

THE IMPORTANCE OF ENVIRONMENTAL CONTROLS IN THE MANAGEMENT OF PEDIATRIC ASTHMA

Robert A. Wood, MD

Aeroallergens play a major role in the pathogenesis of asthma and allergic rhinitis. Indoor allergens are of particular importance and principally include the allergens of house dust mites, domestic pets, cockroaches, and molds. The relative importance of these different allergens varies in different parts of the world depending on a variety of geographic and climatic factors. All studies agree, however, that children with asthma will have a high likelihood of becoming sensitized to allergens prominent in their local environment.

There are three basic lines of evidence that support the relationship of indoor allergens to asthma. The first relates to the frequency with which sensitization to these allergens is seen; the second is based upon an extensive body of evidence supporting a connection between allergic sensitization, allergen exposure, and disease activity; and the third relates to the markedly salutary effects that have been demonstrated with allergen avoidance. These data will be reviewed in detail for each of the major indoor allergens, with a particular emphasis on the environmental control measures that should be recommended to reduce ongoing allergen exposure.

DUST MITES

Dust mites are arachnids that live in accumulated dust in homes, particularly in the dust contained within fabrics. Favorite habitats include carpets, upholstered furniture, mattresses, pillows, and bedding materials. Their major food source is shed human skin scales that are present in high numbers in most

From the Department of Pediatrics, Division of Allergy and Immunology, Johns Hopkins University School of Medicine, Baltimore, Maryland

IMMUNOLOGY AND ALLERGY CLINICS OF NORTH AMERICA

of these items. The major dust mite species known to be associated with allergic disease are *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*.^{62, 63} Other mites, including *Euroglyphus maynei* and *Blomia tropicalis*, are also important in some areas, although their distribution is considerably more limited. Dust mites grow optimally in areas that are both warm and humid and they grow very poorly when the relative humidity remains below 40%.² Dust mites grow from eggs to adults over the course of about 4 weeks and adult dust mites live for about 6 weeks, during which time females produce 40 to 80 eggs.²

A variety of dust mite allergens have been identified and characterized.^{62, 63, 85, 89} Group 1 allergens, such as *Der p* 1 and *Der f* 1, are cysteine proteases that are found predominantly associated with mite fecal pellets.⁸⁶ Group 3 and 4 dust mite allergens are also enzymes associated with fecal pellets. Group 2 allergens are not found in significant concentrations in fecal pellets although their source and function have not been fully elucidated.

Assessment of dust mite exposure has largely been accomplished through the analysis of settled dust samples. Although some studies have not been able to show a relationship between dust mite levels and allergic sensitization or disease activity, there is now general agreement that dust mite levels of greater than 2 micrograms of Group 1 allergen per gram of dust should be considered a risk factor for sensitization^{42, 45, 60, 82} and that levels greater than 10 µg/gram of dust are a risk factor for acute asthma.¹³ Airborne sampling for dust mite has proven difficult or impossible in the absence of substantial disturbance. This is a reflection of the fact that dust mite allergens are carried on relatively large particles, most ranging from 10 to 20 µm in mean aerodynamic diameter, which settle within minutes of disturbance.⁶⁵

The prevalence of dust mite sensitivity in asthmatic patients varies considerably from one geographic area to another. For example, studies have demonstrated prevalence rates ranging from 5% in asthmatic children in Los Alamos, New Mexico, to 66% in Atlanta, Georgia, to 91% in Papua, New Guinea.^{13, 28, 35} These differences are roughly proportional to differences in mite exposure in these different areas of the world.

At least as significant as the relationship between mite exposure and mite sensitization is the evidence that mite exposure is capable of inducing not just sensitization, but the asthmatic state itself. In a prospective trial, Sporik et al demonstrated a significant increase in asthma, as well as mite sensitivity, in 11-year-old children who had experienced high mite exposure during infancy.⁸² Other studies have demonstrated a striking association between asthma development and mite sensitivity,^{12, 28, 59, 77} although these studies lacked a prospective evaluation of mite exposure. These studies are exciting in that they indicate that allergen avoidance early in life could prevent the development of asthma in some patients, an idea that has recently been studied with encouraging results.³³

Extensive evidence also exists to support a relationship between ongoing mite exposure and disease activity.^{22, 39, 93} With regard to chronic symptoms, Vervloet et al demonstrated a significant correlation between medication requirements and current mite exposure in a group of mite-sensitive adult asthmatics.⁹³ Custovic et al also demonstrated a relationship between mite exposure and asthma severity as evidenced by bronchial hyperreactivity, peak expiratory flow rate variability, and FEV₁.²² Several studies have also demonstrated mite exposure to be a risk factor for acute asthma and emergency room visits.^{13, 66} In a study by Call et al, inner city children in Atlanta were evaluated after presentation to the emergency room with acute asthma.¹³ Seventy-two percent of these children were found to be allergic to either dust mite alone or both dust mite and cockroach allergen. The combination of mite exposure and mite sensitization

was highly associated with the development of acute asthma (21 of 35 asthmatic patients versus 3 of 22 control subjects, $P < .001$).

The most compelling evidence for the role of dust mites in asthma comes from studies of allergen avoidance, either through environmental control in the home or the removal of mite-allergic patients from their homes. Two classic studies from the early 1980s provided dramatic evidence as to the potential benefits of dust mite avoidance. Platts-Mills et al investigated the effects of mite avoidance by placing nine young adults with mite-induced asthma in a hospital setting for a minimum of 2 months.⁶⁴ All patients experienced reduced symptoms, seven patients had reduced medication requirements, and five patients showed at least an eightfold reduction in bronchial reactivity, as measured by the concentration of histamine required to induce a 30% fall in FEV₁. In the second study, Murray and Ferguson studied 20 mite-allergic asthmatic children in a controlled trial of mite avoidance in the patients' homes.⁵⁵ They found significant reductions in asthma symptoms, days on which wheezing was observed, days with low peak flow rates, and bronchial hyperreactivity in the group using active mite control measures.

The vast majority of subsequent trials of mite avoidance have yielded similar results.^{14, 26, 29, 30, 61} Ehner et al studied 24 children with asthma and mite sensitivity in a 1-year trial of mite avoidance.²⁹ The patients were divided into three groups. The first had their mattresses, pillows, and comforters covered with impermeable encasements, the second had their mattresses and carpets treated with an acaricide (benzyl benzoate), and the third had their mattresses and carpets treated with placebo. Significant reductions in dust mite allergen levels were found only in the group with mattress and pillow encasements. Similarly, a highly significant reduction in bronchial hyperreactivity was noted in that group compared with the other two.

One final study of mite avoidance deserves note. It has long been recognized that dust mite levels are significantly reduced at high altitude. Peroni et al performed an extensive clinical study of mite avoidance by moving asthmatic children to a high altitude environment.⁶¹ The study was divided into two groups, one with 22 children and the other with 23 children, who were admitted during successive years. They demonstrated significant reductions in total IgE levels, dust mite-specific IgE levels, methacholine reactivity, and response to dust mite bronchoprovocation. These differences were first detected after 3 months in the high altitude setting and continued through the entire 9-month study. They were also able to study 14 of the 22 children from the first cohort 3 months after returning to their usual home environment. These children had experienced significant increases in their total IgE levels, methacholine reactivity, and response to exercise challenge. This important demonstration of reduced disease activity in the mite-free environment, followed by increased disease activity after returning to usual mite exposure, provides a remarkable demonstration of the power of both mite exposure and avoidance.

Dust Mite Control Measures

Although there should be no doubt as to the benefits of dust mite avoidance, there is still some controversy as to the specific measures that are necessary to sufficiently reduce mite exposure to control disease. This controversy arises from three major factors. First, some environmental control measures have not been adequately studied to make any accurate conclusions. Second, for some measures studies of their efficacy have yielded conflicting results. Third, in many

studies a combination of environmental control measures were utilized, making it difficult to determine which measures actually led to the benefit that was observed. Specific environmental control measures will therefore be reviewed individually.

It is very clear that impermeable plastic or vinyl encasements for mattresses and pillows significantly reduce dust mite exposure.^{29, 58, 88} In the study by Ehnert et al, polyurethane mattress encasings produced a 91% decrease in mite allergen by day 14 of treatment, which rose to 98% by month 12 of the study.²⁹ In another study by Owen et al, *Der p* I levels on encased mattresses were only 1% of those on control mattresses.⁵⁸ These encasements should therefore be recommended for all patients with mite sensitivity.

The effects of vacuum cleaning on mite levels have been extensively studied. Live mites are difficult to remove from carpeting and it is clear that vacuum cleaning in the absence of other measures will provide only limited benefit. However, regular vacuum cleaning does remove significant amounts of dust from carpets that will help to reduce the allergen reservoir.⁵⁴ Patients should also be warned that vacuuming creates considerable disturbance with transient increases in airborne mite levels. Vacuum cleaners equipped with special bags or filters to help prevent this problem are available and may be of some added benefit,³⁷ although it should be noted that because dust mite allergen is carried on large particles that settle quickly, it is not clear whether these specialized vacuums are of clinical importance. There is little evidence that wet vacuum cleaning or steam cleaning provides any additional benefit. In one study, carpet shampooing was found to be no more effective than dry vacuum cleaning,⁸ while in another study wet vacuum cleaning was shown to lead to a subsequent increase in mite numbers.⁹⁸ This was presumed to have occurred because of elevated humidity in the carpet after wet vacuuming.

A variety of carpet treatments have also been developed in an effort to control dust mite allergen exposure. These are classified as either acaricides or denaturing agents. A variety of acaricides have been investigated and shown to kill house dust mites in laboratory conditions.^{17, 18} These range from caffeine⁷¹ to potent and potentially toxic organophosphates.⁵¹ Only one acaricide, benzyl benzoate, is available for use in the United States.

Although there is little doubt that benzyl benzoate is effective in killing dust mites, studies regarding the efficacy of this compound in home environments have provided varying results.^{26, 32, 46, 105} For example, while both Hayden et al³² and Woodfolk et al¹⁰⁵ demonstrated significant reductions in dust mite allergen after treatment with benzyl benzoate, the changes were not always in a range that would be expected to produce clinical benefit and were relatively short-lived. In the Hayden study, mite levels were still reduced 2 months after treatment, but some increase was clearly evident compared with 1 month post-treatment, suggesting that repeat applications might be required every 2 to 3 months to maintain effect. In another study by Huss et al, benzyl benzoate was compared with placebo in a group of 12 patients.³⁴ The products were applied at baseline and after 6 months and allergen levels were measured at 0, 3, 6, 9, and 12 months. They detected no decrease in mite allergen in the benzyl benzoate group compared with the control group. Likewise, no effect on clinical asthma was detected. It should be noted that the application of benzyl benzoate every 6 months as performed in this study was based on the manufacturer's recommendations, and that the lack of effect may have occurred simply because the product was not applied more often, or because allergen levels were not measured sooner after application.

Tannic acid is a denaturing agent that has been extensively studied for the

control of dust mite allergen. This product is designed to reduce allergen levels without affecting dust mite growth or allergen production. It has also been shown in the laboratory to be highly effective. Much like benzyl benzoate, however, its efficacy in home environments is less convincing. Woodfolk et al evaluated the effects of tannic acid on 17 carpets.¹⁰⁶ The carpets were treated on day 0 and 28 and dust samples were collected on days 0, 1, 7, 14, 28, and 42. The treated carpets exhibited reduced mite allergen levels compared with control carpets, although the effects were not dramatic and were not maintained for long periods.

The recommendation regarding the use of benzyl benzoate and tannic acid is that these products may be useful adjuncts for the control of dust mite exposure in homes where carpets, particularly bedroom carpets, cannot be removed. Especially with benzyl benzoate, its use must be followed by intensive vacuum cleaning to remove residual allergen. It is likely that the combination of benzyl benzoate and tannic acid would produce the greatest effect,⁸⁷ although even this could never be a substitute for carpet removal.

Bed linens, stuffed animals, and other soft furnishings also provide excellent environments for dust mite growth. Objects such as stuffed animals should be removed whenever possible. The mite content of bedding materials and other objects that cannot be removed can typically be reduced by washing. Washing in hot water (greater than 55°C) is ideal in that it both removes allergen and kills dust mites.⁵⁰ These water temperatures, however, may not be available in many home environments because of safety concerns. It is important to note, therefore, that washing in cooler water does not kill mites but does remove mite allergens very effectively. Weekly washing of all bed linens in a hot cycle is therefore recommended for all mite-allergic patients. Dry cleaning also kills dust mites,^{50, 91} as does tumble drying at greater than 55°C for at least 20 minutes.⁵⁸

Dust mites are susceptible to the effects of low as well as high temperature. Freezing in a typical household freezer for 24 hours will kill most dust mites²⁷ although the mite allergen in the object will not necessarily be reduced. Exposing carpets to direct sun for several hours will also kill dust mites because of the high temperature, the low humidity or both.⁹⁰ It has also been shown that electric blankets will reduce mite growth.⁵² None of these methods have been established in clinical trials.

Because of the reliance of dust mites on humidity for growth, it has been suggested that methods capable of reducing relative humidity would be useful in the control of mite exposure.^{19, 41} Korsgaard and Iversen demonstrated that dust mite growth could be significantly reduced by keeping indoor humidity below 7 g/kg by ventilation.⁴¹ Air conditioning and dehumidification may also help to deter mite growth and should be used whenever possible.²³ It is clear, however, that such measures are difficult or impossible in environments with very high relative humidity. A prime example of this fact is the difficulty in eliminating dust mites from carpets over cement slab floors in basements.

Finally, air filtration devices are frequently purchased by patients for the control of their dust mite allergy. However, there is little evidence to support their use.^{3, 56, 69, 96} In addition, one would not anticipate much effect because of the fact that dust mite allergens do not remain airborne for extended periods and would therefore not be available for filtration in most instances.

In summary, effective dust mite control can be accomplished in most homes with a combination of mattress and pillow covers, hot washing of bed linens, removal of stuffed animals and other soft furnishings, and carpet removal. In the absence of carpet removal, intensive vacuum cleaning and the use of acaricides and denaturing agents may prove helpful in many homes. Because of the

extraordinary benefits provided through dust mite avoidance in mite-sensitive asthmatics, these measures should be routinely recommended, and compliance with these recommendations should be reassessed at each subsequent visit.

ANIMAL ALLERGENS

Animal allergens are also potent causes of both acute and chronic asthma symptoms. Cat and dog allergens are the most important, although significant exposure to a wide variety of other furred animals is not uncommon. Sensitivity to cat and dog allergens has been shown to occur in up to 67% of asthmatic children and in some settings these are clearly the dominant indoor allergens.^{35, 70, 83} This fact was best demonstrated in the study by Ingram et al conducted in Los Alamos, New Mexico.³⁵ In this environment where cat and dog allergens are common but exposure to dust mite and cockroach allergens is rare, IgE antibody to cat and dog was detected in 62% and 67% of asthmatic children, respectively. The presence of this IgE antibody was highly associated with asthma whereas sensitivity to mite or cockroach allergen was not associated with asthma.

As with dust mites, it has been shown that intense exposure to cat allergen early in life leads to an increased risk of developing cat sensitivity.⁹⁷ Warner et al found that 88% of 21 asthmatic children who had a cat in their home at the time of birth developed cat sensitivity compared with 36% of children whose homes did not contain a cat through the first year of life. On the other hand, it is clear from that and other studies that cat sensitivity is common even in the absence of obvious exposure. This is most likely related to the widespread distribution of cat and dog allergens even in homes that do not contain pets.

The allergens of domestic cats and dogs, as well as a wide variety of rodents and farm animals, have been identified and characterized.⁷⁵ At least 12 proteins from cats have been found to be allergenic with one major cat allergen, *Fel d 1*, being the most important.^{1, 47} *Fel d 1* is produced in hair follicles and to a lesser extent, salivary glands.^{6, 15} It has been demonstrated that male cats produce more allergen than female cats and that castration of male cats reduces allergen production.^{15, 36, 99}

Several dog specific antigens have also been identified.^{25, 44, 48, 76, 80} The most important of these is *Can f 1*, which is produced in hair, dander, and saliva. Major allergens from many rodents have been identified, including the mouse, rat, guinea pig, and rabbit.^{57, 68, 78, 84, 94, 95} Urine is the major source of these rodent allergens with hair, dander, and saliva providing lesser quantities.

A number of studies have investigated the distribution of cat and dog allergens in home and other environments.^{35, 53, 83, 100, 101} Using settled dust analysis, it has been shown that levels of cat and dog allergen are clearly highest in homes housing these animals. However, it is also clear from a number of studies that the vast majority of homes contain cat and dog allergen even if a pet has never lived there. This widespread distribution of cat and dog allergen has also been documented in a variety of other settings, including office buildings and schools. Although most of these non-animal-containing environments have relatively low allergen levels compared with those with a cat or dog, it is not uncommon to find rather high levels in some of these homes. This widespread distribution is presumed to occur primarily through passive transfer of allergen from one environment to another. These allergens appear to be very sticky and, unlike dust mite allergens, can be found in high levels on walls and other surfaces within homes.¹⁰²

The characteristics of airborne cat allergen have also been extensively studied. Cat allergen has been shown to be carried on particles that range from less than one micrometer to greater than 20 micrometers in mean aerodynamic diameter.^{49, 103} Although estimates have varied, studies agree that at least 15% of airborne cat allergen is carried on particles less than 5 micrometers. Less information is available for dog allergen, but evidence to date suggests that it is distributed very much like cat allergen, with about 20% of airborne dog allergen being carried on particles less than 5 micrometers in diameter.²¹

Cat allergen can also be detected in air samples from all homes with cats and from many homes without cats. Bollinger et al detected airborne cat allergen in 10 out of 40 air samples from homes without cats.⁹ In addition, when a subset of those homes was reinvestigated on a weekly basis for 4 weeks, all had detectable airborne cat allergen on at least one occasion. In an attempt to determine the clinical significance of this unsuspected cat exposure, patients were challenged in an experimental cat exposure facility to varying levels of cat allergen. It was found that allergen levels of less than 100 nanograms per cubic meter were capable of inducing upper and lower respiratory symptoms as well as significant pulmonary function changes. These levels are similar to those found in homes with cats as well as a subset of homes without cats, suggesting that even patients without known cat exposure may be exposed to clinically significant concentrations of airborne cat allergen on a regular basis.

Control of Animal Allergens

At the present time, much less is known about the control of animal allergens than about the control of dust mite allergens. In particular, there are still no convincing studies on the clinical benefit of environmental control measures for animal allergens. Although it is assumed that removing an animal from the home will lead to clinical improvement in patients who have disease related to their pet, even this has not been proven. Even less data are available regarding the potential benefits of methods that might be used in lieu of animal removal. Cat allergen will be specifically discussed here because the most information is available regarding this important allergen. Most of the information should be applicable to other allergens, although a great deal of study will need to be done before that statement can be made conclusively.

To begin, it should be stated that in any asthmatic patient who is known to be cat sensitive and whose asthma is believed to be related to any significant degree to a cat, the most appropriate recommendation is to remove the cat from the home. This is clearly the correct advice from a medical standpoint and physicians should not shy away from strenuously recommending it. A number of potential alternative measures are also to be discussed, however, because of the high proportion of patients who are either reluctant or completely unwilling to remove a household pet.

Once a cat has been removed from the home, it is important to recognize that the clinical benefit may not be seen for a period of at least several months since allergen levels fall quite slowly after cat removal.¹⁰¹ In most homes, levels in settled dust will have fallen to those seen in homes without cats within 4 to 6 months of cat removal. Levels may fall much more quickly if extensive environmental control measures are undertaken, such as removal of carpets, upholstered furniture, and other reservoirs from the home, while in other homes the process may be considerably slower. This information points to the fact that thorough and repeated cleaning will be required once the animal has been

removed. It has also been shown that cat allergen may persist in mattresses for years after a cat has been removed from a home,⁹² so that new bedding or impermeable encasements must therefore also be recommended.

A number of studies have investigated other measures that might help to reduce cat allergen exposure without removing the animal from the home. DeBlay et al demonstrated significant reductions in airborne *Fel d 1* with a combination of air filtration, cat washing, vacuum cleaning, and removal of furnishings, although these results were based on a small sample size and did not include any measure of clinical effect.²⁴ When cat washing was evaluated separately in that study, dramatic reductions in airborne *Fel d 1* were seen after cat washes. Subsequent studies, however, have presented conflicting results. Klucka et al studied both cat washing and Allerpet-C (Allerpet, Inc., New York, New York) and found no benefit from either treatment.⁴⁰ Most recently, Avner et al studied three different methods of cat washing and found transient reductions in airborne cat allergens after each.⁵ There was no sustained benefit, however, with levels returning to baseline within 1 week of washing.

Information is very limited as to the clinical benefits of these environmental control measures if one or more cats is allowed to remain in the home. Three recent studies, which have thus far only been reported in abstract form, have evaluated different combinations of control measures and although all have shown reductions in allergen levels, clinical effect was less consistent.^{7, 79, 104} One study showed a clear benefit, one showed benefit only in the group in which environmental control was done along with intranasal steroid treatment, and the third showed no clinical benefit. It still remains to be seen whether allergen exposure can be sufficiently reduced to produce a clinical effect in the absence of cat removal.

In families who insist on keeping their pets, the following should be recommended pending more definitive studies. The animals should be restricted to one area of the home and certainly kept out of the patient's bedroom. HEPA or electrostatic air cleaners should be used, especially in the patient's bedroom. Carpets and other reservoirs for allergen collection should be removed whenever possible, again focusing on the patient's bedroom. Finally, mattress and pillow covers should be routinely employed. Although tannic acid has been shown to reduce cat allergen levels, the effects are modest and short-lived when a cat is present so that this treatment should not be routinely recommended. Similarly, cat washing appears to be of such transient benefit that it is not likely to add significantly to the other avoidance measures.

COCKROACH ALLERGENS

The importance of cockroach allergens in asthma and allergy has only been recognized over the past 30 years. It is now clear that cockroach allergens represent a major cause of asthma, particularly in urban areas. Significant cockroach exposure has been demonstrated in a number of cities and the prevalence of cockroach sensitivity in urban patients with asthma has been shown to range from 23% to 60%.^{13, 38, 72} In addition, the combination of cockroach exposure and cockroach sensitization has been shown to be a risk factor for acute asthma exacerbations.^{13, 66, 70}

In the most comprehensive study to date on the problem of asthma in inner city children, 1,528 children with asthma from 8 major inner city areas were extensively investigated with regard to the factors, both allergic and otherwise, that contributed to their disease.⁷⁰ Although sensitivity to cockroach, dust mite,

and cat were all common (36.8%, 36.9%, and 22.7%, respectively), exposure to cockroach allergen was much more common than exposure to either dust mite or cat (50.2%, 9.7%, and 12.8%, respectively). The combination of cockroach sensitivity and high cockroach exposure was associated with significantly more hospitalizations, unscheduled medical visits for asthma, days of wheezing, missed days from school, and nights with sleep loss owing to asthma. Such a correlation was not seen for dust mite or cat allergens. These data argue persuasively that cockroach allergen is a major factor, if not the major factor, in the high degree of morbidity seen in this patient population.

Although there are at least 50 cockroach species in the United States, only four or five are domiciliary. Two species, the German cockroach (*Blattella germanica*) and the American cockroach (*Periplaneta americana*) are the most common causes of both household infestation and allergic sensitization. Several allergens from each species have been identified and characterized.^{4, 67} The most important among these are *Bla g 1*, *Bla g 2*, and *Per a 1*. There is significant cross reactivity between *B. Germanica* and *P. Americana*, although most patients in the United States appear to be primarily sensitized to *B. Germanica*. The source of the major cockroach allergens is still not completely clear although they do appear to be secreted or excreted, suggesting that they may also be digestive proteins.

The distribution of cockroach allergens has been studied in a number of settings. Highest levels tend to be found in kitchens, although the allergen is widely distributed through the home including the bedroom.^{67, 70, 72} In fact, in the inner city asthma study noted above, the 50.2% exposure rate was found in bedroom dust samples.⁷⁰ It has been suggested that cockroach allergen levels of greater than 2 units per gram are associated with sensitization and levels greater than 8 units per gram are associated with disease activity. Cockroach allergen has also been detected at significant concentrations in schools in urban Baltimore.⁷⁴ Finally, limited study on airborne cockroach allergen has suggested that cockroach is very much like dust mite with little or no measurable airborne cockroach allergen in the absence of significant disturbance.

Cockroach Allergen Control

Extensive studies have been performed on the chemical control of cockroach infestation and a variety of pesticides and traps are readily available. These include chlorpyrifos (Dursban), diazanon, boric acid powder, and bait stations that contain hydramethylnon. Very little is known, however, about the effects of extermination procedures on cockroach allergen levels. In one limited study, Sarpong et al did demonstrate a short-term reduction in cockroach allergen in settled dust samples after extermination in an inner city dormitory.⁷³

Other measures that should help to reduce cockroach infestation include eliminating food sources and hiding entry points. All foods should be stored in sealed containers and the kitchen should be cleaned regularly. Finally, extensive cleaning should be performed after extermination to remove the cockroach debris as completely as possible. Even with the most aggressive measures, however, it is unlikely that cockroach exposure will be adequately reduced in some environments. This is particularly true of the older, multiple dwelling units that house a preponderance of inner city asthma patients. It may be necessary to exterminate in the homes or apartments surrounding the patient's home to obtain maximum effect and some patients may need to find new housing altogether. No studies have been reported to date on the clinical effects of extermination or other control measures.

MOLD ALLERGENS

A wide variety of mold species can be present in both indoor and outdoor environments. *Aspergillus* and *Penicillium* species are generally regarded as the most numerous indoor molds,^{11, 81, 100} while *Alternaria* is important in both indoor and outdoor environments. Several mold allergens, including Alt n 1 and Asp f 1, have been identified and characterized.

Sensitivity to *Alternaria* has been shown to be associated with asthma in Tucson, Arizona³¹ and in inland regions in Australia.³¹ In the Tucson study, sensitivity to *Alternaria* was demonstrated in 60.8% of 6-year-old children with persistent asthma, compared to only 11.8% for dust mite. In fact, *Alternaria* was the only allergen for which sensitivity was associated with an increased risk of asthma at both ages 6 and 11.

Molds tend to grow best in warm and moist environments and mold exposure is therefore roughly correlated with these conditions. Basements, window sills, shower stalls, and bathroom carpets are common sites of mold infestation. Air conditioners and humidifiers have also been shown to be sources of significant mold exposure.^{10, 43} To date, the assessment of mold exposure has been more difficult than for the other indoor allergens because of the lack of readily available immunoassays to measure major allergens. The currently available methods are very time consuming, including culture and microscopic examination of air or dust samples. Airborne mold allergens have been shown to be carried on particles ranging in size from less than 2 to greater than 100 microns.¹¹

The control of mold allergens requires a concerted approach combining fungicides, measures to reduce humidity, and the removal of mold infested items whenever possible. A variety of fungicides are commercially available that are highly effective as long as the sites of mold growth are carefully investigated. Any measures that can be taken to reduce humidity should be recommended, including dehumidification, air conditioning, increased ventilation, and absolute abstinence from the use of humidifiers and vaporizers. Moldy items, such as a basement carpet that has suffered water damage, should be removed altogether. Although no specific data are available, air filtration devices may also assist in reducing mold exposure. No clinical studies on the efficacy of mold avoidance measures has been undertaken.

INDOOR AIR POLLUTION

Although a detailed discussion of indoor air pollution is beyond the scope of this review, it should be emphasized that effective environmental control cannot be achieved without attention to a variety of nonspecific irritants. The deleterious effects of passive cigarette smoke on pediatric asthma have been well documented in a number of studies.^{16, 107} No studies to date have assessed the clinical benefit of removal from a smoke-containing environment, but one would predict that this would have highly beneficial effects. In addition to passive cigarette smoke, a variety of other indoor pollutants such as nitrous oxide and wood smoke have been documented to exacerbate pediatric asthma.

All patients must be queried about these exposures and counseled as to their control. The parents of asthmatic children who smoke need to be reminded at each visit about the ongoing damage that they are causing.

CONCLUSION

Indoor allergens are potent triggers for acute and chronic asthma. Environmental control of these allergens, as best evidenced to date for dust mite-induced asthma, should be considered first line treatment measures. Allergen avoidance can produce changes in disease activity and bronchial hyperreactivity that are difficult to duplicate with even the most potent medications. Such therapy is safe, cost effective, and logical.

References

1. Anderson MC, Baer H, Ohman JL: A comparative study of the allergens of cat, urine, serum, saliva, and pelt. *J Allergy Clin Immunol* 76:563–569, 1985
2. Arlian LG: Biology and ecology of house dust mites *Dermatophagoides* spp. and *Euroglyphus* spp. *Immunol Allergy Clin N Amer* 9:339–356, 1989
3. Antonicelli L, Bilo MB, Pucci S, et al: Efficacy of an air-cleaning device equipped with a high efficiency particulate air filter in house dust mite respiratory allergy. *Allergy* 46:594–600, 1991
4. Arruda LK, Vailes LD, Mann BJ, et al: Molecular cloning of a major cockroach (*Blattella germanica*) allergen, Bla g 2. *J Biol Chem* 270:19563–19568, 1995
5. Avner DB, Perzanowski MS, Platts-Mills TAE, et al: Evaluation of different techniques for washing cats: Quantitation of allergen removed from the cat and effect on airborne *Fel d 1*. *J Allergy Clin Immunol*, in press
6. Bartholome K, Kisler W, Baer H, et al: Where does cat allergen come from? *J Allergy Clin Immunol* 76:503, 1985
7. Bjornsdottir US, Jakobinudottir S, Runarsdottir V, et al: Environmental control with cat *in situ*, reduces cat allergen in house dust samples—but does it alter clinical symptoms [Abstract]. *J Allergy Clin Immunol* 99(1):S389, 1997
8. Bohr R de: The control of house dust mite allergens in rugs. *J Allergy Clin Immunol* 86:808–814, 1990
9. Bollinger ME, Eggleston PA, Wood RA: Cat antigen in homes with and without cats may induce allergic symptoms. *J Allergy Clin Immunol* 97:907–914, 1996
10. Burge HA, Solomon W, Boise JR: Microbial prevalence in domestic humidifiers. *Applied and Environmental Microbiology* 39:840–844, 1980
11. Burge HA: Fungus allergens. *Clin Rev Allergy* 3:319–329, 1985
12. Burrows B, Sears MR, Flannery EM, et al: Relations of bronchial responsiveness to allergy skin test reactivity, lung function, respiratory symptoms and diagnoses in thirteen-year-old New Zealand children. *J Allergy Clin Immunol* 95:548–556, 1995
13. Call RS, Smith TF, Morris E, et al: Risk factors for asthma in inner city children. *J Pediatr* 121:862–866, 1992
14. Carswell F, Birmingham K, Weeks J, et al: The respiratory effects of reduction of mite allergen in bedrooms of asthmatic children: A double blind controlled trial. *Clin Exp Allergy* 26:386–396, 1996
15. Charpin C, Mata P, Charpin D, et al: *Fel d 1* allergen distribution in cat fur and skin. *J Allergy Clin Immunol* 88:77–82, 1991
16. Chilmoneczyk BA, Salmun LM, Megathlin KN, et al: Association between exposure to environmental tobacco smoke and exacerbations of asthma in children. *N Engl J Med* 328:1665–1669, 1993
17. Colloff MJ: House dust mites—part II: Chemical control. *Pestic Outlook* 1:3–8, 1990
18. Colloff MJ, Ayres J, Carswell F, et al: The control of allergens of dust mites and domestic pets: A position paper. *Clin Exp Allergy* 22:1–28, 1992
19. Colloff MJ: Editorial: Dust mite control and mechanical ventilation: When the climate is right. *Clin Exp Allergy* 24:94–96, 1994
20. Colloff M, Taylor C, Merrett T: The use of domestic steam cleaning for the control of house dust mites. *Clin Exp Allergy* 25:1061–1066, 1995
21. Custovic A, Green R, Picjering CAC, et al: Major dog allergen *Can f 1*: Distribution

- in homes, airborne levels, and particle sizing (abstract). *J Allergy Clin Immunol* 97:302, 1996
22. Custovic A, Taggart SCO, Francis HC, et al: Exposure to house dust mite allergens and the clinical activity of asthma. *J Allergy Clin Immunol* 98:64-72, 1996
 23. Custovic A, Taggart S, Kennaugh J, et al: Portable dehumidifiers in the control of house dust mites and mite allergens. *Clin Exp Allergy* 25:312-16, 1995
 24. De Blay F, Chapman MD, Platts-Mills TAE: Airborne cat allergen (*Fel d 1*): Environmental control with the cat *in situ*. *Am Rev Respir Dis* 143:1334-1339, 1991
 25. deGroot H, Goei KGH, VanSwieten P, et al: Affinity purification of a major and a minor allergen from dog extract: Serologic activity of affinity-purified *Can f 1* and of *Can f 1*-depleted extracts. *J Allergy Clin Immunol* 87:1056-1065, 1991
 26. Dietemann A, Bessot JC, Hoyet C, et al: A double-blind, placebo controlled trial of solidified benzyl benzoate applied in dwellings of asthmatic patients sensitive to mites: Clinical efficacy and effect on mite allergens. *J Allergy Clin Immunol* 91:738-746, 1993
 27. Dodin A, Rak H: Influence of low temperature on the different stages of the human allergy mite *Dermatophagoides pteronyssinus*. *J Med Entomol* 30:810-811, 1993
 28. Dowse GK, Turner KJ, Stewart GA, et al: The association between *Dermatophagoides* mites and the increasing prevalence of asthma in village communities within the Papua New Guinea highlands. *J Allergy Clin Immunol* 75:75-83, 1985
 29. Ehnert B, Lau-Schadendorf S, Weber A, et al: Reducing domestic exposure to dust mite allergen reduces bronchial hyperreactivity in sensitive children with asthma. *J Allergy Clin Immunol* 90:135-138, 1992
 30. Gillies DRN, Littlewood JM, Sarsfield JK: Controlled trial of house dust mite avoidance in children with mild to moderate asthma. *Clin Allergy* 105-111, 1987
 31. Halonen M, Stern D, Wright AL, et al: *Alternaria* as a major allergen for asthma in children raised in a desert environment. *Am J Respir Crit Care Med* 155:1356-1361, 1997
 32. Hayden ML, Rose G, Diduch KB, et al: Benzyl benzoate moist powder: Investigation of acaricidal activity in cultures and reduction of dust mite allergens in carpets. *J Allergy Clin Immunol* 89:536-545, 1992
 33. Hide DW, Matthews S, Tariq S, et al: Allergen avoidance in infancy and allergy at 4 years of age. *Allergy* 51:89-93, 1996
 34. Huss RW, Huss K, Squire EN, et al: Mite allergen control with acaricide fails. *J Allergy Clin Immunol* 94:27-32, 1994
 35. Ingram JM, Sporik R, Rose G, et al: Quantitative assessment of exposure to dog (*Can f 1*) and cat (*Fel d 1*) allergens: Relationship to sensitization and asthma among children living in Los Alamos, New Mexico. *J Allergy Clin Immunol* 96:449-456, 1995
 36. Jalil-Colome J, Dornelas de Andrade A, Birnbaum J, et al: Sex differences in *Fel d 1* allergen production. *J Allergy Clin Immunol* 98:165-168, 1996
 37. Kalra S, Owen SJ, Hepworth J, et al: Airborne house dust mite antigen after vacuum cleaning. *Lancet* 336:449, 1990
 38. Kang BC, Johnson J, Veres-Thorner C: Atopic profile of inner city asthma with a comparative analysis on the cockroach sensitive and ragweed sensitive subgroups. *J Allergy Clin Immunol* 92:802-811, 1993
 39. Kivity S, Solomon A, Soferman R, et al: Mite asthma in childhood: A study of the relationship between exposure to house dust mites and disease activity. *J Allergy Clin Immunol* 91:844-849, 1993
 40. Klucka CV, Ownby DR, Green J, et al: Cat shedding of *Fel d 1* is not reduced by washings, Allerpet-C spray, or acepromazine. *J Allergy Clin Immunol* 95:1164-1171, 1995
 41. Korsgaard, Iversen M: Epidemiology of house dust mite allergy. *Allergy* 46(suppl)11:14-18, 1991
 42. Kueher J, Frischer J, Meiner R, et al: Mite exposure is a risk factor for the incidence of specific sensitization. *J Allergy Clin Immunol* 94:44-52, 1994
 43. Kumar P, Lopez M, Fan W, et al: Mold contamination of automobile air conditioner systems. *Annals Allergy* 64:174-177, 1990
 44. Larsen JN, Ford A, Gjesing B, et al: The collaborative study of the international

- standard of dog, *Canis Domesticus*, hair/dander extract. J Allergy Clin Immunol 82:318-325, 1988
45. Lau S, Falkenhörst G, Weber A, et al: High mite-allergen exposure increases the risk of sensitization in atopic children and young adults. J Allergy Clin Immunol 84:718-725, 1989
 46. Lau-Schadendorf S, Rusche AF, Weber AK, et al: Short-term effect of solidified benzyl benzoate on mite-allergen concentrations in house dust. J Allergy Clin Immunol 87:41-47, 1991
 47. Leitermann K, Ohman JL: Cat allergen 1: Biochemical, antigenic, and allergenic properties. J Allergy Clin Immunol 74:147, 1984
 48. Lindren S, Belin L, Dreborg S, et al: Breed specific dog-dander allergens. J Allergy Clin Immunol 82:196-204, 1988
 49. Luczynska CM, Li Y, Chapman MD, et al: Airborne concentrations and particle size distribution of allergen derived from domestic cats (*Felis domesticus*): Am Rev Respir Dis 141:361-367, 1990
 50. McDonald LG, Tovey ER: The role of water temperature and laundry procedures in reducing house dust mite populations and allergen content of bedding. J Allergy Clin Immunol 90:599-608, 1992
 51. Mitchell EB, Wilkins S, Deighton J, et al: Reduction of house dust mite levels in the home: Use of the acaricide, pirimiphos methyl. Clin Allergy 15:235-240, 1985
 52. Mosbech H, Korsgaard J, Lind P: Control of house dust mites by electrical heating blankets. J Allergy Clin Immunol 81:706-710, 1988
 53. Munir AKM, Björkstén B, Einarsson R, et al: Cat (*Fel d 1*), dog (*Can f 1*) and cockroach allergens in homes of asthmatic children from three climatic zones in Sweden. Allergy 49:508-516, 1994
 54. Munir AK, Einarsson R, Dreborg SK: Vacuum cleaning decreases the levels of mite allergens in house dust. Pediatric Allergy Immunology 4:136-143, 1993
 55. Murray AB, Ferguson AC: Dust-free bedrooms in the treatment of asthmatic children with house dust or house dust mite allergy. Pediatrics 71:418-422, 1983
 56. Nelson HS, Roger Hirsch S, Ohman JL Jr, et al: Recommendations for the use of residential air-cleaning devices in the treatment of respiratory diseases. J Allergy Clin Immunol 82:661-669, 1988
 57. Newman Taylor A, Longbottom J, Pepys J: Respiratory allergy to urine proteins of rats and mice. Lancet 2:837-839, 1977
 58. Owen S, Morganstem M, Hepworth J, et al: Control of house dust mite antigen in bedding. Lancet 335:396-397, 1990
 59. Peat JK, Tovey ER, Toelle BG, et al: House-dust mite allergens: A major risk factor for childhood asthma in Australia. Am J Respir Crit Care Med 153:141-146, 1996
 60. Peat JK, Tovey E, Mellis CM, et al: Importance of house dust mite and *Alternaria* allergens in childhood asthma: An epidemiological study in two climatic regions of Australia. Clin Exp Allergy 23:812-820, 1993
 61. Peroni DG, Boner AL, Vallone G, et al: Effective allergen avoidance at high altitude reduced allergen-induced bronchial hyperresponsiveness. Am J Resp Crit Care Med 149:1442-1446, 1994
 62. Platts-Mills TAE, De Weck A: Dust mite allergens and asthma: A world wide problem. Bull WHO 66:769-780, 1989
 63. Platts-Mills TAE, Thomas WR, Aalberse RC, et al: Dust mite allergens and asthma: Report of a 2nd international workshop. J Allergy Clin Immunol 89:1046-1060, 1992
 64. Platts-Mills TAE, Tovey ER, Mitchell EB, et al: Reduction of bronchial hyperreactivity following prolonged allergen avoidance. Lancet ii:675-678, 1982
 65. Platts-Mills TAE, Heymann PW, Longbottom JL, et al: Airborne allergens associated with asthma: Particle sizes carrying dust mite and rat allergens measured with a cascade impactor. J Allergy Clin Immunol 77:850-857, 1986
 66. Pollart SM, Chapman MD, Fiocco GP, et al: Epidemiology of acute asthma: IgE antibodies to common inhalant allergens as a risk factor for emergency room visits. J Allergy Clin Immunol 83:875-882, 1989
 67. Pollart S, Smith TF, Morris EC, et al: Environmental exposure to cockroach allergens:

- Analysis with monoclonal antibody-based enzyme immunoassays. *J Allergy Clin Immunol* 87:505-510, 1995
68. Price JA, Longbottom J: Allergy to mice: Further characterization of two major mouse allergens (Ag 1 and Ag 3) and immunohistochemical investigations of their sources. *Clin Exp Allergy* 20:71-77, 1990
 69. Reisman R, Mauriello P, Davis G, et al: A double-blind study of the effectiveness of a high-efficiency particulate air (HEPA) filter in the treatment of patients with perennial allergic rhinitis and asthma. *J Allergy Clin Immunol* 85:1050-1059, 1990
 70. Rosenstreich DL, Eggleston P, Kattan M, et al: The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma. *N Engl J Med* 336:1356-1363, 1997
 71. Russell DW, Fernandez-Caldas E, Swanson MC, et al: Caffeine, a naturally occurring acaricide. *J Allergy Clin Immunol* 87:107-110, 1991
 72. Sarpong SB, Hamilton RG, Eggleston PA, et al: Socioeconomic status and race as risk factors for cockroach allergen exposure and sensitization in children with asthma. *J Allergy Clin Immunol* 97:1393-1401, 1996
 73. Sarpong SB, Wood RA, Eggleston PA: Short-term effects of extermination and cleaning on cockroach allergen Bla g 2 in settled dust. *Ann Allergy Asthma Immunol* 76:257-260, 1996
 74. Sarpong S, Wood RA, Karrison T, et al: Cockroach allergen (Bla g 1) in school dust. *J Allergy Clin Immunol* 99:486-492, 1997
 75. Schou C: Defining allergens of mammalian origin. *Clin Exp Allergy* 23:7-14, 1993
 76. Schou C, Svendsen VG, Lowenstein H: Purification and characterization of the major dog allergen, Can f 1. *Clin Exp Allergy* 21:321-328, 1991
 77. Sears MR, Herbison GP, Holdaway MD, et al: The relative risk of sensitivity to grass pollen, house dust mite, and cat dander in the development of childhood asthma. *Clin Exp Allergy* 19:419-424, 1989
 78. Siraganian R, Sandberg A: Characterization of mouse allergens. *J Allergy Clin Immunol* 63:435-442, 1979
 79. Soldatov D, De Blay F, Greiss P, et al: Effects of environmental control measures on patient status and airborne Fel d 1 levels with a cat in situ [abstract]. *J Allergy Clin Immunol* 95(1):263, 1995
 80. Spitzauer S, Schwiger C, Anrather J, et al: Characterization of dog allergens by means of immunoblotting. *Int Arch Allergy Immunol* 100:60-67, 1993
 81. Sporik RB, Arruda LK, Woodfolk J, et al: Environmental exposure to *Aspergillus fumigatus* (Asp f I). *Clin Exp Allergy* 23:326-331, 1993
 82. Sporik R, Holgate ST, Platts-Mills TAE, et al: Exposure to house-dust mite allergen (Der p I) and the development of asthma in childhood: A prospective study. *N Engl J Med* 323:502-507, 1990
 83. Sporik R, Ingram JM, Price W, et al: Association of asthma with serum IgE and skin-test reactivity to allergens among children living at high altitude: Tickling the dragon's breath. *Am J Res Crit Care Med* 151:1388-1392, 1995
 84. Swanson M, Agarwal M, Yuninger J, et al: Guinea pig derived allergens: Characterization, airborne quantification and size distribution. *Am Rev Resp Dis* 129:844-849, 1984
 85. Stewart GA, Thompson PJ: The biochemistry of common aeroallergens. *Clin Exp Allergy* 25:1020-1044, 1995
 86. Tovey ER, Chapman MD, Platts-Mills TAE: Mite feces are a major source of house dust mite allergens. *Nature* 289:592-593, 1981
 87. Tovey ER, Marks GB, Matthews M, et al: Changes in mite allergen Der p I in house dust following spraying with a tannic acid/acaricide solution. *Clin Exp Allergy* 22:67-74, 1992
 88. Tovey E, Marks G, Shearer M, et al: Allergens and occlusive bed covers. *Lancet* 342:126, 1993
 89. Tovey E, Johnson MC, Roche AL, et al: Cloning and sequencing of a cDNA expressing a recombinant house dust mite protein that binds human IgE. *J Exp Med* 170:1457-1462, 1989
 90. Tovey E, Woolcock A: Direct exposure of carpets to sunlight can kill all mites. *J Allergy Clin Immunol* 93:1072-1074, 1993

91. Vendenhove T, Soler M, Birnbaum J, et al: Effect of dry cleaning on the mite allergen levels in blankets. *Allergy* 48:264-266, 1993
92. Van der Brempt X, Charpin D, Haddi E, et al: Cat removal and *Fel d 1* levels in mattresses. *J Allergy Clin Immunol* 87:595-596, 1991
93. Vervloet D, Charpin D, Haddi E, et al: Medication requirements and house dust mite exposure in mite sensitive asthmatics. *Allergy* 46:554-558, 1991
94. Walls A, Longbottom J: Comparison of rat fur, saliva, and other rat allergen extracts by skin testing, RAST and RAST inhibition. *J Allergy Clin Immunol* 75:242-251, 1985
95. Walls A, Taylor A, Longbottom J: Allergy to guinea pig II: Identification of specific allergens in guinea pig dust by crossed radio-immuno-electrophoresis and investigation of the possible origin. *Clin Allergy* 15:535-546, 1985
96. Warner JA, Marchant JL, Warner JO: Double blind trial of ionisers in children with asthma sensitive to the house dust mite. *Thorax* 48:330-333, 1993
97. Warner JA, Little SA, Pollock I, et al: The influence of exposure to house dust mite, cat, pollen, and fungal allergens in the home on primary sensitization in asthma. *Pediatr Allergy Immunol* 1:79-86, 1991
98. Wassenaar DPJ: Effectiveness of vacuum cleaning and wet cleaning in reducing house-dust mites, fungi and mite allergen in a cotton carpet: A case study. *Exp Appl Acarol* 4:53-62, 1988
99. Wentz PE, Swanson MC, Reed CE: Variability of cat allergen shedding. *J Allergy Clin Immunol* 85:94-98, 1990
100. Wood RA, Eggleston PA, Ingemann L, et al: Antigenic analysis of household dust samples. *Am Rev Resp Dis* 137:358-363, 1988
101. Wood RA, Chapman MD, Adkinson NF, et al: The effect of cat removal on allergen content in household dust samples. *J Allergy Clin Immunol* 83:730-734, 1989
102. Wood RA, Mudd KE, Eggleston PA: The distribution of cat and dust mite allergens on wall surfaces. *J Allergy Clin Immunol* 89:126-130, 1992
103. Wood RA, Laheri AN, Eggleston PA: The aerodynamic characteristics of cat allergen. *Clin Exp Allergy* 23:733-739, 1993
104. Wood RA, Flanagan E, Van Natta M, et al: The effect of a HEPA room air cleaner on cat-induced asthma and rhinitis [Abstract]. *J Allergy Clin Immunol* 99(1):S388, 1997
105. Woodfolk JA, Hayden ML, Couture N, et al: Chemical treatment of carpets to remove allergen. *J Allergy Clin Immunol* 96:325-333, 1996
106. Woodfolk J, Hayden M, Miller J, et al: Chemical treatment of carpets to reduce allergen: A detailed study of the effects of tannic acid on indoor allergens. *J Allergy Clin Immunol* 94:19-26, 1994
107. Wright AL, Holberg C, Martinez FD, et al: Relationship of parental smoking to wheezing and nonwheezing lower respiratory tract illnesses in infancy. *J Pediatr* 118:207-214, 1991

Address reprint requests to

Robert A. Wood, MD
CMSC 1102
Johns Hopkins Hospital
600 N Wolfe Street
Baltimore, MD 21287