned earlier, most airborne pollen grains are 25 μm (range 15-40 μm) in diameter and if they obey Stoke's law would have a free fall velocity of 7.5 cm sec^{-1}. If released from a height of 1m, assuming a wind speed of 10 knots, the pollen would travel 67 meters before deposition. And if released at a height of 20 m, it would travel 1333 meters. Nonetheless, because of various other factors such as turbulence, many pollen grains are deposited close to the source. Thus, regional differences, based on the nature of surrounding and plantation may occur and, provided equal potency of cross skin reactivity among the pollen encountered is confirmed, these differences may have an impact on the allergic population living in the different regions of Saudi Arabia.

The nature of this problem in Saudi Arabia could be specially serious as planting, agricultural and horticultural activities have increased many fold during the past several years, and with the continuation of such practices, it is most likely that airborne level of pollen grains and other allergenic and hazardous agents in the atmosphere may continue to increase. Rain and drizzle are most effective in cleaning the atmospheric particles including pollen grains. Little or no rain for a long period in the Kingdom present another problem and eliminated the efficacy of this natural eradication. Thus the atmospheric concentrations of various allergenic pollen grains are likely to reach or exceed the threshold levels. Skin prick test materials for diagnostic purposes are usually imported into the Kingdom from Denmark and USA and because of the lack of local data until recently, selection of species for skin testing were based on Western findings related to their climate and environment. The nature of pollen involved in allergic reactions may not necessarily be the same as in the West. For example, in Chenopodiaceae (order, Chenopodiales) which is the most prevalent pollen family (23%) in Riyadh sites, there are more than 22 species while it is represented normally by only one SPT extract *Chenopodium album* (Lamb's quarters). Our specialized identification on selected days revealed that *Atriplex* spp. (commonly known as Aliscale, Lenscale, Wingscale, etc.) and *Salsola* spp. (Russian thistle and salwort) are major contributors to the pollen and in the air in Chenopodaceae rather than *C. album*. Published reports indicate neutralizing or desensitizing effect for only 50% of the time between some species of the family Chenopodiaceae, while Lamb's quarters could not desensitize members of Amaranthaceae, another family of Chenopodiales. Thus,

until there are clear reports on the cross-reactivities including cross-antigenicities and cross-allergenicities amongst the members of Chenopodiaceae in general and weeds in particular, the reliability of antigen(s) selected for SPT or other diagnostic procedures remain questionable as regards "false negative" reactions. Contrary to this there may be circumstances when 'false positive" reactions occur.

Of the major practical implementations of our current investigation on various aeroallergens has been the establishment of a preliminary SPT profile which lists pollen, fungal and other allergens found in the Saudi Arabian environment (both outdoor and indoor) to which our allergenic patients are directly exposed (19). Wherever SPT antigens of the listed species are not available commercially for diagnostic purposes, we have taken steps to produce such antigens locally [20]. In fact, several such diagnostic antigens have already been prepared in our laboratory using local species and strains. A complete and comprehensive profile will require all aspects of airborne pollen data from as many locations as possible within the Kingdom. Once completed, the allergens profile for the diagnosis of allergic diseases may be introduced to all clinics and hospitals involved in diagnosis and management of such diseases. Based on the findings, production of diagnostic kits using locally collected species can also be adopted involving purification and characterization of allergens, according to the W.H.O. guidelines. This will not only help to diagnose allergic children with more relevant allergenic extracts but will also provide support for immunotherapy, if so desired. With a good knowledge and information of pollen release seasons [21], avoidance and/or environmental control by elimination (with limitation) may be exercised.

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