

Indoor Allergen Avoidance and Asthma

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Sensitization and exposure to indoor allergens, including house dust mite, cat and dog allergens, is an important risk factor for asthma in children and young adults. With the purification of the major allergens associated with house dust mite, cat, dog, cockroach and mouse and the consequent availability of ELISA assays for their detection, we have learned a great deal about their distribution in homes and their elimination from homes. House dust mite allergens are associated with bedding and exposure can be reduced by over 90% with practical treatments for bedding. In most studies, exposure reduction to this extent has been shown to

reduce asthma severity among children and adults with asthma. Elimination of cat and dog allergen has proven much more difficult because the allergen is carried on small particles that remain airborne and can be widely distributed on clothing; allergen avoidance is less complete and avoidance trials have had only small effects on asthma. Primary prevention of asthma, i.e. prevention of incident cases in at genetically predisposed infants, has proven to be possible in the few trials conducted to date. (*Korean J Asthma Allergy Clin Immunol* 2006;26:10-16)

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While it is impossible to make indoor environments allergen free, we can decrease excessive indoor allergen exposure with the hope of improving the symptoms of our patients with allergic rhinitis and asthma. The most effective method of reducing exposure dose is to remove the source of the contaminant. In practice some sources (house dust mites, cockroaches) have been easier to remove than others (pets). When the source cannot be removed, pollutant removal should start as close to the source as possible.

A number of excellent and complete reviews have summarized the details of allergen reduction¹⁻³⁾ and their health effects on sensitized individuals, so this review will concentrate on recent advances in reducing exposures, without summarizing health effects.

HOUSE DUST MITE AVOIDANCE

House dust mite allergens are carried on relatively large particles (10~30µm) that only become airborne after vigorous disturbance and do not remain airborne for long.

The notion that exposure occurs primarily in the bed when the patient's nose and face are burrowed into contaminated bedding has not actually been proven, but it is still an attractive notion and allows us to focus interventions on the bed. The mites infest fabrics especially bedding, are not particularly mobile and have fastidious growth requirements, making the source elimination relatively easy. At the top of the list of effective methods to reduce house dust mite is allergen proof encasings fitted to the mattress and pillow.¹⁻³⁾ These covers are available by mail or in retail stores are breathable, comfortable and nearly 100% exclusive.⁴⁾ More than a dozen clinical trials of allergen-proof encasings have been published that were at least 3 months long and reported mite allergen levels in bedding.⁵⁻¹⁹⁾ All of these trials report reduced allergen concentrations, but the degree of allergen reduction varied widely, from 39 to 99.9% (median 89%) as did the final allergen concentrations achieved (range 0.01 to 8.50µg/gm, median 0.77µg/gm). It is not clear why such a wide range of effectiveness was seen in these trials, but the variations were not easily explained by the level of mite contamination, and many of the trials included, inclusion of aggressive laundering or the use of tannic acid or acaricides. In addition, bedding allergen levels have been shown to continue to decrease with observations up to a year, suggesting that repopulation of bedding cover

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fabric is not common.

Other essential measures include thorough vacuum cleaning, and washing all bedding (sheets, blankets, comforters, bedspreads). Vacuuming reduces the bulk of household dust and reduces the overall exposure burden, but does not change the concentration of allergen, i.e. mg per gram of settled dust.²⁰⁾ Washing sheets, pillowcases blankets and mattress pads at least weekly in warm water with detergent and with 8~10 minute cycles removes virtually all mite and animal allergen.²¹⁾ Dry cleaning²²⁾ and prolonged tumble drying²³⁾ effectively kills mites, but is less effective at removing allergens.

Second line measures include relocating the bedroom, application of acaracides such as benzyl benzoate, dehumidification and removing wall-to-wall carpeting. Relocating the patient's bedroom out of the basement has been recommended but the only reported study of basement carpets found that mite allergen concentrations were almost identical to carpets elsewhere in the home.²⁴⁾ Removing fabrics such as curtains and furniture seems logical since they might support mite growth, but this has not been shown to increase the effect of vacuuming and bedding covers alone. Removing wall to wall carpeting is difficult but justifiable since house dust mite levels are higher in wall-to wall carpet compared to uncarpeted areas and bedroom floor levels are reduced when carpeting is removed.¹⁶⁾ Acaracides are effective in the laboratory but field trials have generally found that carpet dust mite allergen is reduced minimally, probably because it is so difficult to get the material into the deepest areas of the carpet.²⁵⁾ The evidence supporting measures to reduce indoor humidity is inconsistent. Trials in England showed that portable dehumidifiers²⁶⁾ were not able to reduce median humidity significantly and mite allergen did not change. Central heat exchangers²⁷⁾ were able to maintain indoor relative humidity below 40% for the 4 months that they were used, but mite allergen levels in carpets and bedding did not decrease. Arlian and colleagues²⁹⁾ installed large portable dehumidifiers in Midwestern US homes and showed that approximately half of the homes were able to maintain relative humidity below 51% throughout a 2 year period. Mite allergen in bedding was not measured, but mites and mite allergen in the carpets from these homes declined 78%. Surprisingly, air conditioning

alone was not able to reduce indoor humidity enough to affect mite growth significantly.

PET ALLERGEN AVOIDANCE

Animal allergens are carried on small particles that remain airborne and are remarkably adherent to surfaces and clothing.³⁰⁾ Because the source is so mobile in a home, inclined to heavily contaminate a favorite chair or bed and because families are reluctant to get rid of the pet, source elimination is almost impossible. An atopic patient who is sensitized to cat or dog allergen should not live with a pet in their home. Air filters should be helpful in reducing exposure to airborne pet allergen particles. Their stickiness leads to widespread distribution, so that animal allergen can be found in public buildings such as schools^{31,32)} and homes without a pet, although at concentrations 10 to 1000 times higher in homes with a pet.³²⁾

Once a pet has been removed from the home allergen levels in settled dust fall to those seen in homes without cats over 4 to 6 months.³³⁾ Levels fall much more quickly if extensive environmental control measures are undertaken, such as removal of carpets, upholstered furniture, and other reservoirs from the home. Cat allergen may persist in mattresses for years after a cat has been removed from a home,³⁴⁾ so the purchase of new bedding or impermeable encasements should also be recommended.

Because so many patients are unwilling to remove their pet, even if they themselves are sensitized, many compromise measures have been suggested. DeBlay et al³⁵⁾ demonstrated significant reductions in airborne Fel d 1 with a combination of air filtration and washing the cat, but later studies showed that the decrease lasted only a few days.³⁶⁾ The use of room HEPA air filters may reduce airborne levels somewhat. When these units are placed in living rooms, airborne levels of cat and dog allergen have been shown to decrease by almost 90%^{37,38)} over a period of hours; but similar reductions were seen in control experiments when the units were not running, so that there was no net effect attributable to HEPA air filtration. A later report extended treatment for a year,³⁹⁾ demonstrating persistent 90% reductions in allergen levels in both treatment and control groups, statistically greater in the treatment group. Both groups also

used a HEPA filtered vacuum cleaner but settled dust animal allergen levels did not decrease. Another report described a “safe” room from which the cat is excluded and vigorous environmental control measures such as vacuuming, mattress and pillow covers, carpet removal and room air filters were tested.⁴⁰⁾ In this case airborne levels decreased 43% over 3 months while settled dust allergen levels did not change.

COCKROACH ALLERGEN AVOIDANCE

Cockroach allergen particles have properties similar to mite allergens; 74% to 80% of aeroallergens are associated with particles larger than 10 μ m that are detectable mainly after vigorous and settle rapidly.⁴¹⁾ Since the cockroach is highly mobile, allergen is spread widely through a home, in bedding as well as kitchens; allergen is concentrated in hiding places behind appliances and in crack and crevices, creating a unique reservoir that is difficult to access.

Cockroach allergen removal begins with insecticide treatment to reduce the allergen source.⁴²⁾ Pesticides incorporated in gels or baits are placed selectively in areas with high insect concentrations and traffic. In addition, bait traps using pesticides such as abamectin and hydramethylnon are available to consumers that are just as effective as the gel baits if used properly. Typically, successful treatments provide significant reduction within two weeks, maximal effect by about a month and sustained reductions for 3 to 6 months, even longer if families change cleaning practices to remove food sources that will attract reinfestation. These practices include cleaning grease and other food debris from the kitchen, storing food in plastic containers or in a refrigerator, and eliminating food debris from the TV room or bedroom. Even with household cleaning after extermination, cockroach allergen persists for months after successful pest control.

Field trials of allergen reduction methods have shown that cockroach populations can be reduced by more than 90% in most cases⁴²⁾ while allergen levels in settled dust and bedding decline slowly over about 6 months. While allergen may be completely eliminated from settled dust in less infested homes, in heavily contaminated areas, with Bla g 1 or Bla g 2 concentrations greater than 100 Units per gram of settled dust, treated rooms still contain allergen at levels

that have been associated with disease. The first large field trial that included cockroach allergen control⁴³⁾ found trivial reductions in cockroach allergen concentration in treated homes. In a recently reported intervention that included integrated pest management, mattress and pillow encasings, HEPA room air filters, and HEPA fitted vacuum cleaners in inner-city homes in 7 US cities, cockroach allergen Bla g 1 decreased by 44% but initial concentrations only averaged 0.2 U/gm; similar changes were seen in the control group so that the net change was not significant.⁴⁴⁾ Arbes and colleagues combined education, bait trap placement and hydramethylnon gel bait placement using IPM principles.⁴⁵⁾ They reported a 67% reduction of cockroach allergen in bedding and an even larger decrease in bedding; they commented that the careful placement of gel baits, guided by inspection was essential to their success.

PRIMARY PREVENTION OF ALLERGIC DISEASE

Logically, reducing environmental allergen should reduce incident cases of asthma since allergy plays such a strong role in symptomatic asthma. Many published studies of asthmatic children and adults have shown a high rate of IgE-mediated sensitization. Atopy, either expressed as family history or as the presence of eczema or food allergy, is one of the strongest risk factors for the development of asthma.^{46,47)} Since it is a strong risk factor for asthma it not only confirms that atopy plays a role in asthma, but suggests that atopy and sensitization actually precedes asthma. Finally, a dose: response relationship e.g. the intensity of exposure to selected indoor allergens are directly related to the frequency of sensitization to that allergen.⁴⁸⁻⁵⁰⁾ Published data from clinical trials of allergen avoidance in infants at risk of developing asthma are summarized in the Table 1.

The Isle of Wight study⁵¹⁾ included recruited 136 families in which both parents were atopic (120) or where one parent was atopic and the baby's cord blood IgE was elevated. Families were randomized to a Treatment Group or Control Group. The Treatment Group, lactating mothers excluded dairy products, fish, egg and nuts from their diet or their infants were fed a protein hydrolysate formula. Milk and soy were introduced at 9 months and egg at 11 months. All infants used polyvinyl-covered mattresses. Der p 1 in home

Table 1. Clinical trials of indoor allergen avoidance for the primary prevention of asthma

	Year 1			Year 2			Year 4~8		
	Mite allergen reduction	Mite sensitivity	Asthma	Mite allergen reduction	Mite sensitivity	Asthma	Mite allergen reduction	Mite sensitivity	Asthma
Isle of wight	↓ 79.7%	0 (A)* ND (C)	7% (A) 19% (C)	ND [†]	1.7% (A) 9.7% (C)	15.5% (A) 27.4% (C)	ND	5.2% (A) 24.2% (C)	24% (A) 35% (C)
CaPPS	↓ 15% (A) ↓ 9% (C)	0 (A) 0.6 (C)	8.7% (A) 5.6% (C)	3% (A) ↑ 68% (C)	0 (A) 0.4% (C)	6% (A) 23% (C)	ND	13% (A) 13% (C)	14.9% (A) 23% (C)
MAAS	↓ 97% (A) ↑ 243% (C)	2% (A) 1% (C)	RR A vs C 0.48 (0.19~1.27)						
PIAMA	↓ 47% (A) 25% (C)	0.7 (A) 0.8% (C)	6.6% (A) 8.3% (C)						

*C = control group, A = active treatment group; [†] ND = no data.

dust samples from the child's bedroom and the living room fell from 26 mg/gm dust at baseline to 6 mg/gm dust at 9 months; concentration in control children's home changed significantly less. Signs of asthma were present in 7% of the Treatment Group infants at 12 months compared to 19% of the Control Group infants. Eczema was less common in the treatment group (11% vs 19%) as was the prevalence of positive skin tests (3% vs 10%). Skin tests to mite allergen were not seen in the treatment group.

The families were reevaluated at 2 years⁵²⁾ at which time all 120 children were available. Significantly more of the children in the control group has positive skin tests (26% vs 5%, $P < 0.005$) and significantly more had positive test to house dust mite. Asthma was somewhat more common (16% vs 27%,) but not significantly so. Rhinitis was more common in control infants (3% vs 11%, $P < 0.1$). The final report on these 120 children⁵³⁾ at age 4 found that asthma was less common in the treatment group (24% vs 35%) but not significantly so. The difference in proportion with positive skin tests was still significant (34% vs 14%, $P = 0.02$) and as was the frequency of positive skin tests to house dust mite (24 vs 5%, $P < 0.02$). Settled dust allergen measures were not repeated after the first year.

The Canadian Asthma Primary Prevention study (CAPPS)⁵⁴⁾ enrolled five hundred and forty-five families with one first degree relative with asthma or two with allergic disease, and were randomly assigned to receive avoidance intervention or control. The intervention group received allergen proof encasings for the parent's and child's mattresses and pillows, visits by research nurses to apply benzyl benzoate to rugs

and furniture before birth and at 4 and 8 months. Families were counseled to get rid of pets or keep them outside. They were also given smoking cessation counseling. They were encouraged to breastfeed up to 12 months and to avoid day care facilities. House dust mite allergen in the bedroom decreased modestly in the treatment group (1.31µg/gm to 0.8µg/gm at 12 months) but the change was significantly greater than in the control group (1.46µg/gm to 1.3µg/gm at 12 months; $P = 0.005$). Breast feeding, parental smoking and use of day care all changed more in the intervention group but not significantly so. At the end of a year few infants had positive skin tests to inhalant allergens. Incidence cases of possible or probable asthma were less common in the intervention group (15 vs 20%; $P = 0.04$) and fewer had a persistent rhinitis without a cold (17 vs 27%; $P = 0.01$). At age 2,⁵⁵⁾ mite allergen levels were still ignorantly different although changes were modest. The prevalence of at least one positive skin test was similar (13.7% vs 15.6%) but only one child, in the control group, has a positive skin test to mite. The prevalence of asthma was now significantly higher in the control group (16% vs 23%). The latest report on this cohort,⁵⁶⁾ now 7 years old, did not include allergen exposure data. The prevalence of positive skin test was still similar in the two groups (49% vs 42%, $P = 0.3$). The prevalence of asthma was still lower in the treatment group (23% vs 15%, $P = 0.006$).

Custovic and colleagues conducted a prevention trial of 291 high-risk couples, defined by both parents being atopic, the Manchester Asthma and Allergy Study (MAAS). Families were randomized to a Control Group and an Interven-

tion Group that began treatment in the 16th month of pregnancy consisting of covering the mattress pillow and quilt with impermeable covers, provision of a HEPA vacuum cleaner, replacing carpet in the child's room with vinyl, and providing the infant with allergen proof encasings. Families with furred pets were excluded from the randomized trial. Bedding was washed weekly in hot water and benzyl benzoate was applied to carpets and soft furnishings. Food restrictions were not practiced. In a preliminary report, it was shown that the aggressive measures reduced mite concentrations in the treated homes by 29 fold and that these levels were maintained throughout the first year.⁶⁾ At the end of the first year, the group randomized to intervention had significantly fewer asthma symptoms in the first year than the high risk control group.⁵⁷⁾ However, only severe wheezing, exercise-induced wheezing and medication requirement reached statistical significance. Skin tests were not common in either group and slightly fewer infants in the control group have a positive skin test to mite. Although a number of publications describe pulmonary function tests and symptoms of these infants, comparisons of environmental treatment and controls have not yet appeared.

The Prevention and Incidence of Asthma and Mite Allergy (PIAMA) study was begun in the Netherlands when 1,327 allergic women were asked to participate in and intervention study in the third trimester of pregnancy. Mothers were randomized to an Active intervention group that received mattress and pillow covers for the mothers and child's bed and a control group that received cotton covers. Mite allergen levels were low on the mattresses but decreased by 47% in the active group and 25% in the control group; levels in samples collected at age 4 and 6 to 12 years were actually higher than during infancy, an effect possibly related to a cold, dry winter in the first year.⁵⁸⁾

At the end of the first year, the rate of the infant's sensitization to house dust mite was low; and treatment and control groups were not different.⁵⁹⁾ Children in the active treatment group had a 6.6% prevalence of recurrent wheezing compared to 8.3% in the control group, a difference that was not significant. The prevalence of eczema was similar, but the incidence of runny nose with out a cold was higher in the placebo group.

In summary, the trend of the only 4 four clinical trials of allergen avoidance in early life suggest that this may be

a successful strategy to decrease incident asthma, especially in those interventions that are successful in reducing allergen exposure and can be applied consistently throughout the first 4 to 7 years of life.

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