

Allergen Avoidance

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The systematic avoidance of indoor allergens by modification of houses, furnishings, or hygiene practices has long been advocated to reduce both the incidence of allergic diseases in at-risk infants and exacerbations or symptoms in those previously sensitized with such a disease. However, such advocacy is now under challenge, due to both a lack of evidence of clinical efficacy of avoidance measures and rapidly changing models of disease causation and pathology. This article reviews the current dilemmas in understanding the complexity of allergen sources, disease risks, nature of bioaerosol exposure, and the inadequacies of many available methods.

Introduction

The mainstream allergic disease community recently strongly endorsed allergen avoidance for the management of allergic disease [1]. However, uncertainties are emerging about such support in the details of research literature and evidence-based reviews—driven partly by new complexities in the relationships of allergen exposure to the expression of asthma severity and exacerbations, and partly by the lack of consistent evidence-based proof of efficacy [2•].

Allergen avoidance is divided into primary avoidance to prevent sensitization or clinical outcomes, and secondary avoidance to reduce indices of disease expression in those with prior sensitization, particularly asthma symptoms. Different doubts apply to each; some [3•] but not all [4•] primary interventions trials applied in infancy have shown disappointing clinical outcome reductions in early childhood. Similarly, some [5] but not all [6] secondary trials in children and adults with asthma or allergic rhinitis have shown disappointing or inconsistent benefits.

Possible explanations for this inconsistency differ. In primary interventions, it can be questioned whether the reductions were sufficient, or paradoxically, whether reducing allergens also reduced nonallergen exposures,

which increased the disease risk. (See later discussion of the hygiene hypothesis.) Similarly, in secondary interventions, it is uncertain whether the reductions in exposures were sufficient, or whether there are limitations on the reversibility of the established disease process.

However, studies in low-allergen alpine environments continue to support the therapeutic benefits of a large reduction in allergen exposure. Children with asthma who are moved from cities to such environments show major improvements in many fundamental indices of asthma [7]. Although such alpine studies strongly support the ultimate benefits of allergen avoidance, they also query whether additional lifestyle changes might be important (eg, changes in diet or exercise), the magnitude of allergen reductions required, and whether these reductions can be achieved in domestic situations.

History

Organized attempts to treat asthma by allergen avoidance date back to the 1920s, when bedrooms furnished in a Spartan style and supplied with filtered air were used with apparent success [8]. Over the subsequent decades, allergen exposure was thought to be associated mainly with acute symptoms. Thus, there was a resurgence of interest in the early 1980s when prolonged residence in clean hospital rooms showed striking improvement in airway hyperresponsiveness, an underlying hallmark of asthma [9]. This coincided with demonstrations of the strong association of mite allergy and asthma, the application of immunoassays to the measurement of allergens, and an alarming increase in asthma prevalence and mortality. Suddenly confidence increased that allergen avoidance could play an important role in asthma prevention and management. Such concepts were inspired by early reports from a primary intervention study in the Isle of Wight. This multicomponent intervention in the first 9 months (anti-mite interventions, plus maternal and infant diet) showed reductions in sensitization and wheeze at year 1 [10], which have been maintained to year 8 [4•]. The early outcomes of at least six longitudinal infant intervention studies that were initiated toward the end of the 1990s have been reviewed: Manchester Asthma and Allergy Study (MAAS), Childhood Asthma Prevention Study (CAPS), Prevention and Incidence of Asthma and Mite Allergy (PIAMA), Canadian Primary Prevention Study (CaPPS), Prevention of Asthma in Children (PREVASC), and Study on the Prevention of Allergy

in Children in Europe (SPACE) [11]. At this time, a burgeoning industry in products designed to reduce exposure emerged. As indicated earlier, the initial optimism has not been fulfilled [12]. It is now appropriate to review progress and to question future directions: is allergen avoidance an effective tool that requires a more sophisticated approach, or are the current presumptions of its mechanisms poorly founded? Numerous other reviews provide a more extensive reference base [13–16].

Indoor Allergens

The allergens found in houses and buildings vary with geography, location, housing type, lifestyles, season, and individual rooms. The amount that is airborne and inhaled depends on the shifting mixture of exposures from different sources over time. For example, we have shown that approximately 50% to 60% of inhaled mite exposure occurs in bed, whereas this proportion of cat exposure occurs in other parts of the house and at work, but not in bed [17]. The clinical effects of exposure may vary—at least for cat allergen, chronic exposure may function subclinically to increase airway hyperresponsiveness [18•], whereas acute exposure may precipitate immediate asthma symptoms. The most commonly identified indoor allergen sources are described in the following paragraphs.

Mites

The most common mite species are *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*, which are mainly found in temperate and humid regions of the world [19]. In more tropical regions, including those of the United States, other mites (eg, *Blomia* spp.) are an important allergen source.

Insects

The most noteworthy insect allergen sources are cockroaches, which are probably “the” major allergen in some inner cities [20]. *Blattella germanica* is the most important of three domestic species. Houses also contain a rich mixture of other arthropods including spiders, silverfish, ants, and carpet beetles (including Asian ladybugs [21]), which can also be allergen sources.

Domestic pets

Cats and dogs can be both indoor and outdoor allergens. These allergens are ubiquitously distributed in schools, workplaces, and the homes of non-cat owners; almost all houses (> 99%) have detectable cat and dog allergens [22]. The recent literature is inconsistent regarding whether high pet exposure in infancy is a risk, is protective, or has no impact on other allergies [23].

Mice and rats

Rodent allergens can be important, both in occupational settings and in some low-income areas of US inner cities,

where infestation is common. Mice cohabit closely indoors with humans, whereas rats occupy the fringes—basements, subway stations, vacant lots, and the like.

Fungi

All normal houses have some fungi as a result of infiltration of different outdoor species, adding to those colonizing indoor substrates [24,25]. Generally 5 to 40 species are recorded as present, although new techniques show additional allergenic species [26•]. Recent attention has focused on differentiating between allergens from spores and the smaller threadlike hyphae [26•]. Many clinical and legal controversies are related to fungal exposure; although the conventional view holds that high exposure is hazardous, some exceptions may exist [27], at least in early life.

Occupational

Occupational allergens can be transported home on clothing and hair, providing a sensitization risk to families [28].

Nonallergen Indoor Exposures Requiring Avoidance

In addition to allergen sources, it is evident that indoor exposure involves a complex mix of gases and nonallergen particles, which may have synergistic and deleterious effects on respiratory health. These include tobacco smoke, nitrogen oxides, and other volatile active compounds from gas cooking and unflued heaters, β -glucans from fungi, endotoxin from bacteria, formaldehyde from particleboard, and ozone from high-voltage sources.

Outdoor Allergens

Outdoor allergen sources are dominated by plant pollens and fungi. They differ depending on season, locality, and opportunity for local exposure and are not generally considered in the context of indoor allergen avoidance. However, outdoor allergens do penetrate into houses, and under appropriate meteorologic conditions, pollen grains produce smaller fragments that may cause profound asthma [29]. Plants also produce nonallergic hairs and other fragments that can irritate the respiratory tract.

Relating Allergen Avoidance and Exposure

Minimizing allergen exposure is based on achieving control at three levels: the allergen sources, the accumulated reservoirs, and the aeroallergens.

It is worth considering the concept of “exposure,” because it is directly linked to the concept of “avoidance.” Although in a few cases exposure is still measured as units of the source (eg, pollen grains per cubic meter of air), in general, immunoassays are now used to quantify specific allergens. Such immunoassay studies

Table 1. Common recommendations for allergen avoidance and comments on their perceived efficacy

Recommendation	Comment
Encase bedding	Preference is for tightly woven cotton or synthetic fabrics; encasings alone not effective, allergen must be removed on regular basis
Wash bedding regularly	Essential to remove accumulating allergens; regular cool/warm wash (every 2–3 weeks) better than occasional hot wash
Wash clothing regularly, especially if stored	Only about 50%–60% of mite exposure is from bed; balance is from other domestic sites, including clothing, furnishings, carpets
Replace items that accumulate dust and are noncleanable with cleanable options; this may require time	Despite limited evidence, preference is replacing carpets with hard floors plus washable (Oriental) rugs, and soft furnishings with leather, washable cushions, etc.; remarkable shortage of data about these items as aeroallergen sources
Vacuuming—probably twice a week, not by person with symptoms, unless with mask and in well-ventilated space	Minor effect on allergens, advantage unclear but preference for double bags, HEPA filters; don't spend a fortune; shortage of quantitative data on this
Acaricides and allergen denaturants	Are not recommended because effects are modest and transitory in real houses, but work well in the laboratory
Air filters	Room filters have some use for cat but not mite allergen; bed-mounted units may be useful for mite allergens
Dehumidifiers	Mechanically reducing humidity consistently to 30%–50% relative humidity reduces mites and fungi, if climate and house structure allow
House choice	Be aware: some houses in same city have 100 × less mite allergen than others, probably on basis of construction, height of building, microclimate
Multiallergens	Mites don't occur in isolation, be aware of all allergies; cat allergen occurs despite no resident cat; remove/treat visible mold; be aware of local plants, trees; particles and pollens invade houses
Nonallergens	Tobacco smoke, nitrogen oxide from cooking and unflued heating, vapors from new carpets, particle board, pain, ozone, food (meta-bisulphite) triggers, outdoor exercise with high pollutant levels
Factors not in the air	Be aware: asthma is a complex, multifactorial disease exacerbated by psychosocial and socioeconomic factors, viruses, diet
HEPA—high-efficiency particulate air.	

are generally performed on reservoir samples of house dust collected with a vacuum cleaner, and exposure is expressed as the allergen concentration in dust. Despite the many shortcomings of this approach and the lack of correlation (allergen reservoirs vary between sites and with methods used, whereas acute personal aeroallergen fluctuates over time), reservoirs probably provide a simple and mildly relevant exposure index, mainly for epidemiologic studies of populations.

Why is this relevant to allergen avoidance? Much of our understanding of avoidance has been based on measurement of reservoirs and not on changes in airborne exposure; however, only the latter is ultimately pertinent to understanding changes that occur with interventions. For example, encasing bedding provides large reductions in allergen reservoirs but only small and short-term reductions in inhaled allergen in the same bed [30], probably because a thin film of allergen is quickly re-established to become the source of exposure, not the bulk of the reservoir dust in the bedding. Additionally, only part of the total daily exposure is associated with any one site. This may be a primary reason why allergen avoidance as

practiced at single sites with single methods has been so ineffective compared with the outcomes from alpine studies, where overall allergen exposure is reduced.

Allergen Avoidance Methods: Source Control

The recommended methods of allergen avoidance and comments are provided in Table 1.

Mites

Mites can be killed by subjecting them to biologically intolerable conditions, such as heat, freezing, and dehydration. The practical opportunities to apply these in houses vary. Dehydration—either mechanical dehumidification [31] or harnessing seasonal changes in humidity [32]—must be applied to all sites simultaneously. It is the most appealing method when it is feasible. However, several trials have shown little impact, and dehydration only works with tight housing and in climates that are not too humid. Heat can be applied via steam cleaning, sunshine, underfloor heating, and hot water washing [13]. Freezing mites to death is possible on a small scale.

The history of acaricides is disappointing. They can be applied as powders, foams, or liquid sprays, but generally do not penetrate deep into carpets and furnishings where mites are found. Denial of habitat by choice of materials, furnishings, and barriers remains a practical method of control when possible.

Cockroaches

Eradication of cockroaches is a professional science, utilizing baits and sprays [33] coupled with removal of food and denial of both sheltered niches and free water.

Feral rodents

Rodent control is an expert business, with approaches similar to those for cockroach eradication. Sources of information include e-magazines such as Pest Control Technology (<http://www.pctonline.com/>).

Fungi

Proliferating spores can be directly treated with bleach, but the essential approach requires removing moisture (< 75% relative humidity). Remedial treatment is also needed to prevent water intrusion and condensation.

Removing Domestic Allergen Reservoirs

Laundry

Laundry is the ideal allergen-removal strategy; it physically removes particles (eg, mites, dander) and solubilizes the allergen from those remaining. Mite allergen solubility/loss in laundry solutions is greatest with enzyme-based detergents, followed by detergent alone, soap, and then water, in that order [34]. Laundry is simple, generally available, and inexpensive. It is excellent for bedding and clothing. Hot washing (> 53°C) kills mites; they may recolonize quickly, but this has not been proven. I argue that when compliance is less certain, the effort is better spent performing more frequent warm washing, than occasional hot washing.

Vacuuuming

Vacuuuming, either wet or dry, is the most common method used for cosmetic cleaning of carpets and floors. In practice, it removes only a small fraction of the total allergen within a carpet. Most allergen is at the base of a carpet, and normal vacuuuming makes little difference to the allergen content of both the lower and upper layers [35]. Care must be taken when interpreting advertised data, which is derived from standardized tests based on adding fresh dust to new carpets and then measuring removal, because this exaggerates the efficiency of removal of dust from old carpets. Wet (steam) cleaning removes more allergens, but the moisture involved can increase fungi and mites in the longer term. The alternative is eliminating carpets and utilizing hard floors (see later discussion). We have no experience with a new generation of cleaners equipped

with ultraviolet C lights to kill mites, which appear to be validated by university-based laboratory tests [36]. Further research is needed to show efficacy in normal houses and clinical benefit.

Frustratingly, quantitative and meaningful studies are lacking on carpets as aeroallergen sources and their comparison to hard floors. Indisputably, carpets are rich reservoirs of allergens, and such allergens are difficult to control by mechanical means. However, it can be argued that allergic dust is more easily aerosolized from a hard floor than from a carpet (data are available about fungi). In our experience, no major difference is found in aeroallergen in rooms with carpeted and uncarpeted floors.

Many advertisements promote vacuum cleaners with high-efficiency particulate air (HEPA) filtration of the exhausted air. Although this seems prudent, a recent study failed to show any difference in personal aeroallergen exposure whether the cleaners were equipped with HEPA filters or not; the activity of cleaning itself generated more aeroallergen than the machine's exhaust [37]. This is supported by studies of ducted cleaning [38].

Encasings

The function of occlusive encasings for bedding is to provide a physical barrier to the movement of allergens and mites. Studies of encasings were reviewed recently [39]. Encasings differ widely in their quality—some cheap brands have large pores, other multilayered encasings delaminate, and others harbor mites [40]. Almost all evaluations have been conducted on new, unused encasings. Tightly woven synthetic or cotton fabrics are preferred [41]. Most trials of encasings have failed to regularly wash them (difficult with some encasings), which renders them ineffective as allergens build up on the outer surface within several weeks. The presence of encasings can provide a false sense of security and may not reduce long-term inhaled exposure.

Feather versus synthetic bedding

Contrary to earlier concern about feather bedding encouraging mites, most data now indicate that both mite and cat allergens are lower with feather bedding due to its tight weave than with synthetic bedding [42].

Cleaning impermeable surfaces

More than 95% of allergens are removed from hard surfaces by electrostatic cloths, surface spraying, or a damp cloth [43].

Chemical modification of allergens

The chemical denaturation of mite, cat, and cockroach allergens has been demonstrated in laboratory situations but is difficult in domestic practice. Methods include tannic acid and sodium hypochlorite [44,45]. These methods are confounded by the large quantity of nonallergenic dust present at these sites, which dilutes any effect, plus

the practical limitations of effectively penetrating deep into the carpet and mattress reservoirs, limiting the treatment to the surface dust.

Commercial products for allergen avoidance

Even the most cursory Internet search of “allergen avoidance” reveals a preponderance of products, all inferring promises of performance unlikely to be achieved in practice. Examples include claims of ridiculous numbers of mites in normal beds, coupled with the inference of complete mite control by their product (and by further inference, symptom control). These claims are not based on published data and are not true. I recently wrote to 100 such companies identified from an Internet search, and requested technical and clinical data. About 20 responded, only one with clinical data. Some of the technical data supplied was simply erroneous. The market is totally unregulated, with no accepted performance standards, no requirement to show efficacy, no validation, and limited information on toxicologic hazards. Although some industry-oriented groups have established systems of certification of products, their criteria are not public [46]. It makes selection of products difficult and uncertain.

Aeroallergens

Avoidance methods should be assessed by their impact on aeroallergen exposure, which can be measured using air filters and pumps, or nasal air samplers [47].

Aeroallergen can be reduced directly by improved ventilation (dilution) and air filtration as well as by control of reservoirs. However, the effect of filters alone on personal exposure is overestimated, as the clean air at the filter outlet quickly becomes diluted. When exposure to particles is generated by a source close to the subject (eg, exposure to mite allergen from bedding), then room filters operating at a distance in the room have only a small impact on exposure; filters mounted on the bed itself may be more useful [48]. On the other hand, if the allergen is continuously airborne (eg, cat allergen), then air filters in a room may have some clinical benefit [47].

We have recently shown that small filters worn in the nasal cavity can be used to reduce rhinitis symptoms associated with pollen exposure [49]. In principle, these also would minimize acute exposure to indoor allergens.

Multitargeted Approach

Only multitargeted approaches and ongoing attention to reducing total exposure is likely to be effective due to the broad dispersal of multiple allergens in houses and their continuous refreshment, ubiquitous distribution, and mobility. The UK MAAS study is an example of a multitargeted approach, utilizing vinyl bedroom flooring, HEPA vacuuming, impermeable mattresses (wiped weekly), hot-water washable toys, and weekly laundering

of bedding [41]. The seven-city intervention study used education and remediation for allergens and tobacco smoke in houses [6]. Their approach was guided by social learning theory, where the importance of the activities was modeled at targeting behavior of the caretakers. Education modules were aimed at dust mites, passive smoking, cockroaches, pets, rodents, and mold, and applied only where needed. The intervention consisted of impermeable encasings, HEPA vacuuming, HEPA air filtration (if tobacco smoke or mite/cat/mold allergens were present), and professional cockroach extermination.

When to Aspire to Allergen Avoidance

Despite all the technical doubts and inconsistencies, practicing allergists and their patients are confident that allergen avoidance does work for many people and is well worth maintaining. The “appropriate” patient is someone who is demonstrably allergic on the basis of allergy tests, has a reliable history of symptom exacerbations on exposure to that allergen, and is committed to making the changes required. Without doubt, some individuals significantly improve their asthma and rhinitis in this way.

Compliance and Acceptability

Patients or caregivers are interested in obtaining information about avoiding allergens when there is an initial diagnosis of asthma. However, the introduction of allergen avoidance within a family home is often daunting and expensive, and the long-term level of compliance is often low [50]. Compliance is improved by the use of trained and skilled counselors [6]. Advice such as relocating a dog or cat is seldom accepted, despite evidence that dog removal can be efficacious [51].

Recent Developments: Implications of the Hygiene Hypothesis and High-dose Tolerance for Allergen Avoidance

The hygiene hypothesis suggests that high microbial exposure early in life may protect from later allergic diseases via innate modulation of immune responses reducing the likelihood of allergy. The best examples involve fewer allergies, hayfever, and allergic asthma (but more symptoms of nonallergic asthma) among rural infants who receive high exposure to cattle barns. Such hypotheses are in contrast to the traditional approaches of allergen avoidance, which results in the increased sterility of domestic life. It can be asked, “Is an allergen-free house actually desirable?” A consistent picture is yet to emerge.

The most rigorous primary allergen-reduction study in infants reported a greater than twofold increase in mite allergy at ages 3, 5, and 7 years, but better lung function [52]. One of three alternative explanations was that the intervention reduced bacterial endotoxin exposure.

The emergence of high-dose tolerance to pet allergen exposure also challenges the linear dose-response basis of allergen avoidance. Although a consistent picture is yet to emerge, indications are that cat, dog, and even mite exposure may all have bell-shaped dose-response curves [53,54].

Conclusions

Despite a long history of advocacy by the mainstream allergic disease community, the role of allergen avoidance in the general prevention and management of allergic diseases is only tentatively supported, although it remains particularly relevant where exposure and symptoms have a clear association. Additionally, sub-clinical exposure may play an important role in asthma exacerbations [18,55]. However, aspects remain uncertain. These include the nature of the dose-response relationship between allergen exposure and clinical outcomes, and how this differs among allergens; how to best achieve clinically relevant reduction in domestic allergen exposure; whether our reliance on reservoir exposure has distorted our understanding of changes in inhaled exposure and led to ineffective interventions; and the differences in clinical impact of exposures at different ages, particularly in early life. Ultimately, we need to know how to intervene in houses generally (for both allergens and nonallergens) to minimize the incidence and symptoms of allergic diseases.

Overall, environmental factors play an important role in the acquisition, expression, and modulation of allergic diseases. Although allergens are only a tiny fraction of the total biologic material inhaled, they are an extremely important component. With a rising global asthma prevalence and in view of the uncertainties about how best to manage and prevent this chronic disease epidemic, an urgent need exists for the study of both the mechanisms and components involved to better understand and minimize the adverse health impacts associated with patterns of modern living.

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