Acknowledgments

Thanks to Dr A Custovic MSc DM MD PhD, National Asthma Campaign Senior Research Fellow and Honorary Consultant Allergist, working at the North West Lung Centre, Wythenshaw Hospital, Manchester; Euan Tovey, PhD, IRM Allergen Diagnostic Project, University of Sydney, Australia; Michelle Allsopp, and members of the Healthy Flooring Network.

The article by the International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee is reproduced with kind permission from the Lancet.

This report was commissioned by the Healthy Flooring Network, to specifically look at the connection between indoor allergens, fitted carpets and allergic diseases.

Report compiled by Dr. Jill Warner, Senior Lecturer in Allergy and Immunology, University of Southampton, UK for the Healthy Flooring Network.
# Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Executive Summary</td>
<td>III</td>
</tr>
<tr>
<td>Fitted Carpets and Allergies</td>
<td>VI</td>
</tr>
<tr>
<td>Introduction</td>
<td>01</td>
</tr>
<tr>
<td>Indoor Allergens</td>
<td>02</td>
</tr>
<tr>
<td>House Dust Mites</td>
<td>02</td>
</tr>
<tr>
<td>Ecology and biology of mites</td>
<td>02</td>
</tr>
<tr>
<td>Life cycle and physiology</td>
<td>02</td>
</tr>
<tr>
<td>Mite Allergens</td>
<td>03</td>
</tr>
<tr>
<td>Allergen nomenclature</td>
<td>03</td>
</tr>
<tr>
<td>Distribution of mite allergen in homes</td>
<td>03</td>
</tr>
<tr>
<td>Cat and Dog Allergen</td>
<td>05</td>
</tr>
<tr>
<td>Distribution of cat and dog allergens</td>
<td>05</td>
</tr>
<tr>
<td>Prevalence of Allergic Diseases across the World</td>
<td>06</td>
</tr>
<tr>
<td>Risk Factors for Allergic Sensitisation</td>
<td>08</td>
</tr>
<tr>
<td>Risk Factors - Mite Allergens</td>
<td>08</td>
</tr>
<tr>
<td>Mite allergens and allergic sensitisation</td>
<td>08</td>
</tr>
<tr>
<td>Mite allergens and asthma</td>
<td>09</td>
</tr>
<tr>
<td>Prevalence of Specific Sensitivities In Different Allergic Conditions</td>
<td>11</td>
</tr>
<tr>
<td>Control of Allergens in the Domestic Environment</td>
<td>12</td>
</tr>
<tr>
<td>Reduction of Allergens in Carpets</td>
<td>12</td>
</tr>
<tr>
<td>Clinical intervention studies</td>
<td>14</td>
</tr>
<tr>
<td>The Importance of Carpet Removal</td>
<td>14</td>
</tr>
<tr>
<td>Is Fel d 1 more susceptible to vacuuming than Der p 1?</td>
<td>15</td>
</tr>
<tr>
<td>Carpet Usage</td>
<td>15</td>
</tr>
<tr>
<td>Conclusions</td>
<td>16</td>
</tr>
<tr>
<td>References</td>
<td>17</td>
</tr>
<tr>
<td>Tables</td>
<td>21</td>
</tr>
<tr>
<td>Article by the International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee</td>
<td>26</td>
</tr>
</tbody>
</table>
Everyone knows at least one person who suffers from some form of allergy. Up to a third of the population in developed countries is affected by allergic diseases such as asthma, eczema and hay fever. Today the prevalence of allergic diseases is extremely high, particularly in the English speaking westernised societies, and it has been clearly shown to have increased over the past few decades. The UK has the highest prevalence of asthma symptoms in 13-14 year olds in the world, at 19.8%; the second highest prevalence of eczema; and the twelfth highest of rhinoconjunctivitis. The indoor environment has been cited as one of the possible reasons for this increase.

Indoor Allergens

The factors that are likely to have the most effect on disease management in the short term are those that, while suggested to be potentially useful in primary prevention, also address the problems of reducing symptoms in already sensitised individuals. Indoor allergens are one such area that might provide possible intervention strategies and it is this theory that is addressed in this report.

It is thought that the trend for tightly sealed, energy conscious homes, with fitted carpets and upholstered furniture creates traps for allergen that previously would have been removed by ventilation through ill-fitting doors and windows. This report assesses available research from around the world on indoor allergens and finds for the first time that fitted carpets are significant reservoirs of mite and pet allergens, whose importance has been underestimated in the past. These allergens play a major role, not just in triggering symptoms but in allergic sensitisation, especially during infancy - a sensitisation which is the very foundation of susceptibility to asthma and allergies in later life.

Prevalence of Allergic Diseases Across the World

Studies in different populations have shown that up to 85% of people with allergic asthma, but only 5-30% of the non-asthmatic population are allergy skin prick test positive to mites. Up to 100,000 mites may live in one square metre of carpet. People are allergic to enzymes found in mite faecal pellets.

Mites and their allergens are found in many countries around the world. The variation in their numbers depends mostly on humidity levels. For example, the level of mite allergens in very cold or dry climates is generally low, whereas higher levels are found in the coastal areas of Europe and the USA, where the climate is more suited to mite reproduction. The highest levels are found in regions where the climate is suited to mite growth throughout the year, such as the eastern coasts of Australia, Singapore and South America.

Distribution of mite allergens

Mite allergens are often ubiquitously distributed throughout houses and are found at many sites that are free of live mites, although sites that mites colonise (beds, carpets, and soft furnishings) generally have the higher allergen levels. Mite populations and their allergens are usually found at their highest level per unit weight of dust in beds, but carpets can contain the largest reservoir in total amount of mite allergens in the house.

The presence of carpets in a home can dramatically increase the total mite allergen load compared to having smooth floors. One study showed that the mite allergen concentration in dust from carpets could be 6-14 times higher than that from smooth floors and in some homes could be as high as that found in mattresses. The concentration of mite allergen increases with increasing age of the carpet and the presence of a dog is associated with higher mite allergen concentrations than found in petless households. Long pile carpets contain significantly more mites than short pile carpets.

Distribution of pet allergens

Pets are the second most important cause of domestic allergy and over 50% of asthmatic children are sensitised to allergens of cats and/or dogs. Despite this, these pets are very common in our society and one or other is found in over 50% of homes in many countries. It has been suggested that up to one third of cat sensitised individuals live in a home with a cat.

The presence of fitted carpets is particularly strongly associated with high pet allergen levels. Even when a pet is removed from a home the allergen levels can remain significantly higher than a home which has never housed a pet. Carpet levels become extremely important in this situation, as should a cat sensitive person move into a home that has previously contained a cat or dog, the allergens will remain in any carpets left in the house and may cause allergic reactions. Cat allergen is also easily spread from home to home on the clothes of cat owners, thus accumulating in the carpets of even non-cat-owners.

In one study, dust from schools with carpeted areas...
contained more cat allergen than the non-carpeted areas. This problem gives a great deal of support to the idea that carpets should not be present in schools as they will increase the chances that pet sensitive children will be exposed to allergen concentrations which can trigger their allergic reactions.

Risk Factors - Mite Allergens
There is no doubt that exposure to allergens can bring about a sensitisation which could lead to allergies in later life. Once sensitised to mites, for example, the likelihood of an individual developing asthma is greatly increased. After adjusting for sensitisation to other allergens, the risk of house dust mite sensitised children having asthma approximately doubles for every doubling of the level of exposure to mite allergens.

Sensitisation is more severe in people who live in regions with high exposure levels, and, in turn, asthma is more severe in people who have become sensitised and are subsequently exposed to high allergen levels.

It is more difficult to demonstrate a direct relationship between mite allergen exposure and prevalence of asthma symptoms. Many other factors can influence the symptoms of asthma such as, other sensitivities, cigarette smoke, pollution and infections.

Other allergic diseases have also been strongly linked to mite allergens. One study demonstrates a clear dose response relationship between exposure to house mites and risk of atopic dermatitis. Another shows that house dust mite allergen can aggravate the symptoms of seasonal conjunctivitis. Several more studies link perennial rhinitis with exposure to house dust mite allergens in mite sensitive patients.

Infant Vulnerability
It is widely accepted that infants are most at risk of becoming sensitised. Studies have shown a significant association between increasing degree of sensitisation and increasing exposure during infancy. Thus the most important time for allergen levels to be low is in infancy.

There are now studies which indicate that maternal allergen exposure during pregnancy can influence the development of fetal immune responses, and also new, sensitive techniques have been able to measure mite allergen in amniotic fluid, suggesting that maternal allergen exposure during pregnancy may play a role in primary sensitisation.

Reducing Allergen Exposure
In all, exposure to domestic allergens is strongly associated with increased risk of allergic disease, and in some cases increased symptoms. This must give strong support to the need to find effective methods of allergen reduction in homes, both for primary prevention of disease and alleviation of symptoms.

If we are to reduce the extremely high prevalence of allergic disease seen in many countries, and improve the quality of life of sufferers, we need to employ effective allergen reduction programmes.

Techniques to reduce allergen concentrations during infancy have the best chance of reducing the risk of asthma. Measures to reduce sensitisation can also be employed to manage established disease.

Epidemiological studies suggest that a 2-fold reduction of allergen exposure at a community level would significantly reduce rates of sensitisation in early childhood, halve the risk of asthma development in sensitised children and similarly reduce asthma severity in clinical terms.

The best results for reducing exposure to house dust mite allergens have been achieved with a combination of encasing bedding and removing carpets and soft furnishings. Obviously allergen control measures need to be directed primarily towards sites in the home that contain most respirable allergen and where people spend most of their time. In most homes this means the living room and bedroom.

Control of Allergens in the Domestic Environment
This report reviews the effectiveness of a number of treatments for fitted carpets. These include acaricidal treatment, disinfectants and detergents such as benzyl benzoate, and tannic acid. The results were not dramatic and were not maintained for long periods of time. The overall conclusion was that if carpets cannot be removed alternative treatments to these will need to be found.
Steam cleaning was found to be very effective at reducing both mite numbers and allergen in the laboratory, but was less effective in real homes. Intensive vacuuming, shampooing and autoclaving of carpet pieces in the laboratory was also very effective in reducing mite allergen, but only autoclaving reduced live mites. Unfortunately, the most effective methods are not practical techniques for fitted carpets in the home, and the vacuuming and the shampooing were less effective and very intensive.

Large reductions in mite densities in beds and carpets were achieved in a controlled clinical trial with adult asthmatics using liquid nitrogen and vacuum cleaning. Unfortunately, the process can only be carried out by an operator who is fully trained in safety aspects of the use of liquid gases.

Overall, studies of mite allergen reduction in fitted carpets are very disappointing. The best results were obtained in the laboratory with little translation into effectiveness in the domestic environment. The most promising results are seen with intensive vacuum cleaning, but this is probably not practical outside a research setting, on fitted carpets in a real home. Several of the authors commented on these disappointing results in carpets.

The Importance of Carpet Removal
It was notable that no study was able to reproduce the 10 fold difference between mite allergen concentrations seen between carpeted floors and uncarpeted floors reported from a study in Melbourne.

Surprisingly, very few studies have incorporated carpet removal into their interventions. The majority of successful clinical trials have either removed the carpets or treated them exhaustively with other cleaning methods. Of the 20 trials reported here, 7 showed significant clinical improvements (and two more showed a decrease in bronchial hyperreactivity). Of the 7 with notable improvements in symptom scores and medication usage, 4 removed the carpets, 1 treated them rigorously with liquid nitrogen, 1 with benzyl benzoate + encasing the mattress and the final one employed a punishing allergen avoidance regimen in the children’s bedrooms. This study may also have removed carpets, but it is not made clear in the methods.

All the above studies concentrated on house dust mite allergen, but it cannot be ignored that cat allergen is the second most common trigger of asthma symptoms in the UK. A recent study showed that intensive cleaning with a high efficiency vacuum cleaner can significantly reduce cat allergen, which would still lead to an improvement in clinical symptoms even if sufferers are sensitive to both cat and mite allergen.

Carpet Usage
The UK has the highest consumption of carpets in Western Europe and North America, at 3.9 m$^2$ per person, nearly twice as much as the next highest carpet consumers, The Netherlands and Germany, at 2.6 m$^2$ per person. In contrast, Finland, Norway and Sweden consume only 0.4 m$^2$ per person between them; in these countries the major trigger of asthma is cat and not mite allergen. It has also been reported that 98% of British homes have fitted carpets, compared with 16% in France and 2% in Italy.

Conclusion
This report has concentrated on the indoor environment and the allergens that accumulate in domestic situations. There is no doubt that there is a dose response relationship between the level of exposure to house dust mite allergens and the risk of becoming sensitised to mites, and that exposure of sensitised individuals is associated with a risk of developing asthma.

If we are to reduce the extremely high prevalence of allergic disease seen in many countries, and improve the quality of life of sufferers, we need to employ effective allergen reduction programmes. The best results for reducing exposure to house dust mite allergens have been achieved with a combination of encasing bedding and removing carpets and soft furnishings.

Fitted carpets, once in place, can be treated with rigorous allergen reduction measures, but these are much more difficult and time consuming than installing encasings for the bed. If people are prepared to follow daily cleaning regimens with effective products, then allergen reduction can be achieved, but such rigorous cleaning is unlikely to be practical for most people. Ultimately, the removal of fitted carpets, which are difficult to treat sources of allergen, is likely to be most practical and beneficial in the long term. Serious consideration now needs to be given to alternative furniture and flooring in order to persuade people to alter, what is, a deeply rooted, cultural practice.
Mite populations and their allergens are usually found at their highest level per unit weight of dust in beds, but carpets can contain the largest reservoir in total amount of mite allergens in the house.

The presence of carpets in a home can dramatically increase the total mite allergen load compared to having smooth floors.

Up to 100,000 mites may live in one square metre of carpet.

One study showed that the mite allergen concentration in dust from carpets could be 6-14 times higher than that from smooth floors and in some homes could be as high as that found in mattresses.

The presence of fitted carpets is particularly strongly associated with high pet allergen levels.

One study showed that dust from schools with carpeted areas contained more cat allergen than the non-carpeted areas. This problem gives a great deal of support to the idea that carpets should not be present in schools as they will increase the chances that pet sensitive children will be exposed to allergen concentrations which can trigger their allergic reactions.

In studies where carpets were intensively treated to reduce mite allergen none of the methods used were able to reduce mite allergen concentrations by 90% to match the low levels found in uncarpeted floors.

It is striking that in all studies where there was significant benefit to allergy sufferers, carpets were either removed or were subjected to intensive treatment.

The UK has the highest consumption of carpets in Western Europe and North America, at 3.9 m² per person, nearly twice as much as the next highest carpet consumers, The Netherlands and Germany, at 2.6 m² per person. In contrast, Finland, Norway and Sweden consume only 0.4 m² per person between them; in these countries the major trigger of asthma is cat and not mite allergen.

It has been reported that 98% of British homes have fitted carpets, compared with 16% in France and 2% in Italy.

The UK has the highest prevalence of asthma symptoms in 13-14 year olds in the world, at 19.8%; the second highest prevalence of eczema and the twelfth highest for rhinoconjunctivitis.
Today, everyone knows at least one person who suffers from some form of allergy. While 30-40 years ago allergies were diagnosed in only a small percentage of people, now up to one third of the population in developed countries are affected by allergic diseases such as asthma, eczema and hayfever. This has great implications for costs, both to the sufferers themselves and the health care providers in each country. It has been estimated that in Europe alone the combined direct and indirect costs of allergic disease amount to about 18 billion pounds per year \(^1\). As the demand on healthcare budgets is so high it is essential that countries with a high prevalence of allergy work towards methods of primary prevention \(^2\). This is not a simple task. We do not have any proven evidence for the causes of the increase and have to rely on reducing known risk factors for the development of disease in individuals, which may not be the same as the factors responsible for the increase in disease in populations.

Known risk factors include: allergen exposure, parental smoking, diet and exposure to infection. Currently none of these, either individually or in combination with others, can be directly implicated as the cause of the increase, but all have been shown to be associated with the onset of disease.

The factors that are likely to have the most effect on disease management in the short term are those that, while suggested to be potentially useful in primary prevention, also address the problems of reducing symptoms in already sensitised individuals. Indoor allergens are one such area that might provide possible intervention strategies and it is this theory that is addressed in this report, with specific attention to the role of fitted carpets. It draws broad conclusions on the role that carpets play in determining the total allergen load in the home and the importance of this on the severity of allergic disease.
The three major sources of indoor allergens associated with sensitisation and subsequent allergic disease are house dust mites, pets and moulds. In some inner city areas cockroaches are also important.

House Dust Mites
Studies in different populations have shown that up to 85% of people with allergic asthma, but only 5-30% of the non-asthmatic population are allergy skin prick test positive to mites (3-6).

Ecology and biology of mites
Mites belong to the class Arachnida, as do spiders and scorpions. At least 50 species have been found in domestic house dust, but in temperate climates the most important, both clinically and numerically, are the mites *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* (and its related species *microceras*) of the family Pyroglyphidae. In the last decade it has also been suggested that another species, *Euroglyphus maynei*, may be clinically important (7,8). In tropical and subtropical regions mites from the genus *Blomia* have been shown to be clinically important (9). A pictorial key to identification of dust mites has been published (10) and a database of the global distribution and abundance of dust mites and their allergens has been established (D.MITEDATA)(11).

Life cycle and physiology
Mites are small and invisible to the naked eye. Identifying species and determining viability can be difficult, but the main morphological characteristics are well-described (12). Mites hatch from eggs and proceed through larval, protonymphal, and tritonymphal stages before reaching adulthood, when they are 300-400µm in length. Data on the proportions of eggs, larvae, nymphs and adults in a population can also be used to predict whether that population is increasing or decreasing in size, and how successful different control measures are likely to be (11). The average life cycle is 3 months, during which the female may lay up to 300 eggs. Up to 100,000 mites may live in one square metre of carpet (14).

Mites feed on desquamated human skin and fungi that grow on the skin scales. Some species of mites (Chelitzidae spp) feed on other mite species (15), but this appears to be of little consequence when it comes to controlling mite numbers. Mites have a well-developed gastrointestinal tract with digestion and food absorption primarily in the midgut and water resorption in the hindgut (16,17).

The faecal pellets vary in size from 10-40µm and each mite will produce about 20 per day. In contrast to the gastrointestinal system, mites have no specialised respiratory structure and oxygen is obtained by passive diffusion across their cuticle. As a result of this relatively hard, but pervious layer they are very sensitive to water loss and are essentially in equilibrium with the atmosphere, the relative humidity determining their water content. Many studies have shown a significantly positive correlation between the air humidity in the home and the concentration of mite allergens in the house dust (18,19). Mites appear to thrive best at 80% relative humidity (RH) and 25°C (20), however the minimum RH that is required to allow a net gain of body water is called the Critical Equilibrium Humidity (CEH) which varies with temperature (21,22). Below the CEH, mites slowly lose water. It may take several weeks before a mite dies from desiccation. Conversely, when the RH rises above the CEH, a severely dehydrated mite can regain a fully hydrated state within 1 day (23). This has important implications for mite reduction programmes as reducing air humidity to very low levels (even 0%) for a short period will not affect mite survival. In order to destroy a dust mite population, it is much more important to ensure that RH remains continuously below the CEH, even if only slightly so (24). The average relative humidity levels in UK homes are 50-68% (145).

As well as being humidity dependent, mites are photophobic, and these two factors influence their choice of habitat – namely, at the base of carpets; inside mattresses; and in bedding, soft furnishings and soft toys.
**Allergen nomenclature**

Patients who are allergic to house dust mites produce specific IgE (allergic) antibodies against various mite allergens (or cat allergens if they are allergic to cats etc.). Originally it was decided that if more than 90% of a population allergic to a particular allergen source produced IgE antibodies to a specific allergen then it would be regarded as a major allergen (25). However more recently this has been modified to define major allergens as those components to which more than 10% of the IgE antibodies of more than 50% of the patients react, or which contribute more than 10% of the allergenic activity of the extract (11). Most mite allergens are proteins that are soluble in water and are found in the faecal pellets. Although as many as 30 or more mite allergens have been identified, five or six appear to predominate, with another four being suitably well characterised to be included in the nomenclature system (11). Table 1 (p 21) shows the structural and functional properties of some common indoor allergens.

The allergens derive their nomenclature from the first 3 letters of the genus (for example Der) followed by the first letter of the species (for example p), followed by numbering of the allergens according to their temporal sequence of purification, which is then modified to recognise homology between allergens from related sources (for example Group 1).

With Dermatophagoides pteronyssinus, for example, the allergens that have been identified and characterised are referred to as Der p 1, Der p 2, Der p 4, Der p 5, up to Der p 10. There are known Dermatophagoides farinae equivalents such as Der f 1 and Der f 2 and the cat and dog allergens are Fel d 1 and Can f 1 and Can f 2 respectively.

Most allergens are enzymes which facilitates their interaction with the host’s immune system. House dust mite allergens are able to increase the permeability of respiratory epithelium thereby gaining access to antigen presenting cells located below the epithelium and initiating allergic sensitisation (26).

**Distribution of mite allergen in homes**

Mites and their allergens are found in many countries around the world (27). Despite the dramatic differences in climate worldwide, we create not dissimilar living conditions for ourselves wherever we are. This means that we create domestic environments that are also shared by mites. They vary in their numbers dependent mostly upon humidity levels. For example, the level of mite allergens in very cold or dry climates is generally <2µg/g of dust (The Italian Alps, Stockholm, Arizona), whereas levels in countries with climates more suited to mite reproduction (coastal areas of Europe and the USA) generally have mean levels in the range 2-15µg/g. Regions where the climate is suited to mite growth throughout most of the year (eastern coasts of Australia, Singapore, South America) have mean allergen levels in the range 10-40µg/g (28).

Mite allergens are often ubiquitously distributed throughout houses and are found at many sites that are free of live mites, although sites that mites colonise (beds, carpets, and soft furnishings) generally have the higher allergen levels (29). It is difficult to make detailed comparisons of mite numbers and mite allergen levels between countries due to different sampling techniques, but results from a selection of different countries are shown in Table 2 (p 21).

Mite populations and their allergens are usually found at their highest level per unit weight of dust in beds, but carpets can contain the largest reservoir in total amount of mite allergens in the house (28). Allergen levels in soft furnishings are often similar to those found in beds and both clothing and soft toys can contain very high numbers of mites (30).

There are a number of factors that are found most frequently to be associated with high mite numbers and high mite allergen concentrations. Numerous studies confirm the association between indoor humidity and mite allergen levels (31-37). Further indirect associations with humidity include: altitude of building floors (38-40), where higher Der p 1 levels are found in rooms on the ground floor than rooms on higher storeys; ventilation rates (31,32,39,41), where low air exchange is associated with higher Der p 1 concentrations; observed dampness (38); use of concrete floors (40); and high occupant densities (32,42).

The presence of carpets in a home can dramatically increase the total mite allergen load from reservoir sites in the home compared to having smooth floors (32,43-46). One study showed that the Der p 1 concentration in dust from carpets could be 6-14 times higher than that from smooth floors (32) and in some homes could be as high as that found in mattresses. If the house was also damp this was associated with higher carpet dust concentrations of Der p 1, but not smooth floor dust concentrations of the allergen. The concentration of Der p 1 increases with increasing age of the carpet (32,40) and the
The presence of a dog is associated with higher mite allergen concentrations than found in petless households (42). Long pile carpets contain significantly more mites than short pile carpets, but short pile carpets do not appear to have significantly more mites than wood or ceramic tiles (43).

Interestingly two studies found no correlation between either mite numbers or mite allergen and the frequency of vacuuming cleaning (42,43). Mite allergen in dust from carpeted floors is significantly higher in homes than it is in institutions such as schools and hospitals (35,45,46,47).

The concentration of house dust mite allergen within a carpet in a single room can be highly variable. It is possible to sample one 1m² area in a living room and find undetectable Der p 1 concentrations, whilst sampling another and finding extremely high levels. The distribution is difficult to predict and in general there is no clear pattern, except that variation is less around furnishings. In one home a difference of 149.2µg Der p 1/g dust was found between one sampling area and another (48). This calls into question the practice of only sampling a 1m² area for research studies, a frequently employed technique.

The literature search performed for this report only found one study that reported smooth floor dust to contain significantly higher mite allergen than carpet dust (49). This study was performed in Sweden where the mite allergen levels are very low and cat allergen poses more of a problem for sensitisation. The authors do not offer any explanation for the unusual finding.
Pets are the second most important cause of domestic allergy and over 50% of asthmatic children are sensitised to allergens of cats and/or dogs (50). Despite this, these pets are very common in our society and one or other is found in over 50% of homes in many countries (51,52). It has been suggested that up to one third of cat sensitised individuals live in a home with a cat (53).

The major cat allergen is Fel d 1 and approximately 90% of cat allergic patients make IgE antibodies to this protein. At least 8 other cat allergens have been identified, but they require further characterisation to determine their relevance to disease. The major dog allergens are Can f 1 and Can f 2.

Fel d 1 is produced primarily in the sebaceous glands and in the basal squamous epithelial cells of the skin. It is stored mainly on the surface of the epidermis and on the fur (54). Fel d 1 production is under hormonal control (55) and a single cat can produce between 3 and 7µg per day (56). Castration of young male cats can result in a 3-5 fold reduction in the level of Fel d 1 in skin washings and testosterone treatment of the castrated cats restores the Fel d 1 level to pre-castration values (57).

The allergen Can f 1 is found in the dander, fur and saliva (58) and induces a positive skin test reaction in 92% of dog sensitive patients (59).

Distribution of cat and dog allergens

The allergens become widely distributed throughout homes in which pets are resident and also in environments visited by people who have close contact with pets. The cat allergen, Fel d 1, has been found in dust from floors and soft furnishings, in the air and even on walls. It is widely distributed in public places, due to it being carried on clothing (60). This wide distribution is probably because Fel d 1 is present on very small particles (they can be as small as 0.2µm in diameter) which readily become airborne. The dog allergen Can f 1 is also widely distributed in homes and public places (61). Both cat and dog allergens are found in highest concentrations on upholstered seats (62), most likely again to the allergens being carried on clothing.

While allergen levels are generally much lower in homes that do not have a cat or dog compared to those where the animal is present (53), Fel d 1 is detectable in most homes and Can f 1 in up to 85% of homes (63). Frequently the levels are higher in the living room than the bedroom (possibly due to the animals not being allowed in bedrooms, or people not sitting in the bedroom in clothes covered in pet allergens). High humidity and poor ventilation give rise to increased pet allergen levels. The presence of fitted carpets is particularly strongly associated with high allergen levels. One study showed that there is a graded association between dog allergen concentration and the presence of the dog indoors, outdoors, or not there at all (64). This study, which was in the homes of farmers, also demonstrated that carpet levels of pet allergens were higher than mattress levels. Another study demonstrated that damp homes have higher concentrations of cat allergen in the carpets than dry homes, which may be due to a greater settling of the dust in these homes (49). However, in general, pet allergens are found in highest concentrations on upholstered chairs (35,62,65). A study, investigating how the allergen was transferred from homes to schools in New Zealand found that the average amount of Fel d 1 carried on the clothes of a cat owning child was 6.1µg compared to 0.72µg on the clothes of a non-cat owning child (66). Wool and polyester garments contained more Fel d 1 than cotton garments (probably due to washing frequency) and girls’ clothes contained more Fel d 1 than boys’ clothes. It was suggested, by the authors, that girls might spend more time indoors than boys, therefore being exposed to more allergen, or that girls’ clothes require less frequent laundering! In the schools where this study was performed dust from carpeted areas contained more Fel d 1 than non-carpeted areas and the amount of Fel d 1 correlated with cat ownership rates. This problem gives a great deal of support to the idea that carpets should not be present in schools as they will increase the chances that pet sensitive children will be exposed to allergen concentrations which can trigger their allergic reactions (67).

Even when a pet is removed from a home the allergen levels can remain significantly higher than a home which has never housed a pet (68). It would seem that there is an initial reduction in aeroallergen when the pet actually goes, but after this the reduction in reservoirs is slow and variable. Cat allergen levels can remain high for years after the cat is removed. Carpet levels become extremely important in this situation, as should a cat sensitive person move into a home that has previously contained a cat or dog, the allergens will remain in any carpets left in the house and may cause allergic reactions.
Until relatively recently it has been very difficult to provide information on the prevalence of allergic disease across the world as so many different criteria have been used to define the conditions of asthma, eczema and rhinoconjunctivitis (hayfever). However in 1998 the results of a world-wide study (The International Study of Allergy and Asthma in Childhood – ISAAC) were published which had used a standardised questionnaire to interview 463,801 13-14 year old children in 155 collaborating centres in 56 countries, about their symptoms of these three atopic disorders (69). It was hoped that this information would provide a better understanding of the global epidemiology of allergic disease, to generate new hypotheses and to assess existing hypotheses of possible causes.

There have been few studies of the population prevalence of allergic rhinitis and atopic eczema, and although hundreds of asthma prevalence studies have been done in various parts of the world, they have seldom used standard approaches. An exception is the European Community Respiratory Health Survey (ECRHS)(70-72), that involved surveys of asthma and allergic rhinitis prevalence in adults aged 20-44 years in 48 centres in 22 countries, although only 9 centres in 6 countries were outside Western Europe. The ECRHS suggested that there were regional risk factors for asthma and allergic rhinitis in Western Europe, but it did not comprehensively assess the global patterns. For children, the largest standardised studies of the prevalence of asthma, allergic rhinitis and atopic eczema have involved, at most, four countries (73-75).

The ISAAC study reports the prevalence of asthma in 13-14 year olds across the world to vary from 1.6% (Indonesia) to 36.8% (UK) i.e. the highest prevalence is about 20 times higher than the lowest.

Rhinoconjunctivitis showed a 30 fold variation in prevalence within the population with a range of 1.4% (Albania) to 39.7% (Nigeria). The UK was the twelfth highest for this disease.

Eczema showed a 60 fold variation with a range of 0.3% (Albania) to 20.5% (Nigeria). The UK was the second highest for this disease. The international patterns differed overall for eczema compared to those for asthma and rhinoconjunctivitis, however there were significant correlations (p<0.001) in prevalence for all disorders across the countries taken as a whole.

The prevalence of having symptoms of at least two out of the three conditions varied from 0.3% to 18.5% Symptoms, in the last 12 months, of only one of the disorders were seen in 72.9% of the children.

It must be noted that the ISAAC questionnaire gives a higher prevalence of asthma and probably the other allergic diseases than more objective clinical based studies. Despite best efforts, translations of questions into different languages may not always diagnose the same clinical condition, particularly where there are no near-equivalent terms to describe symptoms and/or where there can be other diseases with similar symptoms.

The ISAAC paper showing all the results across the world is attached to this report (p 26), but to summarise the findings:

For asthma symptoms the highest prevalences were found in the UK, New Zealand, Australia, and the Republic of Ireland, followed by most centres in North, Central and South America. The lowest prevalences were reported from centres in several Eastern European countries, Indonesia, Greece, China, Taiwan, Uzbekistan, India and Ethiopia. There were some very wide variations between different regions in similar parts of the world, which may prove useful information to investigate causative factors within countries.

By contrast to asthma, rhinoconjunctivitis was reported from areas scattered around the world. Several countries with the highest symptom prevalences were not represented in the highest asthma prevalences; therefore this may indicate that the risk factors differ for the two diseases. For example, the highest prevalence of rhinoconjunctivitis was found in Nigeria, but this country is found only half way up the list for asthma prevalence.

For eczema the highest symptom prevalences included centres from many regions of the world, including some from Scandinavia (Finland and Sweden) and Africa (Ethiopia), which were not represented among the highest asthma prevalences. However the centres with low eczema prevalences tended to be the same as those for asthma and rhinoconjunctivitis.

When self reported symptoms of more than one atopic disorder were taken into account the highest prevalences were observed predominantly in English speaking Western countries. The ECRHS also showed
that the presence of at least one positive allergen specific IgE was strongly associated with English speaking populations (72). The presence of at least one specific IgE ranged from 16% in Spain to 45% in New Zealand.

Studies from China and Africa showed striking differences in asthma prevalence within populations despite a similar prevalence of allergic sensitisation. Therefore risk factors other than allergy may be important in some populations (76,77).

The global pattern of allergic disorders was consistent with the belief that outdoor air pollution is not a major risk factor (78,79). Regions such as China and Eastern Europe with the highest air pollutants generally had low asthma prevalence. Those, such as Western Europe and the USA, with high ozone levels had intermediate prevalences and some with low outdoor pollutants (e.g. New Zealand) had high asthma prevalences.

Therefore, patterns of allergic disease do appear to follow English speaking westernised societies, however there are some areas with a high prevalence of disease, but low allergic sensitisation, indicating that other factors can be important and must not be ignored when considering how to reduce the numbers of people with asthma, rhinoconjunctivitis and eczema across the world.
As the previous section has demonstrated, the prevalence of allergic diseases is extremely high in certain parts of the world, and has been clearly shown to have increased over the past few decades (80-82). This has led to much research investigating the possible reasons for this increase that might lead to ways in which primary prevention can be implemented. Three major areas have been cited:

1) Indoor environment;
2) Changes in diet;
3) Increased hygiene (2).

This report will concentrate on the evidence suggesting a role for the indoor environment and will mostly be focussed on the role of mite allergens with reference to the small number of reports on cat allergen and the mould Alternaria, as being the cause and/or trigger factors for allergic disease.

It is very important to differentiate between factors (and levels of factors) that cause allergic disease and those that trigger symptoms in already sensitised individuals. These may be very different. Most studies have concentrated on the role of these factors in asthma, with little information available on other allergic diseases.

Researchers have tried very hard to develop threshold values for allergen exposure which are associated with 1) sensitisation and 2) exacerbation of disease symptoms. The most widely quoted are those proposed by The First International Workshop on Mite Allergens and Asthma (27). They suggested that exposure to 2µg or more of Group 1 mite allergens per gram of dust (e.g. Der p 1 or Der f 1) be regarded as a risk for the development of IgE antibody and asthma, and a higher level of 10µg Group 1 mite allergens/g be regarded as a risk for an acute attack of asthma. Similar values have been placed on the cat allergen Fel d 1 (83) with 1µg/g representing a risk for being sensitised to cats and a higher level of 8µg/g being the level at which most cat allergic patients will experience symptoms. Similarly levels of 2µg/g and 10µg/g Can f 1 are the levels significant for sensitisation and symptoms for dogs (84).

While quoting these thresholds one must be aware that it is difficult to make direct comparisons between different studies as the method of sampling the dust will vary from one to another, affected by issues such as: which vacuum cleaner was used, what filter head was employed, what filter size was incorporated, how long the sampling continued and even the enthusiasm of the operator (85)! Nevertheless the collection of dust samples from domestic environments has remained basically little changed for two decades (86)!

There has been much discussion over the years about whether reservoir or airborne levels are more meaningful in terms of exposure and whether allergen should be measured in ng/g of dust or ng/m² of surface sampled. Overall it is generally agreed that reservoir levels should be reported as both allergen per unit weight and allergen per unit area and that while airborne levels are probably most closely related to exposure, they are difficult to measure (unless notable disturbance is occurring in the sampling environment) and cannot, as yet, form part of a standardised allergen measurement programme. New techniques are currently under development that may make the sampling of airborne allergens more available and thereby provide allergen assessments that are more meaningful in terms of actual exposure (ER Tovey – personal communication).

Risk Factors – Mite Allergens

Mite allergens and allergic sensitisation

The evidence for risk factors with a direct role in asthma causation is most complete for house dust mite allergens. The previously mentioned ability of the enzymes to actively damage airway epithelium (26) makes their biologic significance highly plausible and there is a great consistency of evidence for there being a dose-response effect in sensitisation (87).

Factors which have been proposed as being important determinants of allergen specific immune responses are: an individual’s degree of susceptibility to allergens, the immunogenic properties of the allergen, and the degree of exposure (88). In any population there is a gradient in the ability to respond to allergens: ranging from individuals who do not become sensitised regardless of exposure to others who show extensive sensitisation to many different allergens. The ability to respond is genetically determined, although the exact pattern of inheritance is disputed (89). Even among individuals with a tendency to respond the development of sensitisation to an allergen is dependent on exposure. This is best illustrated by patterns of exposure: in Northern Europe, where ragweed pollen is rare, sensitisation to it is equally rare; similarly the pollen of the olive tree is not recognised as an allergen in North America; additionally among groups where it is rare to
find a domestic cat, sensitisation to cat is uncommon. Between the extremes of no allergen exposure and excess allergen exposure there is a gradation of exposure to a particular allergen. If sufficient exposure occurs the probability of sensitisation for susceptible individuals becomes extremely high. House dust mite allergens are highly immunogenic and in areas where mite exposure is high, such as the UK, parts of mainland Europe, Australia, New Zealand, coastal areas of North America and South America, the level of mite exposure appears to sensitise “most” potentially atopic children (90).

The most vulnerable time appears to be during infancy and both retrospective (91) and prospective (92) studies have shown a significant association between increasing degree of sensitisation and increasing exposure during infancy. However, it must be emphasised that the role of allergen exposure is a two-stage process whereby exposure leads to the development of sensitisation and exposure of sensitised subjects leads to the development of asthma (93). Thus levels of sensitisation become more severe in people who live in regions with high exposure levels (94), and asthma becomes more severe in people who have become sensitised and who are exposed to high allergen levels (95).

Most studies which have investigated the relationship between exposure and sensitisation have concentrated on individuals at high risk of developing atopy, but one group looked prospectively at the effect of allergen exposure on an unselected group of school children, performing skin prick tests to inhalant allergens at 12 month intervals over a period of two years, and measuring Der p 1 levels in mattresses (96). The children were divided into those with previous positive skin tests (other than to mites) and those without. In non-atopic children, only extremely high exposure to Der p 1 (>60µg/g) represented a significant risk of sensitisation. Exposure to levels of Der p 1 of >9µg/g conferred a definite risk of sensitisation in the whole population. For children already sensitised to other inhalant allergens, a significant risk of sensitisation was conferred by >2µg/g of Der p 1, as suggested by The First International Workshop.

Once an individual is sensitised to mites the likelihood of their developing asthma is greatly increased. After adjusting for sensitisation to other allergens, the risk of house dust mite sensitised children having asthma approximately doubles for every doubling of the level of exposure to mite allergens (97).

It must not, however, be forgotten that in areas where mite allergen is very low, or unmeasurable, other allergens will take this role. For example, in Los Alamos, New Mexico, 67% of asthmatic children are sensitised to dog and 62% to cat. In this location the levels of mite allergens are very low, but more than 75% of families keep a cat or dog (84,93). In areas of Australia and the USA (Arizona) where the climate does not favour mite population growth and reproduction, sensitisation to the mould Alternaria represents the most important risk factor for asthma (98,99). In some parts of Scandinavia, with low levels of mite allergen, sensitisation to domestic pets has the strongest association with asthma (100), but should sensitisation to mites occur at these low levels then there is still a close association between the mite sensitisation and asthma (19, 101).

Mite allergens and asthma
The relationship between mite allergen exposure and sensitisation is very clear, but it is more difficult to demonstrate a direct relationship between mite allergen exposure and prevalence of asthma. Many other factors can influence the symptoms of asthma such as, other sensitivities, cigarette smoke, pollution and infections.

Most difficulty in determining whether mite exposure in its own right is affecting the development of asthma occurs in areas where the general level of exposure is high. A study performed in the south west of France concluded that the risk of the occurrence of asthma in sensitised individuals depends upon the degree of atopy (number of positive skin tests), but that mite allergen exposure was not predictive of the occurrence of asthma. The authors’ hypothesis is that house dust mite exposure is so ubiquitous in this area that virtually all genetically predisposed individuals become sensitised to mites, whatever the house dust mite allergen level, which in most cases was above the threshold for sensitisation (102). Another study, in New Zealand, also showed that current Der p 1 levels showed no association with current asthma (103), as did a study of 8-10 year old children in Sydney, Australia (104). However all these areas have very high mite and mite allergen levels. In all three studies the majority of homes had Group 1 allergen levels >10µg/g.
Other studies in areas where the allergen levels are lower or more variable have been able to demonstrate a relationship between severity of asthma symptoms (as determined by bronchial hyperresponsiveness [BHR] and lung function measurements) and mite allergen exposure in mite sensitive patients\(^\text{[105-109]}\). The majority of these studies reported house dust mite allergen levels up to a maximum of 15µg/g and the only one that was higher (approximately 650µg/g)\(^\text{[109]}\) showed a huge variation between the low and high Der p 1 levels, giving room for differences in symptoms.

This ability to demonstrate a difference in symptoms in relation to house dust mite allergen levels, despite the inability to identify a simple threshold level for provocation of asthma symptoms, is central to the hypothesis that reducing allergen concentrations in the domestic environment is a viable method for the management of allergic disease. If different allergen levels were not associated with different degrees of symptom severity there would be little point in instigating allergen reduction programmes.

Nevertheless, it is fairly uniformly accepted that the most important time for allergen levels to be low is in infancy and that this is the most vulnerable time for sensitisation to occur. Techniques to reduce allergen concentrations at this time in life have the best chance of reducing the risk of asthma\(^\text{[91,92,110,111]}\), There are now studies which indicate that maternal allergen exposure during pregnancy can influence the development of fetal immune responses\(^\text{[112,113]}\) and also new, sensitive techniques have been able to measure Der p 1 in amniotic fluid\(^\text{[114]}\), suggesting that maternal allergen exposure during pregnancy may play a role in primary sensitisation.

One of the most frequently asked questions concerning domestic allergens is "Are we exposed to higher concentrations of allergens in homes than during the periods when asthma prevalence was lower?" The answer is not simple as, although it seems likely that in certain environments, such as in Australia and New Zealand, the levels of cat and house dust allergens have been high for many years, the homes themselves have changed\(^\text{[115]}\). Our energy conscious, tightly sealed homes with fitted carpets and upholstered furniture may be traps for allergen that previously would have been removed by ventilation through ill-fitting doors and windows. The concentrations measurable in the dust may be the same, but the amount trapped in the air in the house may have increased. Until we have more reliable methods of sampling airborne allergen this cannot be measured and even then we will not have comparisons from 30 years ago. However, this lack of evidence should not deter us from attempting reduce the allergen load in the future.

As mentioned at the start of this section, most research on the role of domestic allergens as risk and trigger factors for allergic disease has been in asthma, but there are a few studies that have investigated the role of house dust mite allergen exposure in other diseases. One study has demonstrated clear dose response relationship between exposure to house mites and risk of atopic dermatitis\(^\text{[116]}\). The study demonstrated a relative risk of 4.7 with exposure to increased numbers of house dust mites in the mattresses of atopic dermatitis patients compared with a control group of asthma patients not sensitised to mite. The authors hypothesise that this could be due to the increased skin scales (mite food) in the mattresses of patients with atopic dermatitis leading to increased mite numbers. This is supported by trials of house dust mite allergen reduction in atopic dermatitis patients, showing an improvement in symptoms\(^\text{[117]}\).

Another interesting study showed that exposure to house dust mite allergen plays an important role in the aggravation of the symptoms of vernal keratoconjunctivitis\(^\text{[118]}\). The study was performed in Israel and the severity of the symptoms of the vernal keratoconjunctivitis in house dust mite sensitive patients peaked at the same time of year (summer) as the numbers of house dust mites.

There are also several studies that show that perennial rhinitis is associated with exposure to house dust mite allergens in mite sensitive patients.

In all, exposure to domestic allergens is strongly associated with increased risk of allergic disease, and in some cases increased symptoms. This must give strong support to the need to find effective methods of allergen reduction in homes, both for primary prevention of disease and alleviation of symptoms.
The allergens that trigger different allergic conditions will differ from one country to another depending upon exposure. In the UK the triggers for asthma have been studied in most detail and have shown that in asthmatic individuals 50-75% are allergic to house dust mites; 50-70% are allergic to grass pollen; 35-55% to cat; 10-40% to dog; 10-20% to tree pollen; 10-15% to moulds and <10% to foods.\(^{(119-121)}\)

In rhinitis 20-40% are allergic to house dust mites, but the greatest trigger is pollen.\(^{(122-124)}\)

In eczema, particularly in early childhood, the major triggers are frequently foods. However, one study showed that inhalant allergens do play a significant role with over 60% of a mixed group of children and adults having specific IgE antibody to house dust mite allergen, even when those with concurrent asthma were removed. Similar responses were seen to grass pollen.\(^{(125)}\)
Control of Allergens in the Domestic Environment

Epidemiological models suggest that a 2-fold reduction of allergen exposure at a community level would significantly reduce rates of sensitisation in early childhood [92,94], halve the risk of asthma development in sensitised children [95], and similarly reduce asthma severity in clinical terms [126].

The optimal allergen avoidance is found in schools and institutions at high altitude, where severe asthma sufferers can spend long periods of time in environments that contain very low or undetectable amounts of the common allergens triggering their disease. Beneficial results have been seen when allergic individuals have moved from the humid Mediterranean coast of France, where house dust mite allergen levels are high, to a low mite environment in the French Alps [127], or from the plains of Italy to the Alps [128]. Impressive reductions in the severity of asthma and levels of anti-house dust mite IgE have been seen in both locations, but they are reversed on returning to the high house dust mite environment. In the Netherlands, children admitted to a high altitude asthma centre showed reduction in blood eosinophils, reduced peak flow variability and improved airway hyperresponsiveness [129].

Unfortunately not all allergic individuals can be sent to such institutions (although they would be excellent places to spend the vulnerable first year of life in any primary prevention study), so attempts have to be made to recreate these low allergen havens in normal domestic environments.

Obviously allergen control measures need to be directed towards sites in the home that contain most respirable allergen and where people spend most of their time. In most homes this means the living room and bedroom. The sites that contain most allergen are: beds, carpets, soft furnishings, soft toys, and, in some cases, infrequently laundered clothes. Levels in clothing can be as high as in any other domestic site. Clothing is constantly disturbed and is a highly proximal source. Not all allergen reduction techniques are suitable for all sites of allergen accumulation. Therefore, specific techniques have been developed to deal with specific areas of the homes e.g. anti-allergy bedcovers, which are likely to be more effective at reducing exposure to allergens in the mattress, duvet and pillow than vacuuming and safer than spraying the bed with potentially toxic chemicals.

Any successful allergen reduction programme is likely to consist of more than one intervention in order to deal appropriately with the different sources of allergens. The most frequently employed techniques include: removal of carpets, high efficiency vacuum cleaning, bedcovers, dehumidification and increased ventilation, acaricides, and heating or freezing. Other techniques that have been investigated include: ionisers and air filtration devices.

The effectiveness of all of these devices is extremely variable in reducing domestic allergens and whilst several have shown significant reductions in house dust mite allergens in specific source materials, few have been able to translate these reductions into clinical benefit. Some studies did not assess clinical benefit, purely measuring changes in allergen concentrations to assess the effectiveness of the intervention. These studies indicate potentially useful interventions, but the components of the allergen reduction regime cannot be specifically recommended to patients as potential additional management for their disease unless clinical benefit has been proven. People who are looking for techniques to reduce allergen concentrations may wish to try them in their own homes as part of an allergen reduction schedule.

In the following sections, studies that have simply monitored allergen concentrations are reviewed first followed by studies on clinical benefits. The effects on carpets are summarised in Table 3 (p 22).

Reduction of Allergens in Carpets

As mentioned previously, carpets are some of the major allergen retaining sources in the domestic environment. Different carpet types may retain greater or lesser amounts of allergen dependent upon their construction and the material of which they are made. One study investigated the retention properties of 26 types of custom made carpets by spiking them with reference dust containing Fel d 1 and then measuring the ability to remove that allergen with a standardised vacuum technique [130]. They found that the carpet properties that render the carpet most likely to release allergen to vacuuming are: low pile density and height, fluorocarbon coating of fibres, high denier per filament, and low surface area fibres (e.g. square hollow fibre rather than trilobal). Another study showed that woolen carpets have significantly higher concentrations of Der p 1 in the air above them than do synthetic carpets, possibly due to electrostatic charge [131]. Should allergic individuals decide to keep their carpets a careful decision on carpet type would need to be made concerning the ability to actively remove allergen from the carpet, whilst not creating an overall high allergen load in the room air.
Acaricidal treatment of carpets is probably the most frequently studied technique for removal of mites and their allergens. The first studies investigated disinfectants and detergents (132) and found that the most effective chemical was benzyl benzoate, although all the agents were more effective on hard floors than carpeted floors. Another detergent (Metsan) was investigated in The Cape Peninsula (where Der p 1 levels are high) for its properties in reducing Der p 1 levels in carpets and mattresses on its own and in combination with an acaricide (Acarosan) (133). The results showed that a single application of Metsan alone could significantly reduce the concentration of Der p 1 in carpets measured 3 months after the single application and that the addition of the acaricide enhanced the effect. No reduction in mattress Der p 1 was seen with either treatment. The reduction in carpet Der p 1 was approximately 50%, with allergen concentrations of >10µg/g still remaining in both treatments. Two studies from Charlottesville Virginia, USA (134,135) investigated the effectiveness of tannic acid, benzylbenzoate and two commercial carpet cleaners on Groups 1 and 2 mite allergens and Fel d 1 in carpet dust. The results were not dramatic and were not maintained for long periods of time, however benzyl benzoate and the two commercial carpet cleaners significantly reduced group 1 dust mite allergens. Tannic acid was more effective on Der f 1 than Der p 1 and nothing was effective on Fel d 1. The overall conclusion was that if carpets cannot be removed alternative treatments to these will need to be found as their effectiveness is extremely limited. There are also concerns about the frequent use of potentially toxic chemicals in the home.

Steam cleaning and hot water washing extraction has captured the interest of several groups with varied results. When carpets in homes were exposed to hot water washing extraction no reduction in mite numbers was seen, although there was a 3.3 fold reduction in Der p 1 (136). The authors concluded that carpet cleaning in this format was unlikely to be effective enough to show any clinical benefit. Conversely, when pieces of carpet were exposed to steam cleaning 100% reduction in mite numbers and 86.7% reduction in Der p 1 was achieved, with the conclusion that the treatment looked highly promising (137).

Several groups have also investigated vacuuming. In Amsterdam comparisons were made between dry vacuuming, wet cleaning, shampooing and autoclaving of carpet pieces. None of the techniques, where the content of live mites was checked after treatment, showed any reduction in mite numbers (it was assumed that autoclaving killed all the mites), but all showed some reduction in Der p 1, with autoclaving proving the most effective. Unfortunately neither the autoclaving nor the wet washing would be practical techniques to treat fitted carpets in situ and the vacuuming and the shampooing were less effective and very intensive (138).

Low temperature washing with detergents and washing with added benzyl benzoate was moderately effective on carpet pieces, showing a 50% and 100% reduction respectively in mite numbers (139).

A comparison of vacuuming with application of tannic acid on a combined concentration of Der p 1 and Der f 1 showed reductions of 50% and 34% respectively in Sweden (140), while in New Zealand daily vacuuming of carpets showed reductions in Der p 1/g and Der p 1/m² of 48% and 68.5% (141).

A study of the application of benzyl benzoate in Bristol, UK did not demonstrate any reduction Der p 1 in the bedroom carpet (142), nor did the application of an anti-mite shampoo to bedroom carpets in Melbourne, Australia (143).

Ventilation systems and dehumidifiers, despite showing reduction in mite numbers and Der p 1 in mattresses showed no effect on either in bedroom or living room carpets (144-148).

Therefore, overall, these studies of mite allergen reduction in carpets are very disappointing. The best results were obtained in the laboratory with little translation into effectiveness in the domestic environment. The most promising results are seen with intensive vacuum cleaning, but this is probably not practical outside a research setting. Several of the authors commented on these disappointing results in carpets. It was notable that no study was able to reproduce the enormous difference between mite allergen concentrations seen between carpeted floors and uncarpeted floors, with dust from uncarpeted floors containing only 10% of the allergen found in dust from carpeted floors, (41.1µg Der p 1/g and 4.1µg Der p 1/g respectively) reported from a study in Melbourne (143).

This report aims to focus mostly on the effect of allergen reduction techniques on allergens in carpets, but it is important to mention other techniques that address the issues of allergens in other sources in
the home. As mentioned above, whilst mechanical ventilation was not effective on allergens in carpets it has been shown to be highly effective on mite allergen concentrations in mattresses (149,150). This is interesting, as the opposite might be expected, due to the mattress containing a greater reservoir of water and more frequent replenishment from human occupancy. The majority of studies have been done in the dry, cold climate of northern Scandinavia and there has been much scepticism about whether the results can be repeated in warmer, damper climates. Originally it was thought that this was not possible (145-148), but newer, more effective products look more promising (151).

Mite densities have been reduced successfully by the use of electric blankets to decrease mattress humidity (152). In field trials, the inert freezing agent, liquid nitrogen, combined with intensive vacuum cleaning, was found to be very effective at killing and removing mites (153); mean densities of live mites in dust samples from five treated mattresses were reduced from 310/g to 3/g in 8 weeks. Large reductions in mite densities in beds and carpets were also achieved in a controlled clinical trial with adult asthmatics (154) using liquid nitrogen and vacuum cleaning. Unfortunately, the process can only be carried out by an operator who is fully trained in safety aspects of the use of liquid gases.

For beds, barrier methods are most effective and studies in which mites are vacuumed through mattress covers showed a reduction in the order of 30-100 fold compared with those in the dust on the mattresses themselves (155,156). The majority of studies suggest clinical improvement following use of mattress covers, usually combined with cleaning measures (155,157-159). Another allergen denaturing solution was tested in both Australia and UK and was shown to produce a moderate reduction in mite allergens in carpets, blankets and soft furnishings (160,161), but, again, not sufficiently effectively to suggest that an improvement in symptoms would be seen.

There are no studies of air filtration devices alone that have shown any clinical improvement and, although HEPA filters have been shown to be effective at reducing cat allergen concentrations in rooms, the opinion is that they cannot be recommended in the absence of other forms of environmental control (162). There is very little scientific evidence to support the claims of manufacturers that ionisers are of benefit to patients with allergy to domestic allergens. A double-blind cross-over study using active and placebo ionisers in homes showed no improvement of asthmatic symptoms during the period of active ionisation, even though a significant reduction was seen in airborne Der p 1. In fact an increase in nocturnal cough was recorded during the active period (163). Ionisers, therefore are not presently recommended for use in the home for symptomatic relief of asthma.

Clinical intervention studies

One of the most important aspects of a clinical study is that it is placebo controlled to account for any improvements in symptoms which can be attributed simply to being part of a trial and therefore receiving extra attention. Unfortunately this is not always easy to achieve with an allergen reduction programme and some reported studies are uncontrolled before and after investigations. Table 4 (p 24) (adapted from Marks GB [179]) gives an overview of the effectiveness of a range of placebo controlled intervention studies, both in reducing allergen and in improving symptoms. The most effective studies comprised a combination of encasing the mattress and removing or rigorously treating the carpet.

The Importance of Carpet Removal

Surprisingly, very few studies have incorporated carpet removal into their interventions. Those that have, have included other measures as well, which makes any assessment of the individual contribution of removing the carpet difficult to ascertain. However, it is clear that the majority of clinical trials that have reported improvements in symptoms have either removed the carpets or treated them exhaustively with other cleaning methods. Of the 20 trials reported here, 7 showed significant clinical improvements (154,155,157,166, 170, 175 and 176) and two more showed a decrease in bronchial hyperreactivity (BHR) (169,177). Of the 7 with notable improvements in symptom scores and medication usage, 4 removed the carpets (155,157,166,170), 1 treated them rigorously with liquid nitrogen (154), 1 with benzyl benzoate + encasing the mattress (175) and the final one employed a punishing allergen avoidance regimen in the children’s bedrooms (176). This study may also have removed carpets, but it is not made clear in the methods. The schedule included "changing" bedclothes, mattress, rugs, carpets, upholstered furniture and soft toys due to them being major sources of house dust.

1. It must be noted that it is not recommended, however, that people sleep with the electric blankets switched on as electromagnetic fields associated with electric blankets have been implicated as a possible risk factor in breast cancer.
accumulation. The rest of the schedule consisted of:
1) daily washing of floors and damp dusting, shaking
of bedclothes outside the bedroom and bedclothes
left on the window sill;
2) weekly vacuuming of both sides of the mattress,
thorough cleaning of all surfaces with a damp cloth,
changing of bedsheets and washing at >60
degrees Celsius;
3) monthly washing of pillows and blankets at 60
degrees Celsius. As it emphasises washing of floors
in the bedroom it can probably be assumed that the
carpets were removed.

Is Fel d 1 more susceptible
to vacuuming than Der p 1?
All the above studies concentrated on house dust
mite allergen, but it cannot be ignored that cat
allergen is the second most common trigger of asthma
symptoms in the UK (and the most common in some
countries where mite allergen is low). A recently
conducted study of the use of high efficiency vacuum
cleaners in the homes of allergic asthmatic patients
confirmed the lack of effectiveness of vacuuming in
the reduction of Der p 1 in carpets, soft furnishing and
mattresses in homes. However, it demonstrated that
Fel d1 concentrations can be significantly reduced with
a daily vacuuming regimen (even in homes where a
cat is present) with an associated improvement in
medication usage, lung function and BHR in cat
sensitive individuals (in non-cat containing homes)
[180]. It must be stated that cat sensitive patients
are frequently also allergic to house dust mite, but it
seems that the reduction of the cat allergen alone,
can result in improvement in the clinical parameters
of asthma in these patients, even when house dust
mite allergen is unchanged. This must be taken
into account when advocating total removal of
allergen sources rather than treating them in-situ.

Carpet Usage
It has proved difficult to obtain accurate figures of
the differences in carpet usage across the world,
however it seems clear that the UK has the highest
consumption in Europe and North America. In 1999
consumption per capita for the countries where
information was available was as follows:

<table>
<thead>
<tr>
<th>Country</th>
<th>Square metres per person</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>-3.9*</td>
</tr>
<tr>
<td>Holland</td>
<td>-2.6*</td>
</tr>
<tr>
<td>Germany</td>
<td>-2.6*</td>
</tr>
<tr>
<td>USA</td>
<td>-2.4</td>
</tr>
<tr>
<td>Belgium</td>
<td>-2.1</td>
</tr>
<tr>
<td>Canada</td>
<td>-1.9</td>
</tr>
<tr>
<td>Denmark</td>
<td>-1.9</td>
</tr>
<tr>
<td>Switzerland</td>
<td>-1.7</td>
</tr>
<tr>
<td>France</td>
<td>-1.5*</td>
</tr>
<tr>
<td>Austria</td>
<td>-1.0</td>
</tr>
<tr>
<td>Portugal</td>
<td>-0.7</td>
</tr>
<tr>
<td>Spain</td>
<td>-0.6</td>
</tr>
<tr>
<td>Italy</td>
<td>-0.4</td>
</tr>
<tr>
<td>Norway, Finland and Sweden</td>
<td>-0.4</td>
</tr>
</tbody>
</table>

All figures are based on personal communication with Laurance W Bird, DuPont Nylon
Marketing. * All figures other than those marked * are calculated using population
from the Swiss Federal Statistical Office.

Across Western Europe the carpet consumption
follows the climate conditions generally with colder
northern countries having the higher consumption.
The average UK consumer is said to replace carpeting
every 6 years (181). This, of course, must be
tempered by the lower use of carpeting in Scandinavia,
where housing is generally more energy efficient,
despite the cold conditions. It must be noted that
the major trigger of asthma in Northern Scandinavia
is cat and not mite. It has been reported (Proctor and
Gamble Concept and Usage Research for Febreze
1997) that 98% of British homes have fitted carpets,
compared with 16% in France and 2% in Italy.
Conclusions

Allergic diseases have increased in prevalence dramatically over the last 3 decades, particularly in Western, English speaking, countries. The UK has the highest prevalence of asthma in the 13 year old population in the world. The theories that have been put forward to explain this have 3 main focuses:

1) Indoor environment;
2) Diet;
3) Hygiene and infection.

This report has concentrated on the indoor environment and the allergens that accumulate in domestic situations, with particular reference to the role of fitted carpets as reservoirs for these allergens. There is no doubt that there is a dose response relationship between the level of exposure to house dust mite allergens and the risk of becoming sensitised to mites, and that exposure of sensitised individuals is associated with a risk of developing asthma. Measures to reduce sensitisation can also be employed to manage established disease and if we are to reduce the extremely high prevalence of allergic disease seen in many countries, and improve the quality of life of sufferers, we need to employ effective allergen reduction programmes. The best results for reducing exposure to house dust mite allergens have been achieved with a combination of encasing bedding and removing carpets and soft furnishings.

It is notable that in almost all of the studies where there was significant benefit to allergy sufferers, carpets were either removed or subjected to intensive treatment. Fitted carpets, once in place, can be treated with rigorous allergen reduction measures, but these are much more difficult and time consuming than installing encasings for the bed.

If people are prepared to follow daily cleaning regimens with effective products, then allergen reduction can be achieved, but such rigorous cleaning is unlikely to be practical for the majority of people.

Ultimately the removal of fitted carpets is likely to be most practical and beneficial in the long term. Serious consideration now needs to be given to alternative furniture and flooring in order to persuade families to alter, what is, a deeply rooted cultural practice.
References


43. Munir AKM, Einansson R, Kjellman NIM, Bjorksten B. Mite allergen (Der p 1, Der f 1) and cat (Fel d 1) in the homes of babies with a family history of allergy. Allergy 1993;48:158-163.
Allergic Diseases and The Indoor Environment


64. Parunesh H, clipboard M, Salvation V, Van Hage-Hamsten M. Exposure to an abundance of cat (Fel d 1) and dog (Can f 1) allergens in Swedish farming households. Allergy 1999:54:229-234.

65. Borge M, Munir AK, Dorebog S. Concentrations of cat (Fel d 1), dog (Can f 1), and mite (Der f 1) and use of medication in the clothing and school environment of Swedish schoolchildren with and without pets. Pediatr Allergy Immunol 1998:9:25-30.


Dreborg SKG. Vacuum cleaning decreases the levels of mite allergens in house dust. Pediatr Allergy Immunol 1993;4:136-143.


156. Sarsfeld J, Gowland G. Reduced mite allergen levels in houses of allergic asthmatic children. Allergy 1994;24:1078-1083.


# Tables

Table 1  Structural and Functional Properties of some common Indoor Allergens

<table>
<thead>
<tr>
<th>Source</th>
<th>Allergen</th>
<th>Molecular wgt</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>House Dust Mite</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dermatophagoides spp</td>
<td>Der p 1</td>
<td>25kd</td>
<td>Cysteine Protease</td>
</tr>
<tr>
<td></td>
<td>Der p 2</td>
<td>14kd</td>
<td>Epididymal protein</td>
</tr>
<tr>
<td></td>
<td>Der p 3</td>
<td>~30kd</td>
<td>Serine protease</td>
</tr>
<tr>
<td></td>
<td>Der p 4</td>
<td>~60kd</td>
<td>Amylase</td>
</tr>
<tr>
<td></td>
<td>Der p 5</td>
<td>14kd</td>
<td>Unknown</td>
</tr>
<tr>
<td></td>
<td>Der p 6</td>
<td>25kd</td>
<td>Chymotrypsin</td>
</tr>
<tr>
<td></td>
<td>Der p 7</td>
<td>22-28kd</td>
<td>Unknown</td>
</tr>
<tr>
<td></td>
<td>Der p 8</td>
<td>26kd</td>
<td>Glutathione-S-Transferase</td>
</tr>
<tr>
<td></td>
<td>Der p 9</td>
<td>24kd</td>
<td>Collagenolytic serine protease</td>
</tr>
<tr>
<td></td>
<td>Der p 10</td>
<td>36kd</td>
<td>Tropomyosin</td>
</tr>
<tr>
<td>Euroglyphus maynei</td>
<td>Eur m 1</td>
<td>25kd</td>
<td>Cysteine protease</td>
</tr>
<tr>
<td>Blomia tropicalis</td>
<td>Blo t 5</td>
<td>14kd</td>
<td>Unknown</td>
</tr>
<tr>
<td>Mammals</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cat - Felis domesticus</td>
<td>Fel d 1</td>
<td>36kd</td>
<td>Uteroglobulin</td>
</tr>
<tr>
<td>Dog - Canis familiaris</td>
<td>Can f 1</td>
<td>25kd</td>
<td>Calycin</td>
</tr>
<tr>
<td></td>
<td>Can f 2</td>
<td>27kd</td>
<td>Calycin</td>
</tr>
</tbody>
</table>

Table 2  Levels of Der p 1 in carpet dust in different countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Carpet Level of Der p 1 (mg/g dust) (Ref. No.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Northern Sweden</td>
<td>0.03 (33)</td>
</tr>
<tr>
<td>Central Sweden</td>
<td>0.08 (33)</td>
</tr>
<tr>
<td>Canada (Winnipeg)</td>
<td>0.13 (34)</td>
</tr>
<tr>
<td>Southern Sweden</td>
<td>0.25 (33)</td>
</tr>
<tr>
<td>Germany (Berlin)</td>
<td>0.41 (169)</td>
</tr>
<tr>
<td>Canada (Vancouver)</td>
<td>0.49 (34)</td>
</tr>
<tr>
<td>New Mexico (Los Alamos)</td>
<td>0.50 (182)</td>
</tr>
<tr>
<td>UK (Manchester)</td>
<td>1.80 (148)</td>
</tr>
<tr>
<td>The Netherlands (Amsterdam)</td>
<td>2.00 (32)</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>2.50 (47)</td>
</tr>
<tr>
<td>North America (Baltimore)</td>
<td>2.70 (173)</td>
</tr>
<tr>
<td>New Zealand (Wellington)</td>
<td>4.50 (141)</td>
</tr>
<tr>
<td>North America (Charlottesville)</td>
<td>5.90 (182)</td>
</tr>
<tr>
<td>Australia (Melbourne)</td>
<td>17.2 (37)</td>
</tr>
<tr>
<td>South Africa (Cape Peninsula)</td>
<td>22.8 (133)</td>
</tr>
<tr>
<td>Technique</td>
<td>Source Material Treated</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Benzyl benzoate</td>
<td>Carpet</td>
</tr>
<tr>
<td>Metsan and Acarosan</td>
<td>Carpet</td>
</tr>
<tr>
<td>Tannic acid</td>
<td>Carpet</td>
</tr>
<tr>
<td>Benzyl benzoate</td>
<td>Carpet</td>
</tr>
<tr>
<td>Commercial cleaners</td>
<td>Carpet</td>
</tr>
<tr>
<td>Steam cleaning</td>
<td>Carpet</td>
</tr>
<tr>
<td>Steam cleaning</td>
<td>Carpet pieces</td>
</tr>
<tr>
<td>Vacuuming</td>
<td>Carpet pieces</td>
</tr>
<tr>
<td>Wet cleaning –cold</td>
<td>Carpet pieces</td>
</tr>
<tr>
<td>Shampoo –cold</td>
<td>Carpet pieces</td>
</tr>
<tr>
<td>Autoclaving</td>
<td>Carpet pieces</td>
</tr>
<tr>
<td>Low temp wash with detergent</td>
<td>Carpet pieces</td>
</tr>
<tr>
<td>As above with benzyl benzoate</td>
<td>Carpet pieces</td>
</tr>
<tr>
<td>Steam cleaning</td>
<td>Carpet + furnishings</td>
</tr>
<tr>
<td>Vacuuming</td>
<td>Carpet + furnishings</td>
</tr>
<tr>
<td>Daily vacuuming</td>
<td>Carpet</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3 Intervention strategies in carpets - non clinical
<table>
<thead>
<tr>
<th>Technique</th>
<th>Source Material Treated</th>
<th>Allergen Measured</th>
<th>Allergen Reduction</th>
<th>% or fold reduction</th>
<th>City</th>
<th>Year</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzyl benzoate</td>
<td>Bedroom carpet</td>
<td>Der p 1</td>
<td>No</td>
<td>-</td>
<td>Bristol, UK</td>
<td>1995</td>
<td>142</td>
</tr>
<tr>
<td>Anti-mite shampoo</td>
<td>Bedroom carpet</td>
<td>Der p 1</td>
<td>No</td>
<td>-</td>
<td>Melbourne, Australia</td>
<td>1998</td>
<td>143</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>Living room floor dust</td>
<td>Der p 1</td>
<td>No</td>
<td>-</td>
<td>Stockholm</td>
<td>1994</td>
<td>144</td>
</tr>
<tr>
<td>Dehumidification</td>
<td>Bedroom carpet</td>
<td>Mite nos. Der p 1</td>
<td>No Not by intervention</td>
<td>-</td>
<td>Manchester, UK</td>
<td>1995</td>
<td>145</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>Living room carpet</td>
<td>Mite nos. Der p 1</td>
<td>No Not by intervention</td>
<td>-</td>
<td>Manchester, UK</td>
<td>1996</td>
<td>146</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>Bedroom carpet</td>
<td>Mite nos. Der p 1</td>
<td>No</td>
<td>-</td>
<td>Wellington NZ Zealand</td>
<td>1998</td>
<td>147</td>
</tr>
<tr>
<td>Mechanical ventilation and dehumidification</td>
<td>Bedroom carpet</td>
<td>Der p 1</td>
<td>No</td>
<td>-</td>
<td>Manchester, UK</td>
<td>1999</td>
<td>148</td>
</tr>
</tbody>
</table>

Table 3 (continued) Intervention strategies in carpets - non-clinical
<table>
<thead>
<tr>
<th>Age Group</th>
<th>City</th>
<th>Intervention(s)</th>
<th>N Intervention/ control</th>
<th>Length Of Follow-up</th>
<th>Reduction in House dust mite/ allergen</th>
<th>Clinical benefit</th>
<th>Year</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult</td>
<td>Cardiff, UK</td>
<td>Washing, vacuuming, encasing mattress</td>
<td>32 cross-over</td>
<td>6 weeks</td>
<td>Not measured</td>
<td>None</td>
<td>1976</td>
<td>164</td>
</tr>
<tr>
<td>Children</td>
<td>Cardiff, UK</td>
<td>Washing and vacuuming</td>
<td>26/27</td>
<td>8 weeks</td>
<td>No</td>
<td>None</td>
<td>1980</td>
<td>165</td>
</tr>
<tr>
<td>Adult</td>
<td>Aarhus, DK</td>
<td>New bedding, vacuuming, washing, reduced indoor humidity, carpets removed</td>
<td>23/23</td>
<td>6 months</td>
<td>Floor, but not mattress</td>
<td>Improved symptom scores</td>
<td>1983</td>
<td>166</td>
</tr>
<tr>
<td>Children</td>
<td>Vancouver, Canada</td>
<td>Encasing, washing, dusting, removal of soft furnishings and carpets</td>
<td>10/10</td>
<td>4 weeks</td>
<td>Not measured</td>
<td>Improved symptom scores, medication usage, lung function, BHR</td>
<td>1983</td>
<td>167</td>
</tr>
<tr>
<td>Adults</td>
<td>Liverpool, UK</td>
<td>Encasing, synthetic and cotton bedding, washing, removal of carpets, reduced humidity</td>
<td>15/20</td>
<td>12 months</td>
<td>Yes</td>
<td>Symptom scores, lung function, medication usage, IgE, BHR</td>
<td>1986</td>
<td>155</td>
</tr>
<tr>
<td>Children</td>
<td>Harrogate, UK</td>
<td>Encasing, vacuuming</td>
<td>13/ 12</td>
<td>6 weeks</td>
<td>Yes</td>
<td>None (except IgE)</td>
<td>1987</td>
<td>167</td>
</tr>
<tr>
<td>Adults</td>
<td>Glasgow, UK</td>
<td>Liquid nitrogen to mattresses and carpets</td>
<td>9/ 9</td>
<td>8 weeks</td>
<td>Yes</td>
<td>Wheezing, BHR</td>
<td>1988</td>
<td>154</td>
</tr>
<tr>
<td>Children</td>
<td>London, UK</td>
<td>Natamycin on mattresses</td>
<td>23/23</td>
<td>6 months</td>
<td>No</td>
<td>None</td>
<td>1990</td>
<td>168</td>
</tr>
<tr>
<td>Age Group</td>
<td>City</td>
<td>Intervention(s)</td>
<td>N Intervention/ control</td>
<td>Length Of Follow-up</td>
<td>Reduction in House dust mite/ allergen</td>
<td>Clinical benefit</td>
<td>Year</td>
<td>Reference</td>
</tr>
<tr>
<td>-----------</td>
<td>--------------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>-------------------------</td>
<td>---------------------</td>
<td>----------------------------------------</td>
<td>------------------</td>
<td>------</td>
<td>-----------</td>
</tr>
<tr>
<td>Children</td>
<td>Berlin, Germany</td>
<td>1) Benzyl benzoate to mattress and carpets 2) Encasing, tannic acid to carpets</td>
<td>8/8</td>
<td>12 months</td>
<td>1) No 2) Yes</td>
<td>1) None 2) BHR</td>
<td>1992</td>
<td>169</td>
</tr>
<tr>
<td>Adults</td>
<td>Washington DC, USA</td>
<td>Encasing, removal of carpets and soft furnishings, hot washing, reduced indoor humidity</td>
<td>26/26</td>
<td>12 weeks</td>
<td>No (reduction in both active and control)</td>
<td>Symptom scores</td>
<td>1992</td>
<td>170</td>
</tr>
<tr>
<td>Adults</td>
<td>Strasbourg, France</td>
<td>Benzyl benzoate to mattress, bedding and furniture</td>
<td>11/12</td>
<td>12 months</td>
<td>No</td>
<td>None</td>
<td>1993</td>
<td>171</td>
</tr>
<tr>
<td>Children</td>
<td>London, UK</td>
<td>Ionisers</td>
<td>20 cross-over</td>
<td>6 weeks</td>
<td>Yes</td>
<td>None</td>
<td>1994</td>
<td>163</td>
</tr>
<tr>
<td>Adults</td>
<td>Sydney, Australia</td>
<td>Benzyl benzoate/ tannic acid to bedding furniture, carpet, encasing</td>
<td>17/18</td>
<td>6 months</td>
<td>Yes (transient)</td>
<td>None</td>
<td>1994</td>
<td>172</td>
</tr>
<tr>
<td>Adults</td>
<td>Baltimore, USA</td>
<td>Benzyl benzoate to carpets</td>
<td>6/6</td>
<td>12 months</td>
<td>No</td>
<td>None</td>
<td>1994</td>
<td>173</td>
</tr>
<tr>
<td>Children</td>
<td>Italy</td>
<td>Benzyl benzoate to mattress</td>
<td>14/10</td>
<td>Short term</td>
<td>No</td>
<td>None</td>
<td>1994</td>
<td>174</td>
</tr>
<tr>
<td>Children</td>
<td>Bristol</td>
<td>Benzyl benzoate to bedding, furniture and carpet, encasing, hot washing</td>
<td>23/26</td>
<td>6 months</td>
<td>Yes</td>
<td>Symptom scores, medication usage</td>
<td>1996</td>
<td>175</td>
</tr>
<tr>
<td>Children</td>
<td>Tel Aviv, Israel</td>
<td>1) Acaricide+ avoidance 2) Placebo + avoidance 3) Avoidance alone</td>
<td>1) 13 2) 17 3) 16</td>
<td>6 months</td>
<td>Yes, in all groups</td>
<td>Symptom scores</td>
<td>1997</td>
<td>176</td>
</tr>
<tr>
<td>Age Group</td>
<td>City</td>
<td>Intervention(s)</td>
<td>N</td>
<td>Intervention/control</td>
<td>Length Of Follow-up</td>
<td>Reduction in House dust mite allergen</td>
<td>Clinical benefit</td>
<td>Reference</td>
</tr>
<tr>
<td>-----------</td>
<td>------</td>
<td>-----------------</td>
<td>---</td>
<td>----------------------</td>
<td>---------------------</td>
<td>--------------------------------------</td>
<td>------------------</td>
<td>-----------</td>
</tr>
<tr>
<td>Children</td>
<td>Southampton, UK</td>
<td>Encasing</td>
<td>31</td>
<td>crossover</td>
<td>3 months</td>
<td>Yes</td>
<td>None</td>
<td>159</td>
</tr>
<tr>
<td>Adults</td>
<td>Groningen, Holland</td>
<td>1) Air Filter 2) Encasing 3) Air filter + 4) Encasing</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>Yes (in mattress in 2)</td>
<td>BHR in (3) compared with 1) and 2)</td>
<td>177</td>
</tr>
<tr>
<td>Adults</td>
<td>Strasbourg, France</td>
<td>Azasan to carpets, encasing</td>
<td>76/81</td>
<td>20 weeks</td>
<td>Yes</td>
<td>None</td>
<td>178</td>
<td></td>
</tr>
</tbody>
</table>

Table 4 (continued) Allergen Avoidance Trials - clinical
Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC

The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee

Summary

Background Systematic international comparisons of the prevalences of asthma and other allergic disorders in children are needed for better understanding of their global epidemiology, to generate new hypotheses, and to assess existing hypotheses of possible causes. We investigated worldwide prevalence of asthma, allergic rhinoconjunctivitis, and atopic.

Methods We studied 463,801 children aged 13–14 years in 155 collaborating centres in 56 countries. Children self-reported, through one-page questionnaires, symptoms of these three atopic disorders. In 99 centres in 42 countries, a video asthma questionnaire was also used for 304,796 children.

Findings We found differences of between 20-fold and 60-fold between centres in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema, with four-fold to 12-fold variations between the 10th and 90th percentiles for the different disorders. For asthma symptoms, the highest 12-month prevalences were from centres in the UK, Australia, New Zealand, and Republic of Ireland, followed by most centres in North, Central, and South America; the lowest prevalences were from centres in several Eastern European countries, Indonesia, Greece, China, Taiwan, Uzbekistan, India, and Ethiopia. For allergic rhinoconjunctivitis, the centres with the highest prevalences were scattered across the world. The centres with the lowest prevalences were similar to those for asthma symptoms. For atopic eczema, the highest prevalences came from scattered centres, including some from Scandinavia and central Europe that were not among centres with the highest asthma prevalences; the lowest prevalence rates of atopic eczema were similar in centres, as for asthma symptoms.

Interpretation The variation in the prevalences of asthma, allergic rhinoconjunctivitis, and atopic eczema symptoms is striking between different centres throughout the world. These findings will form the basis of further studies to investigate factors that potentially lead to these international patterns.

Lancet 1998; 351: 1225–32

See Commentary page 1220

Introduction

There have been few studies of the population prevalence of allergic rhinitis and atopic eczema, and although hundreds of asthma-prevalence studies have been done in various parts of the world, they have seldom used standard approaches. An exception is the European Community Respiratory Health Survey (ECRHS), which involved surveys of asthma and allergic rhinitis prevalence in adults aged 20–44 years in 48 centres in 22 countries, although only nine centres in six countries were outside western Europe. The ECRHS suggested that there were regional risk factors for asthma and allergic rhinitis in western Europe, but it did not comprehensively assess the global patterns. For children, the largest standard studies of the prevalences of asthma, allergic rhinitis, or atopic eczema have involved at most four countries.

Thus, in some respects, the epidemiology of asthma and other allergic disorders is currently similar to that of cancer epidemiology in the 1950s and 1960s, when the international patterns of the incidence of cancer were studied. These studies revealed striking international differences that gave rise to many new hypotheses, tested in further epidemiological studies that identified previously unknown risk factors for cancer. These risk factors may not have been in the hypotheses investigated if the initial international comparisons had been confined to few western countries. More specifically, Roset has noted that whole populations may be exposed to risk factors for disease (eg, high exposure to house-dust mite allergens) and the patterns may be apparent only when comparisons are made between, rather than within, populations.

Therefore, we carried out systematic, standardised, international comparisons of the prevalence of asthma and allergies to generate new hypotheses and to investigate existing hypotheses in the International Study of Asthma and Allergies in Childhood (ISAAC). The detailed findings for the prevalence and severity of the symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema in children aged 6–7 years and 13–14 years will be reported elsewhere. Here, we give an overview of the findings for children aged 13–14 years (the age-group that was studied by all participating centres), assess the relationship between the findings for the three disorders, and discuss the potential for future ecological and case-control studies.

Methods

Phase one of the ISAAC programme used a simple standard approach at minimum cost in as wide a range of centres and countries as possible, based on school populations to ensure...
Allergic Diseases and the Indoor Environment

We decided that phase-one studies would involve no invasive or expensive tests. We recruited collaborating centers through professional networks. Each center agreed to adhere to the study protocol and to complete a registration document and obtain their own funding. Regional coordinators were responsible for the participation of centers within their regions.

The compulsory core sample of the study for all centers was children aged 13–14 years who completed single one-page written questionnaires about symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema. We report the answers to selected questions or combinations of selected questions: for asthma—"Have you had wheezing or whistling in the chest in the last 12 months?"; and for allergic rhinoconjunctivitis—"Have you had sneezing or a blocked nose when you DID NOT have a cold or the flu?" If yes: in the past 12 months, has this nose problem been accompanied by itchy-water eyes?"; for atopic eczema—"Have you ever had an itchy rash which was coming and going for at least 6 months?" If yes: Have you had this itchy rash at any time in the last 12 months? If yes: Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears, or eyes?"

We also used a video asthma questionnaire, that showed clinical signs and symptoms of asthma followed by questions, which was strongly recommended for use in this age-group. The European and international versions of the video showed five sequences of clinical asthma in different situations, of which two sequences were common to both versions. After each sequence, the children were asked to specify whether their breathing had been like the person in the video; the terms asthma or wheezing were not mentioned at any stage. We report answers to the first video sequence, which showed a person wheezing at rest. This video sequence was at least as sensitive and specific for predicting bronchial hyperresponsiveness as the written questionnaire, and more repeatable. The video questionnaire was shown after the compulsory written questionnaire, to the same children, on the same occasion to keep any potential bias to a minimum, although the order has been shown not to affect the outcome.

We calculated that a sample size of 3000 per age-group was needed to provide sufficient precision for estimates of symptom severity, but smaller sample sizes—minimum 1000—were sufficient to calculate rates. We determined the sampling frame mainly by geographical areas and most centers (65%) chose to sample within their study area by random selection. Standard guidelines for translation of the questionnaires from English were provided in an attempt to decrease difficulties associated with the use of the questionnaires in many different languages. These guidelines included the use of translators familiar with asthma terminology, consultation with the local community, back-translation into English by an independent translator, and pilot testing of the translation.

We present data received and verified by the ISAAC International Data Centre by June 30, 1996, which was checked by Nov 24, 1997 (table I). For some collaborating centers, the data-collection and checking processes had not been completed by these deadlines; their findings will be included in future analyses.

For each of asthma, allergic rhinoconjunctivitis, and atopic eczema symptoms, we calculated 12-month prevalences by dividing the number of positive responses to each question by the number of completed questionnaires. Data are presented for each center by country, with the results ordered by weights mean rate of the country, from highest to lowest. We calculated variations in data by finding the difference between the highest and lowest center rates, and between the highest and lowest rates from the 10th to 90th percentiles. We assessed the association between the rates of the different disorders by calculating Spearman's rank correlation coefficient. We compared the written and video asthma questionnaires by cross-tabulation of the results in tertiles. We calculated the
proportion of children who reported symptoms of asthma, allergic rhinoconjunctivitis, or atopic eczema, or combinations of these symptoms. We also calculated the overall 12-month prevalence rates of symptoms of at least two of the three disorders and categorised them in ranges of 2-9% or less, 3-0-5-9%, 6-0-8-9%, and 9% or more.

**Results**

463801 children aged 13–14 years participated in 155 collaborating centres in 56 countries (table). The video questionnaire was used as well as the written questionnaire in 99 (64%) of these centres in 42 countries, for 304790 children. Response rates were more than 80% in 149 (96%) centres. Written questionnaires were translated into 39 languages, including English (50 centres [32-2%]), Spanish (21 centres [13-5%]), Italian (13 centres [8-4%]), Chinese (nine centres [5-8%]), and Portuguese (nine centres [5-8%]).

**Table 1: Language and video questionnaire used, response rates, and sample sizes by centre**

<table>
<thead>
<tr>
<th>Centre</th>
<th>Collaborator</th>
<th>Video Response rate (%)</th>
<th>Number of children</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Korea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Provincial Korea (Kor)**</td>
<td>SI Lee</td>
<td>98-3</td>
<td>6990</td>
</tr>
<tr>
<td>Social Kor**(1)**</td>
<td>SI Lee</td>
<td>98-5</td>
<td>2993</td>
</tr>
<tr>
<td>Spain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barcelona (Sp)</td>
<td>R M Buquet</td>
<td>91-2</td>
<td>3031</td>
</tr>
<tr>
<td>Bilbao (Sp)</td>
<td>A R Rubio</td>
<td>89-8</td>
<td>3212</td>
</tr>
<tr>
<td>Cadiz (Sp)</td>
<td>AR Aparicio</td>
<td>90-6</td>
<td>3277</td>
</tr>
<tr>
<td>Cartagena (Sp)</td>
<td>L Garcia Marro</td>
<td>91-5</td>
<td>3017</td>
</tr>
<tr>
<td>Castellon (Sp)</td>
<td>A Amado-Pena</td>
<td>93-6</td>
<td>3094</td>
</tr>
<tr>
<td>Pamplona (Sp/Bas)</td>
<td>F Guzman</td>
<td>94-3</td>
<td>3040</td>
</tr>
<tr>
<td>Valencia (Sp)</td>
<td>M L Mest Mest</td>
<td>99-8</td>
<td>3178</td>
</tr>
<tr>
<td>Sweden</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linkoping (Swe)</td>
<td>Nl Kjellman</td>
<td>95-7</td>
<td>3377</td>
</tr>
<tr>
<td>Stockholm (Swe)</td>
<td>T Fosuay</td>
<td>95-2</td>
<td>3075</td>
</tr>
<tr>
<td>Finland</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Helsinki (Fin)</td>
<td>R M Anderson</td>
<td>93-3</td>
<td>11400</td>
</tr>
<tr>
<td>Thailand</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bangkok (Tha)</td>
<td>P Vichayson</td>
<td>74-8</td>
<td>3713</td>
</tr>
<tr>
<td>Chiang Mai (Thai)</td>
<td>M Traivkitawak</td>
<td>94-7</td>
<td>3927</td>
</tr>
<tr>
<td>USA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chicago (Eng)**</td>
<td>V Persson</td>
<td>89-9</td>
<td>1422</td>
</tr>
<tr>
<td>Chicago (Sp)**</td>
<td>V Persson</td>
<td>93-5</td>
<td>3756</td>
</tr>
<tr>
<td>Seattle (Eng)**</td>
<td>G Redding</td>
<td>80-3</td>
<td>2330</td>
</tr>
<tr>
<td>Uzbekistan</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Samarkand (RU)**</td>
<td>T Arnoosa</td>
<td>87-9</td>
<td>1758</td>
</tr>
<tr>
<td>Tashkent (RU)**</td>
<td>T Arnoosa</td>
<td>96-8</td>
<td>2904</td>
</tr>
</tbody>
</table>

**Note to Table 1:** 1) Data recorded to eliminate inconsistent responses. 2) No age or date of birth on questionnaire. 3) No sex information provided.
12-month prevalences of asthma from the written questionnaires for each centre by country are shown in figure 1. The highest prevalence was about 20 times higher than in the centre with the lowest prevalence (range 1.6–36.8%), with an eight-fold variation seen between the 10th and 90th percentiles (3.9–30.6%). 12-month prevalences of asthma symptoms from the first video sequence are shown in figure 2. Worldwide patterns were similar to those from the written questionnaire: results were concordant in 63 (64%) of 99 centres for distribution of centres by tertiles (table 2). The rank correlation coefficient between centre prevalences for written and video questionnaires was 0.76 (p<0.0001). The prevalence of asthma symptoms reported on the video questionnaire was generally lower than that reported on the written questionnaire, probably because the video questionnaire asked for information on more severe asthma symptoms (wheezing at rest) than the written questionnaire (any wheezing).

12-month prevalences of symptoms of allergic rhinoconjunctivitis for each centre by country are shown in figure 3. We found about a 30-fold variation in the rate of allergic-rhinoconjunctivitis symptoms between centres (range 1.4–39.7%), with a four-fold variation seen between the 10th and 90th percentiles (4.9–21.0%). The grouping of centres with a high prevalence of allergic-rhinoconjunctivitis symptoms into specific regions was less well defined than for asthma; by contrast, the centres with the lowest symptom prevalences for allergic rhinoconjunctivitis were similar to those for asthma symptoms (figures 1–3).

12-month prevalences of symptoms of atopic eczema for each centre by country are shown in figure 4. There was more than a 60-fold variation in prevalences of atopic-eczema symptoms between centres (0.3–20.5%), with an eight-fold variation between the 10th and 90th percentiles (2.0–15.6%). The international patterns for the prevalences of atopic-eczema symptoms differed in some ways from those for asthma and allergic rhinoconjunctivitis (figure 5). Nevertheless, significant correlations were seen between the prevalences of the different disorders.

The prevalence of symptoms of at least two of the three disorders varied from 0.3% to 18.5%, with an 11-fold variation between the 10th and 90th percentiles (1.4–15.6%; figure 6). Among symptomatic children, 72–9% had had symptoms of only one of the three disorders in the previous 12 months (figure 6).

**Discussion**

The ISAAC programme has allowed a worldwide assessment of the prevalence of self-reported symptoms of asthma, allergic rhinoconjunctivitis, and atopic...
eczema in children by standard methods. For many
collaborating centres, the measurements were the first in
their country of symptoms of these disorders, and for
many countries, the participation of more than one
centre enabled comparisons within countries. The
worldwide variations in rates, and partly the variations
seen within some countries, suggest that environmental
factors (in their broadest sense) may be critical to the
development of these disorders in childhood.

Despite the use of standard simple questionnaires,
validated study protocols, including those for the use
and translation of questionnaires, and stringent quality-
control measures, difficulties in the comparability of
information will unavoidably influence the results to
some degree. For example, the questionnaires were
translated into 39 languages, some of which had no
colloquial terms for symptoms such as wheezing.
Another difficulty is the sensitivity and specificity of
the listed symptoms to identify children with the specific
disorders. Although the questionnaires had been
validated before the study,11-15 our findings may not be
applicable to countries in which infectious disorders
with similar symptoms may be prevalent.

Our method of population sampling may also have
been a potential source of bias, with school-based
samples not being representative of children aged 13–14
years in some communities. However, the proportion
of children who did not attend school would have been
small in most centres. Response bias could have
occurred if there were great variations in response rates
and if participation was related to symptoms. However,
a similar study in adults14 that had lower response rates
than our study showed little evidence of response bias.
Our response rates were high for most centres, and after
exclusion of the few centres with response rates of less
than 80%, the overall global patterns changed little.
Therefore, response bias is unlikely to have seriously
affected this study.

The international patterns of prevalences of these
disorders should be considered with these potential
biases in mind. For asthma symptoms, the highest
prevalences from the written and video questionnaires
were from the centres in the UK, New Zealand,
Australia, Republic of Ireland, followed by most centres
in North, Central, and South America. The lowest
prevalences were reported from centres in several
Eastern European countries, Indonesia, Greece, China,
Taiwan, Uzbekistan, India and Ethiopia. Although
asthma symptom prevalence rates were generally similar
in centres within the same country, in some countries,
such as India, Ethiopia, Italy, and Spain, large variations
were seen between centres. There were also wide
variations within regions, especially within Europe and
Asia. Therefore, in addition to analyses of the global
ecological patterns, there are opportunities for
investigation of possible causative factors within
countries and regions.

We believed that by showing rather than describing
the signs and symptoms of asthma to children the video
questionnaire would provide more accurate recognition
of clinical asthma, which would be useful to compare
information between populations with different cultures
and languages.12-15 Some differences in the findings for
the written and video questionnaires for some centres in
Several centres with the highest symptom prevalences were not represented among the centres with the highest asthma prevalences; therefore, the major risk factors for these related disorders may differ or may involve different latency periods and time trends.

For atopic eczema, the highest symptom prevalences included centres from many regions of the world, including some from Scandinavia and Africa not represented among the highest asthma rates. The centres with low prevalences of atopic-eczema symptoms were generally the same as those with low prevalences of asthma and allergic-rhinoconjunctivitis symptoms.

The interpretation of these large between-country differences for allergic rhinoconjunctivitis and atopic eczema is likely to be partly influenced by validity of the written questionnaires, despite the translation guidelines, and the avoidance of diagnostic labels such as allergic rhinoconjunctivitis and atopic eczema in the written questionnaires. For example, some of the high or low values for atopic-eczema prevalences could relate to differences in the interpretation of the written questionnaire based on the presence of a flexural skin rash, or differences in the frequency of other skin disorders, such as ectoparasites, which involve the skin flexures in children. Findings from the validation study of the rhinitis questionnaire led to the use of the symptoms of rhinoconjunctivitis rather than rhinitis alone since it was more closely related to positive skin-test reactivity. Further validation exercises and studies that include objective clinical assessment (planned for phase two of ISAAC) will be required to better understand these international differences and the large variations seen within some countries.

When self-reported symptoms of more than one atopic disorder were taken into account, the highest prevalences were observed predominantly in English speaking Western countries, decreasing prevalences were found in northwest to southeast Europe, higher prevalences were seen among many Spanish-speaking and Portuguese-speaking communities in Latin America than in centres in Spain and Portugal, and widely differing prevalences were found between centres with populations of similar ethnic origins within countries such as China (including Taiwan and Hong Kong), India, Italy, and Ethiopia. These findings were dominated to some extent by the asthma and allergic-rhinoconjunctivitis results, because of their relatively higher symptom prevalences.

We looked at the relation between the different disorders in individual children: most symptomatic children had had symptoms of only one disorder in the previous year, which indicates that many different risk factors may be required for the clinical expression of these related disorders. Studies from China and Africa have shown that striking differences in asthma prevalences may occur in populations, despite similar prevalences of atopic sensitisation. These findings support the view that in addition to atopic sensitisation, other risk factors may be important in the development of asthma, allergic rhinoconjunctivitis, and atopic eczema in susceptible populations.

Despite the difficulties in interpretation of our findings, there is substantial potential for ecological analyses. For example, the global pattern of asthma prevalences was consistent with evidence that air pollution is not a major risk factor for the development...
of asthma in populations, although it may exacerbate asthma in individuals. Regions such as China and Eastern Europe, with some of the highest degrees of air pollutants such as particulate matter and sulphur dioxide, generally had low rates of asthma prevalence, whereas those such as western Europe and the USA, with high degrees of air pollutants such as ozone, had intermediate prevalences of asthma, and some centres with the lowest degrees of air pollution, such as those in New Zealand, had high prevalences of asthma. Ecological analyses will also be possible of the international prevalences of these disorders and other putative risk or protective factors, or their surrogate measures. These analyses will need to be based on standard international public-health, socioeconomic, demographic, and environmental data.

Comprehensive comparisons between ISAAC phase-one findings and those from the ECRHS are difficult since the ECRHS primarily involved centres in western Europe. Nevertheless, the ECRHS also showed the highest asthma-symptom prevalences in the UK, Australia, New Zealand, the Republic of Ireland, and the USA, with lower prevalences in non-English-speaking countries in Europe, North Africa, and India. In addition, the centres with the highest prevalences of atopy (defined as the presence of at least one positive allergen-specific IgE) were mainly in English-speaking populations, which is also consistent with our findings.

Phase one of the ISAAC study has shown a wide variation in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema throughout the world, with differing international patterns for the different disorders. Although we acknowledge the limitations of international prevalence comparisons of this kind, we have provided a framework for further actiological research into the genetic, lifestyle, environmental, and medical-care factors affecting these disorders.

Writing group—R Beasley, Wellington School of Medicine, Wellington, New Zealand; U Knell, Universitätskinderklinik, Münster, Germany; E von Mutius, Kinderspital der Universität, München, Germany; N Pearce, Wellington School of Medicine, Wellington, New Zealand.

ISAAC Steering Committee—N Ait-Khaled (regional coordinator), ICAST, Paris, France; G Aebischer (regional coordinator), Pragmat Kliniken Basel, Basel, Switzerland; H R Anderson, St George's Hospital Medical School, London, UK; M Aicher (regional coordinator), University Children's Hospital, Münster, Germany; L Bjermer (regional coordinator and ISAAC executive), University Hospital, Linköping, Sweden; M L Bousvaros, University of Washington, Seattle, WA, USA; D C READ, University of Auckland, Auckland, New Zealand; J Connor, Wellington School of Medicine, Wellington, New Zealand; P Ellwood, University of Oxford, Oxford, UK; A Haninger, University of Auckland, Auckland, New Zealand; C K W Lai (regional coordinator), The Chinese University of Hong Kong, Hong Kong; J Malo (regional coordinator), University of Santiago, Santiago, Chile; F D Martinez (regional coordinator), University of Arizona, Tucson, USA; E A Mitchell (ISAAC International Data Centre), University of Auckland, Auckland, New Zealand; S Monteforti (regional coordinator), University of Malta Medical School, Malta; G Mangia, Malta; N Pearce, Wellington School of Medicine, Wellington, New Zealand; C P Robertson, Royal Children's Hospital, Melbourne, Australia.
Acknowledgments

We thank the collaborators in the participating centres and all parents, children, teachers, and other school staff who participated in the surveys; the field workers and funding agencies who supported data collection; and national, regional, and international meetings, including the meetings of the ISAAC Steering Committee, the funders who supported the ISAAC International Data Centre including: the Health Research Council of New Zealand, the Asthma and Respiratory Foundation of New Zealand, Glaxo Wellcome International, the Child Health Foundation of New Zealand, the Hawke’s Bay Medical Research Foundation, the Waikato Medical Research Foundation, Glaxo Wellcome New Zealand Ltd, and Astra New Zealand. The regional coordinating centres were supported by Glaxo Wellcome International Medical Affairs.

References