Aeroallergens and asthma

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The main aeroallergens in both the indoor and outdoor environment that have been implicated in the pathogenesis of allergic asthma are reviewed. Pollen and fungal spores are important outdoor aeroallergens that cause sensitization in atopic subjects, leading to rhinitis and asthma in a proportion of the sensitized subjects. Each pollen type displays a particular seasonal periodicity: tree pollen are prevalent in the late winter and spring, grass in the spring and summer and weed mainly in the fall. There are regional differences in the type of pollen grains in Canada. Although the pollen grains are large, fragments less than 10 µm can reach the lower airways to cause asthma. Some fungal spores, such as *Alternaria* and *Cladosporium*, have been implicated in asthma. The full clinical impact of fungi in asthma has yet to be clarified. With the construction of homes that are tightly sealed to conserve heat and the use of wall to wall carpet, the type and concentration of indoor aeroallergens have become increasingly different from outdoors. House dust mite and pet allergens have now been shown to be important aeroallergens that sensitize children in infancy and are risk factors for asthma. Clinicians should recognize the importance of aeroallergens in asthma because avoidance and/or reduction of exposure is an important part of the management besides drug therapy.

Key Words: *Allergens, Asthma, Cockroach, Fungi, House dust mites, Hypersensitivity, Pets, Pollen*

Les aéroallergènes et l'asthme

RÉSUMÉ : Les principaux aéroallergènes présents dans l'environnement intérieur et extérieur et, impliqués dans la pathogenèse de l'asthme allergique, sont passés en revue. Les pollens et les spores des moisissures sont des aéroallergènes majeurs de l'environnement extérieur qui provoquent une sensibilisation chez des sujets atopiques puis, de la rhinite et de l'asthme chez un pourcentage des sujets sensibilisés. Chaque type de pollen démontre une périodicité saisonnière spécifique. Les pollens d'arbres prévalent vers la fin de l'hiver et au printemps, ceux du gazon au printemps et en été et, ceux des mauvaises herbes surtout en automne. Au Canada, on a observé des différences régionales dans le type de grains de pollens. Bien que les grains de pollens soient gros, des fragments de moins de 10 µm peuvent atteindre les voies respiratoires inférieures et causer de l'asthme. Certaines spores de moisissures telles que *Alternaria* et *Cladosporium* ont été impliquées dans l'asthme. L'importance de l'impact clinique des moisissures dans l'asthme reste à clarifier. La construction de maisons hermétiques pour conserver la chaleur et la pose de moquettes font que le type et la densité des aéroallergènes de l'environnement intérieur se distinguent de plus en plus de ceux identifiés à l'extérieur. Les acariens de la poussière et les allergènes de source animale sont maintenant identifiés comme des aéroallergènes majeurs qui sensibilisent les enfants dans l'enfance et sont des facteurs de risque pour l'asthme. Les cliniciens devraient reconnaître l'importance des aéroallergènes dans l'asthme puisque leur éviction et/ou une réduction du contact à ces substances jouent un rôle important dans la prise en charge en plus du traitement médicamenteux.

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ASTHMA IS A MULTIFACTORIAL DISEASE, DETERMINED BY a combination of genetic and environmental factors. While scientists are still struggling to discover an asthma gene, a great deal of information has become available in relation to environmental factors in asthma.

Environmental factors can be divided into two groups: air pollutants and aeroallergens. Both groups are present indoors and outdoors. For many aeroallergens, indoor levels are dependent on outdoor levels. However, with the construction of homes that are tightly sealed to conserve heat during the past decade and the use of wall to wall carpeting, the type and concentration of indoor aeroallergens have become increasingly different from those outdoors. As most people spend more than 90% of time indoors, the indoor environment deserves more attention and study than it used to.

This is a review of the main aeroallergens in both the outdoor and indoor environment that have been implicated in the pathogenesis of allergic asthma. Occupational exposure will not be considered. The mechanisms by which these aeroallergens cause airways inflammation and bronchial hyperresponsiveness as well as the allergic evaluation of the asthmatic patient are beyond the scope of this review.

OUTDOOR AEROALLERGENS

Pollen and fungal spores are the most important outdoor aeroallergens that cause sensitization in atopic subjects.

Pollen

The pollen grain is the specialized structure that houses the sperm or male gametes of flowering plants. It comprises two to four cells combined as a unit. The pollen grain typically is composed of approximately 20% protein, 37% carbohydrate, 4% lipid and 3% minerals. Pollen is formed within the anther, which is an elongate structure containing the pollen sacs. Pollen grains are transferred to the female reproductive body mainly by wind or vector insects. Only 30 out of more than 300 families of flowering plants show adaptations for pollen dispersal in air currents and are termed anemophilous. Wind transported pollen tend to be between 10 and 40 µm in size, dry, round and with little surface ornamentation. The germinal apertures are a major feature of pollen morphology. Families in which most of the genera are wind-pollinated, and of allergologic interest, include: Gramineae (grasses), Betulaceae (birches), Fagaceae (beeches, oaks), Cupressiaceae (junipers, cedars), Salicaceae (poplars), Ulmaceae (elms), Chenopodiaceae (docks) and Urticaceae (nettles). Among several families that are predominantly pollinated by animal vectors, some genera are wind-pollinated, for example, the ragweed, *Ambrosia*, in the Compositae and the ash, *Fraxinus*, in the Oleaceae (1).

Pollen constitute a small part of the aeroplankton or air spora present in the atmosphere, since most frequent particles of biological origin are microorganisms, especially the spores of fungi. However, tree, grass and weed pollen are also common airborne particles in the ambient atmosphere. Pollen grains may travel long distances before they are deposited. The pollen season in temperate climates is restricted to the warmer months of the year from late winter through autumn. As the flowering season progresses, different pollen are present in the atmosphere, so that each type displays a particular seasonal periodicity.

In most temperate climates, the seasonal progression first involves tree pollen in late winter and early spring. The pollen of birch, alder, hazel, oak, ash and elm lead the pollen calendar. The grass season begins in late spring and early summer. This is followed closely by various weeds, for example nettle, dock, sorrel and plantain. In North America, various amaranths and ragweeds begin to pollinate in the autumn (1). Both the time of commencement and duration of the pollen season have been shown to be dependent on elevation above sea level and geographic position. However, marked differences in onset of the pollen season and in the total amount of pollen released occur from year to year.

Atmospheric conditions such as temperature, relative humidity and wind speed and turbulence affect the release and dispersal of pollen grains. Epidemics of asthma have been associated with thunderstorms. On two consecutive occasions after thunderstorms in Melbourne, Australia there were 10-fold increases in cases of asthma admissions (2) which was thought to be due to the release of micronic particles from grass pollen after substantial rainfall.

Pollen have been implicated in several allergic diseases, including allergic rhinitis, bronchial asthma, as well as in several eye and skin disorders (3,4). In fact, atopic diseases, particularly those induced by pollen allergens (rhinoconjunctivitis and asthma), have become more common during the past two decades (5,6). Pollen grains are usually too large to penetrate the lower airways. However, allergenic activity has been found in airborne fragments smaller than pollen for both ragweed (7) and ryegrass (8). In the case of ryegrass, it has been shown that pollen grains are ruptured in rainwater by osmotic shock, each grain releasing about 700 starch granules into the atmosphere. These granules are small enough to enter the airways (less than 3 µm in diameter) and tests in asthmatics have shown that suspensions of these granules provoked immunoglobulin (Ig) E-mediated responses (8).

An increase in nonallergic bronchial hyperresponsiveness to methacholine has been demonstrated in pollen-sensitive asthmatic subjects during and after the pollen season (9). The number of pollen grains required to elicit symptoms is unclear but studies indicate that the number is greater at the beginning than at the end of the season, an effect known as priming. Empirical data suggest that the threshold concentration lies between 10 and 50 grains/m^3.

A characteristic feature of pollen sensitivity is its seasonal pattern of occurrence, usually at the time when the pollen count is highest in the atmosphere. Because the diagnosis of pollen sensitivity is partly dependent on patients' symptoms during the pollen season, physicians need to know the season and the amount of pollen from allergenic plants.

Different devices are used for aerobiological sampling such as Durham greased slide (gravitational), the rotating impaction sampler (impaction) or the volumetric Burkard spore trap (suction) (4). Chatterjee and Hargreave (10) stud-

TABLE 1
Flowering period and relative abundance of relevant allergenic plants in Canada

	Flowering period	BC	Alta	Sask	MB	N Ont	S Ont	N Que	S Que	NB	PEI	NS	Nfld	Yukon	NWT
Grasses															
Grass, Kentucky blue (*Poa pratensis*)	May-July	++++	+++	+++	+++	+++	++++	+++	++++	+++	++++	++++	+++	+	+
Grass, orchard (*Dactylis glomerata*)	June-July	+++	+	+	+	+	++++	+	++++	+++	+	+++	+	+	
Grass, Timothy (*Phleum pratense*)	June-July	+++	+++	+++	+++	+++	++++	+++	++++	+++	+++	+++	+++	+	+
Weeds															
Ragweed common (*Ambrosia artemisiifolia*)	July-Sept	+	+	+	+	+	++++	+	+++++	+	+	+	+		+
Lambs' quarters (*Chenopodium album*)	July-Sept	++++	+++	+++	++++	+++	++++	+++	++++	+++	+++	+++	+++	+	+
Mugwort (*Artemisia vulgaris*)	Aug-Sept	+	+	+	+	+	+	+	+	+	+	+	+		
Pigweed, redroot (*Amaranthus retroflexus*)	July-Aug	+++	+	+	+	+	+++	+	+++	+++	+++	+			
Plantain, English (*Plantago lanceolata*)	June-Oct	++++				+	+++	+	+++	+	+	++++	+++		
Russian thistle (*Salsola pestifer*)	July-Sept	+++	++++	++++	++++	+	+	+	+	+	+	+			
Sorrel, sheep (*Rumex acetosella*)	June-Aug	+++	+++	+	+	+++	+++	+++	+++	+++	+	+++	+++	+	
Trees															
Elm, white (*Ulmus americana*)	Apr-May			+	+	+	+++	+	+++	+++	+	+++	+		
Oak, red (*Quercus rubra*)	May-June					+	+++	+	+++	+++	+	+++			
Birch, white (*Betula papyrifera*)	Apr-May	++++	+++	+	+++	++++	++++	++++	++++	++++	+++	++++	++++	+++	+++
Ash, white (*Fraxinus americana*)	May-June					+	+++	+	+++	+++	+++	+++			
Juniper, common (*Juniperus communis*)	Apr-May	+++	+++	+	+	+++	+++	+++	+++	+++	+	+++	+++		
Maple, Manitoba (*Acer negundo*)	May-June	+	+	+++	++++	+	+++		+						

Data modified from reference 11

ied the atmospheric pollen and fungal spores in Hamilton, Ontario using an automatic volumetric spore trap. Immunological methods of identifying and quantifying airborne allergens have been developed in recent years. Table 1 shows the flowering period and the relative amount of pollen from the most common allergenic plants in Canada (modified from reference 11). Note the important regional geographical differences, particularly for weed and tree pollens. The above information is very useful to pollen-sensitive patients when they plan trips and in the prevention of severe allergic symptoms by appropriate medication or other measures (12).

Grass pollen sensitivity is the most common cause of allergic disease worldwide (4). This is due to the wide distribution of wind-pollinated grasses. The allergens from ryegrass (*Lolium perenne*) and timothy (*Phleum pratense*) have been most extensively studied and some have been isolated. The original studies carried out by Marsh (13) and Matthiesen and Lowenstein (14) showed that the pollen from these grasses contained several allergens. In the past, four of the most important allergens in ryegrass were designated groups I to IV, and the main allergens in timothy were termed groups V, VI and VII. Recently, allergens from grass pollen have been isolated and characterized and they are now designated according to the new allergen nomenclature. These individual allergens include *Lol p* I-IV from *L perenne*, *Phl p* V from *P pratense*, *Cyn d* I from *Cynodon dactylon*, *Dac g* I and V from *Dactylis glomerata*, and *Poa p* I from *Poa pratensis*. Allergens from different grass species show a high degree of cross-reactivity (4).

The ragweed tribe is the most important cause of allergic rhinitis and pollen asthma in North America (4). Short ragweed pollen (*Ambrosia artemisiifolia*) contains 22 allergens (15), and the two major allergens, *Amb a* I (former antigen E) and *Amb a* II, have been isolated. Other allergens have been purified from additional weeds, such as *Sal p* I from *Salsola pestifer* (Russian thistle) (16) and *Par j* I from *Parietaria judaica* pollen (17). Members of the two closely related Chenopodiaceae (lamb's quarters, Russian thistle) and

Amaranthaceae (redroot pigweed) families show varying degrees of cross-reactivity.

The allergenic fractions of trees have not been studied as well as ragweed or grasses. A few major allergens have been isolated, including *Bet v* I from *Betula vulgaris* (birch) (18), and *Cor a* I from *Corylus avellana* (hazel). The latter only differ in two residues from the major allergen of birch (19). *Jun s* I has been isolated from *Juniperus sabinoides* (mountain cedar) (20), and *Ole e* I from *Olea europaea* (olive) (21), which is shared by other species of the Oleaceae family (22).

Fungi or moulds

Fungi or moulds are a heterogeneous group of nonphotosynthetic organisms that are grouped in the plant kingdom because of the presence of a cell wall. They are 80 to 90% polysaccharide in composition (23). Fungi grow best at relative humidity of 75 to 95%, but others like *Aspergillus* can grow in lower humidity because they can extract water from the atmosphere.

The spores of fungi range between 3 to 200 µm, with the majority at around 10 µm. However, it has been pointed out by Licorish and co-workers (24) that some spores are quite small, such as *Penicillium* (less than 5 µm) and the young spores of *Alternaria* (less than 10 µm). Moreover, the snowshoe-shaped *Alternaria* spore has different aerodynamic properties that keep it from having an impact in the upper airways.

There are four major groups of fungi: (a) Phycomycetes *Rhizopus, Mucor* – sugar and bread moulds; (b) Ascomycetes (sac fungi) – black moulds and blue moulds, yeast; (c) Basidiomycetes (club fungi) – rusts, smuts, mushrooms, puffballs; (d) Deuteromycetes (fungi imperfecti) – *Cladosporium, Alternaria, Aspergillus, Helminthosporium, Penicillium*. The last group consists of most of the fungi allergenic for humans. There are studies to indicate that the basidiospores may also be important particularly in the southern United States (25). Many fungal spores are virtually always present over large land masses. They are present in higher concentration than pollen, sometimes 40 times higher. The particular species and concentration in the air at any given time are dependent on temperature, rainfall, prevailing winds, seasonal climatological factors, circadian patterns of sunlight and darkness, availability of substrates, and the degree of both substrate and atmospheric moisture (23). For example, the dispersal of basidiospores and their growth are affected by atmospheric moisture; the spores are propelled into the atmosphere during periods of rainfall and dampness. Circadian rhythms in humidity and temperature interact to foster nocturnal or diurnal increases in certain basidiospore concentrations (26). *Cladosporium* and *Alternaria* are blown free by wind, and these spores increase in concentration with diminishing humidity and increasing airflow. Thus, these species are often abundant during mid-day periods with maximal sunlight.

Most of the fungal spores found indoors are from the outside. However, high levels of fungi are present inside damp houses particularly on garbage containers, food storage areas, wallpaper, damp basement, shower curtains and window mouldings. New buildings are being constructed tightly to avoid air leaks in order to save heating cost and, as a result, indoor humidity increases. There is a possibility that occasionally buildings or homes may become sufficiently contaminated with mould to cause asthma (23).

The role of fungi in asthma is not fully understood. This is due to many factors: the choice and method of preparing fungal extracts for skin testing and bronchoprovocation testing vary markedly among investigators; the quality and potency of mould allergenic extracts have often been poor; relatively few fungi have been studied in detail; a single, brief well-defined 'mould season' usually does not occur (23). In addition, there are difficulties with identification of mould allergens (27). Many fungi have very specific growth requirements that prevent culture in the laboratory. The spores are not discrete in morphology, while culture methods may be misleading because some spores may not germinate. Moulds may be airborne in amorphous particles and enumeration of spores may underestimate the total amount of antigen in the air. Thus, identification of fungal aeroallergens may require a combination of methods including microscopic counts, culture and immunochemical assay.

During the past 15 years, several studies have demonstrated the relationship between increase in asthma severity and high fungal spore counts. Salvaggio and Aukrust (25) showed that an increased incidence of asthma admissions in New Orleans, during the months of September to November, was associated with very high outdoor total spore counts. Hasnain et al (28) also showed similar findings in New Zealand. In the Netherlands, Beaumont et al (29) showed a positive correlation between decreased peak flow rates with high outdoor spore levels. In 24 patients with asthma who had positive skin and bronchial reactions to *Cladosporium*, Malling (30) found a positive correlation between the weekly symptom scores, medication scores, total scores and the *Cladosporium* spore counts. Lopez and coworkers (31) studied eight asthmatic patients who had positive skin tests to extracts of basidiospores and asthmatics with negative skin test. Those with positive skin test had positive inhalation challenge to extract of basidiospores. O'Hollaren and colleagues (32) reported that exposure to *Alternaria* in the summer or early fall may be responsible for the severe attack of asthma in 11 patients, fatal in two cases, in the upper midwest of the United States. The study by Licorish et al (24) provided confirmation that inhalation of *Alternaria* or *Penicillium* spores can cause asthma in mould-sensitive patients.

The level of fungal spores in the atmosphere correlates with the level of IgE synthesis. Agarwal et al (33) found that the level of *Alternaria* spore counts correlated with the ability of the extract to induce positive skin test; similarly, the immunochemical activity of the allergens paralleled the mean symptom scores. Roby and Sneller (34) studied 137 patients with allergic rhinitis or asthma and performed spore counts indoors and outdoors. The prevalence of positive skin test to different fungal extracts correlated with the levels of the different indoor spore counts.

Thus, there is good evidence that allergy to fungi play a

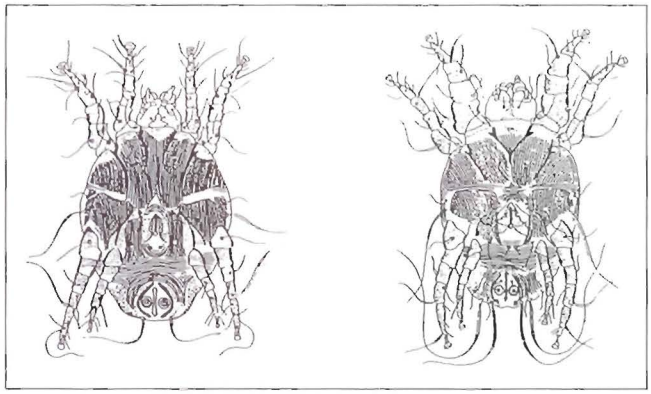

Figure 1) *Male specimens of the house dust mites* Dermatophagoides pteronyssinus **(left)** *and* Dermatophagoides farinae **(right)**. *(Reproduced with permission from 83)*

role in asthma. The full clinical impact of airborne fungi on asthma will not be known until there is standardization of allergens from a wide range of fungal species (35).

INDOOR AEROALLERGENS

The indoor aeroallergens of importance are house dust mites, pets and cockroaches. In parts of the United Kingdom, Australia, New Zealand and the United States, house dust mites are the most important allergen, with 70 to 80% of asthmatics reacting on skin test to the mite allergens (36). Pets are the second most common important cause of allergy in developed countries, and up to 40% of asthmatic children are sensitized to allergens of cats and/or dogs (37). In recent years, cockroaches have become important allergens responsible for symptoms in asthmatics in inner cities of the United States (38).

House dust mites

Dust has been recognized as a triggering factor for asthma for many centuries. In 1964, Voorhorst and co-workers (39) first suggested that the most important source of house dust allergen was mites of the genus *Dermatophagoides*. Miyamoto and associates in Japan (40,41) expanded the work and showed that the potency of house dust allergen is related to the number of mites in the dust. Skin tests, radioallergosorbent test and bronchoprovocation tests performed with extracts from pure cultures of mites correlated well with results obtained using house dust extracts. The equivalent potency of mite extracts was 10 to 100 times that of dust.

Mites are sightless, eight-legged, about 1/3 mm long, and are members of the order Acaridae (close relatives of ticks and spiders). Species of known importance are *Dermatophagoides pteronyssinus*, *D farinae* (Figure 1) and *Euroglyphus maynei*. The main determinants for survival are high humidity, moderate temperatures and an adequate food source that are provided amply by human skin scales. *D pteronyssinus* and *E maynei* are the most common European species, while *D farinae*, which is more resistant to desiccation, is more common in North America (42). The key determinant for excess mite growth appears to be an indoor relative humidity of 60% at 21°C and 75% at 16°C. When the relative humidity falls below 40 to 50%, mites are unable to survive more than 11 days at temperatures above 25°C, because increased transpiration of water leads to dehydration (43).

In the United States, house dust mites multiply in the months of July and August when humidity is highest. Mite allergens are found in dust samples collected from mattresses and bedroom floors from July to December as these allergens are found mostly in feces of mites, which persist long after the mites are gone (44).

There are two major groups of mite allergens. Group I allergens (*Der p* I, *Der f* I) are proteolytic enzymes secreted from the digestive tract and found in high concentrations in fecal pellets (45). Mites are coprophagic, ie, they re-ingest fecal pellets, and it is possible that the presence of these enzymes allows a more extensive digestion to occur after defecation. Group II (*Der p* II, *Der f* II) allergens are found both in fecal pellets and mite bodies.

There are three methods of estimating exposure to mites: mite counts, assay of mite allergens and measurement of guanine (36). The most widely used assays for measuring group I allergens are the enzyme-linked immunosorbent assay (ELISA) method with species-specific monoclonal antibodies to bind the allergen, and labelled group-specific antibodies for detection (46). Counting of house dust mites is tedious and may not give the mite allergen content in the dust. The quantitative assay for guanine is not commercially available (36). Theoretically, measurements of airborne allergen should be more representative of exposure than assays on settled dust. However, there have been few data demonstrating a relationship between airborne dust and sensitization and respiratory symptoms. In general, levels of airborne allergens are low and undetectable in the absence of dust disturbance. After disturbance, concentrations of allergens fall rapidly, because the particles are large (47).

There are many studies providing evidence that the house dust mite is an important cause of asthma in many parts of the world. First, there is an ecological relationship between the levels of house dust mites and the prevalence of asthma. A low prevalence of asthma has been found in areas of low mite exposure such as in high altitudes where the absolute humidity both indoors and outdoors is low (48). These areas tend to be climatically inhospitable and sparsely inhabited. Reports from Papua New Guinea described how contact with western civilization was followed by an increase in the prevalence of asthma. An explanation for this has been the introduction of blankets infested with mites to this native population, leading to sensitization and subsequent development of asthma (49). In areas with high mite exposure such as in the United Kingdom, coastal areas of Australia, New Zealand, Japan and Brazil, 'all' atopic children can become sensitized (43).

Second, there is a dose-response relationship between the level of mite allergen exposure and the risk of sensitization. In the United Kingdom, where mite allergen levels are in general high, approximately 80% of asthmatic children were

sensitized to house dust mites (43). The prevalence of positive skin test reaction to mite allergens was about 45% in two Canadian cities where the mite allergen levels were found to be relatively low (50). The risk of asthma was seven times higher in German children if their current exposure to *Der p* I was greater than 2 µg/g of dust, and 11 times higher for exposure above 10 µg/g than those with less than 2 µg/g (51).

Third, reduction of exposure to house dust mites resulted in improvement in asthma in subjects allergic to them. Placing children in a sanatorium at high altitude, where mite levels are low, had been a traditional treatment of severe asthma and usually resulted in improvement of their symptoms (52). Adult asthmatics allergic to house dust mites improved considerably in an allergen-free environment in a hospital although it took two to three months for improvement to occur (53). The use of acaricides and enclosure of mattresses have been shown to reduce the mite allergen level and severity of asthma (54,55).

The most convincing evidence that house dust mite is important in asthma comes from two prospective studies. Sporik and colleagues (56) conducted a longitudinal study of children at high risk for developing asthma and allergies at birth, and followed them for 11 years. They found that children whose homes had high mite allergen levels during the first year of life were at a much higher risk for developing asthma than those with low levels. Arshad and co-workers (57) conducted a randomized clinical trial on infants at high risk for developing allergy and asthma. The prophylactic group had measures to reduce house dust mite exposure and dietary restriction. The control group had no treatment. At the end of 12 months, those in the control group had four times the risk of developing asthma as those in the prophylactic group.

In a study of environmental risk factors in patients with asthma in Vancouver and Winnipeg, a positive correlation was found between mite allergen levels in the homes of patients and the degree of skin test reactivity to mites (50). There was also an inverse relationship between the levels of mite allergens and the levels of lung function in children with asthma, indicating that mite allergen levels are of clinical relevance.

There are now effective means of reducing mite allergens such as the use of a dust cover for mattresses and pillows, the use of hot water for washing all beddings, and the removal of carpets particularly in the bedroom. The availability of acaricides adds another armament to the regimen.

Pets

Hypersensitivity to pet allergens is extremely common. Surveys have shown that 5 to 15% of the general population and 40 to 70% of patients with asthma have positive skin test reactions to cat and/or dog dander (37,58-60). Close human contact accounts for the high prevalence of pet sensitivity in Western societies. It has been estimated that either cats or dogs are found in over 50% of homes in many countries (61). Laboratory animals (mouse, rat, guinea-pig, rabbit) and farm animals (horse, cow) can also give rise to allergic sensitization in exposed persons, mainly in an occupational context (62). These mammals secrete proteins that may act as potential aeroallergens when they are inhaled. Several of these allergens have been identified and a few of them characterized.

Cats are the most prevalent cause of pet allergy (63). The sources of the allergens in cats are the pelt, dander, saliva, urine and serum (62). Several molecules in cat extracts have been shown to be allergenic and the relative concentration of these allergens varies depending on the source of extract. The most important allergen from a clinical point of view is *Fel d* I (64). Most of the IgE antibodies elicited in cat-sensitive patients are directed against this allergen. *Fel d* I is found in salivary glands, hair follicles, saliva and lacrimal fluid (65). The existence of B and T cell epitopes in the *Fel d* I molecule has been demonstrated (66). The most important allergen derived from dogs is *Can f* I and is present in high concentrations in dog hair, dander and saliva (67). This allergen accounts for at least half of the allergenic activity in dog hair and dander extract (67).

The development of monoclonal antibody-based assays has made it possible to determine the level of environmental exposure to *Fel d* I (68) and *Can f* I (69) and to study the relationship between exposure and development of sensitization and exacerbation of symptoms. Exposure to a level of *Fel d* I in the house greater than 8 µg/g of dust in a sensitized subject is a risk factor for acute asthma episodes leading to emergency room visits (70). It is likely that clinically relevant threshold limits for pet allergen exposure will be proposed within the next few years.

Throughout the home *Fel d* I has been found in dust from floors, mattresses and soft furnishings, on walls and in the air (61). The wide distribution of the allergen is due to a significant proportion of *Fel d* I present on particles smaller than 2.5 µm in diameter, which readily become airborne and remain in the air for long periods even in undisturbed conditions (71). Interestingly, measurable amounts of *Fel d* I have been found in almost every home investigated, including those without cats in residence, and in public buildings (72,73). It has been suggested that *Fel d* I is carried into cat-free buildings on the clothing of people exposed to cats (73). Studies in Scandinavian schools have shown that while mite allergen levels were low in the classrooms, a high level of both cat and dog allergen was found on either smooth or carpeted floors, with approximately 11 times more on the carpeted floors (74). It was estimated that 30 ng *Fel d* I/m^3 was brought into the classroom every day, and this is highly significant for children with cat sensitivity. Another recent study from Sweden showed that levels of both *Fel d* I and *Can f* I were much higher on chairs than on floors, suggesting that allergens were brought in by students and teachers on their clothing. These levels were probably high enough to sensitize children and to induce asthma in most children who are allergic to cats or dogs (75).

In a study of patients with asthma in Vancouver and Winnipeg, levels of *Fel d* I in dust samples collected from

mattresses and bedroom floors were measured. Cat allergen was present in every home, even in those without a cat (76). *Fel d* I levels were highest in homes of patients with cats, and rather high levels were also found in homes of patients without a cat but who had visited others with cats. The lowest levels were found in homes of patients without a cat and where the occupants did not visit others with such a pet. Cat allergen levels were highest during the winter and spring and lowest in summer and autumn in Winnipeg, probably due to the tighter insulation of the homes during winter months. Such seasonal variation was not found in Vancouver. There was no relationship between sensitization to cats and previous or current cat ownership. The findings are in keeping with recent studies showing that *Fel d* I is a ubiquitous allergen. It is likely that the cat allergen was brought into homes on clothing of occupants when they visited homes with cats.

Once a diagnosis of pet allergy has been made, several therapeutic options are available. The most effective method is to remove the animal completely, although this may not be possible in all situations. Even after removal of the pet, it may take several months to reduce the allergen content within the home. Aggressive cleaning measures should be instituted as rapidly as possible. If the symptoms are mild and the patient or the family refuses to give up the pet, some preventive measures should be taken to limit exposure. The allergen content may be reduced by limiting the pet's access to the home, removing carpets and upholstered furniture, increasing ventilation, and by using room air cleaners, particularly those with high efficiency particulate air or electrostatic filters. There is some evidence that washing cats weekly will reduce the amount of *Fel d* I in the home (77). Nevertheless, the effectiveness of these measures on allergen levels and patients' symptoms remains to be defined. Further, even if a patient can avoid animal exposure at home, pets are so common that some degree of exposure outside the home is inevitable (78).

Cockroaches

Cockroaches have been described as allergens based on skin test data on allergic subjects (79). Kang and associates (80) extended the work to include radioallergosorbent and bronchoprovocation studies with cockroach extract. Asthmatics with positive skin tests to cockroach extracts had higher total serum IgE levels than their allergic counterparts with negative skin tests. Bronchoprovocation test induced transient peripheral eosinophilia in those who reacted positively. Immunophoretic studies have shown that roach allergens were mostly found in the whole body and cast skin fractions. Feces and egg casings were less allergenic (81). Hypersensitivity to cockroach allergens is particularly important in inner city asthmatics (38).

SUMMARY AND CLINICAL RELEVANCE

The relative risks of sensitivity to various outdoor and indoor aeroallergens in the development of childhood asthma were investigated by Sears and colleagues (82) in a longitudinal study of a birth cohort of New Zealand children up to the age of 13 years. Of the 714 children skin-tested, 45.8% were sensitive to at least one of 11 allergens, the most common responses being to rye grass pollen (32.5%), house dust mite (30.1%) and cat dander (13.5%). Sensitivity to house dust mite, cat dander and *Aspergillus* were independent risk factors associated with the development of asthma, while grass sensitivity and sensitivity to a number of outdoor aeroallergens were not. Gelber and coworkers (70) conducted a case-controlled study on adult patients (137 in each group) presenting to an emergency room over a period of one year. They found that 38% of the asthmatics, but only 8% of the controls, were allergic to one of the three indoor allergens and had high levels of the relevant allergen in their houses. They concluded that the risk for asthma related to sensitization to indoor allergens applies to many adults with acute asthma. These two studies showed that indoor aeroallergens are important determinants for asthma in children and in adults.

Exposure to indoor household allergens is a leading cause of perennial IgE-mediated asthma and rhinitis. Ongoing daily exposure to allergens leads to perpetuation of the inflammatory process in the airway that is the likely cause for the persistence of symptoms and airway hyperresponsiveness. Clinicians should recognize the importance of indoor aeroallergens in asthma because avoidance and/or reduction of exposure is an important part of the management besides pharmacological management. Finally, clinicians should also be aware that high levels of pet allergens may be found in schools and other public places and may account for the persistence of symptoms despite stringent measures of avoidance at home.

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