

Review article

Avoidance of allergens and air pollutants in respiratory allergy

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Recent epidemiologic studies that used similar methodologies suggest that the prevalence of allergic airways diseases, particularly bronchial asthma, has increased over the last two decades (1–4). This trend involves many industrialized countries but also some developing ones where these disorders were unknown until recent years (5–9). It has been shown that the development of respiratory allergies depends on an interaction between genetic predisposition and environmental stimuli (allergens and adjuvant factors such as the components of urban air pollution) (10–14).

Since we cannot assume a sudden variation of genetic background, it is likely that changes induced by human activities in indoor and outdoor environments, as well as a Westernized lifestyle, might play important roles in the increasing rate of atopic diseases in the general population (15–22). However, many other hypotheses have been proposed to explain these findings (Table 1).

Relationship between allergen sensitization/exposure and development of respiratory allergy

Atopy is now considered the main risk factor for bronchial asthma, particularly in children (12, 23–25). The increasing exposure to indoor-derived materials (allergens and chemical agents) increases the risk of allergic sensitization to mite, pets, and cockroach products (26, 27).

Many different epidemiologic findings suggest that exposure early in life to high levels of inhalant allergens such as Der p 1, Fel d 1, and Bla g 1 may constitute an important risk factor for developing atopic bronchial asthma in childhood (28–30). On the contrary, the possibility that rural environments may induce a lower prevalence of hay fever, asthma, and allergic sensitization in children has recently been suggested by some authors (31, 32). Moreover, early exposure to pet allergens could protect against later allergy development (33).

It has been clearly demonstrated that exposure of sensitized patients to allergens is a risk factor for asthma (34, 35). For example, the association between exposure to indoor allergens and development of chronic asthma has been shown in a study of wheeze-discordant monozygotic twins (36). Exposure to allergens derived from dust mites constitutes an important risk factor for developing allergic sensitization of the airways in geographic areas where climatic factors, such as the rate of humidity, favor the growth of mite populations (37). In contrast, in areas with a cold climate, such as northern Europe, or in some dry regions of the southwestern USA, allergens derived from pets represent the most common sensitizing agents (38, 39).

Various studies have demonstrated the certain association between bronchial asthma and cutaneous/

Table 1. Theories explaining increasing rate of atopic diseases in susceptible populations

General hypothesis	Factors of indoor environments and lifestyle
Low birth weight (254)	Use of energy-saving insulation on doors and windows (86, 265, 266)
Absence of common infections (255, 256)	Upholstered furniture and wall-to-wall carpets (86)
Early use of vaccination (257)	Central heating systems and/or humidifiers (10)
Early use of antibiotics (258, 259)	New building materials (244, 267)
Changes in intestinal flora (260)	
Early exposure to indoor/outdoor air pollution (261)	More time spent indoors (89)
Intrauterine immunity (261)	Increase in furred pets indoors (88)
Dietary factors (262)	
Breast-feeding (263)	
Socioeconomic factors (264)	

serologic sensitization to allergens (40), the possibility that large amounts of indoor allergens are able to trigger asthma exacerbations (41–43), and the effects on clinical symptoms of removal of the sensitizing allergens (44, 45).

A direct correlation between exposure to large amounts of dust-mite allergens and resultant development of allergic sensitization is generally easy to demonstrate, especially in children. On the contrary, the relationship between exposure to allergens and development of bronchial obstruction in previously sensitized subjects or in adults is complex since the symptoms of asthma in each individual may be induced by different doses of allergen and inhalation of many nonspecific agents (46, 47). However, several studies have suggested that atopic asthma is more severe in sensitized patients exposed to higher levels of allergens, mainly those from indoor environments (41, 48–54).

Relationship between exposure to air contaminants and development of respiratory allergy

A large body of evidence suggests that environmental air pollutants play an important role in the development of respiratory allergy (21, 55, 56). They may enter indoor environments from outdoors or be produced by human domestic activities. Unfortunately, energy-saving systems, such as insulated doors and windows, increase the levels of indoor chemical agents by reducing the natural ventilation and consequently the removal of these agents (57–59).

The associated exposure to allergens and outdoor and/or indoor air contaminants may cause an increase in airway hyperreactivity through various mechanisms (direct damage to epithelial barrier, mucosal inflammation, etc.). Other mechanisms are possible. For example, diesel exhaust particles can induce an increase in IgE-mediated hypersensitivity in both man and animals (60, 61). These particles may interact with airborne pollen allergens such as Lol p 1 and Bet v 1 and enhance their sensitizing capacity (62). On the contrary, only a few studies have demonstrated an adjuvant effect

of chemical agents in enhancing specific IgE production when they are associated with inhalation of mite allergens (63).

All this information suggests the crucial role of the efforts to minimize exposure to allergens and chemical agents in the management of atopic airway diseases, especially bronchial asthma (Fig. 1). Therefore, a well-designed prevention strategy might control the inflammatory mechanisms inducing tissue damage and airway remodeling, thus modifying the chronic evolution of these diseases.

It is also likely that avoidance of pollutants and allergens might reduce the need for anti-inflammatory and symptomatic drugs in asthmatic patients (64).

In this review, we will focus on the main strategic target of environmental preventive measures in patients suffering from airway allergic disease.

Prevention strategies

How to predict populations at high risk

An early recognition of infants at higher risk of developing sensitization of the airways later in life by using simple, effective, and inexpensive screening methods is essential for an efficient prevention strategy (65). Establishing family history of allergic diseases is considered a practical way to assess atopic risk in the clinical setting, but its low screening efficiency does not recommend its use for screening purposes (66). Moreover, various predictive tests such as cord-blood IgE, IgE antibodies in the skin and/or serum, type and level of cytokines, and presence of inflammatory markers and cells have all been suggested as a means to assess atopic risk. Unfortunately, none of them have shown a sufficient degree of accuracy for routine clinical use (66).

Possible modalities of prevention according to the stages of airway sensitization and clinical symptoms

Primary prevention should be performed during gestation or in early infancy. Its objective is the inhibition of IgE sensitization (67). In fact, several studies have suggested that the process of sensitization to foods and

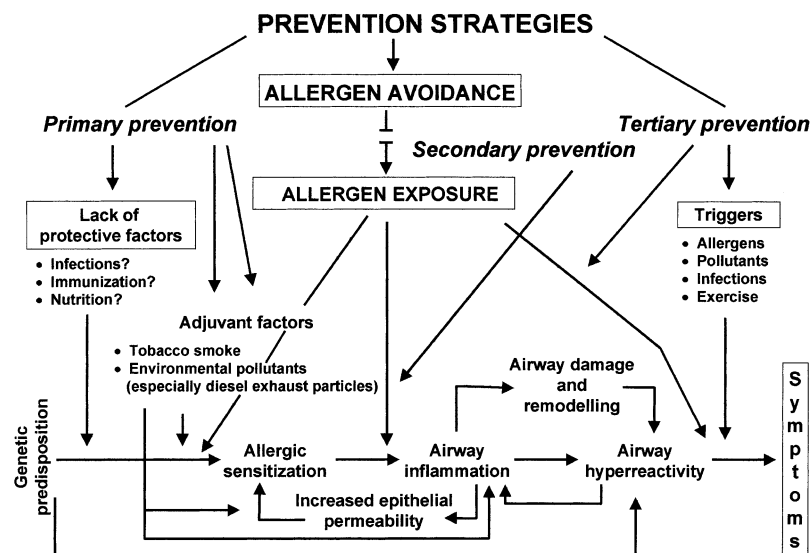


Figure 1. Role of prevention strategies in natural history of atopic bronchial asthma.

inhalant allergens might be initiated in the last months of pregnancy (14, 68–70). Theoretically, this should be the best way to reduce the prevalence of allergic diseases in the future. Unfortunately, there are no convincing data on the efficacy of primary prevention in the later development of allergic diseases.

However, we must emphasize that the majority of mothers of infants at high risk of developing asthma are not aware of the need to avoid the main risk factors in the postpartum period (72). It has been demonstrated that only 13% of them reported that they had been trained by their physicians to improve their domestic environments (72). Consequently, it is likely that the atopic fate of most of the potentially allergic neonates is sealed at their birth (73).

Secondary prevention should be applied during the first months of life to abolish (or delay) the clinical expression of bronchial asthma despite prior IgE sensitization (67). The available data suggest that the first months of life constitute a period during which the immune system is particularly vulnerable. In this period, a high exposure to environmental allergens may induce a prevalence of the Th2 phenotypic pattern (68).

As previously described, there is conflicting evidence that early exposure to allergens, mainly those from indoor environments, constitutes a risk factor for development of allergic sensitization later in life. Although there are no studies suggesting that allergen control in the first months of life effectively delays the onset of clinical expression of asthma, it is likely that it could be useful in high-risk infants (74, 75).

A pharmacologic approach, as a preventive measure to block the “atopic march” from atopic dermatitis to bronchial asthma, has also been suggested for patients in the first years of life. Two studies have been carried out with ketotifen, the first in infants with atopic

dermatitis and the other in infants with a family history of allergy and raised serum total IgE levels (76, 77). Both studies showed a significant reduction in the later prevalence of asthma. Since neither levels of serum IgE nor inhalant allergen sensitization was modified by ketotifen, it is likely that this drug merely masked the onset of symptoms and did not inhibit allergic sensitization.

Recently, the ETAC (Early Treatment of the Atopic Child) Study Group carried out a double-blind, randomized, placebo-controlled trial to evaluate the preventive potential of cetirizine (0.25 mg per kg body weight b.i.d.). A total of 817 infants suffering from atopic dermatitis, who were 1–2 years old with a history of atopic disease in a parent or relative, were enrolled. After an 18-month treatment, cetirizine significantly reduced the incidence of asthma in patients sensitized to grass pollen or to house-dust mite (78).

Tertiary prevention is commonly applied from childhood onward. The objective of this prevention is to reduce the frequency and/or severity of clinical symptoms in subjects with airway allergic diseases (67). It aims to minimize the exposure to allergens (especially those produced indoors) and chemical agents from domestic and outdoor environmental sources. We emphasize that secondary and tertiary prevention use the same procedures of allergen avoidance.

Allergen avoidance

Objectives of preventive measures

The objective of preventive measures is to lower the levels of allergens and pollutants in the indoor environment and, consequently, reduce the rate of exposure to these materials. However, the success of any preventive action rests on various requirements

Table 2. Preliminary considerations on allergen avoidance

- Identify allergen reservoir
- Utilize either short- or long-term environmental control measures
- Evaluate amount of allergen in indoor environment before and after avoidance measures in order to monitor results (103, 268, 269)
- Adapt preventive strategy according to allergen involved, patient sensitization, environmental characteristics, and available economic resources (270)
- Encourage patient compliance (271)
- Utilize only scientifically validated materials and devices (253)

*The presence of some domestic products such as carpet fresheners, powdered pesticides, table salt, and chemical agents such as tannic acid and detergents can cause systematic errors in immunoassays for arthropod allergens (272, 273).

(67). In fact, it is necessary to predict the high risk, demonstrate effective intervention strategies, utilize acceptable interventions, minimize adverse effects, and generate cost-effective efforts.

The control of allergen exposure requires a complex strategy that depends upon some preliminary considerations (37) (Table 2).

How to evaluate and monitor allergens

The levels of mite and pet allergens indoors may be determined by using specific monoclonal antibodies in dust samples (79). The consistency of mite populations may also be calculated indirectly by a simple method such as the Acarex test, which measures the levels of guanine (a metabolic excretion product of chelicarite arthropods) in dust samples (80, 81). Some studies have shown that both measurements are effective in predicting the rate of exposure to mite allergens (82, 83).

The problem of threshold levels of indoor allergens

Various levels of indoor allergens inducing sensitization and/or asthma exacerbation have been suggested (37, 84, 85). However, these threshold amounts of allergen may differ according to the individual degree of bronchial hyperresponsiveness and the possibility of inhalation of other nonspecific irritants (46). In view of the susceptibility of sensitized patients and the rate of allergen exposure, it is hard to calculate the standard amount of allergen, expressed as $\mu\text{g/g}$ of dust or $\mu\text{g/m}^2$, that may constitute the recommended target (86, 87).

Platts-Mills demonstrated that 2 μg Der p 1/g of dust constitutes the threshold amount of this allergen that induces sensitization, whereas 10 $\mu\text{g/g}$ represents the threshold concentration of Der p 1 that may trigger asthma exacerbation in mite-allergic individuals (88). This is why a rate of exposure below 2 $\mu\text{g/g}$ of dust might be the ideal target for obtaining positive clinical results (89). Other authors have suggested that the threshold concentration of Der p 1 inducing airway sensitization is lower because highly susceptible young children may become sensitized at concentrations 10–100 times lower than 2 $\mu\text{g/g}$ (90, 91).

In patients sensitized to cat allergen, the threshold concentration of Fel d 1 inducing sensitization and triggering bronchial obstruction should be considered 1

and 8 $\mu\text{g/g}$ of dust, respectively (92). However, there are conflicting opinions on the threshold of cat-allergen concentrations because the amounts of this allergen in the dust may not represent the real level of the environmental exposure. Since Fel d 1 can be largely detected in the air of indoor environments, this threshold level should be determined by airborne samplers (93).

Although threshold levels of cockroach allergen have not yet been determined, it is likely that they are similar to those of dust-mite allergens (94).

The experience of removing patients from allergen/pollutant-contaminated environments

The transfer of allergic asthmatics to low-allergen environments, such as a hospital room (44) or a high altitude (> 1500 m) where humidity is too low for mites to survive is an important experimental model to demonstrate the effectiveness of measures to avoid mite allergens (45).

In these conditions, mite-allergic asthmatic children show a significant reduction in asthma symptoms (45), and in markers such as nonspecific bronchial hyper-reactivity (95), mite-induced basophil releasability (96), mite-serum specific IgE levels (97), serum markers of eosinophil activation (96), and exhaled nitric oxide (99). Re-exposure to high levels of allergen generally results in the loss of the clinical benefits and recurrence of asthma symptoms (95), suggesting that these measures do not suppress allergen sensitivity. However, treatment with budesonide can prevent the onset of asthmatic symptoms in these children (100).

Occupational allergen exposure also constitutes a model for studying the effectiveness of avoidance measures (101). Some simple control measures such as improved ventilation systems, workplaces designed to minimize allergen exposure, and the use of effective filters and protective respiratory gear are likely to reduce the prevalence of occupationally induced respiratory diseases (67). Moreover, early removal of the worker from the source of occupational agents may frequently induce a reduction in and/or suppression of respiratory symptoms.

Successive studies have been carried out to determine the effectiveness of allergen reduction in indoor environments by various other methods. However, it

is difficult to evaluate the clinical benefit of these environmental interventions, particularly their impact on quality of life, rates of severe exacerbation, and economic resources (102).

Allergen-carrying particles

The determination of sources and aerodynamic characteristics of allergen-carrying particles is an important tool for designing allergen-avoidance strategies (93, 103). Group 1/group 2 mite allergens and cockroach allergens (Bla g 1, Bla g 2) are carried by relatively large particles ($>10\text{ }\mu\text{m}$ diameter). Therefore, these particles can be detected in large amounts in the air of indoor environments only after a strong disturbance (104–106). In undisturbed conditions, these allergens may be found only in reservoirs (107).

On the contrary, allergens derived from domestic animals such as cat (Fel d 1) and dog (Can f 1) are carried both by large particles of about $10\text{ }\mu\text{m}$ diameter (75%) and by small particles of $<5\text{ }\mu\text{m}$ diameter (approximately 25%) (108–110). After a minimal disturbance, these small allergen-carrying particles readily become airborne and remain so for long periods. Consequently, these particles may induce the onset of respiratory symptoms in sensitized patients a few minutes after they enter a home containing a dog or a cat.

These considerations suggest that air-filtration devices are not effective in removing mite and cockroach allergens from their reservoirs. However, these devices may constitute an important means to reduce the amount of pet allergens in the air (106) by approximately two- to fourfold (111). In fact, the use of air cleaners in living rooms and bedrooms may induce a significant improvement in airway hyperresponsiveness and a decrease in peak flow amplitude in children sensitized to pet allergens (112).

Preventive measures to minimize exposure should be applied to allergens produced by dust mites, domestic animals, cockroaches, pollens, and molds.

House-dust mites and measures to avoid their allergens

The procedures to minimize exposure to mite allergens constitute a complex mixture of environmental intervention, and use of chemical and physical methods. Peat & Li (113) demonstrated that the prevention of exposure to mite allergens should be considered the most important intervention to reduce the prevalence of asthma. In fact, these allergens constitute a higher risk factor than the absence of breast-feeding, exposure to environmental tobacco smoke, and ω -3 fatty acid-deficient diet (114).

A recent meta-analysis has demonstrated that environmental control is not effective in providing positive clinical benefits in mite-allergic individuals (115). However, several authors still emphasize the

necessity of measures against mites, although it is necessary to study possible new intervention procedures (116).

The objective of avoidance measures should be not only killing mites but also removing fecal particles containing allergens, since these particles usually remain unmodified in indoor environments for long periods after mites die (117).

The bed is the most important source of mite allergens because dust mites may find great amounts of food (human skin scales and other epithelial products) on its surface. In this case, the measures against mites are fundamental because they protect the patient's airways from the source of allergen for long periods of time (118).

In particular, the mattress constitutes an important reservoir of living dust mites and allergens. Unfortunately, its treatment is very difficult because its thickness does not permit the penetration of antimite agents. Nonetheless, Wickman et al. (119) demonstrated that intensive vacuum cleaning by various systems did reduce the allergen reservoir in the mattress although the number of living mites was not affected by this method.

Encasings for mattresses and pillows that are impermeable to mite allergens, but not to air and water vapor, may be considered the most effective avoidance measure (120–123). Encasings should be used also on mattress bases since they may constitute a relevant source of mite allergens (124). The covers should be robust (their damage could reduce the effectiveness), easily fitted, and easily and frequently cleaned since mite allergens can accumulate on their surface (125). Vaughan et al. (126) showed that tightly woven fabrics and unwoven synthetic fabrics can block common indoor allergens such as those of mite and cat. Consequently, these materials are recommended for use in encasing pillows and mattresses. All exposed bedding and covers should be washed at 55°C , as this is the ideal temperature to kill mites in bedding (127). However, higher temperatures (120 – 140°C) are required to denature Der p 1 and Der p 2, as well as the group 1 and 2 allergens of *Dermatophagoides farinae* (128). Exclusive washing in cool water may remove mite allergens, but the associated use of a soluble form of benzyl benzoate (0.03%) or some essential oils is an alternative way of hot washing (129).

Recently, the use of eucalyptus oil in washing clothing and bedding has been found to be associated with high acaricidal activity (130). Conversely, preliminary data suggest that laundry additives, such as detergents and enzymes, may have only a small additional effect on allergen removal (102). Dry cleaning may also be useful either to kill mites or to remove allergens from blankets (131), although it is less effective than washing in hot water (132).

Fitted carpets represent an important reservoir of

Table 3. Mechanisms by which chemical agents reduce mite numbers

- Some agents, such as benzyl benzoate and pyrethroids, can kill mites directly. Phenyl salicylate seems to be a promising alternative acaricide (274).
- Natamycin reduces mite populations by killing mold spores, which are an optimal food for mites (249, 275).
- Tannic acid has no direct effect on mite growth but does alter chemically the mite allergens and consequently reduces their allergenicity (276). The allergen-denaturing properties of tannic acid could be reduced by the presence of high levels of other environmental proteins, such as pet allergens (277).
- Liquid nitrogen may kill mites by freezing (-195.8°C), but this procedure can be carried out only by a trained operator (84, 278).

* Some commercially available products containing an acaricide associated with tannic acid are usually more useful than separated materials (279, 282).

mites and mite allergens, from which bed and bedding may probably be colonized (133). When the option of removing fitted carpets and replacing them with wood, vinyl or tiled floors is not possible, other preventive measures, such as wet or dry vacuum cleaning, and acaricide/denaturant agents, must be taken. Direct exposure of carpets to sunlight can also kill mites (134). However, this procedure is not applicable to mattresses, owing to their thickness, or to wall-to-wall carpets, because these materials cannot be easily removed.

Steam cleaning may help to kill mites and remove their allergens from carpets, but this procedure could lead to a higher level of humidity in the carpet microhabitat owing to the difficulty of obtaining the complete removal of residual water. In any case, the benefits of these measures last only 2–3 months before mite reinfestation (135).

Regular and intensive vacuum cleaning is considered to reduce the amount of mite allergens in the reservoir (84, 136), but the simultaneous use of other measures is indispensable for effective elimination of allergens in carpets and furnishings (137, 138). Recently, Bellanti et al. (139) demonstrated that reduction of mite allergens was more pronounced with weekly than monthly vacuuming. On the contrary, no reduction in the concentration of indoor endotoxin was found. However, the use of vacuum cleaners with optimal exhaust filtration systems (e.g., HEPA filters and double-thickness bags, the electrostatic filtration system) is necessary to avoid an increase in the indoor airborne levels of mite allergens (138, 140).

Antimite products may achieve their effects in indoor environments by various mechanisms (Table 3). Although these agents demonstrate an optimal *in vitro* activity, their efficacy in indoor environments depends upon other factors (Table 4). The results of clinical studies of these products are still controversial. In fact, some authors demonstrated positive benefits in

controlling mite populations and, consequently, clinical symptoms in allergic patients (141–143), but others failed to find these positive effects (144–147).

Most studies of acaricides or allergen-denaturing agents suggest that repeated applications (every 2–3 months) are needed to prevent reinfestation (143). Although the occasional use of acaricides, such as benzyl benzoate, rarely causes side-effects (148), we still do not know the effects on human health of their long-term use. In any case, some pyrethroids may cause contact allergies (149), whereas other acaricides, such as deltamethrin (150) and S-bioallethrin, possess *in vitro* immunotoxicologic properties (151).

The control of indoor humidity, which should be kept under 45%, is an important measure to reduce mite growth. However, evidence that a reduction in indoor humidity induces a concomitant reduction in humidity in mite microhabitats, such as the middle of a mattress, is still lacking (106). An increased natural ventilation rate may be useful in those geographic areas in which the outdoor air is sufficiently dry. Several studies (152, 153) have demonstrated that the use of mechanical ventilation heat recovery (MVHR) units elicits a significant reduction in indoor humidity and, consequently, mite population. However, this finding has not been confirmed by other studies (154, 155).

Recently, Warner et al. (156) have demonstrated that a combined use of mechanical ventilation and highly efficient vacuum cleaning may induce a reduction in mites and Der p 1 concentrations, but this effect was not sufficient to cause a real improvement in clinical symptoms. Some authors think that dehumidifiers can also influence mite-allergen levels (157), but studies have been unable to confirm this assumption (158). In particular, Niven et al. (159) failed to reduce mite allergens by using mechanical ventilation and dehumidification in British houses.

Air-filtration units and/or ionizers do not reduce the

Table 4. Factors influencing efficacy of antimite agents

- Method of application (e.g., benzyl benzoate moist powder should remain on carpet for almost 12–18 h before removal)
- Type of formulation (liquid, moist powder, foam, spray, etc.)
- Local conditions:
 - Type of carpet and sofa (agents are generally ineffective on mattresses and upholstered furniture)
 - Amounts of accumulated dust or dirt
 - Thickness of carpet and fitted carpets
- Effectiveness of vacuum cleaning in removing dead mites and their products from reservoir after use of these agents

Table 5. Measures to minimize exposure to allergens of dust mites

- Carpets and wall-to wall carpets, curtains, and upholstered furniture should be avoided if possible.
- These materials should be replaced, respectively, with washable surfaces such as vinyl or linoleum, washable cotton curtains, and leather furniture.
- Allergen-proof casing on mattresses and mattress bases, pillows, and quilts should be used.
- Pillows, blankets, eiderdowns, and other materials, such as stuffed toys, must be washed in hot water (55–60°C) weekly.
- An efficient vacuum cleaner equipped with HEPA filter and double-thickness bags should be used at least twice a week on all surfaces of upholstered furniture, carpeting, floors, and bedding (283).
- If not removed, carpets and wall-to wall carpets should be treated every 4–6 months with an acaricide and/or a denaturing agent such as tannic acid.
- Indoor humidity should be kept under 45% by encouraging natural ventilation or, in humid climatic areas, by using a dehumidifier.
- Mite-sensitized patients should wear face masks during vacuuming. Allergic children should be kept out of rooms during and for 2–3 h after cleaning.

* Recently, various authors demonstrated that synthetic pillows contain higher amounts of mite allergens than feather pillows; consequently, these materials may constitute a risk factor for asthma symptoms in mite-sensitized patients (284–286). A possible explanation could be that the tightly woven fabrics used in feather pillow encasement may act as a barrier (287).

levels of mite allergens in indoor environments. In fact, the greatest amount of these allergens remains in settled dust.

Less common antimite measures include freezing of household articles such as soft toys in a domestic freezer for 24 h (86, 160), use of an electric heating carpet in the bedroom (161) or an autoclave to heat rugs (162), and hot tumble drying (163).

Table 5 shows the main measures to minimize exposure to mite allergens in the bedroom and living room, the rooms where people spend most of their time.

Measures to avoid cat and dog allergens

Sensitization to animal allergens is a common occupational hazard in laboratory workers (164, 165). However, the increased exposure to cat and dog allergens due to the increasing frequency of keeping pets indoors, associated with changes in house characteristics and the increased proportion of time spent indoors, is more important (38, 39, 90, 166, 167). For example, cat ownership is associated with the highest prevalence of current asthma (168).

Cat and dog allergens (Fel d 1 and Can f 1, respectively) are characterized by great heat stability. In fact, only 30% and 50% of these allergens, respectively, are modified by the use of dry heat (about 140°C) for 60 min (128). The cat allergen Fel d 1 is produced in large quantities by the sebaceous glands/salivary glands, skin basal squamous epithelial cells (169–171), and anal glands (172). Cat face skin represents the major area of Fel d 1 production (173). Since a Fel d 1-like molecule has been demonstrated in big cats species such as Siberian tiger, lion, puma, and jaguar (174), exposure to these animals should be avoided.

Fel d 1 production is higher in males than in females (175, 176). Vervloet's group (177, 178) have shown that production of Fel d 1 by the sebaceous glands of male cats is controlled by testosterone and decreases after castration. On the contrary, castration in females does not cause any change in Fel d 1 concentrations on their fur (179). However, since both female and castrated male cats may produce enough Fel d 1 to induce

symptoms in sensitized patients, castration of male cats or keeping female cats cannot reduce exposure to cat allergen (179).

The best way to prevent cat/dog allergy is to remove the animal. However, many pet-sensitized patients, particularly children, refuse to give up their pets. In this situation, intensive avoidance measures are necessary to reduce the degree of allergen exposure and to control respiratory symptoms.

Recently, Lewis & Breyse (180) have reported that some characteristics of carpets, such as low pile density and height, fluorocarbon coating of fibers, high-denier filaments, and a fiber shape with a low surface area, can affect the retention of cat allergen. Moreover, other studies have demonstrated the persistence of high levels of Fel d 1 in carpets (181) and in mattresses (182) many months after the removal of cats.

Therefore, HEPA-equipped air cleaners/vacuum cleaners must be used intensively and for a long time. However, although new generations of vacuum cleaners and vacuum cleaner bags reduce the leakage of cat allergens, methods of testing for these allergens should always be applied to these devices before recommending them for allergic patients (183).

Since animal dander may constitute a food for mite populations, the removal of these materials from indoor environments is a preventive measure not only for patients sensitized to pet allergens but also for those sensitized to *Dermatophagoides* allergens.

The main measures to minimize exposure to the allergens of cat/dog are shown in Table 6.

Unfortunately, pet allergens, particularly Fel d 1, are usually found also in many indoor environments, such as day-care centers for atopic children, public buildings, and means of transport, where cats have never been kept (184–189). This finding seems surprising, but winter clothes (skirts and trousers) of patients with a cat in the home contain higher levels of Fel d 1 than those of subjects who have a dog in the home and those of control subjects without animals at home (190). Therefore, clothing may constitute an important means for the distribution of this allergen in cat-free environments and may consequently represent a risk factor for triggering asthma in cat-sensitized individuals

Table 6. Measures to minimize exposure to allergens of cat/dog

- Pets must be removed from home. After their removal, it is necessary to vacuum-clean and wash all surfaces, including wall surfaces, on which Fel d 1 may accumulate in large quantities (288). Carpets and upholstery should be cleaned and bedding should be washed.
- If patients choose to keep cat/dog at home
 - They should use a vacuum cleaner equipped with HEPA filter and double-thickness bags to remove pet allergens from reservoirs as described for dust-mite control (289, 290).
 - They should remove carpeting from all indoor environments, and replace with linoleum or wood flooring.
 - They should use high-efficiency particulate air (HEPA) cleaner to remove airborne Can f 1/Fel d 1 allergens (111, 283).
 - They should use the same preventive methods with bedding as described for mite control.
 - Pets should be washed twice a week to reduce Fel d 1 (291, 292) and Can f 1 (293) shedding; pet bedding also should be washed.
 - The use of Allerpet/c (Allerpet, Inc., New York, NY, USA), a product that removes pet allergens if applied directly on animals, has had mixed results (294–296).
 - Pets should be kept outdoors as much as possible. In any case, pets should not enter bedrooms and living rooms (297, 298).
 - Indoor environments should be naturally ventilated (299, 300).
 - Washing the clothes of cat owners, together with the avoidance of using allergen-contaminated clothes outdoors, can prevent the dispersal of cat allergen (192).

(190). This is also possible for dog allergens (Can f 1) (191). Therefore, the removal of cat/dog allergens from the clothes of pet owners should be considered an important tool for the prevention of pet allergy (192). Washing contaminated cotton fabrics in water is a simple and effective method with which to remove cat allergen from clothing. This procedure, in association with the avoidance of wearing allergen-contaminated clothes outdoors, can prevent the dispersal of cat allergen (192).

Measures to avoid cockroach allergens

Cockroach allergens are the second greatest cause of indoor allergic sensitization after *D. pteronyssinus* in the USA, especially in urban/suburban areas (193–195), and they may constitute a relevant risk factor for emergency room visits (196) and asthma hospitalization (197). The increasing significance of cockroach sensitization has also been demonstrated in Switzerland (198), Spain (199), France (200), Italy (201, 202), Turkey (203), the Dominican Republic (204), and East Germany (205).

An association has been shown between sensitization to *D. pteronyssinus* and cockroach allergens, as assessed by measuring the wheal areas of skin prick tests (202, 206). This finding is in agreement with the results of some studies suggesting cross-reactivity between these allergens (207). For example, Santos et al. have demonstrated that tropomyosin produced by *Periplaneta americana* shows a high degree of identity to that produced by dust mites and shrimp (208). However, some authors believe that this association is probably due to the coexistence of mites and cockroaches in the same indoor environments (209).

Effective methods to exterminate cockroaches are

available. The entomology literature reports that pesticides may reduce populations up to 100% and maintain these results for at least 3 months (210, 211). Nonetheless, the analysis of floor dust of homes with recent cockroach extermination showed high levels (up to 3899 ng Bla g 1/g dust) of the major allergen of *Blattella germanica* (212).

The National Cooperative Inner City Asthma Study (NCICAS) used a combination of education, cleaning, and extermination with Abamectin (Avert) to reduce indoor levels of Bla g 1 in kitchen, bedroom, and TV/living room (213). The results of this study demonstrated that despite a significant but short-lasting decrease, the amounts of cockroach allergens remained well above levels previously found to be clinically significant. Consequently, long-term treatment of indoor environments is probably needed to reduce the level of cockroach allergens and prevent reinfestations (213).

Allergens may be found in cockroach skin, feces, whole-body extracts, and nest debris. For this reason, extermination without adequate vacuum cleaning to remove all cockroach-derived materials is unlikely to be an optimal preventive measure (214–216).

Measures to prevent cockroach allergy are shown in Table 7.

Measures to avoid allergenic pollen

Effective avoidance of outdoor allergens, such as those released from pollens, is very difficult because of the very high atmospheric concentrations of these particles during pollination periods (Table 8). Atmospheric concentrations of allergenic pollens may partially depend upon changes in native vegetation made by man for agricultural, reforestation, and ornamental

Table 7. Measures to minimize exposure to cockroach allergens

- Remove waste food and water leakage, which can facilitate the growth of cockroach populations.
- Maintain the integrity of plasterwork and floors in order to avoid cockroach access indoors.
- Use available chemical agents for cockroach extermination (diazinon, chlorpyrifos, hydromethylnon, abamectin, etc.) in different formulations (bait stations, paste, etc.)
- Use intensive vacuum cleaning to remove cockroach-derived materials (such as bodies and allergens) after extermination with chemical agents.
- Encourage patient compliance with long-lasting prevention measures with appropriate educational programs.

Table 8. Measures to minimize exposure to pollen allergens

- The introduction of weeds, plants, and trees that produce pollens with high sensitizing capacities must be avoided.
- Pollinosis patients should be informed of pollination periods and the levels of airborne allergenic pollens all over the world (221, 222).
- During the pollen season, people suffering from pollinosis should move to an area with a low pollen count.
- Patients should remain indoors with doors and windows closed on days with high pollen counts (220).
- Patients should keep car windows closed or use air conditioning with an antipollen filter while driving.
- Patients must not cut grass, walk in new-mown grass, or exercise in the open during the pollination period. If necessary, a face mask to prevent pollen inhalation should be worn.
- Incoming air should be filtered by air conditioners or indoor air cleaners fitted with HEPA filters.
- Wild plants of the Urticaceae, Gramineae, and Compositae families should not be allowed to grow near inhabited areas.

purposes (217, 218). Thus, an effective but long-term preventive measure would be to avoid the introduction of weeds and/or trees producing pollens with high sensitizing capacities, especially in public urban areas (219).

The indoor levels of the major allergen of *Parietaria judaica* pollen (Par j 1) during the pollination periods are significantly lower than the outdoor levels when the doors and windows are kept closed (220). For this reason, remaining indoors may constitute a useful preventive measure to reduce exposure to pollen allergens when pollen counts are high (221, 222). Obviously, filtration of incoming air by air conditioning or indoor air cleaners with HEPA filters may be useful to remove airborne particles (223).

In view of the cross-reactivity between several pollen allergens and fresh fruits/vegetables, pollinosis patients should be informed of the possibility of intraoral symptoms after the ingestion of these foods to avoid generalized manifestations (224, 225).

Measures to avoid mold allergens

Alternaria allergens from outdoor sources represent the most common agents of mold sensitization in major parts of the world such as the USA (226), Australia (227), and Europe (228–230). Moreover, sensitization to *Alternaria* allergens may constitute a risk factor for asthma exacerbation (226, 231) and sometimes also for death from asthma (232).

Although damp and other microclimate characteristics may facilitate mold growth in indoor environments, only half of the studies indicate the presence of a significant association between the occurrence of respiratory symptoms and the presence of damp and mold (233). For example, Williamson et al. found a weak correlation between the severity of asthma and the degree of damp at home (234). When the correlation is present, cough and wheeze are the most common

symptoms (233). Indoor mold levels depend upon outdoor spores entering the home and indoor sources. These levels differ according to geographic area (235, 236).

The available data on the efficacy of preventive measures to reduce mold growth are few (237, 238); some suggestions are included in Table 9.

Avoidance of environmental pollutants

The control of exposure to environmental pollutants must be considered in all stages of allergy and asthma prevention. In fact, components of air pollution, particularly ozone, particulate matter, and sulfur dioxide, induce an inflammatory effect on the airways of susceptible subjects. This effect can cause increased permeability, more conspicuous penetration of pollen allergens into the mucous membranes, and, consequently, interaction with immune system cells (239). This effect facilitates the increase in bronchial responsiveness to inhaled pollen allergens in predisposed subjects (240, 241). Moreover, some components of air pollution seem to have an adjuvant immunologic effect on IgE synthesis in atopic subjects (239, 242, 243).

Measures to reduce the exposure to outdoor air pollutants should be issued by health authorities since control procedures must be applied to the sources of these air contaminants (industries, transport vehicles, etc.).

In recent years, increasing interest has been focused on the indoor environment as a source of air pollutants. In effect, some pollutants may be more concentrated indoors than outdoors. Therefore, remaining indoors is not a real protection from air pollution, as generally believed (57). Since we spend about 90% of our time indoors, the health risks associated with inhalation of indoor pollutants may be greater than from inhalation of outdoor agents (244).

Table 9. Measures to minimize exposure to mold allergens

- Control of the level of indoor humidity ($\leq 35\%$) with a dehumidifier or an exhaust fan; improvement of spontaneous ventilation.
- Avoidance of hygroscopic materials on which mold colonies may proliferate.
- Use of air cleaners with HEPA filters, which may remove airborne mold spores.
- Use of air conditioning, which can reduce the penetration of outdoor spores indoors. However, the filters of these systems should be changed frequently to avoid mold proliferation.

Table 10. Measures to minimize exposure to indoor air pollutants

- Avoidance (whenever possible) of toxic construction materials (e.g., synthetic carpeting, sealants, paints, adhesives, formica-rolled sections, furniture, combustion appliances, etc.).
- Separation or isolation of toxic materials from indoor environments (244).
- Adequate interchange between indoor air and outdoor air. This objective should be obtained by increasing natural ventilation of the structure and/or by using a central ventilation systems (267).
- Appropriate educational programs should be available for home owners, home builders, designers, engineers, physicians (particularly allergists), and hygienists in order to improve the air quality of homes.
- Humidity control.

Environmental tobacco smoke is the most common indoor pollutant. Its effects on respiratory symptoms are well recognized, particularly in children (118, 245).

Other indoor chemical pollutants include combustion-derived agents, such as sulfur dioxide, nitrogen oxide, carbon monoxide, carbon dioxide, formaldehyde, and domestic materials (paints, solvents, detergents, polish, furniture, plastics, and inorganic fibers) (59). Gas-fueled cooking stoves, space heaters, heating systems, clothes dryers, hot water heaters, and fireplaces frequently introduce large amounts of these agents into the indoor air. These pollutants cannot be easily removed by natural air exchange, especially in tightly insulated houses (244).

The main measures to control indoor air pollutants are listed in Table 10.

Since modern houses are smaller than old houses, ventilation rates play an important role in determining air quality in indoor environments (246, 247). An adequate degree of natural or forced air circulation can control indoor levels of humidity and temperature, remove air pollutants, and dilute toxic agents with outdoor air.

Conclusions

A large body of clinical and experimental evidence suggests that the increasing prevalence of allergic

diseases, particularly bronchial asthma, may be caused by changes of indoor/outdoor environments, although this is a controversial issue.

Allergens and air pollutants cause inflammatory events in airways that may induce chronic damage and the loss of normal respiratory function after various periods of time. These considerations suggest the necessity of frequent monitoring of the levels of indoor/outdoor allergens and air pollutants (248).

Adequate environmental control measures should be taken to maintain the levels of these agents under the threshold concentrations identified in the available literature that cause airways sensitization and/or triggering of asthma exacerbation in predisposed individuals (249). Avoidance of allergens and air pollutants constitutes the keystone in the overall management of bronchial asthma (250). Therefore, these measures should be applied in all phases of this disorder (Fig. 2).

Patient education should be encouraged in order to obtain an increase in the general awareness of the role of environmental allergens and pollutants in the development of allergic asthma (251, 252).

There is a lack in the literature of studies convincingly demonstrating that a reduction of allergen exposure early in life prevents the later development of atopic disorders. However, it is likely that allergen avoidance in the first years of life would delay the onset of clinical

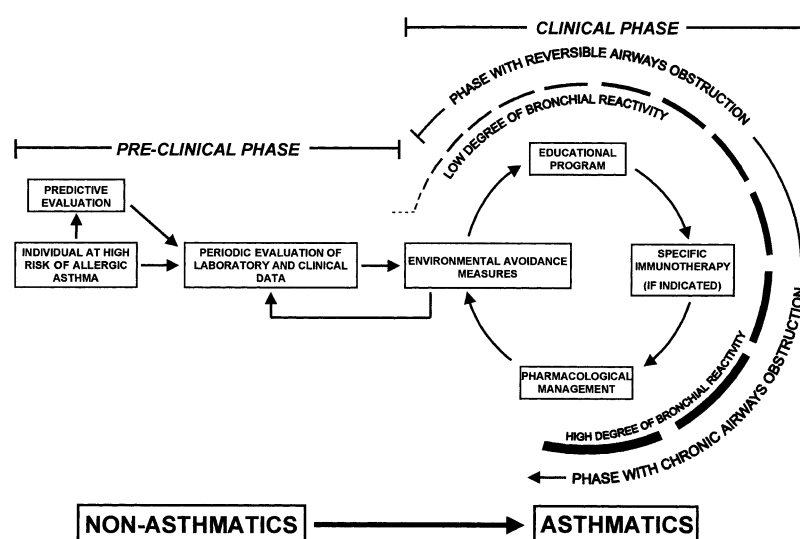


Figure 2. Overall management of bronchial asthma; role of prevention strategies.

expressions of asthma or reduce the frequency and/or severity of clinical symptoms. Therefore, early recognition of infants at high risk of developing allergic diseases, particularly bronchial asthma, combined with avoidance of allergens and air pollutants, should be considered an essential means to reduce both the prevalence and the high social costs of these disorders.

Further studies should be performed to improve the current prevention strategies, because the use of validated, easier to perform, and less expensive procedures is essential to obtain appreciable clinical benefits (253).

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