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Allergen Control in Asthma

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Abstract

Asthma is one of the most prevalent chronic diseases especially among children so that it continues to be a public health problem. Even though genetics is an important factor for asthma, dramatic increase of the asthma recently is related with environmental triggers and lifestyle factors. Understanding of the interaction of multiple factors causing asthma is absolutely necessary for the planning interventions strategies. Exposure to allergens is a key factor for asthma morbidity. Environmental exposure leads allergen sensitization for genetically predisposed individuals and persisting of exposure is a risk element for asthma and other allergic diseases as well. Evidences suggest that environmental triggers avoidance and control interventions preclude asthma attacks, decrease the frequency of symptoms, and the need for drugs. Thus, environmental control should be focused in the management of asthma. Identifying and controlling of indoor and outdoor environmental triggers is the cornerstone for a successful asthma management. Figuring out the reasoning factors and developing primary preventive precautions are necessary to decrease asthma development frequency throughout the world.

Keywords: Allergen, asthma, environment, sensitization, trigger

1. Introduction

Asthma and asthma-related allergic diseases are most prevalent chronic diseases in developed countries. In recent years, a dynamic increase has been observed in prevalence of allergic diseases [1–3]. Even though the exact reason for such an increase is not know, home environment design and quality of indoor allergens are thought to be the factors for those diseases [4, 5]. Allergen induced diseases like asthma is an important public health problem and a burden for health resources [6]. Asthma and allergic reactions are life threaten conditions. Additionally, such diseases have negative influence on children and adults [1, 2, 4, 7]. Although increase

in asthma for children and adults has been discussed widely in recent years, it is believed that the leading factor for this increase is environmental factors. Genetic heterogeneity and ethnicity variety, lifestyles and changes in the type of accommodation are the key factors for the development of asthma [8, 9]. Since avoidance from allergens is an important part for the management of allergic diseases, taking required precautions to prevent exposing to the allergens is the first step of symptom control. A successful identification and avoidance from environmental triggers might prevent inflammation of diseases. Avoidance from allergens in allergic diseases like asthma is more effective than treatment itself [7, 10]. So international asthma guides recommend environmental control implementations as a part of systematic approach to asthma [2]. This chapter focuses on the importance of allergens and control of allergens for the management of allergic asthma.

In the asthma pathogenesis, the role of environment is getting more obvious. Asthma develops through the interaction of genetic agents with environmental exposure [1, 11, 12]. Individual allergen sensitivity is the most important feature and exposing to allergens play the key role to trigger asthma symptoms and inflammation. Asthma management might be controlled by multifaceted interventions since the reasons for asthma are multifactorial. Studies have suggested that combination of different interventions would be much more effective than a single intervention. Thus, it is essential that a successful asthma management should include multiple strategies covering pharmacological and nonpharmacological methods [1].

In allergen control, the risk of exposure should be identified for sensitive individuals, and some interventions should be planned to decrease or to remove the risk, accordingly [4, 6, 13]. In recent years, large number of strategies aiming at reducing of asthma based morbidity and mortality rates have been developed and tested [14, 17]. Within the scope of those strategies, it has been stated in many studies that the education provided for allergen control is not an effective intervention on its own to change environmental control behaviours [18]. To sum up, individual interventions are usually ineffective. Yet, effective allergen avoidance requires a detailed approach.

2. Indoor Allergens

Asthma is characterized by chronic airway inflammation caused by genetic-environment interaction [2, 3, 19]. Even though seasons are accepted as triggers for allergens, exposure to indoor allergens and their presence throughout the year means a greater risk for asthma. Many environmental factors might trigger asthma, but the most important ones are indoor allergens [20]. Indoor environment is a source of risk for health, and exposure to indoor allergens occur in indoor areas [11, 21]. Indoor environment means not only the house but also schools, offices, restaurant, and cars [22, 23]. A strong relation between pathogenesis of allergic diseases like asthma and exposure to indoor allergens has been emphasised in many epidemiological cohort studies and population surveys as well. Biological functions of allergens enhance IgE response and cause allergic inflammation directly. Environmental exposure to allergens and atopic predisposition affect the development of IgE and Th2 responses [8].

Modern life conditions and long hours spent indoors leads to high level allergen exposure, enhancing sensitization, and asthma symptoms [24, 25]. Major indoor allergens, which has been proved as triggers of allergy are dust mite, cockroach, mouse, pet dander, and mold [11, 26]. Although major allergens are present in all of the inner city houses, their presence differ in geographic regions due to climatic variety of geographic regions. Controlling of indoor allergens need much more effort compared to seasonal allergens since the presence of indoor allergies continue throughout the year [27]. In studies, it has been suggested that sensitization prevalence of children to indoor allergens is higher and those children with indoor allergen sensitization are also sensitive to outdoor allergens [28, 29].

Poor housing condition is more often the reason for exposure to the triggers and allergen sensitization. Exposure to indoor allergens may produce symptoms for asthmatic individuals [23]. It has been commonly believed that cats and dogs provoke the symptoms. However, high levels dust mites allergens in the house are the major risk factor for sensitized individuals. Excessive moisture, inappropriate or bad heating/cooling systems, overcrowding, cockroaches, structural problems are the triggers for asthma [26]. Decreasing indoor allergen exposure causes healing in the asthma symptoms, and lessens drug use [22, 26, 27].

2.1. Dust mites

Although people have lived with dust mites for centuries, dust mites allergy has increased dramatically in recent times. Such an increase might be explained by the suitable conditions for dust mites due to the modernization of dwellings and long hours being spent in indoor areas. [16]. Dust mites are the first discovered indoor allergens. Two of the most common house dust mites are *Dermatophagoides pteronyssinus* (Dp), and *Dermatophagoides farinae* [27, 30, 31]. High levels of mites might be found in from the dust of mattresses, pillows, carpets, upholstered furniture, bed covers, clothes, and soft toys. Ninety percent of children with asthma have IgE sensitization to home dust, this might be attributed to dust mite allergens that are carried by bigger substances and that stays on the air hanging a short while. These mites occupy clothes and they are immobile. Distribution of allergens inside the house differ between rooms, more commonly in the bedroom particularly on the bed [20, 23]. Dust mites can be found in hot and humid places. Dust mites exposure is a risk factor for sensitization, and a trigger for asthma attacks [8, 16, 28, 32]. Asthma development, severity, and morbidity are strongly linked with dust mite allergy [15, 24, 31].

Numerous studies have been carried out to test the effect of dust mites removal on asthma symptoms. The most effective method to remove dust mites on the bed is to cover the bed and pillows with dust resistant clothes [30]. In a clinical study, it has been suggested that seven dust mites allergens are removed due to dust resistant cloth used to cover bed and pillows [18]. However, bed-focused interventions to remove dust mites is not effective enough to decrease the exposure. Instead, interventions focusing on patient's total exposure in a day are much more effective [30, 32]. If possible, carpets should be removed and replaced with *polietilen* coverings. Halcken et al. [15] have stated in their study that semipermeable *poliuretan* bed and pillow coverings are important for children and has clinically long-term significant effects. In

addition, toys might be a source of mites and constitutes as a serious risk for asthma symptoms. Toys should be cleaned in hot water or kept in deep-frozen once in a week [15].

Acaricides is recommended as a temporary solution to remove dust mites in soft furnishings. However, some studies have suggested that it might be an effective method if combined with allergen-impermeable mattress to remove dust mites [17, 33]. Vacuum cleaning is another effective method for the removal of dust mites. Vacuum cleaners should be equipped with a special bag or high efficiency particulate air (HEPA) filters in order to diminish mites levels in the air. Additionally, wet vacuum cleaning or steam cleaning are beneficial to remove mites. Bedding staff and other items should be washed in hot water with detergent [11, 17]. Water temperature should be more than 55°C because colder water doesn't kill mites. Dry cleaning might be effective to kill the mites [30].

2.2. Cockroaches

Cockroach allergens are the second agent of indoor allergic sensitization after dust mites [34, 35]. Urban environment, low socio economic status, old buildings, and multifamily homes are all risk factors for cockroach occupation and high level cockroach allergens [23]. In some geographic regions, sensitization to cockroach allergens are rather common especially for children. In those regions, climate is a determinant factor and spending long hours inside the home during winter months means higher exposure to cockroach allergen. Cockroach allergens might be present in all body including shit or split [27, 34]. The most common cockroach allergens are produced by *Blattella Germanica* and *Periplaneta Americana* [20, 34].

Removing cockroach allergens in closed environments is a long term process. Although it has been considered as the best way to exterminate cockroaches, allergic material stays in the closed environment long after its extermination [28]. Thus, following the extermination of the cockroaches, the material including active allergen proteins should be cleaned with an intense vacuum cleaner. The National Cooperative Inner-City Asthma Study (NCICAS) has recently carried out a phase II study emphasising that a complete extermination of cockroach allergens in closed environments is not an easy task [2]. Education, cleaning and extermination interventions ensure a short term decrease, yet, the quantity of allergens is even higher in long term period. For the extermination of cockroaches allergen reservoirs, all the rooms should be cleaned. Studies have stated that pesticides used by professional pest control teams are highly effective to exterminate cockroach allergens. More effective interventions or chemical agents need to be tested to exterminate cockroach allergens but those agents shouldn't harm human health [10, 34].

2.3. Animals

Pet sensitization is an important risk element for asthma and allergic rhinitis. Some studies report that 50–70% of the children with bronchial asthma have sensitivity to pets [34, 36, 37]. Such high rates are the results of the trend of feeding pets at home that leads to high level exposure sensitization [38]. Among pets, cat allergy is the most common type of animal allergy. Sensitized individuals may expose to allergens directly or indirectly. Cats and dogs allergens

stay in the form of little particulates and they are very adherent to floor or clothes. People might be exposed to allergens directly by living with them or they might be exposed indirectly in animal-free areas such as schools, hospitals, or transportation vehicles. Preventing exposure to pet allergens completely is not possible. Lower dose indirect exposure to pet allergens might initiate breathing symptoms for sensitized individuals [34, 39].

Ventilation, humidity and regular house cleaning have been shown as the most effective strategies to remove pet allergens. [25]. Utilizing air-filter tools is not useful to remove mites and cockroaches allergens, however, they may constitute as an important means to reduce the quantity of pet allergens on the air – approximately 2–4 times. In the studies conducted on that issue, it has been reported that HEPA filters and vacuum cleaning lead to short term decrease in the cat/dog allergen levels, however, they do not change the levels of dust allergen concentrations [11, 14, 40]. Results of studies have suggested that the removal of pets from house has provided optimal pharmacotherapy reduced airway responsiveness significantly to methacholine, but no significant differences has occurred in the change of FEV1 [37, 38, 41]. Furthermore, it has also been stated in this study that the removal of pets from the house has led to a reduce in the doses of inhaled corticosteroids and in the frequency of follow-up visits. Alternatively, air cleaners and pet washing are other measures when the pets are not removed from the house [31]. Washing cats is an ineffective short time intervention. Allergen level of the cat increases dramatically within a week after washing. Past studies have shown that repeated washing progressively decreases the amount of cat allergen, and also reduces the amount of airborne allergens originating from the animal. Animal washing procedure is important to reduce allergens, washing with tap water for at least three minutes and pet shampoo is recommended. Washing is an effective method of reducing allergens, but it is not an effective for a long-term time [14, 31]. Avner et al. [14] indicated that the amount of allergen is significantly reduced after washing, but this reduction could not be maintained for a week. As a results, removal of the pets reduce airway responsiveness in patients with pet allergic asthma more than optimal drug use [37]. Even if the pet is excluded from home environment, allergic material keeps living for several months in the same environment. Thus, removal of carpets, covering of bed and mattresses are necessary for the exclusion of allergens for highly sensitive individuals [11, 42]. For pet allergies, use of HEPA filters, mattress covers, and exclusion of cats from the bedroom leads to airway hyperresponsiveness development, and decrease in peak flow variation [28]. For highly sensitive individuals, removal of carpets and upholstery, and encasement of mattresses might be essential to diminish cat allergen levels to a reduce in allergic symptoms. High proportion of sensitized people are not willing to remove pets from their houses because they accept the pets as a member of their family. In this case, environmental control precautions should be taken seriously, such as keeping the pet outside of the bedroom, room air filtration, washing the pet once a week, keeping it in a separate area inside the home, and using HEPA filters. Nevertheless, presence of pets inside the houses always poses a risk for sensitized people [38].

Even though a consensus is available on the role pet allergens for asthma development, it has been tested by some studies that on early interaction with pets can prevent allergy and asthma development for children [27, 43, 45]. The issue whether pet exposure is a risk factor or a

protective factor for allergic symptoms and allergic sensitization has still been under discussion. Studies have focused on the possibility that pet exposure might be beneficial as they can obstacle the development of atopic diseases particularly on the early years of life [43, 46]. Ownby et al. [44] suggested in his study that living with cats and dogs relates to a lower risk of developing atopy during childhood and young adulthood. Collin et al. [36] emphasises in their study that there is no relation between having a pet and bronchial response to methacholine for an 8 year old child. The relation between exposure to allergens and allergy sensitization is a matter of discussion. The results of recent studies confirms hypothesis that keeping pets at home might lead to development of tolerance in a certain degree [46, 47].

2.4. Environmental tobacco smoke

Tobacco smoke is a public health issue and 25-35% of the people with asthma are regular smokers. Approximately 30% of the children has a difficulty to control asthma exposure to environmental tobacco smoke [19]. Environmental tobacco smoke affects individuals at all ages. Negatively, the effect of it on children is stronger, and they can not prevent themselves appropriately [13]. Passive smoking is the most important source of indoor air pollution [48]. Children are exposed to smoke not only at their homes but also in car, other public areas, or restaurants. However, home is the most common place for exposure [49].

The results of exposing to tobacco smoke at pre or postnatal stages are different. Exposure to maternal smoking at prenatal period has long-term effects on the respiratory health of children [50, 51]. Chemical substances available in smoke, transmits to the placenta and affects the health of fetal growth negatively [19]. Prenatal smoke exposure of the baby is associated with deficiency in both functional residual capacity and index of tidal respiratory flow. Furthermore, maternal smoking is associated with increased serum IgE levels, and prevalence of skin-prick test responses in children. Additionally, many studies have suggested that maternal smoking increase the risk of snarling respiration for children under 6-years old [52]. Smoking exposure size at prenatal period and lung irritation are the factors leading allergy development [28, 48, 50].

Children whose parents smoke, experience more severe asthma symptoms and have exacerbations more often [23]. It has been stated in Lang et al.'s [19] study that children exposed in indoor environmental tobacco smoke had more respiratory infections, and significantly worse asthma related quality of life. In addition to its prenatal relation with reduced airway size and its postnatal behavior as a proinflammatory lung irritant, some have proposed that environmental tobacco smoke might also affect allergy development [28].

Tobacco smoke, affecting respiratory and circulatory systems, is the primary reason for many diseases and death, thus, it is a critical issue for public health throughout the world [19]. Although there are several interventions aiming at educating and raising consciousness in people, they are not common enough as desired. Unfortunately, such a public health issue is still waiting for a solution, although lots of strategies has been developed so far. The sole way to prevent children from tobacco smoke is to giving it up inside the house and to inform parents and family members about the mandatory tobacco education programmes helds at school. This is one of the recommended strategies to raise the awareness of environmental tobacco

smoke. In addition, strong national and international policies are required for solution of this issue [2, 19, 28, 49, 52].

3. Outdoor Allergens

People expose to outdoor allergens directly or indirectly is their life-span [53]. Controlling of outdoor allergens is more difficult than controlling of indoor allergens [1]. The most common sources of outdoor allergens are pollens, fungal spores, and air pollutions. Pollens are important risk factor for allergic rhinitis. Furthermore, they cause asthma through their particules penetrating lower respiratory ways. Some evidences suggest that exposure to pollens and airborne allergens increase asthma exacerbations. In order to reduce the pollen based respiratory symptoms, sensitized people should stay at home with closed windows at certain periods of the day that is an effective method to reduce allergen inhalation. Furthermore, wearing masks in outdoor areas might be useful to reduce exposure [53].

Urbanization is an important contributor for asthma since it increases air pollution. Air pollution is a crucial risk factor for health and quality of life in urban life [54]. Children are more sensitive to air pollution and meteorological factors because their lungs have not completed development and developing immune and respiratory systems make them vulnerable to pathogens [55]. There is a consensus on the idea that air pollution might trigger asthma symptoms but the role of air pollution in the development of asthma is a matter of discussion. Air pollution is associated with asthma inflammation, increasing bronchial sensitivity, admitting to emergency departments and increasing rates in the use of drugs. The effects of air pollutants on lung functions depend on type of pollutants, their environmental concentration and duration of exposure to the pollutants. Airway mucosal induced by air pollutants and ruined mucociliary clearance facilitate transmitting and penetrating of allergens to immune system [56]. Concentration and nature of air pollutants changes among regions while the most common ones are ozone (O₃), nitrogen dioxide (NO₂), particulate matter (PM), sulfur dioxide (SO₂), and carbon monoxide (CO) [53].

Modern lifestyle, emission gases of vehicles and air pollution are important risk factors for respiratory allergy for urban life. Controlling those allergens identified as outdoor is rather difficult however reducing exposure to those allergens might be an ideal approach [3, 38]. Individual efforts to control outdoor allergens might be insufficient since their sources are outdoor environment. Primarily, in order to reduce air-pollution based asthma inflammation high level ozone and PM_{2.5} levels warning should be done, traffic should be reduced in urban areas, emission rates of vehicles should be controlled by local authorities [54]. On certain days when air-quality is poor patients should avoid outdoor activities and indoor activities should be included in asthma management plan. Air pollution is a global problem and the solution

requires local national and international efforts by governments, industries and private sector authorities [55, 56].

4. Sensitization

Sensitization is the production of specific IgE antibodies to allergens and immune response begins with sensitization [3]. Asthma prevalence and incidence are affected by many factors. Allergic sensitization is one of the most important factors especially for children and adolescents [9]. Allergic sensitization increases the risk of asthma 4–20 times [23]. The effect of lifestyle factors have still been a matter of debate. On the other hand allergic disease history of the family is doubtlessly an important factor for allergic sensitization [40]. The importance of living conditions and environmental factors exposed at early childhood have been emphasised in many studies [4, 9, 22, 57].

Allergens are a kind of protein and able to penetrate the nasal and respiratory mucosa [58]. Sensitization to inhaler allergens is a major risk factor for asthma however the strength of this factor has still been debated. Furthermore, dose-response relation is another issue that has still been examined. Epidemiological evidences suggest that high level exposure to inhaler allergen is an important risk factor for atopic bronchial asthma especially in the first years of life [13, 20, 57]. It has been reported in many studies that sensitization to allergens is directly related with development of asthma symptoms, exacerbations and severity of asthma symptoms. Childhood asthma, particularly is associated with allergy sensitization and allergy exposure (**Table 1**) [13, 24, 28].

Exposure to high level allergens at early childhoods means a risk for childhood asthma. For the development of sensitization, exposure to indoor allergens at early childhood is an important determinant compared to outdoor allergens. Inner city and urban population studies have indicated that more 80% of school children with asthma sensitized to at least one indoor allergen [4, 23]. Allergic sensitization is a strong determinant for the continuity of disease at later life [40].

Skin prick test, which is the most common method to determine allergic diagnosis, is the basic test procedure to prove IgE based allergic disease sensitization. In the test different allergen extracts is pricked on upper-arm with little quantities and reaction of the person to these extracts is assessed [57]. It provides confirming the type of allergy for sensitization and different allergens can be tested simultaneously as well. The test ensures confirmation of sensitization to allergens objectively [59]. National Asthma Education and Prevention Program (NAEPP) recommends to use the test to assess exposure to allergens besides the patient's history [2]. It is helpful for specific immunotherapy since it makes right interpretation of sensitization children from the birth. As for children, the test can be re-applied if changes in symptoms or new environmental allergens are available. Experienced health professionals perform the test according to international standardized allergens. In test, ≥ 3 mm swollen tissue is accepted as positive allergen reaction (**Figure 1**) [58].

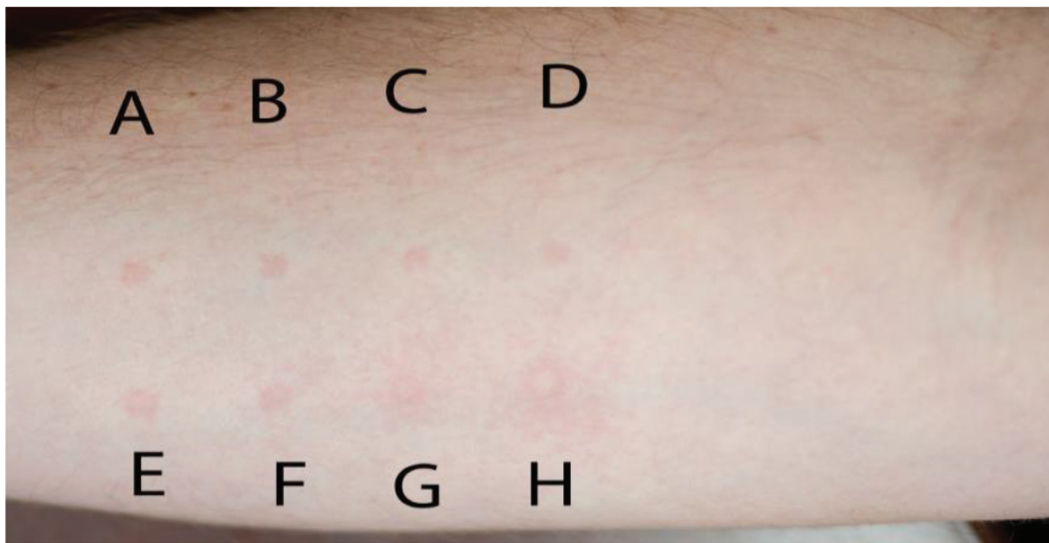


Figure 1. Skin prick test. Kwong et al. [60].

Another sensitization test is the measuring of specific IgE antibodies for a certain antigen such as Enzyme-Linked Immunosorbent Assay (ELISA) or Radioallergosorbent test (RAST). ELISA identifies IgE with a colored reaction product whereas RAST uses radioactively labelled allergen [8, 59].

Allergy history of family	Genetic influence on allergic sensitization
Gender	Underdebate
Childhood environment	Rural and farming environment
	Close interaction with furry animal at early childhood
	Air pollution
	Crowded family
	Exposure to tobacco smoke

Table 1. Factors affecting allergic sensitization.

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