

It's time to rethink mite allergen avoidance

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The role of allergen exposure in the etiology of allergic sensitization and asthma is complex. Advice on strategies to avoid domestic allergens remains contentious because trials of interventions aimed to prevent asthma or reduce symptoms have often failed to demonstrate benefits. Asthma management guidelines differ widely in their recommendations, while Web-based information often claims benefits associated with products. In this rostrum we argue that although many factors have a role in both the etiology and the exacerbation of asthma, allergen exposure probably remains an important contributor to the manifestations of the disease. Currently, there is no evidence-based framework for effective domestic allergen avoidance interventions to reduce chronic aeroallergen exposure. The development of an effective approach to allergen avoidance requires a better understanding of (a) the physical nature of chronic aeroallergen exposure and methods for measuring and reducing this, (b) the interaction between allergen exposure and innate immune modulators at different disease stages, and (c) markers enabling the identification of individuals who would benefit from this. The strategic risk of overemphasizing other novel mechanisms and approaches to asthma management is that we will prematurely abandon and fail to improve an existing approach that could have a significant impact on the development, progression, and symptoms of the disease. (*J Allergy Clin Immunol* 2011;■■■:■■■-■■■.)

Key words: Allergen avoidance, prevention, house dust mite, aeroallergen

There have been many changes in our understanding of the role of allergen exposure in the development of allergic sensitization and expression of asthma over the last 30 years. In the 1980s, exposure to house dust mites (HDMs) was advocated as providing an important key to understanding the etiology, prevalence, and pathology of asthma and to controlling and preventing the disease. This confidence was captured by the first International Mite Workshop,¹ which reviewed emerging data on the global distribution of mites, the dominance of mite sensitization, and its

Abbreviations used

HDM: House dust mite

HEPA: High-efficiency particulate arrest

association with asthma. This view was reinforced by 2 later international workshops and the success of the first primary mite intervention study in the Isle of Wight.

The subsequent decline in confidence was heralded by recognition of the importance of viruses in acute exacerbations of asthma, inconsistent data about exposure thresholds, the recognition of other mechanisms such as allergic tolerance, and the role of innate immunity in modulating disease outcomes.² In addition, analysis of several large primary prevention trials based on mite avoidance failed to confirm earlier hopes,³ and a Cochrane-structured meta-analysis of 54 intervention trials in established asthma did not demonstrate overall clinical benefits.⁴ The “Golden Age of the Dust Mite” was over.

It has also become increasingly apparent that asthma is a complex disease with many manifestations and endo/phenotypes, and wide-ranging generalizations about the role of specific environmental factors cannot be made.⁵ This heterogeneity is demonstrated in many ways, including different patterns of asthma presentation, large differences in the proportion of asthma attributable to allergy in different countries, and the function of genes associated with asthma risk.⁶ Despite this complexity, new evidence, and uncertainty, sensitization to a few domestic allergens remains strongly associated with asthma in cross-sectional studies and is a key prognostic indicator for wheezing illness among children.^{2,7} Furthermore, recent data show that allergy and allergen exposure are predictive of inflammatory markers such as FENO⁸ and may increase susceptibility to virus-induced asthma exacerbations.^{9,10} It remains likely that domestic allergen exposures frequently play a synergistic and critical role in the etiology and outcomes of the disease. The strategic risk is that by focusing only on the novel mechanisms and interventions, we dismiss opportunities to understand the complex nature and impact of domestic aerosol exposures. In failing to fully elucidate exposure, we also lose the opportunity to design and test feasible domestic interventions to reduce the incidence, progression, and symptoms of asthma. It is time to rethink allergen avoidance.

CURRENT MEDICAL GUIDELINES AND ALLERGEN AVOIDANCE

Although most professional guidelines for asthma management advocate the avoidance of acute allergen “triggers,” there is a diversity of views about the role of allergen avoidance practices in long-term disease management. At one end of the spectrum, the 2007 National Heart Lung and Blood Institute (US) report advises

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that the first and most important step in controlling allergen-induced asthma is to reduce exposure. At the opposite end of the spectrum, the Finnish Allergy Program 2008-2018 promotes holistic “allergy health” through diet and physical activity and advocates allergen avoidance only “in mandatory situations.” Both the 2009 Global Initiative for Asthma and the British Thoracic Society guidelines reflect the conclusions of the Cochrane review⁴ that there is no consistent evidence for allergen avoidance in preventing asthma and only tenuous evidence that reducing allergen exposure can reduce asthma morbidity (see references E31-E34 in this article’s Online Repository at www.jacionline.org).

CONSUMER INFORMATION ABOUT ALLERGEN AVOIDANCE

The majority of people with Internet access use it to obtain medical information about their disease.¹¹ Asthma foundations and consumer groups are highly ranked by Web search engines and typically identify themselves as being sources of reliable, evidence-based information. However, in an informal survey of 50 such sites (see Table E1 in this article’s Online Repository at www.jacionline.org), only 2 communicated the uncertainty about the role of avoidance as described in the Global Initiative for Asthma and British Thoracic Society guidelines, while 15 were associated with proprietary products promoted for allergen avoidance. These product recommendations are apparently based either on a review of the manufacturer’s technical data or testing against confidential technical standards, not on direct evidence of clinical efficacy of the specific product. It is likely that the appearance of these products on consumer groups’ Web sites and the labeling of products with consumer group logos at the point of purchase are likely to be interpreted by the public as an endorsement of superior allergen avoidance capacity and/or of a clinical benefit. This is neither evidence based nor reliable, but a commercial arrangement.

HDMS AND OTHER DOMESTIC ALLERGENS

The most common domestic allergens associated with asthma are sourced from HDMS, cockroaches, cats, dogs, mice, and fungi. The relative importance of these differs between people and demographic regions and changes with location, season, activity, and other factors. We would argue that HDM, comprising the 2 species *Dermatophagoides pteronyssinus* and *D farinae* (plus *Blomia* species in tropical regions), is the single most important allergen source in the world. This is based on the global distribution of mites, the frequent dominance of mite allergy among atopic populations, the proportion of total IgE that is specific for mite allergens, and their strong association with asthma.^{7,12} While this rostrum deals with mite allergens, the concepts of rethinking exposure and avoidance also apply to other domestic allergens.

ALLERGEN AVOIDANCE—WHAT HAVE INTERVENTION STUDIES SHOWN US SO FAR?

Mite allergen avoidance can be divided into 2 categories, primary interventions for the prevention of sensitization and asthma in infants and tertiary interventions to improve multiple clinical markers in established allergic asthma. (“Secondary” refers to the progression of allergy to asthma and is rarely studied.)

Primary interventions have been trialed in at least 7 major studies and recently compared.³ All were well organized, involved large numbers of subjects, and generally achieved small-to-large reductions in reservoir allergens. However, the clinical effects have been inconsistent and generally disappointing. Some of the observed effects are paradoxical and have changed both our understanding of the allergic pathways in early life and our clinical expectations of such interventions. In the Manchester Asthma Allergy Study, which achieved large reductions in allergens, the intervention group had 1.6 to 2.8 times more (not less) mite allergy than the control group at 3 years of age,¹³ although its members also had better lung function. One hypothesis is that stringent avoidance also removed other protective environmental factors. In our Childhood Asthma Prevention Study, the intervention group had more eczema at 5 years and in the overall group there was a “bell-shaped” dose-response relationship between cumulative mite allergen exposure and the prevalence of both sensitization and asthma.¹⁴ Furthermore, in those who were not sensitized by the age of 18 months, eczema at this age predicted the subsequent onset of allergic sensitization, a phenomenon also observed in other studies (see references E35-E39 in this article’s Online Repository at www.jacionline.org).

Several reviews of tertiary intervention studies have been published; of these, the Cochrane meta-analysis⁴ is the most exacting and influential. This analysis examined 54 studies and found no overall significant differences in morning peak flows, the numbers of patients improved, asthma symptom scores, or medication usage. These interventions often involved single methods (eg, bedding encasings, acaricides, vacuuming, air filters—in decreasing order of occurrence) or combinations of these, plus other methods. However, reliance on meta-analysis as the basis of evidence-based guidelines has limitations when the trials are of very different designs and engage different subjects, time frames, controls, seasons, and methods of interventions. Many of the trials were simplistic and had limited effect on allergens; indeed, only 17 of 54 reported reductions in allergens or mite numbers. One large and well-conducted trial that did show clinical benefits¹⁵ lay outside the criteria for inclusion. Other multifaceted interventions, including those tailored toward individual needs, have also reported more positive outcomes.¹⁶ Compelling evidence for a clinical role of allergens in chronic disease and for the potential for mite allergen avoidance (albeit limited because of the lack of randomly allocated controls) comes from the few studies where subjects have been moved to virtually allergen-free environments for extended periods.^{17,18} In one study,¹⁸ 5 of 9 subjects had an 8-fold or greater improvement in airway hyperresponsiveness, a benefit that is comparable with that of high-dose inhaled steroids (see references E40-E53 in this article’s Online Repository at www.jacionline.org).

WHY HAS DOMESTIC ALLERGEN AVOIDANCE BEEN CLINICALLY UNSUCCESSFUL?

Primary and tertiary interventions need to be considered separately. The lack of benefit in the primary prevention of asthma in infancy probably reflects the complex nature of the pathways involved in the genesis of asthma, as well as differences in susceptibility between individuals that cannot presently be identified prior to selection. It is apparent that although the

allergen dose may be relevant, there is not always a linear dose-response over a wide range of allergen exposures and many other factors are involved in disease expression. These factors include microbial exposures, allergic tolerance, susceptibility and interaction with viral infections, diet, breast-feeding, vitamin D levels, irritant exposures such as environmental tobacco smoke, chemicals, and gas combustion products, the existence of susceptible periods during infancy, and preceding disease patterns such as nonallergic eczema. All these may be influenced by individual genetic factors, either directly, such as in the case of the *filaggrin* gene and eczema, or indirectly by gene-environment interactions, such as in the case of oxidation pathways and susceptibility to oxidants. It is also unclear whether the protective effect of exposure to pets, barns, childcare, or siblings operates only via the microbiome or whether other modulatory mechanisms are involved in different populations (see references E54-E77 in this article's Online Repository at www.jacionline.org).

Additional and different factors probably apply to generating the mixed outcomes of tertiary interventions. The first and most plausible explanation for a lack of success was identified by the Cochrane meta-analysis as "a failure to adequately reduce mite allergen levels."⁴ This is supported by a recent analysis that concluded that interventions with the largest reductions in allergens were the most clinically successful.¹² Second, changes in "exposure," where they occurred, were measured as changes in mite counts or allergen concentration in reservoir dust. While these are useful measures of abundance, and perhaps community exposure, they are weak proxies of acute aeroallergen exposure¹⁹ and are likely to grossly overestimate the total reductions in chronic inhaled exposure. Third, it has been presumed in designing interventions that the majority of mite exposure occurs in beds. Emerging data exist that this assumption is probably incorrect. The only study to make continuous aeroallergen measurements over the 24-hour period in children found that the bedroom had the lowest airborne mite allergen concentrations (pg/m^3) of 3 indoor locations sampled,²⁰ despite it having the highest reservoir mite allergen concentrations ($\mu\text{g}/\text{g}$). We have recently explored this in a pilot study and confirm that significant daily mite and cat aeroallergen exposure occurs away from the bedroom and is associated with reaerosolization of dust during the day. O'Rourke et al's earlier study of daily exposure,²¹ which measured inhaled exposure only at bed entry, failed to recognize that this drops markedly during undisturbed sleep. Fourth, the pattern of individual responses to large reductions in allergen exposure may be very different between individuals, and we lack markers to predict who might benefit. Individual differences have been previously observed and speculated on.¹⁸ Although mite sensitization is widely used as an inclusion criterion, it may not distinguish different phenotypes at risk for asthma²² and therefore may not be a reliable marker of response to reduced exposure. No studies have used information from the patient's history, for example, benefit from avoidance during vacations or the presence of seasonal rhinitis or other allergic symptoms, to select participants for allergen avoidance. In addition, there is the phenomenon of tolerance to allergen exposure, and the effects of reducing exposure may not be uniform in all people and exposure ranges. Fifth, reducing exposure to mite allergens also reduces exposure to other nonallergen exposures that may, at least for chronic exposure, be protective.²³ Finally, responses to individual domestic allergens may differ (see references E78-E102 in this article's Online Repository at www.jacionline.org).

THE LIMITATIONS OF CURRENT METHODS OF MITE ALLERGEN AVOIDANCE

Previous approaches to avoidance of mite (and other domestic allergens) have been based on the principles of control and removal of sources, reservoirs, and aeroallergens, in that order. Current information is increasingly directed toward the differentiation of specific consumer products, such as types of encasings or vacuum cleaners, rather than evidence-based protocols for the effective use of these items, plus broader approaches. When the question is asked "How should they be used to reduce chronic aeroallergen exposure?" the answers tend to be anecdotal and almost evidence free. Issues with each of the major methods, briefly, are as follows. *Encasings*: The effectiveness of microporous barrier encasings has been exaggerated by the use of reservoir measurements of allergens, which overestimate both the magnitude and the duration of reduction in chronic aeroallergen exposure. The frequency of laundry of all bedding required to maintain low exposure needs to be determined. *Floor coverings*: While it is commonly recommended that carpets should be substituted by hard floors, the little available data of aeroallergens in houses suggest that the difference may be small²⁴ and the effects complex. The loading and 3-dimensional distribution of allergens in floor coverings, their capacity to be cleaned, their role as an allergen source and a sink, the physical structure and the electrostatic nature of the materials, and the different ways disturbances create allergen reaerosolization all contribute to their function as an aeroallergen source.²⁵ This requires a better understanding. *Vacuum cleaners*: Vacuum cleaners are heavily promoted. Probably all cleaners cause a brief increase in personal aeroallergen exposure under normal domestic conditions and high-efficiency particulate arrest (HEPA) filters make little difference.²⁶ The relationship of cleaning frequency and efficiency and resultant reductions in chronic aeroallergen exposure in houses needs to be quantified. *Washing machines*: Both dust and cat and mite allergens are effectively removed by laundry. While washing at $>55^\circ\text{C}$ is advocated, studies comparing the effect of washing temperature or frequency on the resultant chronic aeroallergen exposure from bedding and clothing under normal domestic conditions are required. *Air filtration and air management*: The role of air filtration continues to be debated. There is some consensus that small benefits exist, mainly for pet allergens. Interventions tailored to deliver clean air directly over the bed have shown some clinical benefits, although other methods of air management are generally less promising. *Acaricides*: Enthusiasm for acaricidal sprays and powders has waned as their effectiveness in laboratory culture was not reflected in houses, plus health concerns. There is a recent trend to incorporate permanent acaricides (eg, tributyltin, permethrin, nanosilver) into "protective" bedding under different trade names. No data on clinical benefit exist, and concerns about human health and environmental toxicity remain (see references E103-E147 in this article's Online Repository at www.jacionline.org).

A NEW WAY OF THINKING ABOUT ALLERGEN AVOIDANCE

We need a new way of thinking about allergen avoidance that integrates emerging data on allergen and nonallergen exposures, innate and adaptive immune mechanisms, and variation in individual susceptibility.

A view that allergen avoidance is not practical is primarily based on experience using selected products in previous interventions, and a more fundamental and holistic approach is required based on integrating this with the combination of evidence-based housing design, furnishing choice, and experimentally validated hygiene/lifestyle practices. Ultimately, exposure needs to be understood in terms of chronic inhaled aeroallergen dose. This requires new models derived from mapping the almost continuous resuspension of multiple reservoirs during the day and night to understand when exposure occurs, what the sources are, and what the effect of different human activities is. This fluid-dynamic approach to the reaerosolization of dust and allergens would inform the development of effective strategies and is emerging in recent studies.^{20,25,27,28}

It is also necessary to tailor interventions to an individual's living situation and patterns of disease.^{15,16} One unresolved question about aeroallergen "exposure" is the particle size most relevant to asthma, which may be the subfraction of smaller respirable particles that reach the lung during chronic exposure and not the larger inhalable fraction that carry most mite²⁹ and cat³⁰ aeroallergen which are generated by disturbance and generally measured. As noted, the concept of "exposure" also needs to include the nonallergen bioaerosol. Current evidence suggests that microbial components probably play a minor role in people with established asthma symptoms but a critical role in modulating the process of sensitization and the development of asthma. Thus, interventions for the primary prevention of asthma in future may focus on minimizing exposure to allergens and other agents promoting airway inflammation while also enhancing exposure to agents that stimulate protective innate responses. The identity, route of exposure, and safety of these innate stimulants remain to be determined. Environments for reducing symptoms in established allergic asthma would primarily appear to be those with minimal allergen, inflammatory, and irritant exposures, and other "protective" aerosols may be less important, although other factors such as diet and nutrition may be relevant. Optimizing such approaches will ultimately need to address the differences in responsiveness between people.

It is also important to consider the potential of allergen avoidance, or more broadly, the modulation of domestic exposures, from the perspective of strategic investment in community health. Asthma affects 300 million people, and the global prevalence is increasing. There are no interventions to prevent the disease other than to ban smoking during pregnancy and no pharmacotherapy to alter its course. Domestic allergens are the most prominently known environmental risk factor, possibly the most important inflammatory exposure, and function synergistically with other factors. To date, the trials to reduce allergen exposure have often been simplistically founded, and because of increased marketing, the emphasis has become increasingly product focused. There is lack of knowledge about when and where aeroallergen exposure occurs, how to reduce it, and how to identify those who will benefit from a reduction in exposure. While previous meta-analyses allow us to avoid the errors of the past, in relying on them for the future we risk dismissing an approach that has not been adequately developed or evaluated. For all the billions of dollars spent annually on asthma treatment and research, it would seem strategically prudent to better understand the processes and components of domestic exposure and properly develop and test the effectiveness of interventions.

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ADDITIONAL REFERENCES AND COMMENTS

References E31 through E34: Professional guidelines for allergen avoidance include E31 through E34.

References E35 through E39: For additional eczema in Childhood Asthma Prevention Study cohort, see E35. For eczema increasing the risk of later allergic sensitization and asthma, see E36 through E39.

References E40 through E53: For other meta-analyses of allergen avoidance interventions, see E40 through E42. For more positive outcomes from selected interventions, see E43 through E46. For studies in low-allergen environments, see E47 through E52, plus E53 for comments.

References E55 through E77: Nonlinearity of mite allergen exposures, besides reference 14 includes E54 and E55. These other factors include microbial exposures,^{E23,E56,E57} allergic tolerance,^{E58,E59} susceptibility and interaction with viral infections,^{E60} probiotics, diet, and vitamin D,^{E61,E62} breast-feeding,^{E63} irritant exposures such as environmental tobacco smoke, chemicals, and gas combustion products,^{E64} the existence of susceptible periods during infancy, and preceding disease patterns such as non-allergic eczema.^{E36-E39} Additional factors are gene-environment interactions, such as in the case of oxidation pathways and susceptibility to oxidants.^{E65-E69} For the occurrence of mechanisms for modulating allergic disease outcomes that lie outside the “hygiene hypothesis” but that depend on environmental exposures or other factors, see E70 to E77.

References E78 through E90: Mite allergen exposure: O’Meara and Tovey’s review¹⁹ provides a comprehensive overview of studies and methods for measuring airborne allergen. Studies of chronic static and personal aeroallergen exposure are less common and as yet, no comprehensive model of the pattern of mite allergen exposure throughout the day has been published. Raja et al’s recent study²⁰ describes using both personal and static sampling for PM10 aeroallergen particles, but it was not intended to provide a detailed analysis of the patterns of exposure. Earlier studies on mite aeroallergen exposure frequently lack detail, while others lacked sufficiently sensitive assays. The foundation studies were performed by Sakaguchi and colleagues.^{E78-E81,E89}

Here, group 1 (Der p 1 and Der f 1) HDM allergen was sampled in 6 subjects during the night, starting after subjects were in bed; the geometric means (GMs) were 223 pg/m³ when bedding with high allergen content was used and 11.5 pg/m³ with new quilts.^{E78} This was compared with the GMs measured by sampling continuously in the lounge room with a static sampler over several days; here, the quantities were 29.5^{E79} and 48.7 pg/m³.^{E80} The only data obtained by using personally worn samplers are also unclear; the samplers were “carried by the young adults when at home” and “placed near the bed during sleep” although aeroallergen measured only before and after new bedding is reported as 102 and 19.9 pg/m³, respectively, for the GMs.^{E81} This 5-fold reduction measured with “personal sampling” is less than the approximately 20-fold difference in GMs measured earlier by using static sampling. These data are difficult to fully interpret. Park et al^{E82} also measured continuous mite aeroallergen exposure by using static samplers in houses and found that these differed over a wide range and were positively correlated with reservoir allergen; only limited data can be extracted from the figures. Samples collected in the breathing zone or with personally worn samplers are frequently have a high concentration of airborne allergen than those collected by static sampling in the same room, as

demonstrated with endotoxin.^{E83} Experience using our nasal air samplers to measure the inhaled dose of mite aeroallergens has been documented in references 21, E84, and E85, including their origins during the day from clothing.^{E86} Studies of low-allergen-exposure schools in Sweden show the ubiquity of allergens and how difficult reduction in cat aeroallergen exposure is.^{E87} As noted, our original attempt to measure the pattern of daily exposure,²¹ which sampled only for 30 minutes on entering bed, failed to recognize that inhaled exposure is high only at bed entry and drops markedly during undisturbed sleep (Tovey, unpublished data, plus E88-E90).

References E91 through E102: The overall phenomenon of allergic tolerance is well described for cats^{E59,E91,E92} and is equivocal for dogs^{E93} and rodents,^{E94,E95} while Tovey et al¹⁴ and others^{E54,E55} have noted nonlinear responses for mite allergens. Whether tolerance occurs following prolonged exposure as a form of adaption after a period of symptoms or whether it reflects a subset of subjects who respond in this way following early and high exposure has not been established. The possibility of increased symptoms with allergen reduction following the establishment of tolerance is hypothesized in an abstract from the most authoritative group,^{E96} but published examples of its occurrence are not known to us. While the mechanism of tolerance is thought to be associated with increased IgG4 and a “modified T_H2 response” following high exposure,^{E59} there is not universal support of the details from other studies.^{E94,E95,E97,E98} The latter also includes speculation on the role of dermal exposure in establishing tolerance, a topic of additional interest given recent data on peanut sensitization via environmental exposure.^{E99} Others have hypothesized that the global increase in allergic disease may be the result of a failure to generate normal tolerance,^{E100} following reduced allergen exposure resulting from greater domestic hygiene or reduced mite-contamination of foods. As mentioned earlier, ample data exist that immune responses differ for different domestic allergens, particularly cats. The limited cockroach data support a linear response, while those for the overall effect of early fungal exposure are controversial.^{E56,E75,E94,E101,E102}

References E103 through E147: Fitting encasings to bedding: This greatly reduces the initial quantity and concentration of allergen in the dust that is recovered from bedding. This effect may be large, variable, and persist for a couple of months. However, when aeroallergens are measured, the magnitude of the reduction in exposure is much more modest and of shorter duration.^{E81,E103-E106} Also see reviews for references to studies and comments on types of encasings.^{E42,E107,E108}

Floor coverings: Surprisingly, few data exist to show that in normal houses, personal exposure to aeroallergens is greater or less with carpets than with hard floors, although observational studies of asthma favor hard flooring. As mentioned, in one of the few observational studies of airborne mite allergens and flooring types, both hard floors and synthetic carpets provided similar lower exposure compared with wool carpets, despite the carpets having similar allergen concentrations.²⁴ In an unpublished report of a study in houses that measured allergen settling into petri dishes as a proxy for airborne exposure, the distribution of airborne allergen in carpeted and uncarpeted rooms was similar.¹² The most likely explanation is that while carpets may contain a large amount of allergen, most is at the base and only a small fraction is reaerosolized, whereas hard floors, if they are only occasionally cleaned, accumulate surface allergen that is more readily

reaerosolized. The carpet industry argues that net allergen exposure is lower with carpets, but their industry-based study is light on detail.^{E109} There is mixed support of the complex dynamics of exposure and disturbance from models.^{E110-E112} Thus, the question is more about their capacity to function as an aeroallergen source under different conditions than the absolute quantity in the reservoir.^{E113} In addition to physical disturbance, the thermal plume around bodies modifies exposure from floors.^{E114,E115} It also means that reducing allergen exposure may also be more about the frequency^{E116} and effectiveness of cleaning and the properties of the surface than the reservoir concentrations or quantity per se. Vacuuming of carpets may have only a small effect on total allergen,^{E117} particularly if carpets are worn,^{E118} and on this basis, hard floors are likely to be preferred as they are more easily kept in a state that minimizes aeroallergen reaerosolization in the long term. Quantitative studies of chronic personal allergen exposure under normal conditions in real houses are required.

Vacuum cleaners: We know surprisingly little about the real usefulness of vacuum cleaners for achieving long-term reductions in chronic aeroallergen exposure. Their capacity to remove dirt from carpets under idealized conditions by using standardized tests is frequently compared in consumer magazines. However, because of the distribution of allergens toward the base of carpets, the large differences in the structure of different carpets, and the effects of wear and compression, such tests likely overestimate these capacities.^{E117-E119} A recent feature of vacuum cleaners is the incorporation of HEPA filtration. This may have arisen after a particular brand of cleaner that ironically directed its marketing at people with asthma was shown to generate a large aerosol of allergen, which was subsequently reduced by the researcher fitting an air filter over its outlet.^{E120} The standard laboratory method of testing vacuum cleaners is to run static tests in an enclosed chamber with the cleaner loaded with allergenic dust and check the aerosol output within the chamber. However, this appears to be a poor representation of real exposure in houses. In a study where HEPA and non-HEPA cleaners were compared, there was a large difference in the aerosol output of the 2 cleaners within the chamber in laboratory chamber tests, but in a normal domestic situation, there was little difference in the inhaled exposure experienced by operators of the HEPA and non-HEPA vacuum cleaners.^{26,E121} Another small study also found marked differences in cat aeroallergen between different HEPA and non-HEPA cleaners in a test rig, but all increased aeroallergen in apartments. The conclusion was that the physical activity of cleaning generates much of the aerosol^{E122} and not the cleaner's exhaust and leakage. This conclusion is supported by a further study showing no difference in aeroallergen generated between ducted cleaners (which emit the exhaust outside) and non-HEPA cleaners.^{E123} Thus, the benefits of HEPA filtration on exposure may have been exaggerated and all cleaners probably provide a brief increase in exposure. The use of high-temperature steam cleaning,^{E124} which denatures some allergens in carpets, has shown some promise^{E125,E126} but is not widely used.

Laundry: Research findings are less conclusive about the details of the effectiveness of laundry at removal of allergens and mites; some studies find almost complete removal without hot (>55°C) washing, whereas others suggest that hot washing is required.^{E127-E131} It is important to review these studies in the context of the combined effects of what occurs in laundry: the elution of allergen from the dust; the physical removal of both dust and mites by the multiple wash and rinse cycles; the effects of detergents,

additives, and the subsequent drying procedures. It can be speculated that frequent cold water washing would be more useful than less frequent hot washing at reducing aeroallergen exposure from bedding and clothing,^{E86} but this has not been established.

Air filtration: The role of air filtration in asthma and rhinitis management continues to be debated, and some studies do show small benefits. Nearly all studies have evaluated room air cleaners as a single intervention and are of short duration. There are 3 reviews of the topic, and a consensus would be that there may be small effects, mainly with pet allergens.^{E132-E134} Studies looking at HEPA filtration of the breathing zone have fared better, and this appears promising and would argue that nocturnal exposure was important.^{27,E69,E135-E140} A Cochrane review^{E141} of ionizers and 3 trials did not find evidence supporting their use.^{E142-E144} Dehumidification has also shown some promise^{E145} although other studies using mechanical ventilation to reduce humidity have had more mixed outcomes.^{E146,E147}

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TABLE E1. List of asthma foundations and associations accessed from the Web showing whether their Web sites appeared to contain endorsements for allergen-avoidance products*

No.	Organization	Country	Web site	Products
1	Allergy Asthma Information Association	Canada	www.aaia.ca/en/index.htm	No
2	Allergic Living	Canada	www.aaia.ca/en/index.htm	No
3	The Allergy Awareness Association Inc	New Zealand	www.everybody.co.nz/page-fdeaf1ba-b4fa-4446-807e-31e4ae7e9568.aspx	No
4	Asthma & Allergy Foundation of America	United States	www.aafa.org/	Yes, "asthma and allergy-friendly" certification program
5	American Asthma Foundation	United States	www.americanasthmafoundation.org/	No
6	Asthma and Allergy Foundation of America (New England Chapter)	United States	www.asthmaandallergies.org/	No
7	Asthma Fonds Netherlands	Netherlands	www.astmafonds.nl/content.jsp?objectid=10062	No
8	Asthma Society of Canada	Canada	www.asthma.ca/adults/	Yes, "asthma and allergy-friendly" certification program
9	AsthmaMoms USA	United States	www.asthamomms.com/	No
10	Calgary Allergy Network	Canada	www.calgaryallergy.ca/marketplace.html	Only links to product suppliers
11	Canadian Allergy, Asthma and Immunology Foundation	Canada	www.allergyfoundation.ca	No
12	Childhood Asthma Foundation Canada	Canada	www.childasthma.com/	No
13	Deutscher Allergie - Und Asthmabund e.v. (DAAB)	Germany	www.daab.de/index.cfm	No
14	Kid's Allergies United Kingdom	United Kingdom	www.kidsallergies.co.uk/	Has links to products including vacuum cleaners
15	National Allergy and Asthma Network/Mothers of Asthmatics	United States	www.aanma.org/	Has store but link did not open
16	The National Asthma Campaign (NAC)	Australia	www.nationalasthma.org.au/	Yes, sensitive choice/blue butterfly campaign
17	Asthma UK	United Kingdom	www.asthma.org.uk/	Links to "asthma and allergy-friendly" certification program
18	The British Allergy Foundation (BAF)	United Kingdom	www.allergyuk.org	Own 3-tier endorsement program
19	World Allergy Organization	Global	www.worldallergy.org/index.php	No
20	Zurich Lung Association	Switzerland	www.lungzurich.org/website.asp	No
21	Asthma New Zealand – the lung association	New Zealand	www.asthma-nz.org.nz/	No
22	Asthma Australia	Australia	www.asthmaaustralia.org.au/	Association with vacuum cleaner
23	Asthma Foundation Northern Territory	Australia	www.asthmant.org.au/	No
24	Asthma Foundation Queensland	Australia	www.asthmaql.org.au/	No
25	Asthma Foundation NSW	Australia	www.asthmafoundation.org.au/	No
26	Asthma Foundation South Australia	Australia	www.asthmasa.org.au/	No
27	Asthma Foundation Tasmania	Australia	www.asthmatas.org.au/	No
28	Asthma Foundation Victoria	Australia	www.asthma.org.au/	Association with vacuum cleaner and air filter
29	Asthma Foundation Western Australia	Australia	www.asthmawa.org.au/	No
30	Asthma Foundation ACT	Australia	www.asthmaact.org.au/	Association with vacuum cleaner and air filter
31	The Asthma and Respiratory Foundation of New Zealand	New Zealand	www.asthmafoundation.org.nz/home.php	Yes, sensitive choice/blue butterfly campaign
32	The European Centre for Allergy Research Federation (ECARF)	Europe	www.european-lung-foundation.org/index.php?id=51	Yes, does its own testing and certification for products and hotels
33	The European Federation of Allergy and Airway Diseases Patients Association (EFA)	Europe	www.efanet.org	No
34	Astma en Allergie Koepel	Belgium	www.astma-en-allergiekoepel.be	No
35	Асоциацията на Българите Боледувачи от Астма (АБВА)	Bulgaria	www.asthma-bg.com	No
36	Astma-Allergi Forbundet	Denmark	www.astma-allergi.dk	Advertisements for products
37	Allergia- ja Astmaliitto Allergi-och Astmaförbundet	Finland	www.allergia.com	Has shop vacuum cleaners, air filters, and more
38	Association Française pour la Prévention des allergies (AFPRAL)	France	www.prevention-allergies.asso.fr	No

(Continued)

TABLE E1. (Continued)

No.	Organization	Country	Web site	Products
39	Asthme and Allergies Association	France	www.asthme-allergies.org/	No
40	Aniksi	Greece	www.allergyped.gr	No
41	Asztmás és Allergiás Betegek Országos Szövetsége (ABOSZ)	Hungary	www.abosz.hu	No
42	Magyar Tudógyógyász Társaság (MTT)	Hungary	www.tudogyogysz.hu/	No
43	Federasma	Italy	www.federasma.org	No
44	Lietuvos astmos klubų taryba (LAKT)	Lithuania	www.astmainfo.lt	No
45	Norges Astma-og Allergiforbund (NAAP)	Norway	www.naaf.no	Vacuum cleaners, heaters
46	Associação Portuguesa de Asmáticos (APA)	Portugal	www.apa.org.pt	No
47	Jugoslovensko UD ruženje za Astmu i Hronicnu opstruktivnu bolest pluća (JUDAH)	Yugoslavia	www.yudah.org.yu	No
48	Associació Asmatològica Catalana (AAC)	Calatan (Spain)	www.asmatics.org	No
49	Respirar	Spain	www.respirar.org/	No
50	Astma-och Allergiförbundet	Sweden	www.astmaoallergiforbundet.se/	Yes, vacuum cleaners, heaters

*This was based on a visual inspection of non-English sites. Because of language constraints, it is possible that associations were missed or misinterpreted.