

Permethrin-Impregnated Mattress Liners: a Novel and Effective Intervention Against House Dust Mites (Acari: Pyroglyphidae)

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ABSTRACT This study tested the efficacy of permethrin-impregnated mattress liners in reducing house dust mites in the homes of volunteers with no previous recorded history of asthma, atopic eczema, or perennial rhinitis. The field trial using permethrin-impregnated (450 mg/m² of pure permethrin in polyester netting weighing 35 g/m²) mattress liners ($n = 9$) was conducted for 27 mo. The permethrin-impregnated bedding significantly reduced house dust mites in mattresses for at least 27 mo. Allergen concentrations were significantly lowered at 15-mo postintervention. No adverse side-effects were reported. This is a promising development in house dust mite control.

KEY WORDS house dust mite, acaricide, allergen avoidance, *Der p 1*, permethrin, placebo-controlled

American house dust mite, (Chisaka et al. 1985) and *D. pteronyssinus* (Trouessart), the European house dust mite (Jean-Pastor et al. 1986). Topical preparations of permethrin for the treatment of scabies and head lice have become the treatment of choice for infants and small children, rather than other insecticides, because they are effective yet have a lower risk of side-effects (Taplin et al. 1990, Paller 1993, Brandenburg et al. 1986, Bowerman et al. 1987, DiNapoli et al. 1988). Permethrin-impregnated bedding would be a more suitable presentation for domestic use because it would eliminate the problem of direct inhalant exposure to potentially damaging mite-killing sprays and the need for repeated treatments (Cameron 1997). Laboratory studies indicate that permethrin-impregnated netting kills mites for at least 2 yr (Hill 1996).

The purpose of the present placebo-controlled blind trial is to determine whether permethrin-impregnated mattress liners, which are simply placed on mattresses without further maintenance, can cause a significant long-term reduction in mite population densities (and hence mite allergen levels) in mattresses.

Materials and Methods

The field trial was placebo-controlled and blind. Volunteers were recruited following approval from the London School of Hygiene and Tropical Medicine ethics committee. Before the trial, each volunteer completed a consent form and a questionnaire to establish: (1) that they were nonsymptomatic to house dust mite allergen (i.e., had no previous record of asthma, perennial rhinitis or skin allergies), (2) that they would be sleeping on the same mattress for at least 5 d per week over the next 2 yr (excluding short holidays), and (3) that their mattress was at least 1-yr-old.

A preintervention study was performed (dust samples collected May–June 1996) to obtain baseline measurements of two parameters: (1) mite counts and (2) mite allergen levels in mattress dust for all prospective volunteers. The volunteers were provided with a dust-collection device and filter (ALK-Laboratories, Hørsholm, Denmark), and were given the following instructions to collect dust samples from their mattress: (1) pull back or remove any blankets and covers including any fitted sheets until the full surface of the mattress is exposed; (2) push the plastic collecting cone onto the hose end of your own vacuum cleaner (the rubber ring will help it form a good, tight seal); (3) remove the lid of the plastic filter and place it paper side up on to the collecting cone; (4) press the plastic nozzle onto the collecting cone until it clicks into place (hold the filter firmly); (5) turn on the vacuum cleaner and press the nozzle down hard on to the mattress surface for ≈ 3 s, then move the nozzle to a new position a few centimeters away from the last position and hold there for ≈ 3 s; (6) keep moving the nozzle a few centimeters after each short collection; (7) try to sample most of the mattress within the 3 min collecting period; (8) after 3 min of collecting, turn off

the vacuum cleaner with the nozzle facing upwards; (9) remove the nozzle and carefully lift out the filter unit; (10) place the lid securely onto the filter to stop dust spilling out; (11) write the initials of the person who sleeps in the bed on the label of the filter lid; and (12) place the filter into the sealed bag and bring in (or post) to LSHTM (do not forget to return the filter and collecting attachments the next day).

Dust samples were weighed to obtain the total dust load collected from each mattress (mg/m²). As the main objective was to determine whether the treatment significantly affects mite numbers, the dust collected was firstly used to obtain mite counts. If there was a sufficient quantity of dust remaining, an allergen assay was performed. Mites were recovered using a modification of an unpublished technique developed by Jeremy Griffiths (AgrEvo Environmental Health, personal communication). 100 mg of fine dust was placed in a 50 ml polythene beaker containing 45 ml of tap water. The beaker was covered with Parafilm and inverted 20 times. The Parafilm was removed, and the beaker was placed in a freezer, at -20°C , for 1 h and 15 min. After this time, an ice block was formed with three distinct layers. The top layer, a thin layer of ice, contained mites that had floated to the surface, the middle layer was unfrozen and contained water and some dust debris, and the bottom layer which contained dust debris in ice. The top layer was carefully removed and placed in the lid of a petri dish, 55 mm in diameter, which was previously marked in a grid to aid observation. When the ice melted, the sample was inspected using a binocular microscope at $\times 40$ magnification. The numbers of dead 'intact' (mites killed recently by the acaricide or vacuuming that have not become desiccated) and live mites were recorded.

If at least 50 mg of dust remained, mite allergen, *Der p 1*, was assayed using a double monoclonal antibody enzyme-linked immunosorbent assay (ELISA) kit, and procedure developed by INDOOR Biotechnologies (Chapman et al. 1987, Luczynska et al. 1989). If another 100-mg sample of dust was available, a second house dust mite count was obtained and the mean of the two replicates was used to estimate mite density.

Volunteers with mite-positive beds (18 of 26 examined) were asked to continue in the trial. Mattresses were ordered according to preintervention mite densities, then paired from the top, and within each pair the allocation of treatment group was randomized. The treatment was a mattress liner made from knitted 100% polyester multi-filament fibers (denier 100, mesh 156, color white, weight 35 g/m²) which was either impregnated with permethrin (450 mg/m² of Technical grade Permethrin BPC, *Cis:Trans* 25:75) or (2) unimpregnated (placebo). The volunteers were asked to place the mattress liners on their beds in August 1996 and to collect their first dust sample 1 mo after the placement of the mattress liner on their bed (1 mo postintervention). They were provided with additional filters for 2-, 5-, 15-, and 27-mo postintervention collections (samples collected September 1996–November 1998).

A RECENT STUDY of 56 countries found that the United Kingdom had the highest prevalence for both asthma and atopic eczema in the world, with the United States not far behind (ISAAC Steering Committee 1998). Among the suspected reasons for the increasingly high prevalence and apparent rise in the severity of allergic diseases is an extended degree of contact with the allergens that trigger the disease. Worldwide, the single most important factor in the development of atopic diseases is exposure to house dust mites (Platts-Mills et al. 1991). Although house dust mites can be present in most areas of the home, they are particularly associated with mattresses and bedding because these remain at an ideal temperature and humidity throughout the year and contain an abundant supply of shed human skin fragments. Because patients spend 6–8 h in close contact with their mattress, pillow, and bedding, the reduction of exposure in the bedroom is critical (Woodcock and Custovic 1998).

The importance of the house dust mites as a trigger of asthma has been known for some time. The World Health Organization published sensitization and exacerbation levels for exposure in 1988 (Platts-Mills and de Weck 1988). These levels have since been reviewed but it is still recommended that, to achieve significant control, a reduction in allergen exposure to $< 2 \mu\text{g}$ of *Der p 1*, preferably $< 1 \mu\text{g/g}$, or 100 mites/g dust, is required (Platts-Mills et al. 1997, Dreborg 1998). The method of patient management preferred by most practitioners is to rely exclusively on drug prescription. Patients are not usually instructed on how to avoid house dust mite allergens despite evidence that

suggests that may decrease asthma symptoms and/or medication requirements (Carswell et al. 1996; Fredrick et al. 1997; van der Heide et al. 1997a, 1997b) render atopic dermatitis less severe (August 1984, Roberts 1984, Colloff et al. 1989, Ricci et al. 2000) and reduce the sneezing symptoms of allergic rhinitis (Kniest et al. 1991, Howarth et al. 1992) for those individuals already sensitized.

To date, the most significant breakthrough in house dust mite allergen avoidance has been the development of semi-impermeable encasings (permeable to air and water vapor, but not to mites or allergens) for bedding. Encasings have been shown to be effective for controlling mite allergens in beds for at least 12 wk (Owen et al. 1990) and clinical improvement in asthma symptoms has also been reported (Ehnert et al. 1993, Marks et al. 1994, Frederick et al. 1997). Efficacy is enhanced and prolonged when used in combination with other methods (van der Heide et al. 1997a, Custovic et al. 2000). Continued efficacy requires maintenance by washing the covers and other bedding at temperatures $> 55^{\circ}\text{C}$ or wiping the surface regularly (Tovey et al. 1993; Platts-Mills et al. 1997). This is because the encasing is a two-way barrier wherein allergens continue to accumulate on top of the encasing (from the bedroom carpet) and inside the encasing (from the mattress). Therefore, encasings do not necessarily represent the long-term, low-maintenance solution for mite allergen avoidance.

Many chemical acaricides have had a mixed success in clinical trials, but permethrin is an efficient killer of mites and has an extremely low toxicity in humans (Cameron 1997). In the laboratory, permethrin is effective against *Dermatophagoides farinae* Hughes, the

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Table 1. Comparison between the two treatment groups regarding relative change in dust load from pre-intervention measurements

Time point	t	P	n	df
1 mo post-intervention	1.64	0.13	18	12
2 mo post-intervention	0.18	0.86	18	15
5 mo post-intervention	0.33	0.75	18	13
15 mo post-intervention	-1.00	0.33	18	14
27 mo post-intervention	-0.16	0.88	10	5

To examine the effect of treatment on dust load, mite densities and *Der p 1* levels in samples of mattress dust, univariate *t*-test analysis was performed on the log-transformed ratios of post and preintervention measurements at each postintervention time point (to compare the population changes in the treated replicates versus the population changes in the placebo replicates). Such a comparison allowed for the seasonal variability of mite populations because replicates for both treatment groups were sampled at the same time. A repeated measurement analysis of variance (ANOVA) was carried out on the whole data set, using STATA 6 software, to test for both within-subject (time) and between-subject (treatment) factors for the former parameter only (there was insufficient data to perform this test using *Der p 1* levels).

Results

Eighteen beds were sampled on six occasions (with only four exceptions at the final time-point), making a total of 104 dust samples. The frequency distribution of mite densities (the total of live and dead mites) was highly skewed. Logging the data helped to normalize the distribution. To deal with zero mite densities (found in 14 samples), 2.5 was added to each mite density per gram before log transformation. The choice of 2.5 was determined on the basis that the

minimum density of mites that can be detected using the described methodology is five per gram (or equivalent to one mite found in one of two samples of 100 mg). The detection of no mites in a sample indicated that the real density was between 0 and 5 (with 2.5 being the midpoint).

The preintervention geometric mean (GM) dust load, with 95% confidence intervals (CI), in mattresses (mg dust/m² of mattress) was 236 (182, 305) and 260 (167, 404) for mattresses to be provided with placebo and impregnated liners, respectively, and there was no significant difference between the two groups (*t* = -0.43, *P* = 0.67, *df* = 12, *n* = 18). In postintervention, there was no significant difference between the two treatment groups regarding the change in dust load from baseline at each time-point (Table 1), suggesting that repeat sampling did not introduce a serious bias by depleting dust. The 95% CI overlapped with preintervention measurements for the corresponding treatment group at each postintervention time point, except at 27-mo postintervention for the placebo group only where the dust load fell to 116 (85-159) mg/m² (Fig. 1).

Before intervention, there was no significant difference between the two treatment groups with respect to either mite densities (*t* = -0.14, *n* = 18, *df* = 15, *P* = 0.89) or *Der p 1* levels (*t* = -0.43, *n* = 12, *df* = 9, *P* = 0.68) (tested by *t*-test analysis on log-transformed data). The GM, with 95% CI, number of mites per gram of mattress dust was 80 (31, 202) and 87 (34, 219) for mattresses to be provided with placebo and impregnated liners, respectively. The GM, with 95% CI, *Der p 1* levels ($\mu\text{g/g}$ mattress dust) 0.0455 (0.0198, 0.1047) and 0.0565 (0.0210, 0.1517) for mattresses to be provided with placebo and impregnated liners, respectively.

Inspection of 95% CI showed that mite densities in mattress dust postintervention for the placebo group

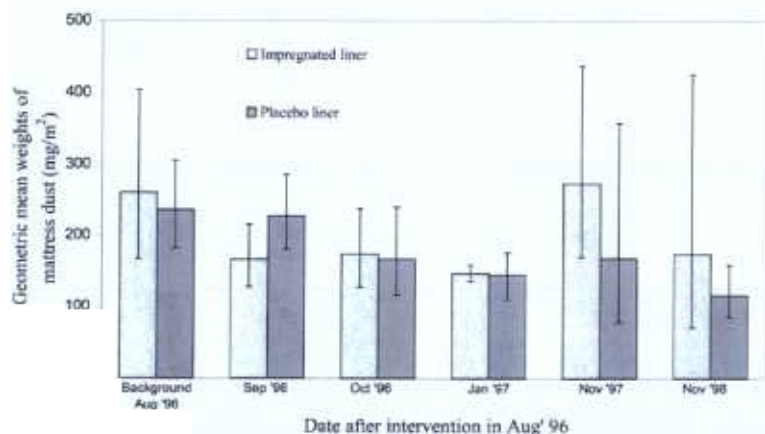


Fig. 1. Change in mattress dust weight during trial.

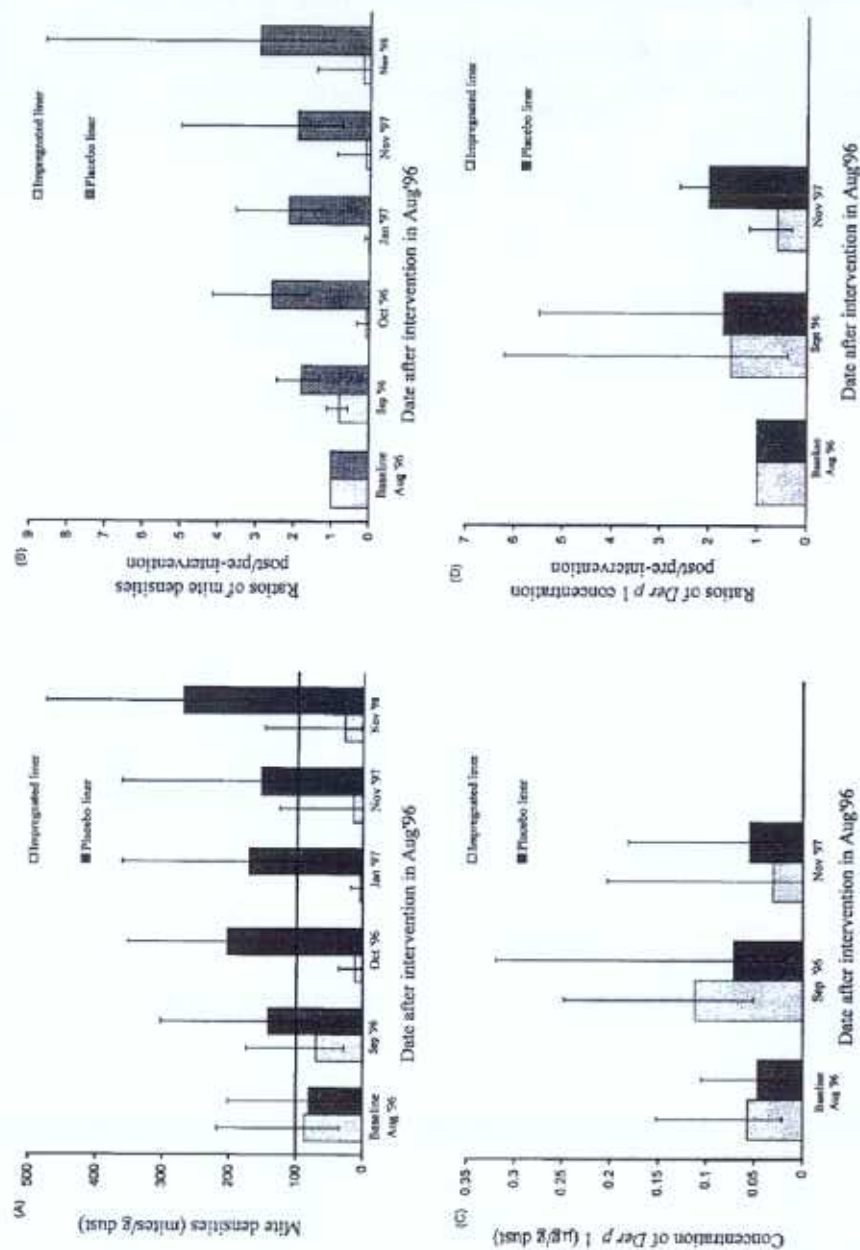


Fig. 2. Effect of intervention with mattress liners. (A) Absolute mite densities (solid line represents desired threshold for effective house dust mite control (100 mites/g dust)). (B) Proportional change in mite densities (per gram of mattress dust). (C) Absolute *Der p 1* concentrations. Geometric means (95% CI.) are represented. (D) Proportional change in *Der p 1* concentration ($\mu\text{g/g}$ dust).

Table 2. Comparison between the two treatment groups regarding relative change in mite densities from pre-intervention measurements

Time point	t	P	n	df
1 mo post-intervention	4.05	0.0011	18	15
2 mo post-intervention	5.40	0.0004	18	9
5 mo post-intervention	6.43	0.0001	18	10
15 mo post-intervention	2.91	0.014	18	11
27 mo post-intervention	2.98	0.021	12	7

increased to levels well above the desired threshold (Platts-Mills et al. 1997) at each postintervention point (Fig. 2A). In contrast, mite densities in dust from mattresses treated with impregnated liners decreased markedly postintervention, and was considerably below the desired threshold even at 15 mo postintervention. In fact, at 5 mo postintervention, mites were almost eradicated from mattresses treated with impregnated liners (GM = 4 mites per gram dust). Mite densities did not reach the exacerbation threshold at any time-point for either treatment groups.

At each time point postintervention, the ratios of post and preintervention measurements for mattresses treated with impregnated liners were <1 (i.e., the mite numbers were always less after intervention than at baseline), and the ratios for mattresses treated with placebo liners were >1 (i.e., the mite numbers were greater after intervention than at baseline) (Fig. 2B). In fact, the geometric mean reduction was 79% of baseline at 1 mo, 7% at 2 mo, 2% at 5 mo, 11% at 15 mo and 19% at 27 mo postintervention for beds treated with impregnated mattress liners. For beds treated with placebo liners, there was a corresponding increase to 180, 258, 214, 193, and 295% of baseline at the equivalent time points. This means that mite levels per gram of mattress dust by 1, 2, 5, 15, and 27 mo use of the impregnated mattress liners were 44, 3, 1, 6, and 6% of the levels in placebo-covered mattresses, respectively.

A highly significant difference in the log-transformed ratios was detected between the impregnated and placebo mattresses ($F = 55.04$; $df = 1, 16$; $P < 0.0001$). There was no significant variation in the log-transformed ratios with time ($F = 2.37$; $df = 4, 58$; $P = 0.063$), but there was a significant interaction between time and treatment ($F = 3.29$; $df = 4, 58$; $P = 0.017$). Hence, the effect of treatment varied significantly with time. From the univariate analysis, it could be seen that this effect was due to the relatively low effect of treatment after 1 mo compared with the later time points (Table 2).

The geometric mean *Der p 1* level per gram of dust for mattresses in both treatment groups remained below the desired threshold (Platts-Mills et al. 1997) postintervention (Fig. 2C). Sufficient samples were available for analysis at 1 and 15-mo postintervention only. At 15-mo postintervention, the ratio for mattresses treated with impregnated liners was <1 (i.e., the *Der p 1* levels were less after intervention than at baseline), and the ratio for mattresses treated with placebo liners was >1 (i.e., the *Der p 1* levels were

greater after intervention than at baseline) (Fig. 2D). The geometric mean change was 154% of baseline at 1 mo but decreased to 61% at 15 mo postintervention for beds treated with impregnated mattress liners, whereas for beds treated with placebo liners there was a continued increase to 169 and 202% of baseline at the same time points. This means that *Der p 1* levels per gram of mattress dust after 1 mo, and 15 mo use of the impregnated mattress liners were 91 and 30%, respectively, of the levels in placebo-covered mattresses. The difference between the two treatment groups was significant at 15 mo postintervention ($t = 5.30$, $n = 6$, $df = 3$, $P = 0.034$).

Discussion

It has been standard practice, when obtaining samples of dust to estimate exposure to house dust mites, to vacuum clean the upper surface of a mattress for 2 min/m², unless a shorter time provides samples of ≥ 200 mg (Platts-Mills and de Weck 1988). The sampling time used in the current study was increased to 3 min/m², to obtain sufficient dust despite the inexperience of our volunteers regarding dust collection. Mite-control trials using repeated measurements of house dust mite population density on the same mattresses, as used here, have been subject to criticism because they may artificially deplete the amount of dust and confound estimates of the size of the population (Colloff 1991, Hill 1998). It has been suggested that expressing mite population densities per unit area, and not per unit weight, may be more appropriate for studies using repeated measurements (Colloff 1991). Both treatment groups in the study herein received the same sampling regime and there is no evidence to suggest that repeat sampling, in this instance, introduced a serious bias by depleting dust.

Many techniques have been developed for isolating mites from dust samples, and as stated by Colloff (1991), there seems to be an inverse relationship between time and effort required by the method and the extraction efficiency. To overcome the problems of previous techniques such as laborious multiple sieving, centrifugation, flotation or filtration steps, Fain and Hart developed a simple 'flotation technique' (Fain and Hart 1986, Hart and Fain 1987) which they claimed to be up to 97% efficient. This estimate has since been disputed and in a re-evaluation of the technique, using samples of house dust rather than laboratory material, a GM efficiency of 27% was obtained (Colloff 1991). The new 'freezing technique' described herein compared favorably to Fain and Hart's 'flotation' method in a pilot study carried out in the laboratory at London School of Hygiene and Tropical Medicine. Significantly more house dust mites (paired $t = 4.7$, $n = 41$, $P < 0.0001$) were extracted from 41 samples of dust collected from a different group of mattresses. The same amount of dust was used for both techniques, 100 mg, and the GM, with 95% CI, number of mites/100 mg mattress dust was 5.7 (4.7, 7.0) and 4.4 (3.7, 5.2) for the freezing and flotation techniques, respectively. Furthermore, results

were obtained in only 2 h using the freezing method (and tap water is the only solution required), whereas overnight preparation of samples was desirable for Fain and Hart's method, to achieve optimal results (and solutions of ethanol and saturated sodium chloride are used).

Another pilot study was undertaken to provide an estimate of the sampling error within different mattresses using the methodology used in this study. House dust mite counts were performed on 2×100 -mg samples of dust from 48 different dust collections and a one-way ANOVA was performed following logarithmic transformation of data (+2.5). The residual sum of squares (the variation between samples on the same mattress) represented only 22% of the total sum of squares indicating homogeneity of samples as the same operator performed all the mite counts.

As the design of the intervention trial was to randomize the choice of treatment between each matched pair, there was no significant difference in the mite densities of the two groups preintervention although there was considerable variation in mite density within both groups. Before intervention, the GM (with 95% CI) house dust mite allergen concentrations in mattress dust, 0.0455 (0.0198, 0.1047) $\mu\text{g Der p 1}$ per gram of mattress dust in the placebo group, were low in this study relative to other reports from the United Kingdom (Reiser et al. 1990, Sporik et al. 1990, Custovic et al. 1995, Carswell et al. 1996, Fletcher et al. 1996, Luczynska et al. 1998). However, the range in mite counts from the same placebo group of mattresses, 80 (31, 202) mites/g mattress dust, did not significantly differ from those obtained in Manchester (Custovic et al. 1995, Fletcher et al. 1996). Only the total amount of mites, regardless of species composition, was provided in the mite counts. It is likely, as in other United Kingdom collections, that 17–32% of the Pyroglyphid mites collected were *Euroglyphus maynei* (Cooreman) and 68–83% were *D. pteronyssinus* (Cunnington 1967, Carswell et al. 1982, Colloff 1987, Hart and Whitehead 1990). This may explain, in part, the discrepancy between the results of the two methods for expressing house dust mite allergen exposure because only *Der p 1* allergen was quantified by ELISA, whereas mite counts will be higher because they represent exposure to other mite species as well as *D. pteronyssinus*. In some studies, houses of allergic patients have higher levels of mite exposure compared with those who are not mite-sensitive (Korsgaard 1983), but this is not always the case (Custovic et al. 1996). Such an association, if true, may explain why the *Der p 1* levels were relatively low in mattresses in this study, which was confined to a population of adults with no history of asthma, eczema or perennial rhinitis.

Permethrin-impregnated mattress liners significantly reduced mite levels in treated beds and this near eradication was maintained for at least 27 mo. Maximum reduction was observed at 5-mo postintervention (where mite levels in treated mattresses were only 1% of the levels in control samples). It was disappointing, but not completely unexpected, to lose

four data points at the last time point because the volunteers changed their address during the 2 yr of experimentation. Three were from mattresses fitted with impregnated liners, and one was from a placebo mattress that was matched with one of the former. As the beds were matched, all three pairs were excluded from the analysis of the final time point resulting in only six pairs of data). The loss of the three beds did not cause any bias in favor of an impact because, at the previous time points, all three showed a consistent significant reduction in their mite densities in comparison with their matched placebo beds. The sample size of the trial was small, but the conclusions are valid because the *P* values obtained when testing the effect of treatment were very low. The fact that a very significant impact was obtained despite the small sample size is clear evidence that the real impact of permethrin-impregnated liners was great.

The finding that permethrin-impregnated liners significantly reduced allergen levels at 15 mo postintervention was encouraging. The international workshop on mite allergens and asthma state that demonstrating a dose-response relationship between house dust mite allergen avoidance and sensitization is relatively straightforward, but it is not so simple for asthma symptoms. They recommend a 90% reduction in allergen exposure for control measures and that levels should be reduced to $<2 \mu\text{g Der p 1}$ per gram of dust (or 100 mites per gram) (Platts-Mills et al. 1997). After using permethrin-impregnated liners for 2 mo, mite levels/g of mattress dust were 97% less than in placebo beds and 94% less after 27 mo. Mite populations crashed in permethrin-impregnated beds but increased in placebo beds. Ideally, an effective control measure should have the same impact on allergen levels and, although a significant effect was observed at 15 mo, where allergen levels in treated beds were lowered by 70% compared with placebo beds, a further reduction is required before any clinical impact may be expected. House dust mite allergen is remarkably stable (de Boer et al. 1995) and further measures are necessary to remove the preintervention allergen loads in mattresses as by vacuum cleaning with an efficient, HEPA-filtered vacuum cleaner (Custovic et al. 1998). A combined allergen avoidance intervention, using permethrin-impregnated liners and a HEPA-filtered vacuum cleaner, is recommended in any proposed large-scale, double-blind, placebo-controlled clinical trials using consenting, mite-sensitive patients to determine whether this novel approach will produce any clinical improvements. Such a trial is in progress by the investigators, in collaboration with The Royal Free Hospital, London.

Remarkably, no studies have been published to assess to what extent patients are compliant with previous allergy avoidance measures, and as yet no cost-benefit analyses of such measures have been undertaken (Schönberger and van Schayck 1998). Intuitively, the easier and cheaper the intervention, the more likely it will be used in the home. Permethrin-impregnated liners are user-friendly. They are simply placed under conventional bedding and require no

further maintenance. However, as experienced in another clinical trial, some patients may refuse to have chemical intervention in their homes due to fears of toxicity (van der Heide et al. 1997b). The types of chemicals that can be used with safety are limited because the chemical will be applied to beds and in close, prolonged contact with people (Colloff 1990). Many conventional acaricides, containing the active ingredients bioallethrin, benzyl benzoate, deltamethrin or pirimiphos methyl, are relatively toxic and are known to cause irritation to the skin, eyes and lungs; such residual insecticides may even cause allergenicity (Colloff 1990). It is essential that a distinction between these irritant acaricides and permethrin is made to promote patient compliance. Permethrin has been in use for many years in a range of different concentrations and has extremely low risk of toxicity in humans when either applied topically for short-term use (Brandenburg et al. 1986, Bowerman et al. 1987, DiNapoli et al. 1988, Taplin et al. 1990, Paller 1993) or when impregnated into mosquito nets for long-term use (Snow et al. 1987; Plestina 1989; WHO 1990, 1991; Lines 1996). No adverse effects were reported in the current study.

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