

Aeroallergens are All Particles in the Air that can Cause an Allergic Reaction

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Abstract

Aeroallergens refer to all airborne particles that can trigger allergic responses. The presence of aeroallergens leads to allergic conditions affecting the respiratory system. In outdoor environments, the primary aeroallergen particles include pollen and spores from fungi and mold, while indoor settings are primarily affected by dust mites and cockroach materials, including their secretions, hair, skin cells, and in damp areas, mold spores.

Keywords: Aeroallergens, Pollen, sIgE, SPT, Health.

INTRODUCTION

Aeroallergens consist of comparatively large and intricate particles such as pollen, spores from fungi, fragments from insects, dander from animals, bits of plants, and dust mites, all of which can provoke allergic reactions in individuals who are predisposed [1]. These particles comprise various molecular components, though only some serve as antigens. Typically, when specific antigenic elements are determined, they are proteins with carbohydrate chains, having a molecular weight ranging from 10,000 to 40,000 D. The antigenic nature of these molecules mainly results from their size, shape, and arrangement of chemical groups. The overall significance of these particles in relation to allergies depends not only on their antigenic properties but also on their prevalence in the environment, making contact with at-risk individuals possible, and their appropriate size for attachment to the respiratory lining.

Sources

Air samples often contain biogenic particulate matter such as grains of pollen and spores from fungi [1]. Some biogenic particulates may not be easily identified, including fragments from insects, plant materials, animal dander, and broken pollen and fungi. These can sometimes be recognized through immunoassays. In contrast, nonbiogenic particles, like hydrocarbons, dirt, salt crystals, and other particulate matter—often from local agricultural or industrial operations—can affect allergic reactions but are classified as non-aeroallergens. Additionally, nonbiogenic gaseous substances, such as chlorine, hydrogen sulfide, formaldehyde, gasoline vapors, smoke from wood and tobacco, and odors from cooking are not considered allergens either but can still alter allergic responses or act as irritants.

Size

Most airborne particles that are significant allergens and can be seen under a microscope range in size from 2 to 60 µm in diameter [1]. The majority of these particles (notably those larger than 15 µm diameter) tend to hit the surfaces of the eyes, nose, and throat due to their momentum. Since most allergenic particles do not penetrate the bronchi, it has been suggested that the features associated with bronchial pathophysiology in asthma may stem from a reflex initiated by receptors in the nasopharynx. Alternatively, allergenic materials could be released from these particles in the nasopharynx and either inhaled or enter the bronchi through the bloodstream.

Pollen

Pollen grains serve as the male reproductive units of seed-producing plants, facilitating the fertilization process by transferring male gametes (sperm) to female gametes (egg), which remain on the plant [1]. Transfer of pollen for plants that have bright, colorful, and aromatic blossoms is often achieved via insects. In such cases, the pollen tends to be large and covered with a sticky layer. Some plants have evolved notable methods for dispersing pollen, relying on birds, bats, mice, or even snails.

The majority of pollen types that are significant for allergies are carried by the wind. Plants that rely on wind for pollen dispersal generally produce dull, small, inconspicuous, and scentless flowers. Their pollen is typically tiny, lightweight, non-sticky, and generated in vast quantities.

Most pollen is released in the early hours of the day, yet wind patterns can lead to peak pollen levels occurring in the afternoon or at dusk. While individual pollen grains

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remain viable for only a limited time, nonviable pollen continues to act as a potent allergen. A mild breeze has the capability to transport pollen from wind-pollinated plants over considerable distances, creating elevated pollen levels in urban and metropolitan settings, away from their original rural or suburban origins.

Animals

Inhaling dander from non-human animals can trigger allergic reactions in sensitive individuals [1]. Any foreign animal dander might cause sensitization, although the most frequently encountered allergens originate from dogs, cats, and animal hair or feathers from species like cattle, horses, sheep, goats, and ducks, which are often used in stuffing. Since it is the soluble dander that causes allergic reactions rather than the hair itself, finished products free from dander (such as furs used in garments) tend to be less allergenic. Many allergens present in dander are also found in animal urine and saliva. Research has identified the typical allergens, which include those from cats (Fel d 1), dogs (Can f 1, Can f 2), and horses (Equ c 1, Equ c 2).

Sensitivity can be quite pronounced, particularly with cat dander, where even a brief or unexpected exposure can trigger a strong allergic reaction. The primary allergens in cat dander exist in extremely small particles (some <2.5 mm); as a result, they fall slowly and remain suspended in the air for extended periods without disturbance. Clinically, this likely explains the abrupt onset of symptoms that occur during encounters with cats or in cat-infested homes. Dander levels can build up within a household or confined location; the heating system can easily facilitate its distribution throughout the dwelling. Vacuuming and bathing pets are only mildly effective, short-term solutions for managing these allergens. Because the allergen is contained in soluble dander, even breeds with short hair or non-shedding dogs can still trigger allergies.

Exposure to laboratory animals in a professional setting can pose significant challenges for individuals with allergies, potentially hindering their ability to work in those environments. Additionally, high levels of rodent dander and urine in rundown apartments and poorly maintained housing can contribute to substantial allergic issues. Recent research indicates that mouse allergens are widely present in homes in urban areas and could be a significant indoor allergen, particularly for asthmatic children.

sIgE

Diagnostic testing for allergen-specific IgE (sIgE) can be conducted using skin tests or blood analyses to verify allergic rhinitis (AR) and identify the specific airborne allergens that may be causing symptoms [2]. Among these, skin prick testing (SPT) is the most cost-effective and dependable method for detecting sIgE. Typically regarded as safe, SPT has not resulted in any fatal incidents; however, there can be infrequent systemic reactions, particularly in infants,

individuals with several positive results, extensive eczema, or uncontrolled asthma when peak flow is below 70%, posing significant risks for systemic responses. Although numerous commercial devices have emerged to minimize skin trauma, the testing procedure remains consistent across them; a sharp solution is applied to the skin, typically on the upper back or the inner side of the forearms, creating a minimal break in the skin through which the allergen solution can enter. After an interval of 15 to 20 minutes, the size of the wheal and flare is assessed and documented in millimeters, serving as an indication of immediate mast cell reactions, with a positive outcome generally characterized by a wheal measuring at least 3 mm at its greatest diameter. It is critical to concurrently assess both positive and negative controls to eliminate the likelihood of false negative and false positive results. False positives generally occur due to dermatographism, while false negatives may result from the technique of the operator, low potency of extracts, or the presence of medications and medical conditions that inhibit histamine responses. In summary, SPT provides a high level of specificity (70–90%) and sensitivity (80–90%) for diagnosing inhalant allergens. Nevertheless, the effectiveness of intradermal testing (IDT) for inhalant allergens remains a topic of debate. Research indicates that positive intradermal tests for airborne allergens, alongside negative SPT results, tend to have a low positive predictive value and are unlikely to detect clinically significant sensitivities, although they might enhance the negative predictive value of the testing process.

In vitro tests also successfully detect allergen-specific IgE (sIgE) with similar levels of specificity and accuracy compared to epicutaneous testing methods. Second-generation clinical assays utilizing fluorescent anti-sIgE in fluorescence enzyme immunoassays yield quantitative and reproducible results, capable of identifying sIgE levels below 0.10 kU/L in blood samples. More recently developed component resolved diagnostic tests employ proteins to assess a patient's sIgE reactivity to recombinant allergenic proteins instead of entire allergens, facilitating a detailed analysis of specific molecules that pose risks and are clinically relevant in terms of sensitization. Additionally, in vitro testing is not influenced by medications or conditions that reduce histamine responses, though false positives may manifest in patients suffering from conditions linked to elevated baseline IgE, like atopic dermatitis. Thus, SPT may present a slightly greater sensitivity compared to in vitro testing involving complete allergens, especially when considering allergen immunotherapy.

SPT

Allergy skin prick testing (ASPT), combined with a comprehensive clinical history, is recognized as the most effective diagnostic technique for identifying IgE-mediated responses to environmental allergens [3]. Comparative evaluations indicate that SPT demonstrates the greatest positive predictive value among the available diagnostic

methods for allergies. SPT is established as a validated, safe, reliable, and relatively low-cost procedure that can be easily conducted in an outpatient environment. An advantage of using SPT is that both the clinician and the patient receive results right after the test is performed.

The SPT technique operates by inducing a localized hypersensitivity reaction in the skin by exposing cutaneous mast cells to liquid allergen solutions. When a patient is sensitized to an airborne allergen, the IgE receptors on their cutaneous mast cells link together and trigger the release of their contents upon sufficient local exposure to the allergen. During this degranulation process, the mast cell discharges pro-inflammatory substances, causing a noticeable raised wheal and redness on the skin's surface. This response is then evaluated and compared to positive histamine and negative saline controls. A positive outcome in SPT indicates sensitization; however, it does not necessarily indicate the existence of a clinically significant allergy. Evidence of sensitization, obtained solely through skin prick or serum tests, is insufficient for a diagnosis without a clinical history of symptoms.

There are two main methods for skin testing: prick/puncture and intradermal testing. The prick technique is generally recognized as the initial and most suitable approach, carried out by placing small drops of aqueous allergen solutions with a concentration of either 1:10 or 1:20 in weight to volume on the skin of the back or the front of the forearms. The droplets can be applied one at a time in sequence, or by utilizing commercially available devices that allow for the application of various aeroallergens to distinct skin areas simultaneously, typically using lanced tips coated with the allergen. It is important to place the droplets at least 2 cm apart to ensure the results can be accurately interpreted. Standardized SPT panels usually include common regional airborne allergens such as trees, grasses, and weeds, as well as animal danders, dust mites, cockroaches, and molds. While many extracts are standardized, SPT can also be tailored for individual patients through puddle testing, where solutions containing inhalants or foods mixed with saline are placed on the skin.

Once the allergens are applied, measurements of both the wheal and erythema are taken, if they manifest. The histamine control is assessed roughly 10 minutes after application, while the other results are read about 15 to 20 minutes post-application. A result is deemed positive if the diameter of the wheal is 3 mm by 3 mm or larger when compared to the negative saline control.

The precision of the Skin Prick Test (SPT) can be influenced by a variety of elements, with the type of allergen extracts and the method or device used for testing being the most significant. Allergen extracts consist of liquid solutions derived from natural allergen sources, such as various animal hairs or dust mites, and these can be either standardized or non-standardized. In the United States, the strength of

certain standardized extracts is represented in allergy units or Bioequivalent Allergy Units (BAUs), serving as an indicator of potency. Extracts available commercially that are not yet standardized are frequently labeled in Protein Nitrogen Units (PNU), which does not indicate the potency accurately. Standardization is more prevalent for aeroallergen extracts compared to food allergen extracts.

Patients underwent skin prick testing (SPT) using a variety of standard allergen solutions for airborne allergens, which included two variations of house dust mites [*Dermatophagoides pteronyssinus* (Dp) and *Dermatophagoides farinae* (Df)], pet dander (from cats, dogs, and horses), pollens from early and mid-blooming trees (including alder, elm, hazel, poplar, willow, birch, beech, oak, and plane trees), olive tree pollen, grasses and cereal grains (Kentucky bluegrass, Timothy grass, Meadow fescue, Ryegrass, Velvet grass, Orchard grass, Barley, Oats, Wheat, and Rye), as well as weeds (Mugwort, Dandelion, Nettle, English plantain, Wall pellitory), molds (*Alternaria alternata*, *Aspergillus fumigatus*, *Cladosporium herbarum*), and cockroaches (*Blattella germanica*) [4]. The choice of aeroallergens was determined by their prevalence in the air and accessibility.

The skin prick testing was conducted in accordance with global standards, utilizing a single examination on both forearms with lancets and standardized allergenic substances. Histamine (10 mg/mL histamine phosphate) was utilized as a positive control, while 0.9% sterile saline served as the negative control. The evaluations of the SPTs were made 15 minutes post-application, and a result was deemed positive if the average wheal diameter was 3 mm or greater when compared to the negative control. Individuals who exhibited sensitivity to two or more allergen categories were categorized as polysensitized. Sensitivity to house dust mites was indicated by a positive reaction to at least one of the *Dermatophagoides* allergens. A positive response to any of the early or mid-season tree pollens was needed to define sensitivity to tree pollen. Fungal sensitivity required a positive reaction to at least one of the species: *Alternaria alternata*, *Aspergillus fumigatus*, or *Cladosporium herbarum*.

AIT

Immunotherapy for aeroallergens is recommended for managing allergic rhinitis or rhino-conjunctivitis, allergic asthma, and atopic dermatitis in patients who exhibit measurable and relevant allergen-specific IgE antibodies (sIgE) [2]. Patients ought to display clinical symptoms when exposed to the allergen in natural settings and have sIgE to that specific allergen shown through either epicutaneous or serum testing. Allergen immunotherapy (AIT) should be evaluated for patients who cannot find symptom relief through conventional pharmacologic treatments and allergen avoidance, as well as for those who may want to minimize long-term usage of medication or suffer intolerable side effects from these drugs. It is crucial that patients are

informed about the time requirements of AIT, and they should be made aware that AIT will not provide immediate symptom relief.

Patients must be assessed every 6 to 12 months while undergoing AIT and should be monitored for adherence, side effects, and effectiveness. A clinical response typically takes place soon after achieving the maintenance dose. If there is no clinical improvement after one year of maintenance treatment and no reasons for the lack of efficacy are identified, it may be advisable to stop AIT. Factors contributing to AIT failure include insufficient allergen dosing, the omission of identifying and including all relevant allergens in the treatment plan, continued high exposure to environmental allergens, and significant contact with non-allergic triggers like tobacco smoke and pollution. The usual length of AIT treatment spans from 3 to 5 years, although some individuals may opt to extend their treatment beyond this period. Certain patients may attain lasting clinical remission of their allergic conditions after stopping immunotherapy, while others may see a recurrence of symptoms one or more years after treatment has ceased. The most effective duration of treatment for AIT has not been thoroughly investigated; however, existing studies indicate a higher rate of relapse among patients treated for less than 35 months compared to those treated for over 36 months. There are insufficient diagnostic methods available to predict which patients will maintain a sustained response, hence the treatment duration should be tailored to each individual patient.

AIT has been confirmed as effective for allergies related to various aeroallergens and insect venom, making it a recognized form of treatment for these allergies today [4]. Although various methods of delivery and different types of allergens have been evaluated in AIT studies, clinical practice exclusively utilizes whole allergen extracts, with subcutaneous immunotherapy (SCIT) recognized as the most efficient method. Despite the proven effectiveness of traditional AIT for treating inhalant allergies and insect venom allergies, it is not currently utilized in clinical settings for treating peanut and other food allergies. This is due to persistent concerns regarding the safety and effectiveness of SCIT, as well as low adherence to SCIT and other conventional AIT types in the management of food allergies.

To this point, AIT remains the sole form of causative treatment aimed at modifying the allergen-specific immune response in allergic patients to achieve a state of tolerance, which seeks to establish enduring immunological and clinical tolerance to allergens following the conclusion of therapy.

Climate Change

It is increasingly critical to acknowledge the effect of the external exposome on the onset of allergies [6]. Environmental influences can be categorized into three interconnected areas: the general external environment, the specific external environment, and the internal, host-dependent environment. The general external environment includes

aspects such as climate, biodiversity, and the urban, social, and economic contexts that influence how humans interact with nature. Conversely, the specific external environment pertains to direct exposures, such as allergens, microbes, diet, tobacco, pollutants, and other harmful substances that have a direct effect on human health. Additionally, the internal environment consists of host-dependent physiological elements—like metabolism, inflammation, and oxidative stress—that influence how people react to these external exposures. Collectively, these three areas constitute the notion of the “meta-exposome,” which illustrates the dynamic relationship between environmental exposures and human health.

Allergic sensitization is largely driven by exposure to allergens, which plays a vital role in the onset of ailments such as asthma, allergic rhinitis, and eczema. The most noteworthy contributors to respiratory allergic illnesses are airborne allergens, especially pollen and dust mites. Additionally, characteristics like age, gender, and location can affect the trends in allergen sensitization.

Climate change presents a significant danger to humanity, primarily caused by greenhouse gas emissions that introduce serious challenges to both human health and healthcare services, potentially undoing years of medical advancements. A prominent health consequence is the increase in allergic respiratory conditions, which are exacerbated by rising levels of atmospheric carbon dioxide and elevated temperatures. These elements elevate the concentration and allergenic properties of airborne allergens such as pollen and fungal spores, resulting in exacerbated symptoms. Moreover, the biodiversity hypothesis indicates that engagement with natural settings enhances the human microbiome and fosters immune system balance, providing defense against allergies and inflammatory issues. Nonetheless, the diminishing presence of these immune-supportive factors in swiftly urbanizing regions facing a decline in biodiversity poses an emerging health concern.

Grasping the influence of the external exposome on allergy development is essential. Innovations in Precision Allergy Molecular Diagnosis (PAMD@) now facilitate the accurate identification of individual IgE reactivity patterns, consequently enhancing diagnostic precision and allowing for tailored therapies.

CONCLUSION

Aeroallergens are biological particles that are conveyed through the air, with environmental elements determining their release and dispersion, alongside their impact on humans and the ecosystem. These airborne allergens rank among the primary causes of allergic illnesses today and pose a considerable public health challenge. The type and intensity of allergic responses triggered by pollen from allergenic plants depend on both the potential of the allergen and the quantity of pollen present in the atmosphere. Furthermore, for a plant species to be considered allergenic,

three additional crucial criteria must be fulfilled: the plant's distribution and prevalence, its ability to produce and release large amounts of pollen, and the reliance on wind for pollination.

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