Occasional review

Allergen avoidance in the treatment of asthma and atopic disorders

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The majority of asthmatic patients are atopic— that is, they have IgE mediated sensitivity to common inhalant allergens. Exposure and sensitisation to allergens from the house dust mite is established as an important risk factor for asthma in most parts of the world. In addition, several recent studies have provided evidence of the importance of exposure to other indoor allergens, particularly those from cats, dogs, and cockroaches. The rate of sensitisation to mites is directly related to exposure, whilst conversion from sensitisation to non-sensitisation may occur in indoor environments with low allergen levels.

The severity of asthma is also related to allergen exposure. Objective indices of asthma severity such as bronchial hyper-reactivity (BHR), forced expiratory volume in one second (FEV₁), and variability in peak expiratory flow rate (PEFR) in patients sensitised to dust mites correlate with the level of mite allergens in their beds. Peat et al found a similar prevalence of sensitivity to mites in children living in areas with two different levels of exposure to mites but BHR was more severe in sensitised children living in the area with the highest mite levels. The relationship between exposure and asthma symptoms in sensitised individuals is complex, with some patients reacting to very low doses of allergen whilst in others the allergen level required to cause symptoms may be considerably higher. Nonetheless, a pattern emerges in which asthma is usually more severe in those sensitised patients who are exposed to higher allergen levels. Avoiding exposure is the logical way to treat asthma when the offending allergen can be identified and effective methods of avoidance have been devised.

Effective allergen avoidance is recognised by the British Thoracic Society as an integral part of the overall management of the sensitised asthmatic patient. Allergen avoidance

The effectiveness of allergen reduction in the treatment of asthma was first suggested by studies in which patients were removed from their homes into a low allergen environment. Later, measures aimed at the reduction in allergen levels were attempted in patients’ homes.

LESSONS FROM HIGH ALTITUDE STUDIES

The levels of mite allergen are dramatically reduced at high altitude (>1500 m) where humidity is too low to support mite populations. Mite sensitive asthmatic children had a progressive reduction in non-specific BHR when taken from their homes in Holland to the mite-free environment of Davos, Switzerland. Similarly, a progressive reduction in asthma symptoms occurred in children admitted to the residential home at Misurina (altitude 1756 m). Further studies from Misurina reported a significant decrease in mite allergen-induced basophil histamine release, mite-specific serum IgE level, and methacholine BHR with reversal of this trend after 15 days of allergen re-exposure at sea level. Peroni et al found a significant reduction in total and mite-specific serum IgE and allergen-induced BHR after three and nine months at Misurina. These results suggest that avoidance of mite allergen leads to a decrease in airway inflammation with consequent improvement in non-specific BHR and symptoms, and that re-exposure results in a rapid relapse. The high altitude studies were not controlled and there is a possibility that avoidance of other domestic factors such as exposure to pets or environmental tobacco smoke contributed to the observed improvement in asthma control. Nevertheless, mite avoidance is the most plausible reason for clinical success. These high altitude studies (table 1) suggest that it is essential to achieve and maintain a major reduction in allergen levels and that, even with such a reduction in exposure, it may take many months for the effect on symptoms, medication use, pulmonary function, non-specific and specific BHR, and immunological parameters to become fully apparent.

An uncontrolled study of the effect of mite-free conditions at lower altitudes in which patients were admitted to the “mite-free” environment of a hospital room (allergen level <0.2 μg Der p 1/g) did result in improved airway reactivity and reduced treatment requirements, but the benefits were transient. Moving asthmatic patients into new “healthy homes” equipped with mechanical ventilation resulted in an increase in lung function and a decrease in medication use.

All the studies reviewed in table 1 suggest that asthmatic subjects allergic to mites improve when moved from their homes into a low allergen environment. They also provide information on the duration of avoidance necessary. For example, studies of mite allergen...
avoidance in patients’ homes have to be sufficiently long – if BHR is the primary outcome probably six months to a year is required.

Allergen avoidance in homes: practical measures
The real challenge facing practising physicians is to create a low allergen environment in patients’ homes. Although not easy, it is possible to achieve substantial reductions in allergen exposure. Effective control strategies should be tailored to individual allergens, flexible to suit individual needs and cost effective. Many different avoidance measures for mite allergens have been tested with some widely exaggerated claims, and only a few have been subjected to controlled trials. It is important to make a clear distinction between those measures that have been only tested in the laboratory, those tested in field trials, and those tested in clinical trials.

DISTRIBUTION AND AERODYNAMIC PROPERTIES OF INDOOR ALLERGENS: RELEVANCE TO AVOIDANCE
Knowledge of the sources and aerodynamics of allergen-carrying particles is essential for the design of successful strategies to reduce personal exposure. Allergens from mites, cats, dogs, and cockroaches have different aerodynamic properties (table 2). Mite and cockroach allergens can be detected in the air in significant amounts only after vigorous disturbance and are contained within relatively large particles (>10 μm diameter). In contrast, airborne cat and dog allergens are readily measured in houses with pets (and in a quarter of the homes without pets), and approximately 25% of airborne Fel d 1 and Can f 1 is associated with small particles (<5 μm diameter). This underlies the difference in the clinical presentation of the disease. Mite and cockroach sensitive asthmatics are usually unaware of the relationship between allergen exposure at home and asthma symptoms (exposure is low grade and chronic). The large particles, however, may contain a large quantity of allergen and even small numbers may cause a significant inflammatory response when impacted in the airways. In contrast, patients allergic to cats or dogs often develop symptoms within minutes of entering a home with a pet due to the inhalation of large amounts of airborne allergen on small particles which can penetrate deep into the respiratory tract inducing acute asthma. Application of this information is important and implies, for example, that air filtration units have no place in mite or cockroach avoidance but may be useful in removing cat and dog allergens from the air. It is important to know where patients receive most of their exposure. The bed is the most important source of mite allergens and lowering exposure in the bedroom is the primary target of avoidance. In contrast, it is likely that most exposure to allergens of domestic pets occurs in the living room area and this must be taken into account when planning avoidance strategies.

Table 1 High altitude studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Location (altitude)</th>
<th>Study design (duration of stay)</th>
<th>Clinical outcome</th>
</tr>
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<tbody>
<tr>
<td>Kerrebijn et al</td>
<td>Davos, Switzerland</td>
<td>House dust sensitive children</td>
<td>Clinical improvement; reduction in BHR (histamine)</td>
</tr>
<tr>
<td>Morrison Smith</td>
<td>Davos, Switzerland</td>
<td>212 children (Davos)</td>
<td>Improvement in symptoms and reduction in medication</td>
</tr>
<tr>
<td>Boner et al</td>
<td>Misurina, Italy</td>
<td>14 mite allergic children</td>
<td>Improvement of LF; reduction in BHR (exercise); reduction in medication</td>
</tr>
<tr>
<td>Piacentini et al</td>
<td>Misurina, Italy</td>
<td>12 mite sensitive children</td>
<td>Drop in antigen-induced basophil histamine release; reduction in BHR (methacholine) and IgE</td>
</tr>
<tr>
<td>Simon et al</td>
<td>Davos, Switzerland</td>
<td>17 mite sensitive children</td>
<td>Change in serum ECP and EPX and total IgE during exposure (3 months summer holidays at home)</td>
</tr>
<tr>
<td>Peroni et al</td>
<td>Misurina, Italy</td>
<td>12 mite allergic children</td>
<td>Decrease in total and specific IgE; reduction in BHR (exercise, histamine and allergen challenge)</td>
</tr>
<tr>
<td>Valeta et al</td>
<td>Misurina, Italy</td>
<td>12 mite allergic children</td>
<td>Decrease in PEF variability and improvement in BHR; after 3 weeks at homes PEF and BHR worsened</td>
</tr>
<tr>
<td>van Velzen et al</td>
<td>Davos, Switzerland</td>
<td>16 mite allergic children</td>
<td>Reduction in antigen-induced basophil histamine release; reduction in BHR (methacholine); decrease in the percentage of sputum eosinophils</td>
</tr>
</tbody>
</table>

LF = lung function; BHR = bronchial hyperreactivity; PEF = peak expiratory flow.

Table 2 Differences in the aerodynamic properties between house dust mite and cockroach and pet allergens

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Particle size</th>
<th>Airborne level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mite: Group 1</td>
<td>Large particles &gt;10 μm</td>
<td>Undisturbed; Detectable with conventional assays (&lt;0.2 ng/m³ for mite allergens, &lt;0.02 ng/m³ for cockroach)</td>
</tr>
<tr>
<td></td>
<td>Disturbed</td>
<td>Detectable after vigorous disturbance</td>
</tr>
<tr>
<td>Cockroach: Bla g 1</td>
<td>Large particles &gt;5 μm (~75%)</td>
<td>Homes with animal detectable in all homes. Levels 4-5 times higher with animal in the room</td>
</tr>
<tr>
<td></td>
<td>Disturbed</td>
<td>Detectable in about one third of the homes without artificial disturbance</td>
</tr>
<tr>
<td>Cat: Fel d 1</td>
<td>Large particles &gt;5 μm (~75%)</td>
<td>Homes with animal detectable in all homes. Levels 4-5 times higher with animal in the room</td>
</tr>
<tr>
<td></td>
<td>Disturbed</td>
<td>Detectable in about one third of the homes without artificial disturbance</td>
</tr>
<tr>
<td>Dog: Can f 1</td>
<td>Small particles &lt;5 μm (~25%)</td>
<td>Homes without animal detectable in all homes. Levels 1-3 times lower without animal in the room</td>
</tr>
</tbody>
</table>

CONTROL OF HOUSE DUST MITES AND MITE ALLERGENS
Bed and bedding
Covers: the most effective and probably most important avoidance measure is to cover the mattress, pillows, and duvet with covers that are impermeable to mite allergens. These covers were initially made of plastic and uncomfortable to sleep on, but the development
of water vapour permeable fabrics which are both impermeable to mite allergens and comfortable have considerably increased compliance. Allergen levels are dramatically reduced after the introduction of covers which should be robust, easily fitted, and easily cleaned as their effectiveness is reduced if they are damaged. Mite allergen can accumulate on the covers, possibly by circulation from the carpet, and it is important that covers are wiped at each change of bedding.

Washing: all exposed bedding should be washed at 55°C as this is the temperature that kills mites in the bedding.64 The cold cycle of laundry washing reduces allergen levels but most of the mites survive.64 Additives for the detergents providing a concentration of 0.03% benzyl benzoate, or dilute solutions of essential oils in normal and low temperature washing, provide alternative methods of mite control.65,66 Feather versus synthetic pillows: asthmatic patients are often told to avoid using feather pillows and to replace them with those filled with synthetic materials. This has been challenged recently, first with the finding that synthetic pillows were a risk factor for severe asthma and then with the report that polyester filled pillows contained more mite allergens than those filled with feathers.65

Carpets and upholstered furniture
Carpets are an important microhabitat for mite colonisation and a possible source of allergen from which beds can be reinfested.66 Ideally, fitted carpets should be replaced with polished wood or vinyl flooring. Exposure of carpets to direct strong sunlight for at least three hours kills mites and this simple and effective treatment may be used in loosely fitted carpets in certain climatic areas.67 Steam cleaning may be used as a method of killing mites and reducing allergen levels in carpets.68,69

Acaricides: a number of different chemicals that kill mites (acaricides) have been identified and have been shown to be effective under laboratory conditions.70 However, data on whether these chemicals can be successfully applied to carpets and upholstered furniture are still conflicting. Le Mao et al reported that long term mite avoidance can be maintained by twice yearly treatments with benzyl benzoate, but other studies could not confirm this.71,72 The method of application of the benzyl benzoate moist powder on carpets is very important.74 When carpets were treated for four hours only a very modest effect was observed, whilst allowing the powder to remain on the carpet for 12–18 hours with repeated brushing followed by vigorous vacuum cleaning reduced the concentration of mite allergens one month later. Allergen levels rebounded after two months, suggesting that repeated application every 2–3 months is necessary to control mite allergen levels.74 Thus, the main problem of chemical treatment is not its ability to kill mites but the means of getting the chemicals to penetrate deep into carpets and soft furnishings, the persistence of mite allergen until recolonisation occurs, and the nuisance of frequent re-applications. Acaricides are ineffective on mattresses and upholstered furniture.72–74

Liquid nitrogen: mites can be killed by freezing with liquid nitrogen.75 The technique can only be carried out by a trained operator which limits its use, especially since treatment needs to be repeated regularly. When used, both acaricides and liquid nitrogen should be combined with intensive vacuum cleaning following administration.

Tannic acid: the protein denaturing properties of tannic acid are well recognised and it has been recommended for the reduction of indoor allergen levels in house dust. Woodfolk et al confirmed the allergen denaturing properties of tannic acid but also showed that high levels of proteins in dust – for example, cat allergen in a home with a cat – blocked its effects.76 This suggests that ≥ 1% tannic acid solution could reduce mite allergen levels, but only with aggressive vacuum cleaning being carried out before and after the treatment and in homes without pets. Products which combine both an acaricide and tannic acid have been shown to reduce skin test reactivity of the extracts prepared from dust taken from the patient’s house and to have a temporary effect on mites and mite allergens.78–80

Vacuum cleaning: intensive vacuum cleaning may remove large amounts of dust from carpets, reducing the size of allergen reservoir.76 However, some vacuum cleaners (with inadequate exhaust filtration) may increase airborne Der p 1 levels during use.81,82 These results suggest that low levels of dust mite allergens are not a significant factor in asthma,39 whilst al-
allergen-specific but also specific to a particular geographical area with housing and climatic conditions being taken into account.

Air filtration and ionisers
Due to the aerodynamic characteristics of mite allergens it makes little sense to use air filtration units and ionisers as the only way of reducing personal exposure.

Conclusions: house dust mite avoidance measures
A large number of proprietary mite allergen control products are currently available on the market with claims of clinical efficacy that have not been adequately tested. Mites live in different sites throughout the house and it is unlikely that a single measure can solve the problem of exposure. An integrated approach including barrier methods, dust removal and removal of mite microhabitats is needed if a comprehensive reduction in mite allergen exposure is to be achieved (table 3). Even in the same geographical area there is a marked difference in mite allergen levels between houses, and the design of houses has a profound effect on mite allergen levels. These issues need to be addressed in designing and building “low allergen houses”.

PET ALLERGEN AVOIDANCE
Up to 60% of asthmatic patients show IgE mediated hypersensitivity to cat and/or dog allergens and up to one third of these sensitised individuals live in a home with a pet. In some parts of the world complete avoidance of pet allergens can be extremely difficult as sensitised patients can be exposed to pet allergens not only in homes with pets, but also in those without pets and in public buildings and public transport.

Breed, sex and castration
The major cat allergen Fel d 1 is produced primarily in the sebaceous glands and in the basal squamous epithelial cells of the skin with very high levels reported in cat anal sebaceous glands. Fel d 1 production is under hormonal control and the castration of male cats results in a 3–5 fold reduction of Fel d 1 concentration in skin washing with testosterone treatment restoring the Fel d 1 levels to pre-castration values. It has recently been suggested that Fel d 1 production is higher in male than in female cats, but the observed gender differences in Fel d 1 secretion are too low to suggest that patients allergic to cats could benefit by getting a female rather than a male cat or by castrating their male cats.

Another important question is whether one breed of cat (or dog) can produce more allergens or different allergens than any other? Since all domestic cats belong to the same species, it is unlikely that different breeds would produce breed-specific allergen molecules although there may be variation in the relative concentration of allergens produced by different breeds – for example, short hair and long hair.

Removal of the animal from the home
The best way to reduce exposure to cat or dog allergen is to remove the animal from the home. Even after permanent removal of the animal it can take many months before reservoir allergen levels decrease. Unfortunately, despite continued symptoms, many patients allergic to cats and/or dogs insist on keeping their pet. Asthma is often severe and difficult to control in pet sensitised asthmatics who continue to be exposed to the high allergen levels because they refuse to get rid of the family pet. Every effort should therefore be made to reduce exposure to pet allergens in homes where pets may coexist with a sensitised individual.

Control of airborne allergen levels with a pet in home
Airborne pet allergen levels increase by approximately fivefold when the pet is in the room, indicating that the immediate presence of a pet contributes to airborne allergen levels. When it is not possible to remove the animal, the pet should be kept out of the bedroom and preferably outdoors or in a well ventilated area such as the kitchen.

Cat and dog washing: there is controversy on the effect of washing the cat on Fel d 1 levels. A recent study showed no effect of washing in decreasing allergen shedding, but only two litres of water were used to wash a cat. Other trials, however, have shown that large quantities of allergen can be removed from cats by immersion in tap water resulting in a decreased concentration of airborne allergen. Washing dogs thoroughly in a bath using shampoo significantly reduces the levels of dog allergen in fur and dander samples.

Air cleaners and vacuum cleaners: HEPA filter air cleaners can significantly reduce airborne concentrations of cat and dog allergens in homes with pets and vacuum cleaners with built-in HEPA filters and double thickness vacuum cleaner bags remove allergen from dust reservoirs without leaking Fel d 1 and Can f 1. As carpets may accumulate allergens up to a level 100 times that of polished floors, carpeting and soft furnishings should ideally be removed.

Since getting rid of the family pet is rarely a viable option, we currently advise a set of measures listed in table 4 to patients who are allergic to cats or dogs and persist in keeping their pet. The clinical benefit afforded by the proposed avoidance measures has not yet been
AVOIDANCE OF COCKROACH ALLERGENS

Sensitisation to cockroach allergens is an important risk factor for asthma in the USA where cockroach infestation is common in substandard housing apartment complexes. Cockroaches have also been reported to be an important cause of asthma in the Far East (Taiwan, Japan) and there have been recent reports of cockroach-induced asthma in France. In the colder climate of the UK cockroach allergens are not routinely used in the evaluation of allergic disease although there have been recent cases of cockroach infestation associated with asthma in the London Borough of Tower Hamlets (Dr C. Luczynska, personal communication). In the USA cockroach asthma occurs primarily among lower socioeconomic groups and minority populations living in substandard housing. This patient population has the highest mortality and morbidity rates from asthma and is also the least compliant with any form of asthma treatment. Both physical and chemical procedures are used to control cockroach populations in houses. Reducing access to food and water is critical so waste food should be removed and surface water should be contained by reducing leakage through faulty taps and pipework and reducing condensation by improved ventilation. Cockroach access should be restricted by caulking and sealing cracks and holes in the plasterwork and flooring. Several chemicals are marketed in the USA and elsewhere for controlling cockroach infestations including diaphanone, chlorpyrifos, and boric acid. The most useful for patients with allergic disease are bait stations where the chemical is retained within a plastic housing. These stations may contain hydramethylnon (marketed as Combat) or avermectin (Avert). A paste formulation of hydramethylnon (Siege) is also marketed for use on cockroach runways and underneath counters etc.

Bait stations are generally effective in reducing cockroach levels for 2–3 months. The effect of cockroach control measures on allergen levels in houses has not been extensively studied, though a number of trials are underway. Cockroaches in apartment complexes are especially difficult to treat because of reinfestation from adjacent apartments. Asthma is the only disease unequivocally associated with cockroach infestation of houses and it is an important public health problem in towns and cities across the USA where housing conditions sustain large cockroach populations. Many patients are unaware that cockroaches may cause asthma so attempts to reduce cockroach allergen exposure must rely on improving patient education and concerted attempts by pest control companies and public health departments to reduce cockroach infestation.

Clinical trials of mite allergen avoidance in patients’ homes

Having explored the science behind allergen avoidance strategies, the important question is whether allergen avoidance in homes by these techniques improves asthma control in sensitised patients. Trials of mite allergen avoidance in allergic diseases are reviewed in table 5. It is difficult to conduct a placebo-controlled trial in this area because the combination of skin weal and home visit is a potent stimulus for a change in behaviour resulting in increased cleaning, removal of mite habitats, and reduction in allergen levels. Virtually every controlled study has observed a significant reduction in mite allergen levels and sometimes improved clinical symptoms in both the control and active groups. A population study on an unselected group of asthmatic subjects with retrospective analysis of atopic status – for example, specific serum IgE determined from the “bank” of blood samples taken at the beginning of the study – would partially address this problem by “blinding” patients to their allergen sensitivities. As stressed previously, a successful trial would need to achieve and maintain a major reduction in allergen levels, be reproduced in another setting (probably not less than a year with a run in period of at least six weeks), and have adequate power.

There are conflicting data on the effectiveness of allergen avoidance carried out in houses, primarily because most of the studies have been small, poorly controlled, and have often used measures that we now realise do not reduce mite allergen exposure. Consequently, many fail to show clinical benefits. Thirty one studies of mite allergen avoidance in homes of asthmatic patients are listed in table 5,71 110–119 seven of which used air cleaners, ionisers or precipitators,114 118 122 124 126 130 131 which is illogical due to the aerodynamics of mite allergens. Of the remaining 24, seven showed little or no effect of avoidance measures on mite/allergen levels,71 112 116 129 132 133 three were uncontrolled,110 115 125 one was not randomised,117 one did not monitor the effects on mite/allergen levels,111 one showed colonisation of bedding during the study,123 one showed no difference in allergen levels between the two study groups at the end of the study,128 and one used an
<table>
<thead>
<tr>
<th>Author and Year</th>
<th>Country</th>
<th>Study design and duration</th>
<th>Avoidance measures</th>
<th>Effect on mite/allergy</th>
<th>Clinical outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sarsfield et al. (Leeds, UK)</td>
<td>Ch, As; MS; n = 14; UC; C; 3–12 months</td>
<td>Mattress encased (plastic covers); synthetic pillows; bed dressed weekly; dusting, vacuuming</td>
<td>Reduction in mite counts (from 80 to 2; p &lt; 0.01)</td>
<td>Improvement in symptoms score (9 to 1.89; p &lt; 0.05)</td>
<td></td>
</tr>
<tr>
<td>Burr et al. (Cardiff, UK)</td>
<td>Ad, As; MS; n = 32; crossover PC; 6 weeks</td>
<td>Mattress encased (plastic covers); vacuum cleaning of the bed; laudering of the bedding</td>
<td>Not monitored</td>
<td>No improvement in daily PEF reading or drug usage</td>
<td></td>
</tr>
<tr>
<td>Burr et al. (Cardiff, UK)</td>
<td>Ch, As; MS; n = 53; PC; 8 weeks</td>
<td>Mattress, carpets and upholstery vacuumed; blankets, sheets laundered; bed dressed weekly; feather pillows, quilts replaced; soft toys removed</td>
<td>No difference in mite counts before and after treatment</td>
<td>Both active and control group improved, no difference between the groups</td>
<td></td>
</tr>
<tr>
<td>Burr et al. (Cardiff, UK)</td>
<td>Ch, As; MS; n = 21; crossover; C; 1 month + 1 month</td>
<td>New sleeping bags, pillows and blankets; mattress encased (plastic covers); carpets vacuumed</td>
<td>Colonisation occurred on new bedding after second study period</td>
<td>PEF variability lower during the treated period, but the difference NS; majority with higher PEF during the treated period (p &lt; 0.01)</td>
<td></td>
</tr>
<tr>
<td>Mitchell and Elliott (Auckland, N. Zealand)</td>
<td>Ch, As; MS; n = 10; C, crossover; 8 weeks (4 + 4)</td>
<td>Electrostatic precipitator in the child’s bedroom</td>
<td>Not monitored</td>
<td>Control vs active period; PEF: NS; medication use: NS</td>
<td></td>
</tr>
<tr>
<td>Korsgaard (Aarhus, Denmark)</td>
<td>Ad, As and/or AR, HDS; n = 23; UC; C; 6 months</td>
<td>Mattress encased (plastic covers), n = 3; synthetic pillows, n = 22; bedroom carpet removed, n = 7; dusting, vacuuming</td>
<td>Not monitored in the study group over time</td>
<td>Beneficial effect reported by 15 patients, no change by 4</td>
<td></td>
</tr>
<tr>
<td>Dorward (Leeds, UK)</td>
<td>Ad, As, MS; n = 46; C; 12 weeks run n = 12 weeks intervention</td>
<td>Mattress vacuumed twice; synthetic pillows and quilts; bed dressed weekly; bedroom carpet removed; bedroom aired 1 day</td>
<td>Difference between groups in BC (p &lt; 0.01) but not in LG or M</td>
<td>Improvement active vs control group: PEFR: NS (both improved), symptoms: p &lt; 0.05, medication: NS</td>
<td></td>
</tr>
<tr>
<td>Murray and Ferguson (Vancouver, Canada)</td>
<td>Ch, As, MS and/or HDS; n = 20; C; 1 month</td>
<td>Mattress, pillows encased (vinyl covers); toys, carpets and upholstery removed (bedroom); washing, dusting, vacuuming</td>
<td>Not monitored</td>
<td>Improvement active vs control group: symptoms (p &lt; 0.01), medication (p &lt; 0.5), PEFR (p &lt; 0.05) and BHR (p &lt; 0.001)</td>
<td></td>
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<tr>
<td>Bowlas (Brisbane, Australia)</td>
<td>Ad, Ch, As, MS; n = 9; PC; crossover; 4 weeks (2 + 2)</td>
<td>Active period: mattress and pillow covered; washing, dusting, vacuuming; dust retardant and anti-static spray; active electrostatic filter of HEPA filter; placebo: inactivated air filter</td>
<td>Not monitored</td>
<td>Control vs active period: symptom scores: NS; PEF: NS</td>
<td></td>
</tr>
<tr>
<td>Walsh and Evans (Liverpool, UK)</td>
<td>Ad, As; n = 50; C; 1 year</td>
<td>Mattress, pillows encased (plastic covers); synthetic duvets; bedroom carpet, upholstery removed (n = 7); washing, dusting, vacuuming</td>
<td>Significant fall in mite counts in the active group (p &lt; 0.001), but not in the control group</td>
<td>Improvement in MS As in active group: FEV1, FVC (p &lt; 0.02), PEFR (p &lt; 0.05), BHR (PC20) (p &lt; 0.01), medication (p &lt; 0.05), total IgE (p &lt; 0.05)</td>
<td></td>
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<tr>
<td>Gillies (Leeds, UK)</td>
<td>Ch, As; n = 26; C; A – 12/52 avoidance, B 6/ 52 observation + n = 52 avoidance</td>
<td>Mattress, pillows encased (plastic covers); synthetic bedding; soft toys and pets excluded from bedroom; vacuuming</td>
<td>Mite counts: A – 40 (start), 1.2 (6/52), 0.8 (12/52); B – 22 (start), 10 (6/52), 2 (12/52)</td>
<td>Fall in total serum IgE in MS Ch (p &lt; 0.005); BHR, symptoms, medication use and PEF: NS</td>
<td></td>
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<tr>
<td>Dowgier (Glasgow, UK)</td>
<td>Ad, As, MS; n = 21; B; 8 weeks</td>
<td>Mattress and bedroom carpet treated with liquid nitrogen; washing, dusting, vacuuming; soft toys, plants and upholstery excluded from bedroom</td>
<td>Fall in number of intact mites in active group (p &lt; 0.001); no change in control</td>
<td>Active vs control: fall in the number of hours wheezing (p &lt; 0.05); reduction in BHR (p &lt; 0.002); total and specific IgE: NS</td>
<td></td>
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<tr>
<td>Verral (Hamilton, Ontario, Canada)</td>
<td>Ad, Ch, As; MS; n = 13; DB, crossover; 4 periods; 3/52 each</td>
<td>Laminar flow air cleaner device in the bedroom</td>
<td>Not monitored</td>
<td>No difference between the groups in the number of symptom-free days and symptom severity and PEFR</td>
<td></td>
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<tr>
<td>Reiser (London, UK)</td>
<td>Ch, As; MS; n = 46; DB PC; 24 weeks</td>
<td>Mattress sprayed once every 2 weeks for 3 months with either Natamycin or placebo; mattress vacuumed</td>
<td>Small, NS trend to a fall in Der p 1 in both groups</td>
<td>No change in BHR, symptoms and LF</td>
<td></td>
</tr>
<tr>
<td>Reisman (Buffalo, USA)</td>
<td>Ad, Ch, As; AR, MS; n = 32; DB PC, crossover; 8 weeks (4 + 4)</td>
<td>Active period: HEPA air cleaner, placebo period: placebo filter</td>
<td>Not monitored</td>
<td>Control vs active period: symptom and medication scores NS; last 2 weeks of each period: nasal congestion, eye irritation (p &lt; 0.05); asthma symptoms NS</td>
<td></td>
</tr>
<tr>
<td>Morrow Brown and Merritt (Derby, UK)</td>
<td>Ad and Ch, As and/or AR and/or AD, MS; n = 25; UC; 12 months</td>
<td>Acarosan foam on mattress and bedding and moist powder on carpets and soft furniture</td>
<td>Reduction in Der p 1 level</td>
<td>Active vs control period: symptom: NS; LF: NS; PEF: NS; BHR (methacholine): NS</td>
<td></td>
</tr>
<tr>
<td>Antoniello (Ancona, Italy)</td>
<td>Ad, Ch, As; MS; n = 9; PC; crossover, 16 hours (8 + 8)</td>
<td>A: mattress, pillow and quilt covered, carpets sprayed (3% tannic acid) 4 months; B: mattress and carpet treated with benzyl benzoate; C: placebo on mattress and carpet</td>
<td>No difference in reservoir levels of mite allergens between the periods; fall within both groups (p &lt; 0.05)</td>
<td>Significant increase in BHR (PC20) in the encasing regimen group (A): within group p &gt; 0.01; no change in groups B and C: between groups p &gt; 0.05</td>
<td></td>
</tr>
<tr>
<td>Ehren (Berlin, Germany)</td>
<td>Ch, As; MS; n = 24; DB PC; 12 months</td>
<td>Investigated the effect of supplementary computer instruction on adherence to mite avoidance measures</td>
<td>Significantly lower group 1 level in bedroom carpet in computer instructed group</td>
<td>No change in FEV1; computer instructed group significantly less symptomatic by study weeks 9 and 10 (p &lt; 0.033)</td>
<td></td>
</tr>
<tr>
<td>Huss (Washington, USA)</td>
<td>Ad, As; MS; n = 52; 12 weeks</td>
<td>Benzyl benzoate foam or placebo on mattress and upholstery; benzyl benzoate powder or placebo on carpets</td>
<td>No significant difference in Der 1 between the groups</td>
<td>Active vs placebo: clinical score, drug score, LF, PEF: NS</td>
<td></td>
</tr>
<tr>
<td>Dieterman (Strasbourg, France)</td>
<td>Ad, Ch, As; MS; n = 26; DB PC; 12 months</td>
<td>Active period: HEPA air cleaner; placebo period: placebo filter; routine house cleaning</td>
<td>No significant difference in Der 1 between the groups</td>
<td>Active vs control period: PEF: NS; symptom scores: NS (trend towards increased cough during active period); medication: NS</td>
<td></td>
</tr>
<tr>
<td>Warner (London, UK)</td>
<td>Ch, As; MS; n = 20; DB PC; crossover; 12 weeks (6 + 6)</td>
<td>Active period: active ionisers; placebo period: placebo ionisers</td>
<td>Active vs control period: airborne Der p 1 (p &lt; 0.0001)</td>
<td>Active vs passive period: symptom scores: NS; LF; NS; PEF: NS (histamine): NS; PEF: NS</td>
<td></td>
</tr>
<tr>
<td>Warburton (Manchester, UK)</td>
<td>Ad, As; MS; n = 12; (active + passive treatment 30 + 24 days)</td>
<td>Active period: HEPA air cleaner; passive period: no HEPA air cleaner</td>
<td>Airborne Der p 1 below detection limit in two thirds of samples</td>
<td>Significant improvement in symptoms in both groups, but active vs placebo: NS; LF and BHR, active vs placebo: NS</td>
<td></td>
</tr>
<tr>
<td>Marks (Sydney, Australia)</td>
<td>Ch, As; PC; 3 months run-in + 6 months treatment</td>
<td>Active tannic acid/acaricide to mattress, pillow, duvet, blankets, carpets and upholstery; mattress, pillow and quilt covered; placebo: inactive spray</td>
<td>At 2 weeks Der p 1 fell to 29% of baseline (p = 0.04) compared with placebo; 3 and 6 months: NS</td>
<td>Significant improvement in symptoms in both groups, but active vs placebo: NS; LF and BHR, active vs placebo: NS</td>
<td></td>
</tr>
</tbody>
</table>
### Table 5 contd

<table>
<thead>
<tr>
<th>Author</th>
<th>Study design and duration</th>
<th>Avoidance measures</th>
<th>Effect on mite/allergen</th>
<th>Clinical outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Settel et al[35] (Verona, Italy)</td>
<td>Ch, As, MS; n = 32</td>
<td>Mattress encased (plastic covers); regular cleaning of mattresses; carpet removed and curtains</td>
<td>Assessed by Acarix test; no difference between 3 study groups</td>
<td>No difference in BHR (P&lt;0.02) between 3 study groups; no change in serum IgE concentrations</td>
</tr>
<tr>
<td>Hus et al[33] (Washington, USA)</td>
<td>Ch, As, AR, MS; n = 32; DB PC; 12 months</td>
<td>Mattress encased (plastic covers); regular cleaning of mattresses; carpet removed and curtains</td>
<td>No change in mite allergen content in BC or LC</td>
<td>No change in LF and PEF between groups</td>
</tr>
<tr>
<td>Geller-Bernstein et al[36] (Rehovot, Israel)</td>
<td>Ch, As, AR, MS; n = 32; DC, DB PC; 12 months</td>
<td>Mattress encased (plastic covers); regular cleaning of mattresses; carpet removed and curtains</td>
<td>Active: fall in Der f 1 from 10.00 to 4.15; control: fall in Der f 1 from 6.01 to 3.01</td>
<td>Significant improvement in severity of asthma; no change in PEFR and wheeze</td>
</tr>
<tr>
<td>Carswell et al[37] (Bristol, UK)</td>
<td>Ch, As, MS; n = 49; DB PC; 6 months</td>
<td>Mattress encased (plastic covers); regular cleaning of mattresses; carpet removed and curtains</td>
<td>Active vs placebo: PEF; NS; BHR (histamine): NS; LF (FEV1): p&gt;0.05; symptoms: p&gt;0.05; medication use: p=0.01</td>
<td>Active vs placebo: PEF; NS; BHR (histamine): NS; LF (FEV1): p&gt;0.05; symptoms: p&gt;0.05; medication use: p=0.01</td>
</tr>
<tr>
<td>Frederick et al[38] (Southampton, UK)</td>
<td>Ch, As, MS; n = 31; single blind, crossover; run in 2/53; treatment periods 3/12</td>
<td>Mattress encased (plastic covers); regular cleaning of mattresses; carpet removed and curtains</td>
<td>Active vs placebo: significantly lower levels of eosinophil peroxidase (p=0.02); within group: symptoms, PEFR, BHR (P&lt;0.05); NS: NS</td>
<td>Active vs placebo: significantly lower levels of eosinophil peroxidase (p=0.02); within group: symptoms, PEFR, BHR (P&lt;0.05); NS: NS</td>
</tr>
<tr>
<td>van der Heide et al[39] (Groningen, Holland)</td>
<td>Ch, As, MS; n = 45; DB PC; 6 months</td>
<td>Mattress encased (plastic covers); regular cleaning of mattresses; carpet removed and curtains</td>
<td>M: 100% reduction in active vs 53% reduction in placebo (p&lt;0.0001); BC: active vs placebo: NS</td>
<td>Active vs placebo: PEF; NS; BHR (histamine): NS; LF (FEV1): p&gt;0.05; symptoms: p&gt;0.05; medication use: p&gt;0.01</td>
</tr>
<tr>
<td>Hallen et al[40] (Odense, Denmark)</td>
<td>Ch, As, MS; n = 60; DB PC 12 months</td>
<td>Mattress encased (plastic covers); regular cleaning of mattresses; carpet removed and curtains</td>
<td>Active vs placebo: significant reduction in Der p 1 in mattress</td>
<td>Significant improvement in BHR (histamine) in group 3; trend to improvement in group 2</td>
</tr>
<tr>
<td>van der Heide et al[41] (Groningen, Holland)</td>
<td>Ch, As, MS; n = 59; DB PC randomised, 3 parallel group; 12 months</td>
<td>Mattress encased (plastic covers); regular cleaning of mattresses; carpet removed and curtains</td>
<td>Significant reduction in Der p 1 with covers (group 3) compared with group 1 and 2</td>
<td>Significant improvement in BHR (histamine) in groups 1 and 3</td>
</tr>
</tbody>
</table>

### Table 6 House dust mite allergen avoidance in allergic rhinitis and atopic dermatitis

<table>
<thead>
<tr>
<th>Author</th>
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<th>Clinical outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roberts[42] (Swansea, UK)</td>
<td>Ch, As, MS; n = 15; UC; 6 weeks</td>
<td>Mattress encased (plastic covers); regular cleaning of mattresses; carpet removed and curtains</td>
<td>Assessed by Acarix test; no difference between 3 study groups</td>
<td>Fifteen patients improved, three remained unchanged</td>
</tr>
<tr>
<td>August[43] (UK)</td>
<td>Ch, As, MS; n = 37; UC; 4–56 weeks</td>
<td>Mattress encased (plastic covers); regular cleaning of mattresses; carpet removed and curtains</td>
<td>No change in mite/allergen content in BC or LC</td>
<td>19% complete remission, 41% almost unchanged</td>
</tr>
<tr>
<td>Colleff et al[44] (Glasgow, UK)</td>
<td>Ch, As, MS; n = 20; PC; 12 weeks</td>
<td>Mattress encased (plastic covers); regular cleaning of mattresses; carpet removed and curtains</td>
<td>Mite counts: 26% fall in NV (p&lt;0.01), 50% fall in nV (p&lt;0.01), 15% rise in NV, 25% fall in nV (both NS)</td>
<td>Symptom scores: improvement rates 24% NV, 20.4% nV, 8.4% NV and 0.7% nV. Fall in mite specific IgE: NV (p&lt;0.05)</td>
</tr>
<tr>
<td>Kniest et al[45] (Utrecht, Holland)</td>
<td>Ch, As; n = 20; DB PC parallel group; 12 months</td>
<td>Mattress encased (plastic covers); regular cleaning of mattresses; carpet removed and curtains</td>
<td>Active vs control group: Acarix test (p&lt;0.05)</td>
<td>Active vs control (matched pairs): symptom scores (p&lt;0.05); physicians’ assessment (NS); medication (NS); total IgE (p&lt;0.01)</td>
</tr>
<tr>
<td>Howarth et al[46] (Southampton, UK)</td>
<td>Ch, As, MS; n = 35; DB PC; 6 weeks</td>
<td>Mattress, pillows and duvet covered in active or placebo covers</td>
<td>Active vs control group: significant reduction in Der p 1</td>
<td>Active vs control: improvement in sneezing (p&lt;0.02), rhinorrhea (p&lt;0.01) and nasal blockage (p=0.006)</td>
</tr>
<tr>
<td>Sando et al[47] (Nagoya, Japan)</td>
<td>Ch, As; n = 30; (3–4 weeks)</td>
<td>Patients hospitalised to clean room</td>
<td>No change in mite/allergen content in BC or LC</td>
<td>Improvement in symptoms, long term remission, decrease in eosinophils and mite-specific IgE</td>
</tr>
<tr>
<td>Tan et al[48] (Liverpool, UK)</td>
<td>Ch, As, MS; n = 48; DB PC; 6 months</td>
<td>Mattress, pillows and duvet covered in active or placebo covers</td>
<td>Der p 1 in carpets: median reduction 91% active, 89% control; mattress: insufficient dust (active)</td>
<td>Active vs control: change in eczema severity score (p&lt;0.001) final eczema severity score (p&lt;0.001); mean final area affected (p&lt;0.001)</td>
</tr>
</tbody>
</table>

For definition of abbreviations see footnote to table 5.

The remaining nine studies showed a significant reduction in mite counts and/or mite allergen levels. In three of these the period of treatment was too short[120,121,126] but nonetheless showed some effect (fall in the number of hours of wheezing and some effect on BHR),[121] fall in total serum IgE,[126] reduction in the levels of eosinophil peroxidase.[136]

The final six controlled studies achieved both a significant reduction in mite/allergen levels and were sufficiently long to show an effect on outcomes.[137,138,139] All six studies showed evidence of clinical benefit such as a significant improvement in lung function, symptoms, and medication use but there was no effect on BHR (six month study, probably too short for this outcome),[139] a significant increase in BHR (PC<0.05) was reported after eight months,[127] improvement in pulmonary function, BHR, medication, and IgE was seen[147] and a reduction in the dose of inhaled steroid, reduction in non-specific BHR, and improvement in symptoms acaricide without good evidence of the effect on mite allergens.[134]
and PEFR was found. In a multiple regression analysis of the factors contributing to the improvement of BHR van der Heide et al concluded that the greatest improvement was found in patients who had the largest decrease in Der p 1 concentration in mattress dust.127

Allergen avoidance in the treatment of other atopic diseases

Allergen avoidance also improves disease control in other atopic disorders such as atopic dermatitis and allergic rhinitis. The relevant clinical trials128–136 are reviewed in table 6.

Conclusions

Minimising the impact of identified environmental risk factors such as house dust mites, cats, and dogs is a first step in reducing the severity of asthma. Although environmental control is difficult, it should be an integral part of the overall management of allergen sensitised patients. As a recommendation for future trials the Third International Workshop on Indoor Allergens and Asthma concluded: “There is an urgent need to develop adequately powered, randomised, controlled studies to investigate the potential benefits of low allergen domestic environments in patients with allergic disease. Such studies need to address compliance, cost effectiveness, be of adequate length (e.g. 12 months), and be tailored for different socioeconomic groups and age groups”.147 The 1995 revision of the British Thoracic Society asthma guidelines states: “Support for house dust mite avoidance measures reflects a change to the 1993 guidelines but further research into methodology and duration of action of these measures is needed”.139 If the benefits attributable to allergen avoidance were instead attributed to a new drug, that drug would be the subject of trials involving thousands of patients. It is unfortunate that the perceived lack of commercial benefit has discouraged large scale, population based trials. There remains an urgent need to develop a large scale trial of the widespread applicability of mite avoidance and the effect on patient symptoms, exacerbation rate, use of medication, and overall health costs.

Dr A Custovic is supported by the Lancardis Foundation.

10 de Blay F, Kassel O, Chapman MD, Ott M, Van der Heide S, De Montchy JGR, de Vries K, Bruggink TM, Kaufman HF. Seasonal variation in airway hyperresponsiveness and natural exposure to house dust mite allergens.
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53 McDonald LG, Tovey E. The role of water temperature and laundry procedures in reducing house dust mite population and allergen content of bedding. J Allergy Clin Immunol 1992;90:599–608.


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A Custovic, A Simpson, M D Chapman and A Woodcock

*Thorax* 1998 53: 63-72
doi: 10.1136/thx.53.1.63

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