

Position paper

The effectiveness of measures to change the indoor environment in the treatment of allergic rhinitis and asthma: ARIA update (in collaboration with GA²LEN)

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Allergen exposure in sensitized individuals is one of the numerous factors which have been related to the worsening of asthma and rhinitis (1–3). If allergen exposure contributes to the severity of symptoms, then one would expect that reducing exposure should improve the symptom control. However, the evidence is equivocal as to whether measures to change the indoor environment are effective in the treatment of allergic airway diseases. In this document we focussed on studies of the effectiveness of environmental control measures aimed at reducing allergen exposure to house dust mites and domestic pets in the management of allergic rhinitis and asthma published between January 2000 and September 2004 (i.e. primary prevention by allergen avoidance and measures to reduce outdoor allergen exposure are not included in this review).

The undisputed facts about allergen exposure and allergic respiratory diseases

Experimental studies have demonstrated that a low-dose allergen challenge which mimics 'real life' increases nonspecific airway reactivity amongst sensitized asthmatics (4). Furthermore, several cross-sectional studies have reported the relationship between domestic allergen exposure and asthma severity. Nonspecific bronchial reactivity, peak expiratory flow rate (PEFR) variability and pulmonary function in mite sensitive subjects correlate with dust mite allergen levels in beds (5).

Patients with very severe (brittle) asthma are significantly more often both sensitized and exposed to high levels of sensitizing allergen compared with patients with mild disease (6). Exhaled NO is higher in asthmatics both sensitized and exposed to the sensitizing allergen compared with those who are sensitized, but not exposed (7). Most markers of asthma severity (airway reactivity, eNO and lung function) in atopic asthmatics are worse in those subjects who are exposed to sensitizing allergens compared with those not exposed (8). In addition, combination of sensitization, high exposure to sensitizing allergen and respiratory viral infection substantially increases the risk of hospital admission (9). However, demonstrating the link between exposure and disease severity does not equate to demonstrating the benefits of allergen avoidance.

Does allergen avoidance work?

In patients with seasonal allergic rhinitis, the absence of exposure outside the season is associated with a dramatic improvement in symptoms (e.g. hay fever sufferers in Europe sensitized to grass pollen do not have any symptoms during the winter months). Removal of atopic asthmatic children from their homes to the low-allergen environment (e.g. high altitude sanatoria) improves airway reactivity and reduces airway inflammation (10, 11). Clearly, this illustrates that complete avoidance of sensitizing allergen may improve symptoms of

respiratory allergic disease. However, the challenge is to achieve this result with measures which can be used in patients' homes, and it remains unclear whether a major 'real-life' reduction in personal exposure can be achieved.

The equivocal findings about allergen exposure and allergic respiratory diseases

Clinical trials of allergen avoidance in asthma

There are conflicting data on the effectiveness of domestic allergen control in asthma. A Cochrane meta-analysis concluded that current chemical and physical methods aimed at reducing exposure to mite allergens seem to be ineffective and cannot be recommended for mite sensitive asthmatics (12). However, it is worth emphasizing that only four of 23 trials included have achieved a reduction in mites/allergen levels and were sufficiently long to show an effect on measured outcomes. This meta-analysis was updated in 2004, and the update comprised 49 studies (search until June 2004). Mite reduction was achieved in 13 trials; reduction was unsuccessful in 24 and was not measured or reported in the remaining 12 trials. The conclusions of the updated meta-analysis remained unchanged, i.e. current methods of mite allergen avoidance should not be recommended for mite sensitive asthmatics (13). A further Cochrane meta-analysis reported on the efficacy of pet allergen control measures for allergic asthma in children and adults. However, only two of 34 studies met the inclusion criteria for the review. Both studies were small (22 and 35 participants respectively). No beneficial effect from the active intervention (use of air filtration units) could be demonstrated (14).

Studies in adults

Several recent studies investigated the effectiveness of mite allergen-impermeable mattress, pillow and duvet encasings as a single intervention (with sham covers for the control group) in adults with asthma. The largest double-blind, placebo-controlled trial was carried out 1122 adult patients with physician-diagnosed asthma who were taking regular inhaled corticosteroids (ICS) and using at least 100 µg/day of salbutamol or equivalent per day (15). The primary outcomes were mean morning PEFR over a 4-week period during the run-in and at 6 months, and the proportion discontinuing ICS in a phased reduction during months 7–12. There was no difference in either of the primary outcomes, or in the secondary outcomes (e.g. mean proportionate ICS reduction for all patients entering reduction phase; 47% *vs* 48%) for the whole group or the mite-sensitive subgroup. Further analysis of a sub-sample of patients highly sensitive to mites (IgE ≥ 10 kU/l) and with high baseline mattress mite allergen levels (> 10 µg/g dust) revealed no significant difference in the outcomes between the groups.

A smaller recent study recruited only subjects on inhaled steroids who were both allergic to dust mites and exposed to high levels of mite allergen in their homes, but were not sensitized to a pet with which they lived (16). Although there was a trend towards an increase in PEFR in both groups throughout the study, there was no difference between the groups at any time point. In addition, there was no difference between the groups in any of the other outcome measures (including symptom diaries and asthma medication).

A recent study demonstrated a beneficial effect of encasings on Der p 1 (reduction 87%) and morning PEFR (20 l/min increase). The number of patients, however, was small (*n* = 52) and the intervention period was short (only 9 weeks) (17).

Most of the studies in adults demonstrate that in the absence of other mite control measures, allergen-impermeable covers are clinically ineffective for routine management of adult asthma. It remains possible that a much more extensive intervention in carefully selected subgroup of patients could have some effect, but that has not as yet been adequately addressed.

Children

A small double-blind randomized study of polyurethane encasings for the mattress and pillows recruited mite sensitized asthmatic children (*n* < 60) with a positive mite bronchial challenge and mattress Der p 1 levels > 2 µg/g (excluding pet-sensitized pet owners) (18). There was a reduction in the dose of inhaled steroid of *c.* 50% in the active group which was not seen in children in the control group (*P* = 0.007). This effect was only apparent after the encasings had been in place for 6 months, and was maintained to 12 months. There was no difference between groups in the secondary outcome measures (PEFR and dose of mite allergen provoking a positive challenge).

The other recent large study in children aged 5–11 years (*n* = 937) tested a comprehensive intervention which was tailored to the child's sensitization and exposure status (included advice on passive smoke exposure where appropriate) (19). Children from seven inner city areas of the USA with high levels of poverty were recruited if they had a physician diagnosed poorly controlled asthma and at least one positive skin test. It is worth noting that less than half of the subjects were on controller treatments, despite moderately severe asthma. Mattress and pillow encasings and a high filtration vacuum cleaner were supplied to all homes. No attempt was made to introduce placebo devices into control homes. Mite, cat and cockroach allergen levels fell in both groups during the intervention, and for mite and cat the reduction was greater in the active compared with the control group. Children in the intervention group had significantly more symptom-free days compared with control; this effect was significant within

Table 1. Practical measures for reducing dust mite and pet allergen levels: effect on allergen levels and the clinical effect on symptoms of rhinitis and asthma

Measure	Effect on allergen levels	Clinical effectiveness
House dust mite allergen avoidance		
Encasing mattresses, pillows and quilts in impermeable covers	Ib	Ia – no effect in adults Ib – some effect in children
Washing bedding in the hot cycle (55–60°C)	IIb	IV
Replacing carpets with hard flooring	Ib	IV
Acaricides and/or tannic acid	III	IV
Minimizing dust accumulating objects in closed cupboards	IV	IV
Vacuum cleaners with integral HEPA filter and double thickness bags	IIb	IV
Removing, hot washing/freezing of soft toys	IV	IV
Pet allergen avoidance		
Removing cat/dog from the home	IIb	IV
Keeping the pet out of the main living areas and bedrooms	IIb	IV
HEPA filter air cleaners	Ib	Ia – no effect in pet allergy
Washing a pet	IIb	IV
Replace carpets with linoleum or wood flooring	IV	IV
Vacuum cleaners with integral HEPA filter and double thickness bags	IV	IV

Evidence level graded according to the Scottish Intercollegiate Guidelines Network recommendations: Ia, evidence obtained from meta-analysis of randomized-controlled trials; Ib, evidence obtained from at least one randomized-controlled trials; IIa, evidence obtained from well designed controlled study without randomization; IIb, evidence obtained from at least one other type of well-designed quasi-experimental study; III Evidence obtained from well-designed nonexperimental descriptive studies, such as comparative studies, correlation studies and case studies; IV, Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.

2 months, and was sustained throughout the 2-year period. The number of Emergency Room visits was also reduced during the intervention year. Thus, this comprehensive intervention in poor, inner-city homes costing *c.* \$2000 per child was associated with a further 34 symptom free days over a 2-year period. Statistical modelling indicated that for mite and cockroach allergen, the increase in symptom free days was seen predominantly in those children with larger (> 50%) reductions in allergen levels.

Clinical trials of allergen avoidance in rhinitis

A systematic review on dust mite avoidance measures for perennial allergic rhinitis was published in 2003 (20). Only four trials satisfied the inclusion criteria, all of which were small and judged to be of poor quality. There was no beneficial effect of physical or chemical intervention. Subsequent to this meta-analysis, a recent large study ($n = 279$) investigated the effectiveness of mite allergen-impermeable encasings in mite sensitized patients aged 8–50 years with perennial rhinitis and a positive nasal challenge test to mite extract (21). The active covers reduced the level of mattress Der p 1 to *c.* 30% of the baseline level, whereas the placebo covers had no effect ($P < 0.001$). Both groups reported a decrease in symptom scores during the 12-month follow-up period, with no difference in the primary outcome measure (symptom scores) between the groups. In addition, there was no difference between groups in any of the secondary outcome measures.

Two small studies addressed the effects of pet allergen control measures in rhinitis. In a randomized-controlled trial of the efficacy of HEPA filters, nasal and pulmonary

symptoms were assessed in 35 patients. No difference in nasal symptoms between active intervention and placebo group was demonstrated (22). In another small study ($n = 31$) a set of allergen control measures (wash all walls and floors, remove carpeting from bedrooms, apply tannic acid, wash bedding, replace duvets and pillows, use impermeable covers, wash cat every 2 weeks, etc.) resulted in a fall in Fel d 1 level to 6.8% of baseline and in a significant improvement in nasal symptoms and nasal peak flow (23).

Conclusions

Although the general consensus is that allergen avoidance should lead to an improvement of symptoms, there is little evidence to support the use of physical or chemical methods to control dust mite or pet allergen levels (Table 1). The use of mattress encasings or HEPA filters as a single intervention for mite and pet allergy in adults with asthma or rhinitis cannot be advocated. Adequately powered multifaceted interventions in large numbers of subjects have not been conducted in adults, and thus there is currently inadequate evidence to advise this as a strategy to this age group. For children the majority of studies suggest that environmental control measures may be of some benefit.

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References

1. Van der Heide S, de Monchy JGR, de Vries K, Dubois AEJ, Kauffman HF. Seasonal differences in airway hyperresponsiveness in asthmatic patients: relationship with allergen exposure and sensitisation to house dust mites. *Clin Exp Allergy* 1997;**27**:627–633.
2. Van Strien RT, Verhoeff AP, van Wijnen JH, Doekes G, de Meer G, Brunekreef B. Infant respiratory symptoms in relation to mite allergen exposure. *Eur Respir J* 1996;**9**:926–931.
3. Nelson RP, DiNicolo R, Fernandez-Caldas E, Seleznick MJ, Lockey RF, Good RA. Allergen-specific IgE levels and mite allergen exposure in children with acute asthma first seen in an emergency department and in nonasthmatic control subjects. *J Allergy Clin Immunol* 1996;**98**:258–263.
4. Arshad HS, Hamilton RC, Adkinson NF. Repeated aerosol exposure to small doses of allergen. A model for chronic allergic asthma. *Am J Respir Crit Care Med* 1998;**157**:1900–1906.
5. Custovic A, Taggart SCO, Francis HC, Chapman MD, Woodcock A. Exposure to house dust mite allergens and the clinical activity of asthma. *J Allergy Clin Immunol* 1996;**98**:64–72.
6. Tunnicliffe W, Fletcher T, Hammond K, Roberts K, Custovic A, Simpson A et al. Sensitivity and exposure to indoor allergens in subjects with differing asthma severity. *Eur Respir J* 1999;**13**:654–659.
7. Simpson A, Custovic A, Pipis S, Adisesh A, Faragher B, Woodcock A. Exhaled nitric oxide, sensitisation and exposure to allergens in asthmatics not taking inhaled steroids. *Am J Respir Crit Care Med* 1999;**160**:45–49.
8. Langley SJ, Goldthorpe S, Craven M, Morris J, Woodcock A, Custovic A. Exposure and sensitisation to indoor allergens: effect on lung function, bronchial reactivity and exhaled nitric oxide in asthma. *J Allergy Clin Immunol* 2003;**112**:362–368.
9. Green RM, Custovic A, Sanderson G, Hunter J, Johnston SL, Woodcock A. Risk factors for hospital admission with acute asthma: synergism between sensitisation and exposure to allergens and viral respiratory infections. *BMJ* 2002;**324**:763–766.
10. Piacentini GL, Bodini A, Costella S, Vicentini L, Peroni D, Zanolli L et al. Allergen avoidance is associated with a fall in exhaled nitric oxide in asthmatic children. *J Allergy Clin Immunol* 1999;**104**:1323–1324.
11. Grootendorst DC, Dahlen SE, Van Den Bos JW, Duiverman EJ, Veselic-Charvat M, Vrijlandt EJ et al. Benefits of high altitude allergen avoidance in atopic adolescents with moderate to severe asthma, over and above treatment with high dose inhaled steroids. *Clin Exp Allergy* 2001;**31**:400–408.
12. Gotzsche PC, Hammarquist C, Burr M. House dust mite control measures in the management of asthma: meta-analysis [see comments]. *BMJ* 1998;**317**:1105–1110; discussion 1110.
13. Gotzsche PC, Johansen HK, Schmidt LM, Burr ML. House dust mite control measures for asthma. The Cochrane Database of Systematic Reviews 2004, Art. No.: CD001187.pub2.DOI: 10.1002/14651858.CD001187.pub2.
14. Kilburn S, Lasserson TJ, McKean M. Pet allergen control measures for allergic asthma in children and adults. The Cochrane Database of Systematic Reviews 2001, Art. No.: CD002989. DOI: 10.1002/14651858.CD002989.
15. Woodcock A, Forster L, Matthews E, Martin J, Letley L, Vickers M et al. Control of exposure to mite allergen by the use of allergen-impermeable bed covers for adults with asthma. *N Engl J Med* 2003;**349**:221–232.
16. Luczynska C, Tredwell E, Smeeton N, Burney P. A randomized controlled trial of mite allergen-impermeable bed covers in adult mite-sensitized asthmatics. *Clin Exp Allergy* 2003;**33**:1648–1653.
17. van den Bemt L, van Knapen L, de Vries MP, Jansen M, Cloosterman S, van Schayck CP. Clinical effectiveness of a mite allergen-impermeable bed-covering system in asthmatic mite-sensitive patients. *J Allergy Clin Immunol* 2004;**114**:858–862.
18. Halken S, Host A, Niklassen U, Hansen LG, Nielsen F, Pedersen S et al. Effect of mattress and pillow encasings on children with asthma and house dust mite allergy. *J Allergy Clin Immunol* 2003;**111**:169–176.
19. Morgan WJ, Crain EF, Gruchalla RS, O'Connor GT, Kattan M, Evans R III et al. Inner-City Asthma Study Group. Results of a home-based environmental intervention among urban children with asthma. *N Engl J Med* 2004;**351**:1068–1080.
20. Sheikh A, Hurwitz B. House dust mite avoidance measures for perennial allergic rhinitis: a systematic review of efficacy. *Br J Gen Pract* 2003;**53**:318–322.
21. Terreehorst I, Hak E, Oosting AJ, Tempels-Pavlica Z, de Monchy JG, Bruijnzeel-Koomen CA et al. Evaluation of impermeable covers for bedding in patients with allergic rhinitis. *N Engl J Med* 2003;**349**:237–246.
22. Wood RA, Johnson EF, Van Natta ML, Chen PH, Eggleston PA. A placebo-controlled trial of a HEPA air cleaner in the treatment of cat allergy. *Am J Respir Crit Care Med* 1998;**158**:115–120.
23. Bjornsdottir US, Jakobsdottir S, Runarsdottir V, Juliusson S. The effect of reducing levels of cat allergen (Fel d 1) on clinical symptoms in patients with cat allergy. *Ann Allergy Asthma Immunol* 2003;**91**:189–194.

Appendix 1

ARIA

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