Asthma diagnosis and treatment

Perspectives in asthma

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Allergen avoidance in asthma: What do we do now?

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Although allergen exposure can clearly aggravate the condition of sensitized patients with asthma, there is uncertainty and controversy about exactly which allergen avoidance interventions should be recommended to patients with asthma. Interventions that appear logical may fail to be clinically efficacious for several reasons. Although narrow interventions, such as allergen-impermeable mattress covers to reduce exposure to dust mite allergens, may offer little benefit if used alone, recent evidence suggests that a multifaceted, home-based environmental intervention focusing on multiple exposures may provide clinical benefits to patients with asthma. The role of allergen avoidance in infancy in the primary prevention of asthma is a subject of active investigation, but data remain too preliminary to make public health recommendations in this regard. (J Allergy Clin Immunol 2005;116:26-30.)

Key words: *Asthma, allergen avoidance, environmental control measures, dust mites, cockroach allergen, pet allergen*

Abbreviations used
HEPA: High-efficiency particle arrest
RCT: Randomized, controlled trial

In 1925, twenty years after von Pirquet coined the term *allergy* and Wolff-Eisner demonstrated a link between asthma and hypersensitivity, Storm van Leeuwen[1] proposed enclosing patients with asthma in an allergen-proof chamber or moving them to high altitude to reduce allergen exposure. Eighty years later, after clinical trials of these and other allergen avoidance interventions, there remains substantial uncertainty and controversy concerning which interventions should be recommended to patients with asthma.

The rationale for allergen avoidance by atopic patients with asthma is clear. Asthma is strongly associated with allergy to common aeroallergens, and asthma exacerbations can be provoked by natural and experimental allergen exposures. In addition, some studies have revealed that among patients with asthma sensitized to a particular allergen, asthma morbidity is directly related to the degree of exposure to that allergen.[2,3] Furthermore, asthma brought on or aggravated by occupational exposure to laboratory animals can greatly improve or even resolve entirely when exposure to the offending source of allergen ceases. Most clinicians can recall a patient whose asthma essentially resolved after finding a new home for a pet cat.

With such a clear rationale, why might specific allergen avoidance interventions fail to provide health benefits to patients with asthma? A given intervention could fail for several reasons. First, it may simply fail to reduce exposure or may not reduce it sufficiently to prevent allergic airway responses. Second, an intervention might be applied to patients who are not sensitized and/or exposed to the allergen targeted. Third, an intervention might reduce exposure in one location but not others (eg, bedroom but not living room, home but not school), permitting sufficient residual exposure to aggravate asthma. Finally, an intervention might reduce exposure to one offending allergen while failing to reduce exposure to other allergens or other environmental factors that aggravate asthma.

CLINICAL TRIALS OF NARROWLY FOCUSED ALLERGEN AVOIDANCE INTERVENTIONS

Dust mite allergens, which play an important role in causing and aggravating asthma in many parts of the world, have been a major focus of trials of allergen avoidance in asthma. The strategies proposed by Storm van Leeuwen in 1925, ie, living in an allergen-free room (in the hospital) and moving to high altitude, have both been studied as means of reducing mite allergen exposure among patients with asthma allergic to mite, with

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reportedly beneficial effects.[4,5] Most studies of mite allergen avoidance, however, have examined the health effect of interventions that are feasible in the patient's own home.

Among the available mite allergen avoidance interventions, encasement of the mattress and pillows in allergen-impermeable covers combined with frequent hot water washing of bedding is the approach offering the best combination of practicality and effectiveness in reducing allergen exposure in the bedroom. Substantial uncertainty exists, however, about whether these measures contribute to improved asthma control among patients with asthma allergic to mite.[6] Recent meta-analyses of published trials reached the conclusion that there were no statistically significant benefits of dust mite avoidance interventions for patients with asthma.[7,8] The conclusion that dust mite avoidance measures should not be recommended,[7,8] however, is not shared by all experts.[9] The restriction of meta-analyses to studies of narrowly focused interventions with sham interventions that permit subjects to be blinded may select for studies in which the difference in allergen exposure between intervention and control groups is limited.

Some of the limitations of the interventions tested in many trials of dust mite avoidance are illustrated by a recent well designed randomized controlled trial (RCT) of allergen-impermeable mattress and pillow covers among patients with asthma in the United Kingdom.[10] The intervention tested included only the encasement of beds. The intervention, which was not targeted specifically to patients with documented dust mite allergy, did not include education about environmental control measures, and exposure to pets and tobacco smoke, which was common in the patients in the study, was not addressed. This report is consistent with others in indicating that mattress and pillow encasement alone has little effect on asthma control, but it does not address the potential benefits of a more comprehensive environmental control program—including allergen-impermeable mattress covers as one component—guided by specific sensitization testing, as recommended in recent asthma management guidelines.[11]

Allergen avoidance has been less often studied for other indoor allergens. Avoidance of cockroach allergen was a focus of several intervention studies,[12-14] but reductions in allergen levels were not obtained or were modest, and clinical benefits were not seen in the trials with clinical outcomes.[12,13] A recent study[15] of an intensive, 6-month extermination and cleaning intervention has shown that substantial reductions in cockroach allergen levels can be obtained in infested apartments, but that particular study did not assess clinical outcomes. Mold exposure can aggravate the asthma of sensitized persons, and case reports of the clinical benefits of eliminating indoor exposure in such cases have been described. The potential clinical effect of interventions to reduce indoor, residential exposure to fungi, however, has not been evaluated in clinical trials.

Although a RCT to test the efficacy of removing pets from the homes of patients with asthma allergic to pets has not been conducted, anecdotal experience and common sense provide sufficient rationale for the recommendation that patients with asthma with documented pet allergy find a new home for their pet. Many patients with asthma, however, continue to live with pets despite such recommendations. Two small RCTs of air filtration to reduce exposure to airborne pet allergen, one with[16] and one without[17] the addition of allergen-impermeable mattress and pillow covers, failed to document clinical benefits of this intervention among patients with asthma allergic to pets. Although high-efficiency particle arrest (HEPA) filters and HEPA filter vacuum cleaners can be shown to reduce environmental levels of pet-derived allergens in indoor environments effectively, there are no convincing data that environmental control measures can reduce asthma morbidity to acceptable levels in patients with pet-allergic asthma who continue to live with a pet to which they are allergic.

The clinical benefits of HEPA filtration units have also been evaluated by some relatively small trials among patients with asthma who were not selected on the basis of pet allergy. A recent meta-analysis of these trials[18] revealed some evidence that HEPA filtration reduces asthma symptoms and sleep disturbance, but other clinical outcomes were not affected, and there was substantial heterogeneity of benefit among the different trials. HEPA filtration may reduce exposure to a variety of airborne allergens as well as environmental tobacco smoke and other particulate air pollution, and published studies have not elucidated which specific exposure reductions were responsible for the clinical benefits observed.

CLINICAL TRIALS OF MULTIFACETED ENVIRONMENTAL CONTROL INTERVENTIONS

Many patients with asthma are exposed to multiple aeroallergens to which they are sensitive, along with other harmful inhalants such as tobacco smoke, in their home environments. It is logical to expect that reducing exposure to one of these environmental factors while leaving the others unabated may have limited effect on asthma control. This logic underlies current environmental control recommendations[11] and provides the rationale for trials of multifaceted environmental interventions for patients with asthma.

One such trial was the recently reported Inner-City Asthma Study,[19] which evaluated a home-based, multifaceted environmental intervention for urban children 5 to 12 years old with moderate to severe atopic asthma. Of more than 1000 children with asthma screened for this trial, only 6% were excluded for lack of at least 1 positive allergy skin test result to an indoor allergen. Many of the 937 children included in the trial were sensitized to multiple indoor allergens, and cockroach infestation, dampness, pets, and environmental tobacco smoke were commonly present in the children's homes.

The year-long intervention evaluated in the Inner-City Asthma Study trial, which was tailored to each child's

allergy skin test profile and to the environmental conditions in the home, included education of the child's caretaker about environmental aspects of asthma along with the provision of equipment, supplies, and services to reduce exposure to indoor allergens and environmental tobacco smoke. All children in the intervention group received allergen-impermeable covers for mattress, box spring, and pillows, and all families were given a HEPA vacuum cleaner and educated to use it regularly. Most intervention group families were given a HEPA filtration unit to run in the child's bedroom, and many families were provided with professional cockroach extermination services. Compared with the control group, the intervention group had significant reductions in asthma symptoms, school absences because of asthma, and unscheduled clinic or emergency visits for asthma, reductions that were observed both during the intervention year and for an additional year after the intervention ended. The intervention had no significant effect on pulmonary function or asthma hospitalizations. Among children in the intervention group, reductions in asthma morbidity were correlated with reductions in the levels of cockroach and dust mite allergens. The multifaceted design of the intervention, however, makes it impossible to determine the degree to which specific intervention components contributed to the benefits observed.

Another trial of a multifaceted, home-based environmental intervention for children with asthma in low-income families has recently been completed in King County, Washington. A high-intensity intervention that included extensive education, support for behavior change, referral to smoking cessation counseling, supplies, and equipment such as mattress covers and a low-emission vacuum cleaner led to a reduction in asthma-related urgent health services and improved quality of life of the asthma caregiver, compared with a low-intensity environmental intervention group.[20] Preliminary results from a trial of a multifaceted environmental intervention among children with asthma in inner-city Baltimore also indicate significant clinical benefits.[21]

ALLERGEN AVOIDANCE IN THE PRIMARY PREVENTION OF ASTHMA

Observational epidemiologic studies linking the occurrence of asthma to exposure to indoor allergens, such as dust mite and cockroach allergens, have led to the hypothesis that reducing such exposure in early life might offer a means of preventing the development of asthma. This hypothesis is complicated by issues including the induction of immune tolerance with repeated allergen exposure and the fact that some sources of allergen, such as pets, may also be sources of endotoxin, exposure to which may protect against the development of asthma.[22]

Several primary prevention trials, focusing on infants at high risk of asthma and allergy because of parental history, have been reported at various stages of follow-up. All of the interventions studied in these trials have included dust mite avoidance with impermeable mattress covers,[23-28] and some have also included reduction in other allergens,[24,28] reduction in environmental tobacco smoke,[24] avoidance of food allergens in early infancy,[23-25] or supplementation with omega-3 fatty acid.[26] Clinical outcomes in these trials have so far been examined at follow-up periods ranging from 1 to 8 years, and results are mixed. Some but not all of these studies have observed intervention-related reductions in wheeze,[23,24] asthma,[24] atopy,[23,25] and mite sensitization.[25,26]

Further follow-up and analysis of these clinical trials will lead to important insights into whether it is possible and feasible to prevent the development of asthma by identifying high-risk infants before they are born and instituting environmental control measures in early infancy. Currently available data suggest that an environmental control program with the goal of primary prevention may need to be multifaceted, including avoidance of inhalant allergens, food allergens, and possibly tobacco smoke. Successful primary prevention may also be enhanced by exposure of infants to endotoxin, or substances with similar immune effects, to help prevent the development of atopy.

ALLERGEN AVOIDANCE RECOMMENDATIONS FOR PATIENTS WITH ASTHMA IN 2005

Further research clearly is needed to resolve the many remaining questions about environmental control measures for asthma. In the meantime, however, clinicians must give recommendations to their patients on the basis of the best information currently available. The following recommendations (summarized in Table I) reflect my own synthesis of what should be recommended to patients with asthma at this time.

1. Although not directly related to allergens, no environmental control recommendations should fail to include the importance of avoiding active tobacco smoking and passive exposure to environmental smoke. Tobacco smoke aggravates existing asthma and is probably a risk factor for the development of childhood asthma.
2. Patients with persistent asthma should undergo assessment for hypersensitivity to aeroallergens by skin testing or serum specific IgE determination by RAST, and allergen avoidance recommendations should be guided by the specific profile of hypersensitivity.
3. Many patients with asthma are allergic to more than one aeroallergen, and avoidance recommendations should deal with all allergens to which a patient is sensitized and definitely or probably exposed. The cornerstone of allergen avoidance activities should be the education of the patient about the role of allergens in asthma and how to reduce exposure to *all* relevant allergens in the home and other environments. Allergen-specific recommendations should include the following:
   a. Pets: Find a new home for the pet(s), followed by scrupulous cleaning of the home after the pet's departure. Patients who cannot or will not remove

TABLE I. Summary of environmental control recommendations for patients with asthma

Exposure	Recommended control measure
Tobacco smoke	• No active smoking by patient • No smoking by anyone else in home • If smoking by others not under patient's control, HEPA filtration is logical
Allergens, general	• Document specific sensitization profile by skin testing or RAST • Allergen avoidance recommendations should deal with *all* relevant allergies • If available, consider home-based intervention by trained staff
Specific allergens	
Pets	• Removal of pet • If removal impossible, logical steps include exclusion of pet from bedroom, HEPA filtration, HEPA vacuuming, allergen-impermeable mattress covers
Cockroach	• Ideally, move to cockroach-free home • If moving not possible, recommend integrated pest management, professional pest control, careful home cleaning, allergen-impermeable mattress covers
Mold	• Move out of damp and visibly moldy home • If impossible to move from such a home, it is logical to fix leaks, use dehumidifier, remove carpets, wash moldy surfaces with weak bleach solution, use HEPA filtration
Dust mite	• Allergen-impermeable mattress and pillow covers • Wash bedding in hot water • Reduce indoor dampness and humidity • Educate to avoid close exposure to carpets and upholstered furniture
Seasonal pollen and outdoor mold	• Air conditioning or other air filtration systems to keep outdoor allergens out of home are logical • Avoid locations likely to have high levels of seasonal outdoor allergens, eg, fields, woods

the pet from the home should be educated that, although there is no clinical trial evidence that environmental control measures will improve asthma control with the pet still in residence, it is possible that their condition could be helped by a multifaceted approach including banishing the pet from the bedroom, allergy-proof mattress and pillow covers with frequent cleaning of bedding, HEPA filtration, HEPA vacuum cleaning, and avoiding direct contact with the pet.

b. Cockroach: Ideally, the patient should move to a home that is free of infestation, but this is often impossible for the low-income families most often affected. A multifaceted intervention involving education (including integrated pest management), professional pest control (including baited gel insecticide rather than sprays), careful home cleaning including vacuuming, and encasement of mattress and pillow in impermeable covers should be recommended, with the understanding that there is some evidence of clinical efficacy but that further studies are needed.

c. Mold: Mold-sensitive patients who live in damp and visibly moldy homes should be advised to seek alternative housing that is free of dampness and mold. If this is not possible, there is certainly a sound rationale for recommending measures to reduce dampness (fixing leaks and dehumidification), removal of carpets, washing moldy surfaces with a weak bleach solution, and HEPA filtration to filter mold spores from the indoor air. There are no clinical trials, however, that address the health benefits of such interventions for mold remediation.

d. Dust mite: Although allergen-impermeable mattress and pillow covers alone appear not to offer clinical benefits, it remains quite possible that a more multifaceted strategy that reduces exposure to dust mites (including avoidance education and allergen-impermeable mattress and pillow covers) and other allergens and irritants may provide clinical benefits.

e. Seasonal pollens or outdoor molds: It is logical to recommend that air conditioning or other filtration systems be used to keep airborne particles bearing these allergens out of the home. Avoiding outdoor environments likely to have high levels of seasonal pollen, such as fields or woods, is logical if the clinical history and allergy test results indicate which seasons and environments are likely to be problematic.

4. Allergen avoidance strategies that involve home-based, multifaceted environmental interventions

conducted by trained staff may be more likely to yield clinical benefits than simple advice given in the doctor's office, and health insurance organizations should consider coverage for such interventions.

5. These recommendations are directed to patients with existing asthma. Allergen avoidance for the primary prevention of asthma among infants and children without asthma is an active area of research, and findings remain too preliminary to make public health recommendations at this time.

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