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Allergen exposure and control

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ABSTRACT

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Allergens produced by the house dust mites (family Pyroglyphidae) are probably the single most important allergens associated with asthma world wide. If exposure to these allergens in houses could be sufficiently reduced, then asthma symptoms may be markedly reduced and even prevented from being initiated. Only about half of the many attempts to reduce mite allergens in houses have shown any clinical benefit. One reason may be that exposure was not reduced enough – however exposure to mite allergens has never been measured in any trial. This review summarises previous allergen control trials and then provides an outline of allergen exposure, including the nature of exposure, the analytical methods available and the recognised risks of allergen exposure. This provides a perspective to evaluate the individual methods used to kill mites and to reduce exposure to the allergens. The object is to provide a framework to improve and develop allergen avoidance as an effective component of asthma management.

INTRODUCTION

Many people with asthma are allergic to specific proteins (allergens) produced by the house dust mites of the family Pyroglyphidae: *Dermatophagoides pteronyssinus*, *Dematophagoides farinae* and *Euroglyphus maynei*. They are probably the single most important allergens associated with asthma world wide.

The avoidance of exposure by reducing the production and distribution of mite allergens has commonly been recommended as the first step in the management of asthma in mite-sensitive subjects. This recommendation is supported by (1) the establishment of the causal link between exposure to mite allergens and the development and maintenance of allergic sensitization and

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TABLE 1

Brief summary of selected allergen avoidance studies

Author name	Year	Beneficial	Active controls	Subject age	Study design	Clinical assess.	Treatment	Exposure	Time	Comment
Storm van Leeuwen*	1927	yes	ng	ng	anecdtl	symp	LAE			outdoor air used
Wright	1963	yes	ng	ng	anecdtl	symp	ob			
Denborough	1971	yes	54	ng	follow up	symp	af		6m-3y	39/54 greatly improved
Zwemer & Karibo	1973	yes	18	ch	dbxo	symp	af		4w	
Molk	1974	no	ng	ng	xo	symp	af		2w	
Sarsfield et al.	1974	yes	14	ch	pre/post	ss,tsE	xv,wb	mc	mths	reduction tE>sE
Burr et al.	1976	no	32	ad	xo	PF,md	xv,wb		6w	limited compliance, mild as.
Villaveces et al.	1977	~no	13	ch	dbxo	PF,ss	af		2w*	ss improved, not PF
Maesen et al.	1977	no	30		placebo	PF,as	af		~7w	only abstract in English
Scherr & Peck	1977	yes	130	ch	placebo	tsE,sk	af		1y	lower ss with active filter
Lund & Dowdle	1977	yes	15	ad		AF,H,	LAE		3m	Symptom free in Antarctica
Tovey et al.	1977	yes	18	mx	pre/post	t,sdE	ob,xv,wb	mc		11/18 AF improved, t,s&dE reduced
Warner & Price	1978	~no	69	ch			"align avoid"			7/69 significant improvement
Østergaard	1979	yes	87	ch			dust control			70% pts satisfied, Eng. Abst.
Mitchell & Elliot	1980	no	10	ch	xo	PF	af		4w	
Burr et al.	1980a	~no	26/27	ch	ctrl gp	PF	wb,xv	mc&align	8w	both gps improved
Burr et al.	1980b	~yes	21	ch	xo	PF	xb,xv		4w	modest improvement
Platts-Mills et al.	1982	yes	9	ad		H,PF, md,tsE,G	LAE	align	2-4m	7/9 improved hist., ss & md change in tE>sE

Korsgaard Murray & Ferguson	1983b 1983	~yes yes	23/23 10/10	ad ch	ctrl gp	PF,ss,md PF,ss, md,H	xv,xb,rc,wb cm,rc, dc,wb Nat	mc	12w 4w	ss,md improved, not PF carpet removal significant
Van de Maele	1983	yes	28			ss,rh			12w	15/28 improved
Bowler et al.	1985	no	9	ch	xo	PF,ss	cm,ob,wb,af		3x2w	brief treatment
Walshaw & Evans	1986	yes	22/20	ad	ctrl gp	PF,Hist, md,ss,tsEG	~rc,cm, wb,xb	mc	1y	RAST 3+, 4+ improved slowly
Gillies et al.	1987	no	14&12	ch	~pre/post	H,tsE,PF,ss	cm,dc,xv	mc	6,12w	only total IgE reduced
Dorward et al.	1988	yes	9/9	ad	pre&ctrl	H,ss,PF	LN,xv	mc	8w	better with young children
Verrall et al.	1988	yes	13	mx	pre & dbxo	H,md	af		6w	laminar HEPA on bed
Colloff et al.	1989	~	20	mx	4 gps + / -	dermatitis	xv,Nat	mc	4m	vac > Nat at reducing mites
Reiser et al.	1990	no	23/23	ch	db placebo	H,ss,PF,sE	Nat	algn	24w	little change in algn or sympt.
Kniest et al.	1991	yes	10/10	mx	db placebo	ss,md,tsE,eo	sbb	gu	1y	% redns: tE=38,ss=47,gu=53

Key to table and abbreviations used in order of appearance. Columns list the Author, (*=similar experiments by others not listed, see historical paragraph in text), year of publication, whether the trial was beneficial or not (~yes and ~no denote minor trend), the number of participants who finished in the active and placebo groups (ng=not given), the age of the subjects (ng=not given, ch=children, ad=adult, mx=mixed), the study design (anecdotal=anecdotal, dbxo=double blind cross over, xo=cross over, pre/post=pretreatment period compared with a post treatment period, ctrl gp=control group used), clinical assessment (symp=symptoms, ss=symptom scores, tsdE,G=total, specific and dust IgE/IgG respectively, PF=peak expiratory flow, md=medication, as=asthma score, sk=skin tests, H=histamine provocation, rh=rhinitis score, eo=eosinophil count), treatment used (LAE="low allergen" environment, ob=oil bedding, af=air filtration, xv=extensive vacuuming, wb=wash bedding, xb=change bedding, rc=remove carpets, ~rc low compliance with former, cm=cover mattresses, dc=unspecified dust control, Nat=spray bedding with Natamycin, LN=liquid nitrogen, sbb=solidified benzyl benzoate), exposure assessment (mc=mite counts, algn=measure mite allergen, gu=guanine assay for mite products), time of treatment period and additional comments.

asthma (see Sporik and Platts-Mills, this issue), (2) the observed recovery after the end of the pollen season in asthmatics who are only pollen-allergic, (3) the observed recovery from occupational asthma when the allergenic stimulus is removed and (4) some trials of allergen avoidance either in the houses or in special "low allergen" environments (see next two sections). Together these suggest that successful domestic allergen avoidance has the potential to (1) prevent the initiation of sensitization and development of symptoms in susceptible individuals, (2) reduce symptoms in established asthma, (3) improve the airway hyper-responsiveness which is a characteristic of asthma, and (4) prevent the increase in the asthma severity which may accompany continued exposure.

Historical perspective

There are several anecdotal reports from the 1920s of the dramatic improvements in asthma symptoms resulting from moving people, who were house dust allergic, from their houses to specialised rooms with minimal clean furniture and a supply of filtered air (Leopold and Leopold, 1925; Storm van Leeuwen et al., 1927; Cohen, 1928; Dekker, 1928). Such uncontrolled demonstrations continued sporadically for the next forty years and although encouraging, were generally too expensive and impractical to apply as a general measure for treating asthma in dust allergic subjects. The recognition in the 1960s that *Dermatophagoides* mites were the principle origin of house dust allergens allowed advice on reducing domestic allergen exposure to be directed at specific practices for both killing the mites and for removing the allergenic dust.

Published trials of allergen avoidance, their implications and future development

Clinical improvement has only been reported in about half the trials of methods used to control mites and their allergens in the home, see Table 1. In general, successful trials were those which involved the most rigorous dust control measures including removal of carpet, encasement of mattresses and vigorous attention to controlling all dust. They usually also ran for longer to allow clinical changes to be apparent and had younger and more highly mite-allergic participants whose disease may be more responsive to changes in exposure. Examples of well-conducted trials are Murray and Ferguson (1983) and Walshaw and Evans (1986), though even these may not have gone far enough in controlling allergens. Comparison of all the trials is limited by the wide variations in methods and design. Several suffer from potential faults including too short a time course, no controls, poor selection of subjects and a limited assessment of responses.

However, the most outstanding difficulty comparing trials to identify useful allergen control methods, is that none have quantified the reduction in

aeroallergen exposure which occurred when specific avoidance measures were applied. Without this, it is difficult to draw conclusions about the usefulness of measures designed, but not demonstrated, to reduce exposure. Indeed the impact of individual methods has rarely been tested for their effect on allergen at the source, and never been tested for their effect on the aeroallergen in a room or the total personal exposure received in the house.

The trials also have implications for the practical application of allergen avoidance. The more successful trials used treatment regimes which were sufficiently severe to make compliance unlikely in the general population. Indeed it is doubtful whether the advice generally dispensed to asthmatics who are mite allergic is useful, as the methods advised are often similar to those employed in some unsuccessful trials.

Two vitally important questions are unanswered: (1) what is the quantitative relationship in mite-allergic asthmatics between reduction in aeroallergen exposure and reversal of asthma symptoms, and (2) how can mite aeroallergen exposure be most effectively reduced in houses?

Two recent developments provide a framework for allergen control to proceed on a more rational, comprehensive and experimental basis. These are (1) the extensive development of immunoassays which allow the quantitative measurement of mite allergens in dust and in the air, and (2) that proposals for the risks of allergic sensitization and acute asthma symptoms which are associated with defined quantities of allergen in dust have now been confirmed in several studies. The background and techniques which established the risks of exposure, can also be applied to reduce exposure effectively.

The aim of this review is to provide an outline of the nature and distribution of mite allergens and aeroallergens in houses and the risks associated with allergen exposure. This is followed by an examination of the methods of control which can be exercised over mite allergens through environmental modifications, with chemicals and by physical methods. The object is to provide a perspective of allergen control based on the agent of exposure, that is aeroallergens. Such a rational perspective is required to make the decisions needed to reduce mite allergen exposure to minimum levels.

MEASURING MITE ALLERGENS

Allergen Der p I as a marker of exposure

Most of the information about house dust mite allergens has been determined for the *D. pteronyssinus* allergen *Der p I*. This is a major allergenic component of mite culture, faeces and aeroallergen. It appears to correlate well with the presence of total mite allergens (Chapman et al., 1987) and another important allergen *Der p II* in dust samples (Sakaguchi et al., 1989; Lau-Schadendorf et al., 1991a,b), and so can serve as a marker of total mite exposure.

Measurement from dust samples

Assessment of aeroallergen exposure has generally been made by two methods – by extrapolation from the allergen concentration of dust samples, and from the measurement of aeroallergen collected at a single site. Dust sampling uses a vacuum cleaner to collect surface dust from items such as beds, floors, furniture etc., and the result is expressed as μg of allergen per weight of sieved dust (Platts-Mills and de Weck, 1989). These units are used through most of this review and are referred to as “allergen levels”. Quantities usually range from $<1 \mu\text{g/g}$ up to over $300 \mu\text{g/g}$. Such a unit is simple and allows useful comparison between similar items. Its main limitation as an index of exposure is that it takes no account of the total amount of dust present at a site or the likelihood of dust becoming airborne. Other expressions of allergen load as the quantity per item (Owen et al., 1990), or per area (Carswell et al., 1991) have also been used. The assessment of items as a sources of aeroallergens would be more useful, though no method for this currently exists.

Measurement and nature of mite aeroallergens

The measurement of total aeroallergen has been performed by collecting airborne dust samples on filters and in devices which fractionate particles according to their size (Tovey et al., 1981; Price and Longbottom, 1988). The quantities of airborne allergen can vary from low pg amounts per m^3 in unoccupied rooms up to 1000 times this in the same room when the dust is disturbed by domestic activity (Sakaguchi et al., 1989). The quantity collected is also affected by sampling rate (Price et al., 1990) and by other factors such as the orientation of the filter and filter material (personal observation). Moreover the nature of the aeroallergen itself changes under these circumstances. The allergen in the sporadic bursts of high exposure associated with the disturbance of dust is largely associated with large ($10\text{--}40 \mu\text{m}$) diameter mite faeces (Tovey et al., 1981). These particles settle out over about 15 min and only small particles $\ll 10 \mu\text{m}$ remain (Platts-Mills et al., 1986), providing a background of almost continuous very low exposure.

Alternative methods of estimating aeroallergen may be developed. We have used large plastic petri dishes to collect settling dust in rooms over a period of 1–14 days, collecting up to 14 ng/day (Tovey et al., 1992), representing a “fall out” of over $400 \text{ ng/m}^2/\text{day}$. Nasal filters (Pasricha and Abrol, 1974) would require no power supply and would monitor personal exposure.

EXPOSURE TO AEROALLERGEN

Inhaled aeroallergens carried by mite faecal particles are mainly trapped in the upper airways and rarely enter the lung, whereas the smaller particles (whose nature and origin are unknown) would easily enter the lower airways.

Although the total mass of inhaled allergen is very small, it has been suggested it could have a profound, local and cumulative effect on the lung. This is because the allergens are concentrated (at least on large particles) and would produce high local concentrations wherever deposited (Tovey et al., 1981; Platts-Mills and Chapman, 1987). At the moment it is unclear whether an inhaled mass of allergen associated with large particles produces the same allergic response as the same mass associated with small particles or whether a short high burst of exposure has the same effect as the same quantity over a long time. Because of their dependence on dust disturbance for generation and uncertainties about the relevance of particle size, aeroallergen should be collected under carefully standardised conditions (yet to be defined) to provide an index of personal aeroallergen exposure. Clearly this is an area which needs further development. Ultimately we are interested in controlling personal aeroallergen exposure, but the theory, technology and background to determine the exposure which is biologically relevant to allergic disease are not sufficiently developed.

Risks associated with allergen exposure

The first Workshop on house dust mite allergens proposed two threshold levels for risk: exposure to levels of $> 2 \mu\text{g/g}$ of *Der p* I in house dust were associated with increased risk of sensitization and levels of $> 10 \mu\text{g/g}$ which were associated with a risk of acute asthma symptoms (Platts-Mills and de Weck, 1989). These thresholds have been supported by case control, cohort and cross sectional studies examining the relationship between allergen levels and the prevalence of allergic disease (Platts-Mills et al., 1991).

Safe levels of allergen exposure

Safe levels of exposure to mite allergens are not known. If $2 \mu\text{g/g}$ is a lower level for sensitization in the general population, then a "safe" level would presumably be much lower. Price et al. (1990) found the level of $0.5 \mu\text{g/g}$ in carpet dust was more significant for predicting sensitization than $2 \mu\text{g/g}$. In the "allergen-free" hospital room, which provided clear evidence of the clinical benefits of allergen avoidance (Platts-Mills et al., 1982), the allergen level was $< 0.24 \mu\text{g/g}$. Such a level functions as a goal for allergen control studies, though in many houses would be extremely difficult to achieve without the development of new approaches. It is unlikely such levels were achieved in any of the successful trials and so any major reduction of exposure may have some benefits.

Depending on the aspect of the disease, i.e. sensitization, community prevalence of asthma, acute or severe attacks of asthma and the quantitative change required for clinical improvement; there may be different risk levels of allergen which may not necessarily be the same (Platts-Mills and de Weck, 1989). Individuals will also vary widely in sensitivity.

Occupational asthma as a model for domestic allergen avoidance

Experience with treating occupational asthma demonstrates that early diagnosis and complete removal of exposure were important factors in ensuring complete recovery. Continued or prolonged exposure was likely to result in further deterioration in lung function and the development of irreversible persistent asthma (Chan-Yeung, 1988). If the occupational model can be generalised, it appears likely that the early implementation of effective allergen control measures in dust mite-allergic asthmatics may halt or reverse the process of the disease. Indeed, allergen control should be instituted in the high-risk babies of mite-allergic parents, as several studies demonstrate that excessive exposure to an allergen (including mites) in the first few months of life increases the risk of sensitization and developing asthma (Bjorksten, 1986).

DISTRIBUTION OF MITE ALLERGENS

International distribution

Mite allergens have been found in many countries around the world (see Platts-Mills and de Weck (1989) for a list). Despite wide differences in climate, we modify our living conditions to provide a "comfort zone". Mites share this zone and their presence is a product of the way we build, furnish and live in our houses. Since mites require a high humidity for survival, the level of mite allergens in very dry or cold climates (Riyadh, Stockholm, Arizona) is generally $< 2 \mu\text{g/g}$, whereas levels in countries with a season suitable for their proliferation (coastal areas of Europe, USA) generally have mean levels in the range $2\text{--}15 \mu\text{g/g}$. Regions where the climate is suitable for mite growth for much of the year (eastern coasts of Australia and South America) have mean allergen levels in the range of $10\text{--}40 \mu\text{g/g}$. It is difficult however to make close comparisons of the international distribution of mite allergen levels from the different studies because different methods, seasons, sampling sites, population groups and expressions of data (as means, ranges etc.) have been used or this information has not been given.

Variation between houses

Dust samples from the same site in different houses in a single locality have a wide distribution of levels. For example, in Sydney the mean level of allergen in 74 samples of bed dust was $38.9 \mu\text{g/g}$ and based on their distribution, 95% of cases range between $7.1 \mu\text{g/g}$ and $213.4 \mu\text{g/g}$ (Marks et al., submitted). Factors influencing the distribution of allergen levels in houses in the same community have not been thoroughly investigated though the availability of humid niches in houses is probably the main factor. Significantly, hospitals (Tovey et al., 1975) and many public buildings (Green et al., 1992) in the same locality are almost uniformly mite free and serve as a model for allergen reduction.

Distribution of mite allergen in houses

Mite allergens are often ubiquitously distributed throughout houses and are found at many sites which are free of live mites, although sites which mites colonise (beds, carpets, soft furniture and clothing) generally have higher allergen levels (Tovey et al., 1981).

Beds: Mite populations and the level of their allergens are usually higher in beds than at other major sites in the house per unit weight of dust. Beds provide a refuge with warmth, food and moisture for mites and therefore require active control of mites and allergens. Exposure to this source occurs for about 11 h a day for children and for about 8 h per day for adults. Low level exposure is probably continuous, though is too low to usually be measured with current methods and peaks of exposure probably occur whenever the dust is disturbed – coughing, bed making, movement in bed, etc.

For beds, generally the highest mite allergen levels are in the dust from blankets (or other upper bedding such as quilts, duvets), followed by mattresses and then pillows, though the differences are not great (personal observation). There is insufficient evidence to choose one form of bedding (duvets, synthetic, cotton or woollen blankets) over another – provided it can be regularly hot washed ($> 55^{\circ}\text{C}$) to remove allergen and to control mites. All types of mattress (inner spring, kapok and foam) can develop high mite populations. Mites are found deep inside mattresses and pillows which serve as a source for reinfestation, are inaccessible to most control measures and function as a buffer against fluctuations in humidity. While extensive use of electric blankets will reduce mite populations, it does not entirely eliminate them (Mosbech et al., 1988). For an allergen-free bed, there is no option but to encase mattresses and pillows with impermeable covers.

“Infant-care” sheepskins because of their frequent occupation, dampness (!) and warmth can contain very high populations of mites (Tovey et al., 1975) and potentially serve as an important source of exposure for infants. In hospitals, such sheepskins are mite-free due to high washing temperatures and frequent changes of bedding – unless these measures can be assured in the home then the use of sheepskins is strongly discouraged, particularly in infants with a high risk for sensitization.

Flooring: Soft floor coverings (carpets) can contain the largest reservoir (total weight) of mite allergen in a house and there is probably no substitute for frequently washed hard floors (wood, ceramics etc.) if minimal allergen exposure is to be achieved. Such washing removes settled aeroallergen from the circulating pool in a room. Even if carpets are temporarily rendered mite free, they cannot be sufficiently cleaned of all dust (see section on vacuum cleaners), are easily reinfested and serve as a collection and distribution point for mite aeroallergen from other sources. It has been speculated that woollen car-

pets, being "organic" and having a higher moisture content, have higher mite populations, though this has not been confirmed. If, for reasons of social prestige, concepts of "warmth" etc., carpets are mandatory, then a few rugs and mats cover less floor area and can be put outside in direct sunlight for complete mite eradication (see control section).

The capacity of different types of flooring to function as a source of aeroallergen has not been systematically investigated. Smooth floors may allow allergen to become airborne by air currents more easily than carpet, which would trap the particles, but carpet fibres may function to "catapult" particles into the air when walked on. In one study (Price et al., 1990), aeroallergen in rooms with woollen carpet was significantly higher than in rooms with synthetic carpet, which was similar to hard floors, despite the fact the allergen level of the dust from both types of carpet was similar. It was suggested that the electrostatic charge on synthetic carpets may release less aeroallergen.

Soft furnishings: Allergen levels found in soft furnishings are often similar to those found in beds. The thickness of cushions and density of the material means that the mites have the opportunity to retreat deep into the matrix for long periods to escape both unfavourable climates and allergen control. Furniture is likely to be an important source of direct aeroallergen exposure and an important source of both allergens and mites for carpets and clothing. Soft and hard vinyl or leather-covered furniture are not colonised by mites. Although they collect surface dust, they are easily cleaned. Like beds, a range of "mite-free" soft furnishings could probably be developed which incorporate an impermeable barrier to mites and dust directly beneath a layer of removable, washable outer fabric.

Clothing and soft toys: Both clothing and soft toys can have very high numbers of mites (Carswell et al., 1982; Bischoff and Fischer, 1990). Mites and their allergens are probably widely distributed by clothing, though their contribution to personal exposure has never been determined. Children are often emotionally attached to toys which are often physically close to their respiratory zone. Appropriate control methods for such toys would include careful choice of materials in the first place, frequent hot washing, dry cleaning, prolonged freezing, heat sterilisation and storage under dry conditions.

House dust: Controlling aeroallergen exposure means removing allergen from all the sites from which it can potentially become airborne in houses. The dust from pelmet boxes above windows, lampshades, the top of wardrobes, indeed almost anywhere where dust will settle contains measurable allergen (Tovey et al., 1981). It seems likely that whenever a room is occupied there is a constant turnover and movement of aeroallergen around the room depending on the different aeroallergen sources present (beds, carpets, furniture etc.), the

level of dust disturbance and the patterns of airflow in the room. In this context, control also means good design to reduce these surfaces and the thorough removal of accumulated dust. Aerosolised sprays to neutralise allergen in inaccessible places could be developed.

Other allergens in houses

Despite the importance of mite allergens for both sensitization and asthma symptoms, other allergens may contribute to the total aeroallergen burden, depending upon the individual situation. This may be one reason that greater reductions of total IgE than mite-specific IgE often occur during allergen avoidance trials. The sources of domestic non-mite allergens include cats, fungi, insects (including cockroaches) and deposited pollen. The approaches to allergen avoidance described here will also reduce this exposure, depending on the method and the allergen.

METHODS OF CONTROLLING ALLERGENS

Methods of allergen control can be grouped as functioning either directly on mites or functioning to control the dust. Methods acting directly on mites are physical changes to the environment (changing humidity, heating, washing or freezing) or chemical control (acaricides or other chemicals). Methods acting in the dust are removal (vacuum cleaning, washing or air filtration), denaturation or by provision of a barrier (occlusive covers). Some methods, e.g. washing, function at a number of levels.

Targets for reduction

As discussed in the section "risks associated with exposure" a level of $<0.2 \mu\text{g/g}$ may be regarded as "safe" though this depends on the benefit required and the individual involved. In houses currently with a level of $20 \mu\text{g/g}$ this would require a reduction by a factor of 100. To achieve such ambitious reductions a combination of highly effective methods applied to both sites of mite colonisation and of dust accumulation would be required. A more practical interim goal would be the lowest ten percentile of the mean allergen level of houses in that community.

Physical changes to control mites

Humidity: Mites will only be active and proliferate when the relative humidity is sufficiently high to allow water to be gained from the surrounding air and humidity is a critical determinant of mite populations (Korsgaard, 1983a). The role of humidity in the water balance of mites is fully covered in this issue by Arlian. At a temperature of 15°C mites require a $\text{RH} > 55\%$, whereas at 30°C this increases to $> 68\% \text{ RH}$. Mites are susceptible to desic-

cation and as humidity declines they will cluster together in niches and between fibres in fabrics in order to maintain a high local humidity. Beds, carpets and furnishings provide a dense refuge with a complex microclimate which may differ from the humidity and temperature in the room and provide opportunities to replenish the water lost at lower humidities. Humidity conditions inside houses differ from those outside. Poor under-floor ventilation and damp-coursing, unflued fuel heating, any cooking, bathing, clothes drying and of course respiration, without adequate ventilation, can all increase indoor humidity. Any warming of outside air will reduce its relative humidity. Simple controls of humidity, such as increased ventilation (many houses have less than 1 airchange per hour) and venting sources of moisture to the outside are useful. Air conditioning, while effective (Lintner et al., 1991), is expensive to install and to continuously operate.

Temperature: The activity and proliferation of mites is restricted to a rather narrow range of temperatures. At the optimum culture temperature of around 25°C, mites require about a month to complete a life cycle, at 15°C, more than a year is required. Although development time is more rapid at >25°C, fewer mites survive (Wharton, 1976). Mites will not survive –15°C for more than 6 h (van Bronswijk and Koekkoek, 1972) and few mites survive 6 h at 50°C (at 60% RH) (Kinnaird, 1974). Mites do not survive hot washing at 55°C. The use of liquid nitrogen is highly effective at killing mites in mattresses and carpets (Colloff, 1986) decreasing their population by 90–100%. Its use requires specialist application and needs to be repeated.

Sunlight: Daily airing in the sun of bedding is a common practice in some countries though its effect on mites has not been studied. We have found that exposing carpets flat in the sun is an extremely efficient method to kill all mites in about 3 h (Tovey et al., in preparation). On a day with ambient conditions of 30°C and 60% RH, direct sunlight raises the temperature under the carpet to >50°C and reduces the RH to <15%. Obviously such a method requires the sun, but exposure is only required monthly.

Diet: The only known way to control mites through their diet is to interfere with their complex relationship with fungi (de Saint Georges-Grèdelet, 1984). The usual diet of mites in houses includes shed human dander and other sources of protein. When house dust is put under culture conditions it can develop much larger populations of mites than ever seen in the wild. Although this is probably the product of multiple factors (constant high humidity, a surplus of breeding opportunities, freedom from predation, imposition of restrictions on their mobility etc.) it does demonstrate that shortage of food is unlikely to be a controlling factor of mite populations.

Chemical control of mites and allergens

Numerous chemicals with different modes of action have been tested to control mite populations and so reduce the production of allergen. A list of those currently available has recently been published (Colloff, 1990). While these compounds completely kill mites *in vitro*, there is difficulty in applying them effectively to the resident mite populations in the matrix of mattresses, carpets and soft furnishings. All the chemicals have low human toxicity, but there is always concern over adverse reactions to chemicals in close physical contact, in enclosed spaces, with repeated applications for extended periods. There is always the additional possibility of mites developing resistant strains.

Acaricides: Three acaricides, benzyl benzoate, pirimiphos methyl and PAR-AGERM have passed from successful *in vitro* assessment onto trials in houses. All showed some effect, none achieved complete control of mites and all would require application about every 2 months if control of mites was to be maintained. The use of acaricides can currently only be viewed as a long-term measure offering partial control.

Benzyl benzoate is the active ingredient of three commercial acaricides for house dust mites: Acarosan, Allerbiocid and Artlin 3A. In two controlled trials, Acarosan reduced mite allergens in carpets but not beds at 1 and 2 months after application compared to controls (Lau et al., 1991) and reduced rhinitis symptoms, IgE and mite products over a year (Kniest et al., 1991). Two uncontrolled trials (Dietmann et al., 1989; Kersten and Musken, 1989), both reported reductions in mite populations and improvement in allergic symptoms. Burr et al. (1988) reported the use of a sheet containing benzyl benzoate on top of a new mattress reduced the surface frequency and degree of mite infestation compared to controls. Pirimiphos methyl has been used in one trial where allergen *Der p* I fell by more than 60% in carpets and > 50% in soft furnishing at 2 weeks while control levels rose (Mitchell et al., 1985). The disinfectant, PARAGERM, contains a complex mixture of chemicals (Penaud et al., 1975), some recognised to be acaricidal. It eliminated surface mites in more than half the mattresses it was applied to in a controlled trial, although subsurface mites survived (Penaud et al., 1977). Numerous other disinfectants have also been screened (Leysen et al., 1974) without identifying any with potent activity.

Fungicides: Because of the relationship between mites and fungi (see diet, above), fungicides can be used to reduce mite populations. Regular use of a natamycin spray on mattresses reduced symptoms in an uncontrolled trial (Van de Maele, 1983), but was not effective in reducing mite numbers in a controlled trial (Colloff et al., 1989) although better control may have been achieved with higher applications (de Saint Georges-Grèdelet, 1988).

Growth regulators and other chemicals: Growth regulators have been successfully used to control insects and can be effective at very low concentrations. When tested with mites, they were not able to establish complete control (Saleh et al., 1976) or high concentrations were required (Downing et al., 1990). However this area is in its infancy. The chemical treatment of carpet fibres with Mitin BC[®], Ultrafresh 300 DD[®] and Zirpro[®] (M.A. Rushforth, pers. commun., 1990) to prevent insect attack has also been shown to be effective at controlling resident mite populations (Jorde, 1988) and this represents another future area of development. The acaricidal effect of some essential oils has been identified (Watanabe et al., 1989), and this again is an area of likely development. The way plants, animals and microorganisms control mites requires further investigation.

Removal and treatment of allergenic dust

Vacuum cleaning: Vacuum cleaners are useful to extract excess surface dust from items and remove it from the circulating pool of aeroallergen. Although some studies have shown reductions of mites and dust by repeated vacuuming (Burr et al., 1980a; Colloff et al., 1989), such treatment is not an effective method for adequately controlling either dust or mites in carpets, soft furnishings or mattresses. Even when impractical and extreme cleaning times have been used, for example 20 min per m², both live mites and allergenic dust still remain (Arlan et al., 1982; Wassenaar, 1988; de Boer, 1990). Little difference was found between a powerful industrial cleaner and a domestic model in removing mites and dust from bedding (Carswell et al., 1982) and in a comparison of cleaning efficiency of 29 different models, only between 6 and 67% of added dust was recovered from a carpet (ACA report, 1989). Vacuum cleaning may also increase live mite populations by selectively removing predatory mites (van Bronswijk et al., 1971; Wassenaar, 1988). However, vacuum cleaning will almost completely remove mites and allergens from hard floors (Mulla et al., 1975).

Modifications to standard cleaners, such as controlled heating of either the dust container or the floor beneath the cleaner, are misdirected in terms of overall control of mites or allergens in a house. Allergic subjects are vulnerable to exaggerated claims made in some advertisements, and anecdotally, more than half of potential purchasers enquire about mites when considering their choice. Studies have shown several fold increases in airborne allergen after regular dry vacuuming (Trudeau et al., 1989; Kalra et al., 1990) and another vacuum cleaner employing a water trap, disperses an allergen aerosol of a size suitable for inhalation (Luczynska et al., 1990). Performance standards for the emission of allergen by vacuum cleaners are urgently needed. A few vacuum cleaners are fitted with high-efficiency (HEPA) filters which do not increase airborne allergen (Kalra et al., 1990; Luczynska et al., 1990). Patients

with asthma who have to perform vacuuming should choose such a cleaner or be advised to at least wear an efficient dust mask and to leave as many windows open as possible during the cleaning and for half an hour afterwards to provide cross ventilation to reduce airborne allergen.

Carpet washing: The combination of vacuuming and washing for carpets has not been adequately explored or developed specifically to remove allergens and control mites. This approach offers both potential benefits and disadvantages. The cleaning units vary from specialised domestic vacuum cleaners to large truck-mounted units employing powerful pumps. All units employ the same principle of washing the carpet and then removing as much water as possible. Many variations in the rate, period and type of application and the efficiency of water removal occur. Enhanced killing of mites could be achieved with very hot washing and the inclusion of residual acaricides. The washing should elute allergen but the primary concern that residual water may greatly increase the proliferation of mites and fungi is justified (Wassenaar, 1988).

Machine washing: Machine washing of clothes and bedding is an essential component of an allergen control programme as it kills mites and removes both soluble allergens and the sources of mite nutrition. All mites are killed in 10 minutes in water at 55°C and there is no enhanced killing effect on mites by the addition of detergents (McDonald and Tovey, 1992). Washing at lower temperatures does not kill mites though it does remove large numbers of them. All mites are killed by dry cleaning in perchlorethylene (Kniest et al., 1989). Remaining heat-labile *Der p* I allergen but not stable *Der p* II allergen should be partially denatured by hot washing.

Air filtration: Specialised HEPA filter units which fit to the head of the bed and supply a small zone of allergen-free air directly to the occupant, reduced symptoms in a placebo controlled trial (Verrall et al., 1988) though the majority of trials with air filtration systems have not shown benefit (see Table 1). Such units offer no protection from allergen exposure once the person moves outside the zone of clean air. Air filtration devices which stand alone in a room are less effective as the clean air is quickly diluted with air containing allergen. Airfiltration would be more useful for mite allergen if the majority of exposure were to particles which were airborne continuously (as for cat).

Allergen denaturation: The use of tannic acid to denature allergens is very effective at treating surface dust (Green et al., 1989; Miller et al., 1989). When combined with an acaricide and applied to beds, floors and furnishings the results have been disappointing, as in less than a month denatured surface allergens are replaced by dust and mites from deeper in the matrix (Price and

Marchant, 1990; Tovey et al., 1992). The original application rates of the order of 150 ml/m² (six times those commercially recommended) probably offer a high level of control.

Occlusive covers on bedding: The use of completely occlusive covers on mattresses and pillows is another essential component of controlling allergens. There is no method to completely control both mites and allergens in uncovered mattresses in humid climates. Such covers provide a barrier both to the escape of allergens and mites from the mattress and to the entrance of skin and humidity into the mattress to support mite growth. Problems of discomfort with waterproof covers, led to the development of permeable plastic covers which allow the passage of water vapour but not mites, skin scales or allergen. Immediately following their introduction, allergen was found to be reduced by 100 fold (Owen et al., 1990) or was too low to be measured (Miller et al., 1991). Under the covers on used mattresses, the mite life continues (Sesay and Dobson, 1972) and we have found allergen levels > 200 µg/g after 1 year. It is important that when mattress and pillow covers are used, that regular hot washing of bedding is maintained otherwise allergen levels in the bedding and on the outer surface of the covers will soon rise (Tovey et al., submitted).

CONCLUSIONS AND FUTURE DEVELOPMENTS

Asthma is a major public health burden, contributing significantly to morbidity, mortality and the cost of health care in many communities. The aim of research should be disease prevention and allergen removal is the only currently known method which is likely to achieve this. Where disease is established, allergen avoidance has the potential both to reduce symptom severity and the progressive deterioration of lung function.

In climates which favour the development of high mite populations, the required reductions in allergen exposure will need major changes to the way we build and live in our houses. Based on current experience it is unlikely that any reasonable amount of normal domestic cleaning activity alone will achieve this. The use of washable hard flooring in all rooms, occlusive covers on mattresses and pillows, regular hot washing of other bedding, replacement of soft furnishings and toys with options which do not retain dust and mites as well as the regular cleaning of items and areas likely to contribute to the pool of circulating aeroallergen will all be required. Reduction of indoor humidity by air conditioning or modified ventilation are probably useful additions in some localities. If the clear benefits of allergen avoidance can be established by well-conducted trials and the methods to avoid allergen can be demonstrated to be effective, then acceptance of the altered patterns of living will follow.

Future developments are particularly required in three broad areas. We need to know more about the asthma in mite-allergic people – in particular, the

quantitative relationship between reductions in exposure and improvement in both immediate symptoms and in bronchial hyper responsiveness. Can patients who will benefit be identified? What is the time course of recovery? How reversible is asthma? Can pharmacotherapy enhance this? Can at-risk children be prevented from becoming asthmatic by early initiation of comprehensive allergen avoidance procedures? One approach under development for investigating the clinical effects of low allergen exposure is shown in Fig. 1.

We need to know more about personal exposure to mite aeroallergens. What should be measured? Is particle size and allergen concentration important? Is the pattern of exposure important? Better methods are needed to measure the very low levels of exposure involved and to allow simple monitoring of allergen exposure in the home by the subjects themselves.

Finally we need to know more about how to reduce exposure to mite aeroallergens. This is a challenge to acarologists, chemists, interior designers, engineers and educators to improve the available methods and develop new approaches. This would include better control of mites through their biology



Fig. 1. An experimental approach to allergen avoidance. A prototype of an "allergen-free" chamber under development by the author for home use by highly allergic subjects with asthma. The $2.5 \times 2.5 \times 3$ -m chamber walls are constructed from thin plastic and the floor from nylon. The shape is maintained by the pressure of the partially recycled, highly filtered air supply. All bedding is either new and encased or hot washed fortnightly. There is sufficient space for recreational activity to extend the time of occupation and clear walls to prevent a feeling of isolation.

(pheromones to disrupt behaviour or other specific biologically active agents?) and with safe and better acaricides; furnishings, bedding and flooring coverings which are attractive, cheap and do not accumulate dust; houses which are less humid and with clean air and the educators to encourage these changes to occur. This would make the allergen-free house a comfortable, cost-effective and desirable choice.

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