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Methods and effectiveness of environmental control

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In recent years the role of allergen exposure and atopy, and the interaction between them in the clinical expression of allergic disease, has been examined in a quantitative manner in epidemiologic studies. Such analyses suggest that avoidance of exposure to domestic allergens is a critical element in integrated strategies for both the prevention and the management of asthma. The promise of primary intervention in high-risk infants, as shown in the Isle of White study, has been confirmed in a recent study in Japan, and at least 4 similar trials are in progress. Applying these principles to the management of symptoms in patients with chronic asthma has proved more difficult, and it is likely that many earlier studies were poorly designed to test the hypothesis that allergen avoidance was clinically useful. Recent studies with patients moved to high altitudes during seasonal reductions in mite exposure and randomized controlled interventions in houses have all shown improvements in clinical manifestations of asthma. These recent trials have also demonstrated something that was less certain—that massive reductions in domestic allergen exposure can be achieved and that people will adopt the significant changes to their domestic environment and lifestyles if the risks and benefits are known. In the future, it seems likely that better study designs, as well as improvements in methods to monitor exposure and clinical outcomes, will provide further support for the role of allergen avoidance in the prevention and management of asthma. (J Allergy Clin Immunol 1999;103:179-91.)

Key words: *Allergen avoidance, allergen exposure, aeroallergens, allergens, risk factors, mites, cats*

Abbreviations used
AHR: Airways hyperreactivity
HDM: House dust mite
HEPA: High-efficiency particulate air
SPT: Skin prick test

The rising prevalence of asthma, particularly among children, has stimulated analyses of the changes in environment, lifestyle, and other causal factors that may be responsible for the increase.[1,2] Some of these factors may be suitable targets for interventions to prevent or reduce the severity of asthma.

In last month's *Current reviews of allergy and clinical immunology* article in The Journal, Peat et al[3] identified exposure to house dust mite (HDM) allergen as a key target for intervention. In communities with high mite exposure, the association between exposure, sensitization, and asthma is very strong. In these communities halving the mean level of HDM allergen could be anticipated to have a greater impact on the prevalence of asthma than interventions directed at other risk factors, such as the absence of breast-feeding, exposure to environmental tobacco smoke, and omega-3 fatty acid–deficient diets.[4] A synergistic intervention addressing all risk factors was proposed.

The concept of allergen avoidance dates back to the 17th century,[5] and clinical studies date back to the 1920s.[6,7] There are already numerous comprehensive[8] and contemporary reviews,[9-12] together with workshop reports,[13] a book,[14] numerous editorials,[15-17] and Internet sites. Some sites are useful,[17] but many contain misinformation and little insight. Although most reviews promote allergen avoidance, the recent Cochrane Review[18] found no significant clinical benefit and recommended larger and more rigorous trials with more careful monitoring of exposure and clinical outcomes.

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The recent availability and use of immunoassays for several major indoor allergens[19] has provided more quantitative data on the role of allergens in atopy and asthma, and this has in turn refined the practice and clarified the potential of allergen avoidance. This is reflected in an increased emphasis on avoidance in asthma guidelines.[20] It is now appropriate to reexamine its status.

This review will focus on recent clinical and research experience. It is outside the scope of this review to explore the causal mechanisms of allergens in asthma; the cultural, social, and economic factors that influence the implementation of avoidance procedures; or other environmental factors, such as the nonbiologic indoor air pollutants and particulates.

THE RELATIONSHIP OF ALLERGEN EXPOSURE TO ALLERGIC DISEASE OUTCOMES

Allergens associated with asthma

The major allergens associated with the risk of asthma differ between and within communities, depending on climatic, seasonal, and social factors. Within the same community, individuals differ somewhat in which aeroallergens they become allergic to. For an individual, the allergen or allergens causing symptoms may differ with time, place, and season.

Numerous community studies (see Table II[13]) show chronic asthma is largely associated with exposure to allergens that occur indoors. This is also supported by a recent study of wheeze-discordant monozygotic twins.[21] Exposure to "indoor" allergens is probably more important than exposure to outdoor allergens because we spend most of our time indoors and indoor exposure is perennial and often at a high level, and it increases with the modernization of housing design.

In general terms, the greatest risk for asthma in temperate and humid regions is associated with allergy to HDMs.[13,22,23] In some arid climates the strongest risk factor is allergy to the fungus *Alternaria* spp,[24-26] whereas in some urban communities allergy to cockroach is most important.[27-30] Allergy to furred pets is important in many places,[31-33] particularly Scandinavia.[34] Although pollen allergy is seldom an independent risk factor for chronic asthma,[35-37] it is strongly associated with acute hospital admissions[38,39] and seasonal changes in airway responsiveness.[40]

The nature of allergens and aeroallergens

Houses can accumulate large quantities of mite, pet, and other allergens in the dust of beds, carpets, soft furnishings, and clothing; all these function as reservoirs and serve as sources of exposure. In temperate climates mean mite (Der p 1) allergen concentrations of 20 to 40 μg of allergen/g of dust are often observed[41-43]; for pet allergens, mean levels of 200 μg/g are not uncommon.[31,32,44] Such houses would contain, in total, many milligrams of pure allergens, of which a few nanograms (ie, <0.001%) may be airborne at any time.[45] The aeroallergen level fluctuates depending on the level of reservoir disturbance, the nature[46] and quantity of dust, allergen concentration at these sites, and the proximity of sources.[31,47] This is balanced against the rate of aeroallergen removal by settling, collection on surfaces, air exchange, and dilution.

Although the current methods of expressing allergen exposure may provide the only practical way to conduct some epidemiologic studies, they limit our ability to relate exposure to symptoms and to refine avoidance methods. Changes in allergen exposure are the desired intermediary between the application of an environmental intervention and the clinical outcomes sought. Such changes in exposure relate to what is inhaled over a period of time. We have a poor understanding of what true personal exposure is and how this relates to any of the present indices of allergen exposure as currently described.

In most studies the micrograms of allergen per gram of fine dust (or area) collected with a vacuum cleaner from beds and floors has been used as an index of allergen exposure.[23] Such indices vary spatially[48] and temporally[49] and are only weakly correlated with aeroallergen levels.[50-52] Our group is currently exploring the relation between various measures of aeroallergen and actual personal exposure.

Different allergens are carried by a range of particles of different shapes and sizes,[53-55] which affects their behavior when disturbed, when airborne, and when inhaled. Mite aeroallergen after dust disturbance is mainly associated with large particles (>10 μm aerodynamic diameter).[53] After 15 minutes, 10% to 20% remains airborne (mainly that associated with smaller particles),[47] whereas hours later less than 0.1% may remain airborne.[56] In contrast, after disturbance, greater than 20% of cat and dog allergens associated with particles less than 5 μm in size remain airborne for prolonged periods (days).[31,32] This persistence of allergen in the inhalable airborne fraction[57] may explain why asthma symptoms may develop in persons allergic to cats on entering a building without any dust disturbance. It also means that there are potentially some differences in avoidance strategies. For cockroach allergen, 74% to 80% of the aeroallergen is associated with particles larger than 10 μm, which are only detected after vigorous dust disturbance.[58]

The site of deposition in the airways, and presumably the subsequent clinical outcome, is determined by particle shape, size,[59] airflow,[60] and density.[61] It is unclear to what extent the outcomes in asthma are determined by the cumulative effects of occasional large aeroallergen particles entering the lung[62] or the chronic exposure of the lower airways to the subfraction of smaller particles.[63] If the latter is important, avoidance should be focused toward strategies to prevent persistent, small-particle exposure (ie, air exchange and ventilation).

Allergen exposure and sensitization risk

Numerous studies demonstrate the relation between risk for sensitization and the level of exposure to allergen. However, there is no "safe" minimum level of expo-

TABLE I. Recommended avoidance measures for mite allergens

Basic principles of methods
- Based on experience and hypotheses (in leu of available practical allergen monitoring)
- Aggressive and continual attention to multiple reservoirs plus control of sources

Beds
- Most important site
- Mattress: encasement plus optional washable "protector" for comfort
- Blankets/duvets: encasement or washing each 1 to 2 months in water greater than 130°F kills mites; any washing removes allergen
- Pillows: encase, wash, or replace each 3 months; only washable toys on bed

Floor coverings
- Cannot render fitted carpets free of allergen
- Where possible, replace with smooth flooring, especially bedrooms
- Smooth floors cleaned by vacuuming plus damp mopping
- Loose rugs may be possible compromise; kill mites outdoors (3 hours direct sunlight in summer or freeze overnight in winter); wash intermittently and thoroughly to remove allergens

Soft furnishings
- Where possible, replace with cleanable items that do not retain dust
- Possible compromise may be regularly washed loose covers of tight-weave cloth

Clothing
- Wash regularly, particularly after storage (unless dry and free of dust); select clothing for ability to be washed

Chemicals
- The use of acaricides or denaturants to provide practical, long-term, and significant control of allergens is no longer supported

Mechanical devices
- Vacuum cleaners, air filters, and dehumidifiers may have a minor secondary role only and should not be a focus of avoidance procedures
- Vacuum cleaners should have a good air filter and use double thickness bags
- Clean all surfaces regularly with damp or oiled cloth, vacuum, or both; avoid irritating cleaners
- Dehumidifiers most useful in climates where mites are not a major problem (mean relative humidity of 50% to 60%)

Housing design
- Because levels vary greatly within communities, design and lifestyle is likely to be important but difficult to be prescriptive
- A dry indoor climate will reduce mite allergen production; factors include ventilation, building type and age, furnishings, and occupant density

TABLE II. Recommended avoidance measures for furred pet allergens

Basic principles of methods (compared with Table I)
- Same strong emphasis on control of reservoirs—beds (encasings and wash), furnishings (cleanable), carpets (removal/cleanable surfaces), and clothing (change contaminated, wash regularly)
- Same low confidence in any current methods relying on chemicals
- Greater confidence in air filtration as component of secondary route for controlling exposure because more pet allergen is airborne for longer time
- Greater confidence in washing cat-contaminated items than in weekly washing of cats; allergen returns to cats within days from both environment and by production; heavily contaminated clothing can be a potent source of exposure (equal to cat)

Control of source
- Encourage eviction of animal, particularly where clinical effects are obvious
- A poor compromise is to limit animal's territory to indoor cleanable areas (kitchen) and to confine to outdoors at other times
- Note: allergen is very persistent (many months), and control may require aggressive cleaning and removal of heavily contaminated items.

Additional notes
- Measures may be required to prevent significant transport of allergen to houses without pets from houses with furred pets and from public buildings
- Production varies widely between animals and over time; not well enough understood to be prescriptive; probably no allergen-free breeds of cats or dogs

sure appropriate to all susceptible individuals. Some become sensitized[51,64,65] at lower mite allergen levels than those originally proposed as a threshold.[66] This is similar for cat and cockroach allergens.[67]

The relation between the incidence of sensitization to mite and cat allergens during the first 3 years of life has been clearly demonstrated by the study conducted by Wahn et al.[68] This quantified the increasing incidence of sensitization with increasing exposure both in a group of infants with atopic parents and in a group without atopic parents. When both parents were atopic, less than 1% prevalence occurred at levels of approximately 0.1 μg of HDM Group 1 allergen/g of dust and gradually rose to 6% prevalence with allergen levels over 10 μg/g. This group had 3% sensitization at an allergen level of 0.75 μg/g, whereas 3% sensitization occurred in the group without atopic parents at 25 μg/g. There was also an increased risk of sensitization at lower cat allergen levels

compared with mite allergen levels. This study reinforces the need to begin allergen intervention early in life.

ALLERGEN AVOIDANCE IN THE PREVENTION AND MANAGEMENT OF ALLERGIC DISEASES

The ideal way to deal with a chronic disease, such as asthma, is to prevent its onset. If this is not successful, the next aim should be to induce remission. Finally, in those with persisting asthma, management is directed at ameliorating the severity of the disease and avoiding severe adverse outcomes, such as impaired quality of life, side effects of treatment, hospitalizations, and premature death. Avoidance of allergen exposure, along with other environmental modifiers and therapeutic inventions, has a potential role in each of these outcomes.

The highest quality evidence for the assessment of therapeutic interventions is derived from randomized controlled trials. This experimental design is the only strategy for investigation that delivers conclusions free from confounding and selection bias, which may seriously interfere with the interpretation of observational strategies. This constraint on evidence also applies to the evaluation of allergen avoidance interventions, whether for primary prevention, induction of remission, or disease management.

Unfortunately, there is no simple "allergen avoidance" intervention that can be prescribed or evaluated. Instead, we have a number of elements of strategies for allergen avoidance. It is these that are tested in randomized controlled trials. Hence trials of allergen avoidance actually test 2 hypotheses: (1) that the specific interventions are effective in reducing allergen exposure and (2) that this reduction leads to the desired clinical outcome. The second is only valid if the first is proven. The additional practical difficulty of describing when avoidance has been achieved on the basis of proxy exposure measurements has been discussed earlier.

Preventing the onset of allergic disease: Primary prevention

Primary preventive strategies have been targeted at infancy because most cases of asthma arise at that time.[69] However, there is a complex relation among the various elements involved in the evolution of allergic disease. The observed pattern of cellular, humoral, and in vivo responses may not fully reflect the effects of allergen exposure, and their relation to clinical outcomes in later life remains uncertain. A further pragmatic problem with primary prevention studies is the difficulty in clinically characterizing wheezing illness, impaired lung function, and airway hyperresponsiveness in infants.

There have been 2 published randomized controlled trials of allergen avoidance in the primary prevention of asthma, one in the Isle of White[70-72] and one in Japan.[73] Several others are currently in progress.

The Isle of Wight study, which commenced in 1990, involved a total of 120 infants with a strong family history of allergic disease. The intervention group (n = 58) received an intensive food and HDM allergen avoidance regimen; the control group (n = 62) did not. The HDM intervention in carpets and furnishings significantly reduced allergen levels at 9 months. The rates of sensitization in the intervention and control groups were 1.7% and 9.7% at 2 years of age[70] and 5.2% and 24.2% at 4 years of age[71] (both significant). The intervention group was 3.4 times less likely to have eczema ($P < .05$) but not asthma or rhinitis.

Unlike the Isle of Wight study and others that are currently in progress, the published report from Japan[73] identified infants at high risk of HDM allergy and asthma postnatally on the basis of early manifestations of atopy (ie, eczema and food allergy). Children were enrolled during the first year of life and randomized to receive impermeable covers for their mattresses and quilts. This intervention resulted in a substantial reduction in HDM allergen levels (0.8 μg/g in the active group vs 3.0 μg/g in the control subjects). At the 1-year follow-up, children in the active treatment group had lower levels of HDM-specific IgE (median, <0.35 IU/mL vs 1.8 IU/mL; $P < .05$), lower prevalence of positive skin prick test (SPT) responses to HDM (31% vs 63%, $P < .02$), and lower incidence of wheezing episodes (11% vs 37%, $P < .05$).

A second wave of primary prevention studies have commenced in the last 2 to 3 years in Europe, North America, and Australia. In each of these trials, high-risk infants identified on the basis of a family history of asthma, allergy, or both are enrolled and randomized antenatally. Few outcome data have been reported, and definitive conclusions cannot be expected for 3 or 4 years.

In Vancouver and Winnipeg 493 infants have been enrolled in a study testing a multifaceted environmental intervention. The intervention includes HDM avoidance (encasing parents' and infants' beds, washing bedding in hot water, and removing carpets or using a topical acaricide), avoidance of pets, maintaining a smoke-free indoor environment, and food allergen avoidance. At the 1-year follow-up, the HDM allergen levels were substantially reduced in beds but not floors, and there were significantly less rhinitis symptoms (17.2% vs 26.7%) and a strong tendency for less asthma-like symptoms (13.6% vs 18.5%) in the intervention group compared with control subjects.[74]

The Manchester (UK) study, which enrolled 300 infants, has used a vigorous HDM avoidance intervention.[75] The intervention includes the replacement of carpets with newly fitted smooth flooring in all the infants' bedrooms, encasement of new infant mattresses and parents' beds, washing of all linen in hot water, provision of a vacuum cleaner with a high-efficiency filter, and application of an acaricide to the lounge room floor and furnishings. Very low HDM allergen levels have been achieved in the actively treated beds. No clinical outcomes have been reported.

The Southhampton (UK) trial has enrolled 200 infants. The active HDM avoidance intervention includes encasings for all parental bedding, boil-washing infants' bedding monthly, dehumidification in the parent's room, heat treatment of soft furnishings, application of an aca-

ricide/allergen denaturant to carpets, and use of a high-efficiency vacuum cleaner. Some preliminary data on allergen reductions in a subgroup have been presented.[76]

The Australian study in Sydney involves 600 infants. HDM avoidance procedures in this trial include the application of encasings to the infants' mattresses and washing all bedding in an acaricidal solution at 3-month intervals. In homes in which the infant sleeps in the parents' bed, this bed is treated in a similar manner.

We are aware of another randomized controlled trial of HDM allergen avoidance in the Netherlands (PIAMA), but no data have been presented so far.

Inducing remission and preventing persistence: Secondary interventions

Between 30% and 70% of children with asthma or wheezing illness in childhood enter remission during the transition to adult life.[77-79] It is not known whether any therapeutic interventions can improve the chances of remission.

If allergen exposure is important in the etiology of asthma, it seems probable that it will be involved in its persistence. This hypothesis is supported by a cohort study in Scandinavia in which of 115 children with positive SPT responses to mite allergen, 66 of 67 whose SPT responses became negative over a period of 2.4 years had a level of mite allergens of less than 2 μg/g, whereas 15 of 48 whose SPT responses remained positive had a level of greater than 2 μg/g.[80] Furthermore, in the setting of occupational asthma, continuing exposure to the relevant occupational allergen is associated with a higher risk of persisting asthma (ie, a reduced chance of remission).[81]

The possibility of "curing" allergic disease by environmental modification has important implications for public health practice. It is important that this hypothesis is tested in long-term, randomized, controlled trials in children with asthma that are similar to the primary prevention trials described above.

Reducing disease severity and improving outcomes in persons with asthma: Tertiary interventions

There are 3 groups of studies that support tertiary interventions: a temporary move from a residence with high allergen exposure to one with naturally low exposure; observations in the same residence during seasonal fluctuations of allergen; and observations within a residence during interventions to reduce exposure.

The most dramatic demonstration of the effect of reduction in exposure to allergens is provided by observations in subjects with asthma who have moved to high-altitude environments where allergen exposure levels are very low. This environmental change is consistently associated with improvements in symptoms, lung function, and immunologic markers. Many of these studies have been reviewed by Custovic et al.[10] Additional trials[82] have shown some interesting features, including reductions in bronchial epithelial shedding,[83] rapid reductions in allergen-specific nasal IgE,[84] and improved outcomes achieved by combining avoidance with immunotherapy.[85]

Natural variations in mite allergen exposure also provide an opportunity to study the relation between this exposure and the severity of asthma. In 3 Dutch studies the large seasonal difference in mite allergen levels in mattresses correlated with differences in peak expiratory flow amplitudes,[86] and changes in the levels in carpets correlated with changes in airway hyperresponsiveness.[87,88] Spontaneous changes in HDM allergen levels in the bed were also correlated with the level of airway hyperresponsiveness in adults with asthma living in a high HDM environment.[89]

Uncontrolled studies, such as those cited above, have encouraged the view that avoidance of exposure to allergens may be an effective form of treatment for asthma. This has been extensively investigated in clinical trials.

The plethora of randomized controlled clinical trials (in addition to uncontrolled trials) testing various HDM allergen avoidance strategies as treatment for people with asthma has been extensively reviewed recently.[10,18,90] Unfortunately, the evidence even for randomized controlled trials is seriously flawed because of a number of problems. First, very few researchers have demonstrated that they have successfully reduced allergen exposure in the intervention group, even using the crude measures of reservoir allergen concentrations. Second, some studies are probably too brief to detect changes in clinical outcomes. Finally, there is a limited range of outcome measures that have been selected for evaluation. These problems, together with the complexity and heterogeneity of the interventions, limit the utility of a simple statistical summary of the existing data as presented in the Cochrane Review.[18]

Four randomized, placebo-controlled trials have successfully achieved a difference between active and control arms of the study over a sustained period of follow-up (6 months or longer). These are the most appropriate studies to test the hypothesis that allergen avoidance, when it is achieved, is an effective treatment for asthma.

The first of these studies was conducted for 1 year in Liverpool (UK) from 1983 to 1984 in 50 adult subjects with asthma and strongly positive SPT responses to HDM allergen.[91] The intervention comprised encasing the mattress, weekly washing of bedding, removing carpets, and taking steps to reduce indoor humidity. Mite numbers in bedding were approximately 100-fold lower in the intervention group compared with the control group at each 3-month follow-up during the 12-month study. Despite some confusion of the allergic status and the absence of a formal statistical comparison between active and control groups, there appeared to be benefits in medication use, spirometry, bronchial responsiveness, symptom score, and serum IgE among allergic subjects in the intervention group compared with allergic subjects in the control group.[91]

The next report of a clinical trial in which prolonged HDM allergen avoidance was successfully achieved was from Berlin and was published in 1992.[92] This study of 24 children with asthma and allergy to HDMs (by SPT and RAST) tested 2 interventions. One intervention,

which consisted of treatment of mattresses and carpets with an acaricide (benzyl benzoate), did not result in a significant reduction in mite allergen levels. However, another group of 8 children, who were randomized to an intervention that included encasing mattress and pillows, did experience a significant reduction in allergen levels in bedding when compared with the untreated control group. This was sustained over the 12-month follow-up period. When compared with the control group, the subjects in this successful allergen reduction subgroup experienced a substantial (and statistically significant) reduction in airway hyperresponsiveness. No other clinical outcomes were reported for this study population.

More recently, Carswell et al[93] have reported on the results of a randomized controlled trial of HDM avoidance in Bristol (UK). Subjects were children allergic to HDMs with asthma who had high levels of HDM allergen in their beds (n = 70). The intervention was focused on the child's bedroom and included acaricidal treatment and vacuuming of mattresses, furniture, and carpets; encasing of mattresses; and washing of bed linen weekly in hot water. This treatment resulted in a substantial and significant reduction in HDM allergen levels in the intervention beds compared with the control beds, which was sustained throughout the 6-month study period. There were no significant changes in HDM allergen levels in carpet. This reduction in exposure resulted in an improvement in symptoms and a reduction in medication requirements compared with the control group at the conclusion of the study period. There were no associated changes in lung function or airway hyperresponsiveness.

Finally, van der Heide et al[94] in Groningen (The Netherlands) have compared 3 interventions directed at HDM avoidance in 45 adult patients with asthma allergic to HDMs. Three parallel groups received either only air filtration with a high-efficiency particulate air (HEPA) filter, only mattress and pillow encasings, or both encasings and air filtration. There was no untreated control group. Subjects in the 2 groups that used mattress encasings had a large reduction in HDM allergen content of mattress dust compared with the other group. The group that used both HEPA filters and mattress encasings experienced an improvement in airway hyperresponsiveness at 3 and 6 months of follow-up when compared with the other 2 groups. There were no significant changes in lung function (measured as peak expiratory flow) during the course of the study.

In these small numbers of trials in which the intervention group experienced a sustained reduction in allergen exposure, clinical benefits have been forthcoming. Unfortunately, the range of outcome measures tested in these studies are limited, and we have little information that allows assessment of the importance of these benefits. In particular, there are no data concerning the impact of these interventions on quality of life or on rates of severe exacerbations. There are no existing data that would support an economic analysis. These deficiencies require data from further randomized controlled trials, which should only be conducted when there is a consensus among investigators about the most effective and efficient method of achieving HDM allergen avoidance.

ALLERGEN AVOIDANCE METHODS

A general strategy

A strategic approach is required that has to be able to address the variety of patients, lifestyles, climates, differences in allergens, and the sites of distribution, as well as resources available over time. Only one attempt to compose a synergistic, outcome-driven strategy has been published.[95] Methods of allergen avoidance are presented below in order of their perceived usefulness. Those for mite allergens are discussed first because there is more experience with these, and many of these may be applied to other allergens.

In theory, control of exposure to indoor allergens combines 3 approaches: (1) control of the reservoirs of allergen in beds, carpets, furnishings, and clothing, which are the main source of exposure; (2) control of the sources of new allergen (eg, live mites and residential cats); and (3) direct control of aeroallergens.[14] A combination of effective measures directed at different sites is required.

Best practice for HDM avoidance

Bedding: Definitely useful. The bed is probably the most important site of allergen exposure because of the high level of mite allergen exposure experienced during sleep,[96] the proximity of the subject to the source, the high proportion of indoor time spent at this one site, and the large amounts of dust present in the bed. The relative success and simplicity of interventions directed at this site make it a key target for allergen control.

In trials in which bedding was encased in impermeable covers, long-term, dramatic reductions (15- to 65-fold)[73,75,97,98] in the amount of allergen recovered, as well as reductions in allergen concentration, were shown. In cross-sectional community studies encased bedding has lower allergen levels, but the difference from unencased mattresses is smaller than in the experimental setting.[99] Some encasings are permeable to air, but not allergens,[100,101] and are more comfortable, although expensive. Even semipermeable cotton may be an effective barrier.[102] Encasings should be wiped down each week with a damp cloth to remove any allergen. There can be an initial reluctance to retain encasings depending on the fabric comfort. There is no advantage in treating mattresses with acaricide in addition to encasement.[93]

If the mattress is encased but the other bedding is not treated in some way to control allergen, there may be some reduction in allergen collected from the mattress surface,[42] although levels in the upper bedding may not be reduced in the long term.[103] Unencased mattresses reach high values within 4 months of use.[104]

Pillows can be washed, encased, or replaced frequently. Issues of allergens and pillow type have arisen[105,106] that are mainly of interest in the epidemiologic/biologic context and not in the context of allergen control. Blankets and duvets, if not encased, should be regularly washed (see below).

Laundry: Definitely useful. Mite[107] and cat[108] allergens are quite soluble in water. Laundry can be done in water greater than 130°F[109] or with an acaricide[110] or an emulsion of an essential oil.[111] All of these will kill mites. However, washing at any temperature will wash out most dust and allergen[109] and will achieve a large (>20-fold) reduction in total allergen level. It is not known whether killing mites, in addition to removing allergen, confers any advantage in reduced allergen exposure or delayed reaccumulation of allergen. There may be problems of subject compliance with regular washing of blankets, even in the setting of a clinical trial. We observed that when subjects did their own laundry the mean reduction was approximately half that when laundry was performed by a technician (Vanlaar, unpublished data; 1998). We have preliminary data to suggest that laundry additives (detergents and enzymes) have a small additional effect on allergen removal.

Replacement of fitted carpets with smooth flooring: Probably useful. Carpets serve as a major reservoir of many indoor allergens and may serve as an additional primary source of allergen. On sampling with a vacuum cleaner, carpets yield more dust[42,112] and have a higher allergen concentration than smooth floors.[42,99,112,113] Houses with carpets contain more allergen than those without,[114] and carpets accumulate cat allergen much faster than smooth floors.[45]

There is no effective method to render fitted carpets free of allergen. To achieve large reductions in exposure, carpets need to be replaced, preferably with smooth flooring that can easily be rendered free of allergen by vacuuming and then damp wiping.

The use of the allergen denaturant tannic acid is not practically useful.[115] The quantity of mite allergen increases markedly from the top to the base of the carpet (Philip Bell, unpublished observations; 1994), which explains why surface treatments only have a short-term effect. Loose carpets can be removed and placed in the sun, which kills all mites,[116] and hand washed to remove almost all allergens. A carpet incorporating an acaricide has been released onto the UK market,[117] although no published data to support its use have been cited.

More research is urgently needed both to quantify the behavior of different floor coverings to function as allergen sources and on methods to minimize allergen exposure from carpets. For a number of reasons (eg, cultural, safety, noise, family, and rented accommodation), it is difficult for some people to avoid having carpets. There are virtually no data about the mechanisms by which carpets function as sources for aeroallergens. The only study done on the subject[51] suggests that electrostatic characteristics are more important than reservoir allergen levels. Contrary to commercial information,[118,119] there is no published data to support the claim that carpets are safer and function as a sink by trapping allergens and preventing them from becoming airborne and therefore are preferable to smooth floors. Anecdotally, the market share of carpets in Europe is declining, and a recent Dutch study found houses of children with asthma were less likely to be carpeted than others,[112] presumably indicating an awareness of health effects among consumers. In the Manchester allergen avoidance study,[75] all 150 parents readily agreed to having smooth flooring fitted in the infant's bedrooms (Custovic, personal communication; 1998). This confirms that people are ready to modify their lifestyles given appropriate information and assistance. Perhaps the continued loss of consumer confidence in this floor covering will stimulate efforts to develop a means of achieving urgently needed better hygiene performance from it (see also the section on vacuming and acaracides).

Hard surface cleaning: Probably useful. Allergens accumulate in the patina of dust on all surfaces[120] and contribute to the turnover of aeroallergen. Because this surface area is large, it may be an important exposure source. In some preliminary studies we found that a single wipe with a dry cloth removes about 70% of surface mite and cat allergen, whereas wiping with a moist cloth removes greater than 90% (DeLucca et al, unpublished observations; 1998). It is recommended that surfaces be damp dusted once per week, although this was performed daily in the low-allergen child-care center.[121]

Vacuuming—dry, wet, or steam cleaning: Possibly useful. Dry vacuum cleaners are useful to pick up excess dust and to reduce reservoirs and allergen concentration.[122] Whether this achieves significant reductions in exposure remains to be demonstrated. There are several vacuum cleaners with low particulate emission rates demonstrable under laboratory conditions.[115,123-125] This reduced emission is partly attributed to better filtration by dust bags and filtration systems. However, their use in houses may still increase aeroallergen levels.[123] Wearing a mask and opening the windows during and after cleaning (or getting someone else to do it) is still advised where practical.

Wet vacuum cleaning may offer the advantage of better removal of allergen by washing it out. Although an earlier small study produced 2- to 3-fold greater reductions in allergen concentration compared with dry vacuuming,[126] a recent larger study found no advantage of an acaricidal shampoo compared with control dry vacuuming or plain shampooing.[42]

The use of super-heated steam was shown to kill mites in carpets and reduce allergen (Der p 1) levels.[127,128] Although slow, it does offer significant allergen and mite reduction without chemicals. This form of cleaning requires further study to determine the extent to which it reduces total aeroallergen exposure in a room.

Air filtration, ionizers, and air conditioning: Possibly useful. A recent review concluded "air cleaning alone has not been proved effective at reducing airborne allergen containing particles to levels at which no adverse effects are anticipated."[129] No recent studies have been published, and this subject has previously been reviewed elsewhere.[130,131] For mite allergens, the usual explanation is that exposure is a very local event and that aeroallergens settle quickly after disturbance and are unaffected by an air filter operating at a distance. Frey[132] proposed that aeroallergen particles are strongly influenced

by electrostatic conditions in a room and are difficult to remove by air filtration. For definitive information on air filtration, see the NAFA guide.[133]

Use of air filtration, in combination with encased bedding, had a greater effect on clinical outcomes than use of encasings alone.[94] The subjects with the greatest benefit were those who had carpets and pets and had the largest decrease in mite allergens from encasing their bedding. In this study the large-pore sham filter removed half the amount of the intervention filter, which brings the need for expensive filtration systems into question.

Several studies have indicated that air filtration will reduce the amount of airborne cat allergen by approximately 2- to 4-fold,[45,134] although there is less reduction in the presence of carpets.[45,54] A recent clinical study by Wood et al[134] found that although cat aeroallergen levels were significantly reduced by HEPA filtration, there was no reduction in any index of disease activity compared with controls over 3 months.

Acaricides: Unlikely usefulness. Intervention trials continue to use acaricides, almost always with disappointing results.[93,135-140] It is important that such trials include a placebo control,[93] or otherwise simple dilution of allergen may produce apparent reductions. Although it is likely that a small effect on allergen can be obtained with acaricides in the long term,[72,75] it remains to be established whether this has an effect on allergen exposure sufficient for clinical benefit. The appearance of acaricidal products in spray cans in supermarkets is disturbing. These are unlikely to be clinically effective. Until there are supportive data based on domestic trials, not laboratory tests, patient resources would be better spent on more useful control methods.

Building modification

The ecologic approach to reducing mite exposure, based on reducing indoor humidity to levels where mites are not sustained[141] rather than site-directed hygiene approaches, has been successfully implemented in Denmark.[142,143] However, its utility appears to be limited to climates with sufficiently low absolute humidity in winter and "tight" houses. It has not been so successful in more humid climates.[144-146] Mechanically reducing[147,148] and raising[149] indoor humidity can, in some but not all cases,[150] affect mite allergen levels.

Characteristics of the housing and furnishing stock or individuals' lifestyles can influence mite allergen levels by affecting aspects of mite ecology. Building age, dampness, occupant density, presence of carpet, double glazing, and single or multi-story height have been found to influence levels of allergen.[131] Chew et al[99] recently confirmed that home characteristics were a weak predictor of allergen levels. Although houses had higher mite levels (but lower cockroach levels) than apartments, levels of mite allergen greater than 2 μg/g were found in 16% of apartments, as well as in 32% of uncarpeted floors and 21% of plastic-encased mattresses. Studies of university student residences,[151,152] in which mean allergen levels are greater than 30-fold lower than that of local houses despite ample dust, carpets, and the same local climate, suggest that low-allergen houses may be possible in any climate if the ecologic and building principles are understood and applied.

In an example of an integrated approach, a special child care center consistently achieved 10- to 30-fold reductions in exposure to pet allergens[121] compared with similar institutions. The measures included ventilation systems, regular and extensive cleaning, and avoidance of direct and indirect contact with pets.

Pet allergen control

In many communities almost all houses contain detectable cat and dog allergen.[44,153] The mean level in houses without pets is about 36[99] to 200[10] times lower than that found in houses with pets. This lower level is still sufficient to cause symptoms in some individuals.[44] Cats carry very large amounts of allergen, only a tiny fraction of which becomes airborne,[108] and production varies with the cat and with time.[154] Transfer of allergen from houses to public places,[155] schools,[33,156] and day care centers[34] where there may be no indigenous allergen sources probably occurs by means of clothing.

Effectively treating the reservoirs is difficult (see the sections on laundry and carpet replacement above). Where cat levels in furnishing are high, replacing the items will accelerate the allergen reduction.[157] The optimum strategy to permanently relocate cats is often not taken due to their social role. When cats are removed from rooms, the aeroallergen levels drop by up to 70%,[31] and when they are removed permanently from houses, the levels in reservoirs decline slowly over months[157] and years.[153] If pets cannot be relocated, the next best option is to keep them out of bedrooms and isolated to rooms with hard surfaces (eg, kitchens) from which the allergen can be removed and to use regular washing for rugs on which pets lie.

The combined strategy of washing the cat, washing hard flooring, and increasing air filtration[45] has been advocated, although it remains controversial.[158] Washing achieves a large and immediate reduction in aeroallergen shedding,[108] but the effect appears to be limited to less than a week.[159] Treatment of cats with drugs or emollients is not effective.[159] A combined strategy that included air filtration achieved reductions in aeroallergen levels, but this was not associated with any significant clinical benefit.[134] A further study obtained a greater than 90% reduction in allergen by using encasement, weekly washing of cat and bedding (separately), and carpet removal,[160] and it was found that environmental control plus inhaled steroids was more clinically effective than either alone.[161]

Other indoor allergens

Cockroaches. Cockroach allergy, combined with high exposure, continues to be strongly associated with asthma risk in some studies of inner-city populations in the US and elsewhere.[27-30,58] Exposure is also associated with accelerated age-related decline in FEV_1.[162] Cockroach allergens are widely distributed in reservoir dust and are highest in kitchens.[163] Methods for decreasing

exposure are still not well established and aim to reduce the populations of cockroaches through control of sources of food and water plus routine cleaning and use of the insecticides hydramethylnon or avermectin.[163]

Fungi. Allergy to *Alternaria* spp is a major environmental risk for asthma in some arid climates.[24-26] However, the extent to which exposure occurs indoors, and is therefore potentially avoidable, is unclear. An association between daily symptoms and spore counts has been shown,[25] although other studies suggest cumulative indoor exposure is sufficient to be significant.[164,165]

There are numerous indoor sources of fungi, particularly in damp buildings. However, establishing the strength of the independent association of indoor fungal exposure to asthma symptoms without confounding by endotoxin or mite exposure has been more difficult.[166] Verhoeff and Burge[167] reviewed the relationship between allergy and domestic fungi in 9 population-based studies, and although positive associations were confirmed, they concluded it was impossible to set guidelines because of inconsistencies and inadequacies in exposure and outcome measures. Avoidance methods for indoor fungi remain focused on preventing the ingress of outdoor fungi into buildings, maintaining a dry indoor environment, and adopting domestic hygiene measures.[168]

Future research

There is strong evidence that allergen exposure is an important factor in the etiology of asthma and in determining the severity of the disease. Existing data support the role of allergen avoidance as a component of both asthma prevention and management strategies. However, many questions remain. The following provides directions for future research.

One group of clinical questions involves the identification and characterization of patients who will (or will not) benefit. For primary prevention, what interventions should be applied to high-risk (and low-risk) groups? How and when should these people be identified? Should measures be instituted antenatally or during infancy, and should they be continued into childhood? Is the effectiveness of aeroallergen avoidance modified by diet (either lipid-type or avoiding food allergens) or by other environmental factors? It is anticipated that significant progress in answering these questions will come from the intervention trials presently in progress (see above). Such studies should enable cost-benefit estimations to be made for populations.

Some information about the role of environmental factors in inducing remissions of asthma is likely to be obtained from several current longitudinal studies, but no secondary intervention studies are known to be in progress.

Targets for tertiary interventions range from children with transient wheezing illness to adults with brittle[169] or steroid-dependant[170] asthma. The dose-response relationship, the extent of reductions in exposure required, individual differences, and expected benefits and risks are all unclear. Although valuable information will come from further high-altitude studies, these are mainly confined to children. Further data on the effects of profound reduction in allergen exposure on a diverse range of subjects is needed. Although there are numerous population studies of increased asthma prevalence or symptoms that are associated with a deterioration of environmental factors, there are no similar population studies of reducing prevalence with an improved environment (eg, population migration/resettlement/transition to college accommodation).

A second group of questions involve allergen control methods. These are enormously important because it is likely that many current strategies may not be effective at reducing total indoor exposure, particularly if only applied to limited sites. It is important that avoidance strategies are well characterized, can be implemented, and are validated before embarking on large resource-intensive clinical interventions. Multifaceted approaches[74,75,121] are necessary. More information about the relative contribution of individual sites to personal exposure is needed to target intervention resources. The development of aesthetic and comfortable houses with lower mite allergen production that are structured for better removal of all allergens and better control of aeroallergen will require the collaboration of hygienists, designers, sociologists, and engineers. Mite population biologists, better acaricides (possibly including pheromones), and an understanding of aeroallergen generation and dispersal from all surfaces will also be needed. This is a major public health issue; unfortunately disproportionate public resources are dedicated to outdoor air quality, and the area of indoor air quality relating to allergens has received too little attention and has been vulnerable to commercial exploitation.

The third group of future issues involves allergen exposure. It seems almost counterintuitive that subjects are expected to apply and to maintain rigorous allergen avoidance procedures only on the basis of allergy tests or diagnoses but without any knowledge of their personal allergen levels and the risks. Some simple, publicly accessible allergen measurement technologies are being developed.[171,172] Their impact on management needs to be evaluated. The second, more esoteric issue, is the description of "exposure" itself in a form relevant to clinical risk and avoidance. A role for measurements in reservoirs (per weight and per area) and in aeroallergens (per volume and settling per time and area) will remain. However, the use of other indices, such as aeroallergen collected after a standardized domestic disturbance of dust as an indicator of the potential of an environment to provide exposure, seem worth exploring. The biologic significance of this exposure measurement might be further enhanced by detecting allergens with the subject's own IgE. Other matters, such as particle size ($< \text{or} > 5\ \mu m$) and accommodating the varying exposure with time, still need to be addressed.

Additional issues occur from a wider social context. Should any avoidance methods be reimbursed by health care funds? Is consumer protection legislation sufficient to prevent exploitation? Is it possible or desirable to set standards for indoor allergen exposure in public building and houses? Should building standards include consider-

ation of indoor allergen exposure? How can the cost-benefit analyses of environmental control be calculated and validated? These environmental issues will soon appear on the agendas of health and social planners. Scientists and physicians need to be prepared to provide information for this planning process.

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