



Control of environmental allergens as a therapeutic approach

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Guidelines from the National Asthma Education and Prevention Program include avoidance of environmental triggers among the other principles of good asthma treatment [1,2]: use of objective outcome measures of lung function, comprehensive pharmacologic therapy, and patient education. The evidence on which these recommendations are based has been summarized in several reviews [3–6]. The most comprehensive assessment of evidence can be found in an Institute of Medicine report entitled “Clearing the Air” that critically assessed experimental evidence supporting the role of environmental control in asthma. The report concluded that the evidence of the effectiveness of avoidance measures of house dust mites in the management of asthma was sufficiently strong and that these measures “should be part of normal management of asthma in mite-allergic individuals” [6]. This article summarizes the generally accepted recommendations [3] and the data supporting them.

The first rule of environmental allergen control is that avoidance is appropriate for allergic patients with asthma. Although this rule is obvious to allergists, it frequently is not considered by families and physicians who are not trained in allergy. For allergists who present suggestions to such individuals, it should be noted that these measures will not benefit the 10% to 30% of children and 50% of adults with asthma who have no evidence of allergy. The next step in environmental avoidance is to determine the specific sensitivity of a patient—removing a cat does not help a person who is allergic to house dust mite. Most of the methods that are discussed in this article are targeted to a single allergen. Because more than half of allergic asthmatics have multiple sensitivities, it is remarkable that clinical trials have shown that treatment of a single allergen improves symptoms, despite exposure to other allergens. Clinically, practitioners have to address reduction of

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exposure to more than one allergen, and it is likely that the complexity of dealing with several treatment regimes decreases compliance.

Avoidance also involves estimation of exposure in terms of intensity and location (Table 1). This step involves a taking a history, inspecting the home, and measuring environmental allergens. Estimation of exposure is more difficult than previously believed. The distribution of house dust mite allergens varies widely (> 1000-fold) among different homes [4,7]. The highest concentrations are found in the bedroom, especially in the bed, but concentrations vary widely at each site. Increased moisture is associated with higher allergen levels, and mite levels are higher in damp houses and basement bedrooms [58]. Allergen levels are higher in summer than in winter [8] and can be reduced with dehumidifiers [9–11]. Chew and colleagues found that dust mite allergen in bedding was higher in houses than in apartments (odds ratio, 2.6), and allergen was lower in beds when an impervious cover was used (odds ratio, 0.5) [12]. Floor dust allergen was higher in carpeted homes, especially with shag carpets (odds ratio, 2.2). Other investigators [13] also found that the age of a home was not a predictor of mite allergen levels [9].

Cat and dog allergen is more than 100-fold higher in homes with pets than in homes without pets [7,14,15]. Levels among homes can vary by 1000 fold and are frequently high in homes with no current pet. Pet allergen also can be found in public buildings that have never housed a pet [7]. Even cockroach allergen may be found in homes with no history of cockroach infestation [58]. In the studies by Chew et al, levels of cockroach allergen were higher in the summer and with the use of boric acid, an ineffective insecticide that probably was used when infestation was obvious.

Home inspection is not practical in most cases, and in epidemiologic studies, it has not predicted allergen levels in the home with much certainty. Inspections should involve measurement of allergen levels in samples of settled dust; such tests can be done commercially in laboratories (Table 2), most of which also mail a collection kit to consumers and provide allergen assays to patients. Do-it-

Table 1
Predictors of high allergen exposure

Allergen	Predictor
House dust mite ^a	Damp houses
	Houses (rather than apartments)
	Basements
	Carpets
	Summer, fall seasons
Cat, dog	No impervious mattress cover
	Current or past pet ownership
Cockroach ^b	Infestation
	Boric acid use
	Summer season

^a Age of house and clutter are not predictors.

^b Age of house and socioeconomic status are not predictors.

Table 2

Resources for allergen measurement in home dust

Laboratory	Website	Telephone number
IBT Reference Laboratory	http://www.ibtrefflab.com	913-492-7145
Indoor Biotechnology, Charlottesville, VA; United Kingdom	http://www.inbio.com	434-984-2709
Aerotech Labs, Phoenix, AZ	http://www.aerotechlabs.com	800-651-4802
Air Quality Sciences, Atlanta	http://www.aqs.com	770-933-0638
Pure Air Control Services, Clearwater, FL	http://www.pureaircontrols.com	800-422-7873
Health Home Air, Kings Mills, OH	http://www.healthyhomeair.com	800-789-0050
DACI Reference Lab, Baltimore, MD	http://www.hopkins-allergy.org/services/daci.html	800-344-3224

yourself allergen detection kits have been developed to help patients assess their exposure (Table 3).

Avoidance of house dust mite allergen

House dust mite allergen first was identified in 1967; since then, a much better understanding of this allergen and methods to reduce exposure have been developed [11]. Beds most often contain this allergen, and large particles are responsible for most of the allergenic activity; therefore, exposure requires close contact with the allergen. Bedding is a logical target for interventions. Vacuuming the floor has not proved to be effective in reducing exposure, and treatment of bedding and rugs with acaricide or tannic acid is also ineffective. Encasing mattress and pillows with materials that exclude small, allergen-containing particles has been shown to be effective and usually reduces allergen concentration by at least 50%. Washing the bedding also has shown to be helpful if coupled with an encased mattress and pillow. Studies show dramatic clinical improvement when asthmatic patients moved to residential care centers in the mountains [19] or into hospitals [20] where mite allergen exposure is very low. These studies also establish an important principal in the effects of allergen avoidance on asthma. Despite almost complete elimination of exposure, disease changes occurred gradually, with significant changes only seen after at least 1 month. In homes, it is impossible to achieve this level of allergen avoidance, and changes are more gradual. When evaluating these trials, data on the degree of exposure reduction should be examined critically. To date, only 32 publications of clinical trial data

Table 3

Home kits for measurement of dust allergens

Kit	Website	Telephone number
Allergen Alert	http://www.stopallergen.com	800-789-0050
Mitest	http://www.inbio.com	434-984-2709
Dustscreen	http://www.inbio.com	434-984-2304
Acloctest	http://www.naturalsolution1.com/dust	847-577-7000

Table 4

Recommended interventions for house dust mites

Type	Intervention
First line (simple or proven effective)	Intall mattress and pillow covers
	Wash bedding weekly
	Vacuum carpets frequently
	Remove stuffed animals, pillows from bed
	Get the bedroom out of the basement
Second line (difficult or unproven)	Dehumidify acaracides
	Remove carpeting
	Replace draperies
	Replace fabric furniture

have appeared, and not all these studies have included measurements of allergen to demonstrate that exposure had changed. Based on the degree of exposure reduction that could be achieved in these trials and the effect on disease activity, recommendations for avoidance of house dust mites can be categorized as first- or second-line measures (Table 4). First-line measures are consistently effective and are feasible, and second-line measures have inconsistent effects and may be difficult to implement.

Allergen-proof encasings for the mattress and pillow are the most effective interventions [11]. Much progress has been made in materials, and these products are breathable, comfortable, and nearly 100% exclusive [21]. Twelve clinical trials have been published that include allergen-proof encasings, seven of which demonstrate a reduction in levels of dust mite allergen and a clinical effect [22–28]. A number of the unsuccessful trials had methodologic problems, such as short duration or no estimation of exposure, but one of the most successful trials [29] also had these problems. Five trials are summarized (Table 5). The

Table 5

Results of clinical trials of house dust mite reduction

Authors	Time (y)	Intervention	N	Decrease in mites ^a	Primary outcome
Walshaw and Evans [23]	1	Covers	18 of 20	++	Syx ^b , medications ^c , FEV1 ^c , PEFR ^b , BHR ^c
Ehnert et al [22]	1	Covers, acaracide	8 of 16	++	BHR ^b
Carswell et al [24]	0.5	Covers, acaracide, washing, vacuuming	24 of 25	++	Syx ^b , meds ^b , FEV1, BHR ^b
Van der Heide et al [50]	1	Covers, acaracide	21/19/19	++	FEV1, BHR ^c
Shapiro et al [26]	1	Covers, laundry, tannic acid	18 of 18	+	FEV1, BHR ^c
Htut et al [27]	1	Steam cleaning, hot air, filters	7/8/8	++	BHR ^c

Abbreviations: BHR, bronchial hyperresponsiveness; Syx, symptoms.

^a ++, >80% reduction; +, 30 to 50% reduction.

^b highly significant ($P < 0.01$).

^c Significant ($p < 0.05$).

most consistent physiologic outcome is a reduction in bronchial hyperresponsiveness, and most trials show improved clinical outcomes.

Walshaw and Evans achieved a 99% reduction in mite numbers with the use of encasings and found clinically important reductions in symptoms, medication use, morning peak expiratory flow rate (PEFR), and histamine inhalation challenge during the course of the year-long experiment [23]. Carswell and colleagues tested the use of mattress and pillow encasings and frequent professional laundering [24]. Levels of dust mite allergen in bedding were low at baseline, and decreased by an additional 90% in the intervention group. Although the intervention group experienced a reduction in chest symptoms and a comparable degree of decrease in bronchodilator requirement, these changes were of marginal significance. There was twofold improvement in bronchial hyperresponsiveness. Although Carswell et al concluded that treatment had a modest effect, these responses compare favorably with responses to treatment with low-dose inhaled corticosteroids or with leukotriene modifiers. Busse and co-workers compared treatment with fluticasone (88 $\mu\text{g}/\text{d}$) and montelukast (10 mg/d) in adult asthmatics and found that symptoms scores were reduced by 52% and 36%, respectively, and that β -adrenergic use was reduced by 61% and 56%, respectively [30]. In the study by Walshaw and Evans, symptom scores were decreased by 69%, and β -adrenergic use was reduced by 67%. The outcomes of the two trials that included asthmatic adults are summarized (Fig. 1). Shapiro et al found that 200- $\mu\text{g}/\text{d}$ budesonide decreased symptom scores by 6% in school-aged children and decreased β -adrenergic use by 28% [31]. These figures compare with those from the study by Carswell et al, in which the number of children in the actively treated group who reported symptoms was reduced by 63%, and the number who required β -adrenergic use was reduced by 72%. Successful dust mite

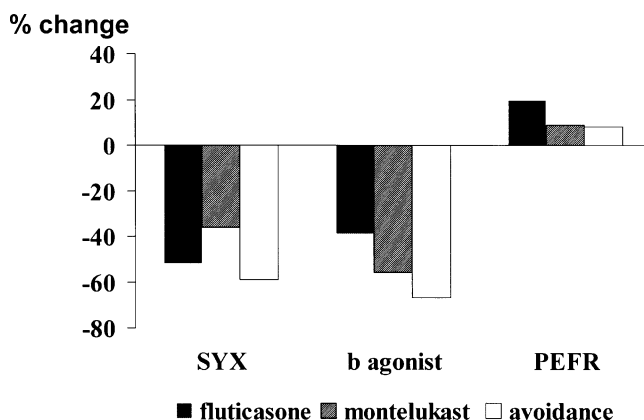


Fig. 1. Comparison of changes from baseline in symptom scores (SYX), β -agonist use, and morning PEFs in two clinical trials. Fluticasone (shaded bars) and montelukast (striped bars) treatment was reported by Busse et al [30], and avoidance (open bars) was reported by Washaw and Evans [23].

intervention can produce clinical improvement comparable with the improvement seen with pharmacologic treatment for mild-to-moderate asthma.

Other first-line measures include thorough vacuuming, which removes bulk dust without changing the concentration of allergen in each milligram of dust; and washing all bedding (sheets, blankets, comforters, bedspreads) in warm water with detergent using 8- to 10-minute cycles, which removes virtually all mite and animal allergens [32] but must be repeated weekly. At least weekly washing of sheets, pillowcases, blankets, and mattress pads in hot water (55°C [130°F]) kills mites and removes most allergen, but this method presents a scalding risk in homes with children, so it may not be practical. Dry cleaning [33] and prolonged tumble drying [34] effectively kills mites, but is less effective at destroying allergens. Vacuuming reduces the bulk of household dust and reduces the overall burden, although it does not change the concentration of allergen per gram of settled dust [35], and low-pile carpeting retains less dust mite allergen [36]. Second-line measures include relocating the bedroom, application of acaricides such as benzyl benzoate, dehumidification, and removal of wall-to-wall carpeting. Relocating the bedroom from the basement or ground floor can help [11], because carpeted slab floors have higher mite infestations. Acaricides are effective in the laboratory, but field trials generally have found that dust mite allergen in carpets is reduced minimally, probably because it is difficult to get acaricides into the deepest areas of the carpet [37,38]. Removing other fabrics from rooms (eg, carpets, curtains, furniture) has been shown to produce minimal changes in levels of settled dust allergens and bedding allergens. Steam cleaning may reduce mite allergen levels in carpets and may reduce levels enough in beds to affect asthma morbidity [21]. The evidence supporting the use of dehumidification is conflicting. Trials in England failed to reduce settled dust allergen levels [10], but a well-done study in the United States [9] achieved significant reduction.

Avoidance of animal allergens

Animal allergens are carried on particles that range from less than 1 μm to greater than 20 μm in mean aerodynamic diameter [14,39]. At least 15% of airborne cat allergen is carried on particles that are less than 5 μm in size. Because the particles are airborne, room air filters should help reduce exposure [40]. The particles seem to be sticky, leading to widespread distribution in homes, where they may be found on walls and other surfaces, and on clothing. This stickiness is believed to be responsible for the finding that animal allergen can be found in homes without pets and in public buildings, such as schools [15,17,18]. Concentrations of the allergen in settled dust and in air are 10 to 1000 times higher in homes with a pet [16].

Studies in Swedish schools have provided tests of the importance of this distribution. Munir and colleagues first reported that substantial levels of cat and dog allergens were present in dust from schools, that the levels were higher in children's desks than on the floor, and that rooms with many pet owners had the

highest levels [41]. These findings suggest that the allergen was brought to the school on children's clothes [40]. Almqvist and co-workers sampled air and found the same relationship; they demonstrated that the airborne levels were highest around the desks of children with pets at home [16]. These investigators gave children with and without pets new T-shirts at home and demonstrated that the shirts of the children who owned cats arrived at school with high levels of cat allergen. The shirts of the children without pets had negligible levels of cat allergen when they came to school, but by the time they left, levels were nearly 100 times higher than the earlier levels [16]. Almqvist examined children as they returned to school from summer vacation [42]. Children who were sensitized to cats but did not live with cats in their homes had increased respiratory problems (low PEFR, more symptoms, more β -agonist use, more steroid use) when they returned to a school in which more than 18% of their class were cat owners (odds ratio, 9.4; $P < 0.05$). These studies demonstrate the difficulty of pet allergen avoidance in a society where many families have pets and where accidental and undetected exposure may occur. They also demonstrate the futility of trying to reduce home exposure significantly while the pet is still in the home. Many patients with asthma and sensitivity to cats or dogs experience a more severe form of the disease because of continuous, ongoing exposure to a family pet. According to these studies, many patients also may have significant cat and dog exposure of which they are not aware. It is likely that animal allergens are important causes of chronic airway inflammation, even in patients without known exposure. Further study will be needed to clarify this issue.

Asthmatic patients who are sensitized to cat or dog allergens should not live with a pet in their homes. Because the risk for sensitization is great in atopic patients, patients with allergic airway disease should not bring a pet into their homes. No other clinical advice is supported by published data (Table 6). Healthcare providers should not shy away from strenuously recommending this precaution. [43]. No clinical trials have tested the effect of removing a cat or dog from the home of a sensitized asthmatic.

Once a pet has been removed from the home, the clinical benefit may not be seen for a period of at least several months, because allergen levels fall slowly [44]. In most homes, levels in settled dust fall to those seen in homes without cats within 4 to 6 months after pet removal. Levels may fall more quickly if extensive environmental control measures are undertaken, such as removal of

Table 6
Recommended interventions for furred pets

Type	Intervention
First line (simple or proven effective)	Do not bring a furred pet into the home Find an existing pet a new home
Second line (difficult or unproven)	Restrict pet from home Keep pet out of patient's bedroom Use encasings and room air filter in bedroom Wash pet weekly

carpets, upholstered furniture, and other reservoirs from the home. Thorough and repeated cleaning is required once the animal has been removed. Because cat allergen may persist in mattresses for years after a cat has been removed from a home [45], the purchase of new bedding or impermeable encasements should be recommended.

Because so many patients are unwilling to remove their pets, many compromise measures have been suggested. DeBlay et al demonstrated significant reductions in airborne Fel d 1 with a combination of air filtration, cat washing, vacuum cleaning, and removal of furnishings [46], but these results could not be confirmed, and the methods were shown to produce only a transient decrease in airborne allergen levels [47]. Although tannic acid has been shown to reduce cat allergen levels in carpets [48], the effects are modest and short-lived when a cat is present, so this treatment should not be recommended routinely. The notion has been tested of creating a clean room from which the cat is excluded and in which vigorous environmental control measures, such as vacuuming, mattress and pillow covers, carpet removal, and room air filters, are carried out. In one study, adults with asthma or allergic rhinitis and cat sensitivity were asked to keep their bedroom doors closed, and a combination of a bedroom air cleaner and covers for mattresses and pillows was provided [49]. A control group was provided with nonactive air cleaners. Airborne cat allergen levels were reduced, but no significant differences were detected between the groups in symptom scores, PEFs, medication requirements, pulmonary function studies, or methacholine challenges. In another study, children with asthma and sensitivity to cat or dog allergens were given active or placebo air cleaners to be placed in the bedroom and living room [50]. The investigators found that the active-treatment group had a significant reduction on airway hyperresponsiveness but no change in other clinical measures. It seems that, at least in some settings, it may be possible to produce a clinical effect without removing the pet from the home.

Avoidance of cockroach allergens

Cockroach allergens are derived from several sources (eg, saliva, fecal material, secretions, cast skins, debris, dead bodies). Significant amounts of allergen can be recovered from cockroach washings and from the secretory debris called frass, which accumulates in jars where cockroaches are kept in the laboratory. The primary site of cockroach accumulation is the kitchen, where levels of cockroach allergens are highest. Lower allergen levels can be found in dust samples from sofas, bedding, and bedroom floors [18]. Allergen exposure may occur at school [51]. Approximately 20% to 48% of homes without visible cockroaches contain detectable cockroach allergen in dust samples [18]. Cockroach allergen Bla g 1 was detected in bedding and bedroom-floor samples of 85% of homes of inner-city children with asthma, and levels of Bla g 1 greater than or equal to 8 U/g of dust, considered high and proposed as a disease-induction threshold, were found in 50% of those bedrooms [18]. Heavy

cockroach infestations in homes may create reservoirs of allergen in carpets, rugs, and inaccessible spaces around appliances and furniture.

Cockroach aeroallergen particles have properties similar to mite allergen particles: they are relatively large ($>10\text{-}\mu\text{m}$ diameter), are detectable mainly after disturbance, and fall to the ground and settle rapidly [53]. For cockroaches, 74% to 80% of aeroallergens are associated with particles larger than $10\mu\text{m}$, in contrast to animal allergens, which are carried on small airborne particles. Patients are usually not aware of their cockroach allergy and do not report symptoms of asthma when entering a cockroach-infested house.

Inspection is an important first step in cockroach extermination. It enables identification of the species and their likely hiding places and travel routes. The inspection should be conducted with an understanding of the ecology of the insects and with the idea that insecticides are most effective and least toxic to humans if they are targeted to hiding areas. Evidence of cockroach habitation should be sought, including body parts, feces (black specks the size of sand grains), and stains from regurgitated digestive juices, which appear as brown stains in the edges of cabinets or inside drawers. Food sources that harbor insects should be targeted. These food sources include grease and other cooking debris in the kitchen, indoor garbage cans, pet food, and open food containers. Water sources, which provide another living requirement and determine migratory patterns, should be identified to provide targets for baiting and pesticide spraying [52].

Cockroach allergen avoidance begins with insecticide treatment to reduce the allergen source (Table 7) [52]. Available insecticides are listed (Table 8) [54]. Although the pesticides can be applied in almost any form, the selected placement of gels or baits is preferred. This approach, called integrated pest management, has become a widespread practice that is employed in inhabited buildings to avoid the risk from pesticides.

In kitchens, it is possible to apply the 5- to 15-mm gel spots to cracks, crevices, the junctures of cupboards or walls with floors, and the junctures of counters with walls without making these areas accessible to children and pets. The materials and the application methods are not more expensive than are the older spray methods. Because the gels contain sugars and other attractants for roaches, the pesticides are carried back to harborage and provide effective

Table 7
Recommended interventions for cockroaches

Type	Intervention
First line (simple or proven effective)	Exterminate (professional usually needed) Vacuum and wet wash home thoroughly
Second line (difficult or unproven)	Put out trash nightly Wash dishes nightly Store food in sealed containers Repair plumbing openings, cracks, crevices Place bait traps

Table 8
Insecticides for cockroach control

Insecticide	Preparations	Effectiveness	LD ₅₀ (mg/kg) ^a	Comment
Organophosphates	Diazinon	90%–98% kill	135	—
Carbamates	Carbaryl (Sevin)	90% kill	500	—
Pyrethrins	Permethrin	85% kill	4000	Also added for quick kill, flushing of insects
Avermectins	Abamectin (Avert, Raid)	92% kill in 1 mo	5000	Consumer bait trap ingredient
Miscellaneous	Fipronil	92% kill in 1 mo	1500–5000	—
	Hydromethylnon (Combat, MaxForce)	—	—	Consumer bait trap ingredient
Growth regulators	Methoprene, hydroprene, fenoxycarb	90% kill in 4–5 mo	10,000	
	Biflubenazaron, alsystin	—	—	
Inorganics	Boric acid	25%–50% kill in 2 wks	2500	

^a LD₅₀ indicates a dose that kills 50% of test rodents.

population reduction that lasts longer than that achieved with previously used methods. Bait traps with narrow openings limit access to the attractant and pesticide; if used properly, these products are as effective as gel baits. Successful use of enclosed or gel baits requires enough coverage for large populations. Hungry roaches may clean out the traps before the whole population is controlled. Most technicians recommend a second pesticide application within 1 or 2 weeks to overcome this problem.

Typically, successful treatments provide significant reduction within 2 weeks, demonstrate maximal effect by about 1 month after application, and keep populations under control for 3 to 6 months. The time frame can be extended by changing cleaning practices to remove grease and other food debris from the kitchen, by storing food in plastic containers or in a refrigerator, and by eliminating food debris from other areas of the home (the television room or bedroom).

Household cleaning is an essential adjunct to successful allergen removal. Before applying insecticide, a good cleaning should remove additional food sources so that the insects are more likely to eat the gels or baits. After the insecticides are applied, cleaning should be delayed for 1 week to avoid removal of the insecticides. After that time, a thorough vacuuming should be performed that concentrates on the tops, bottoms, and insides of kitchen cabinets; and the spaces behind stoves, refrigerators, and other kitchen appliances that are likely to harbor dead cockroaches and frass. Hard surfaces in the kitchen and the rest of the house should be scrubbed thoroughly with detergent and water to remove allergen in sticky secretions. Adding liquid bleach to wash water can facilitate this cleaning [55]. In the rest of the house, attention should be turned to furniture and cracks that have been identified as likely harborage by the initial inspection. Rugs should be vacuumed thoroughly and must be repeated several times a week

for months to remove most of the contaminating dust. Allergen is likely to be left adherent to walls, floors, appliances, countertops, and woodwork; these areas should be scrubbed with water and detergent. Bedding, curtains, and clothing usually are contaminated and should be washed.

Field trials of allergen reduction methods have shown that extermination is easier than allergen removal [56,57]. After successful extermination, repeated cleaning for 6 months can result in a 95% reduction in allergen concentrations in settled dust. In less contaminated environments, this intervention may result in complete elimination of allergen from settled dust. In heavily contaminated areas with Bla g 1 or Bla g 2 concentrations greater than 100 U/g of settled dust, treated rooms still will contain allergen at levels that are associated with disease. The only reported clinical trial of the health effects of allergen reduction is the National Cooperative Inner City Asthma Study [58]. In this trial, cockroach allergen treatment was only one part of a global intervention. Disease activity was improved significantly, but median cockroach allergen concentration in treated homes was not reduced; the improvement of disease activity could not be attributed to allergen reduction. Other trials are underway.

Avoidance of fungal allergens

Although sensitization of asthmatic patients to mold is common and the relationship of mold sensitization to severe asthma is not questioned [59–61], the treatments for mold-related asthma in Box 1 [62] have not been as well tested as treatments for asthma related to other indoor allergens. Some interventions have been tested for their ability to reduce mold spore [63,64], but none have been tested for their ability to reduce mold allergens or allergic symptoms, in part because there is a disconnect between the mold allergens, mold allergen-specific IgE, and disease activity. Allergens have been purified from *Alternaria*, *Aspergillus*, *Cladosporium*, and *Penicillium* that bind specific IgE and elicit skin test

Box 1. Recommended interventions for mold

- Control moisture with dehumidification, bathroom fans, leak repair, clothes drier vents, air conditioning
- Clean contaminated materials with chlorine bleach, quaternary ammonium compounds
- Remove contaminated materials
- Regularly maintain HVAC systems
- Use air filters
- Close windows during summer and during other periods of high prevalence

Abbreviation: HVAC, heating, ventilation, and air conditioning.

reactions in sensitized allergic patients [62]; however, the allergens are not found commonly in indoor or outdoor environments, despite the ability to culture viable mold colonies from these same environments. Consequently, the laboratory measurements that have expanded the understanding of the exposure–morbidity relationships for other allergen sources have not been applied to fungal allergens. The second phase of experimental evidence (ie, the ability to reduce exposure by interventions) has not been accomplished, so the treatment recommendations cannot be considered as solid as those for other allergens.

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