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## Allergen avoidance

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## Allergen exposure and allergic diseases: allergens and relationship to allergic diseases

Exposure to allergens plays an important role in allergic diseases. It is essential for the induction of sensitisation (production of allergen-specific immunoglobulin E) and in communities with 'affluent' lifestyles that the prevalence of sensitisation to mites has been directly related to domestic mite-allergen concentrations.<sup>1</sup> However, the relationship of exposure to asthma occurrence and symptoms is more complex. Many factors affect this role, including genetic factors, immune/pathology patterns established in infancy, the nature and continuity of the allergen exposure, asthma phenotypes, other non-allergen factors affecting the disease (e.g. viral infections), concurrent pharmacotherapy, and time.<sup>2</sup> While events involving major increases or decreases in allergen exposure such as moving location may have parallel effects on asthma indices, the clinical effects of smaller changes in allergen exposure such as seasonal fluctuations<sup>3</sup> or domestic interventions are often more difficult to distinguish.

While most allergen avoidance studies have focused on asthma, there is accumulating support that reducing exposure should also be applied to reducing the incidence of sensitisation (primary intervention)<sup>4</sup> and in reducing the severity of atopic eczema.<sup>5</sup> The role of allergen avoidance on managing perennial rhinitis is also underexplored.

## Important allergens and their domestic ecology

Internationally, for asthma, the most important allergens are those from house-dust mites.<sup>6</sup> In temperate regions, these are mites of the genus *Dermatophagoides*, and in tropical regions *Blomia tropicalis*. Their occurrence and distribution is largely driven by microclimate factors, which favour consistent warmth and humidity.<sup>7</sup> Thus, domestic mite populations in coastal regions are greater than those in drier inland regions, and those in damper houses are greater than those in drier houses. Allergen levels > 10 µg allergen/g dust would be regarded as 'high' and those < 1 µg/g as 'low'.<sup>6</sup> The mites populate reservoirs of shed human skin, particularly in beds, clothing, soft furnishings, toys and carpets. The allergens are associated with accumulated mite faeces and other dust particles, which become ubiquitously distributed throughout houses.<sup>8</sup>

Sources of other domestic allergens include pets, particularly cats and dogs,<sup>9,10</sup> and, in some urban poorer groups, cockroaches.<sup>11</sup> When houses have a resident cat, allergen levels can exceed 10 µg allergen/g dust;<sup>12,13</sup> in cat-free residences, allergens are usually present by ~300-fold less. 'Outdoor' allergens, particularly in dry regions, the spores of *Alternaria alternata* fungi and pollen grains, accumulate indoors and may be regarded as 'domestic' allergens.<sup>14</sup> Many other domestic allergens also occur less frequently - sourced from plants, insects, rodents, foodstuffs, domestic products and furnishings. The original source of allergens may not always occur in the home - the presence of cat allergen in houses without a cat is the classic example;<sup>15</sup> other allergens may also be introduced from occupational sources.

In addition, houses may contain additional materials that modulate the effects of allergens; these include biological materials such as endotoxin,<sup>16</sup> chemicals in building and domestic products, and combustion products such as tobacco or wood-smoke.

## Practising allergen avoidance

Numerous reviews and all comprehensive guidelines for asthma management advocate the avoidance of allergen exposure and of other airborne trigger factors.<sup>17</sup> Such minimising of exposure is the logical extension of a causal role for allergen. It provides parents of at-risk infants and also people with asthma with an active role in long-term prevention and management of disease, and it is consistent with their anecdotal experiences and with cultural views that diseases can be controlled with greater attention to domestic hygiene.

However, the evidence base advocating avoidance of allergens in on-going symptoms is less conclusive. A recent meta-analysis of trials found no conclusive support for mite-allergen avoidance<sup>18</sup>

and new data for cat allergen suggested tolerance may occur at high exposure levels.<sup>19</sup> Exploring and developing a more rigorous basis for allergen avoidance requires: (1) measurement of the changes of the actual allergen exposure that are occurring before and after exposure, (2) practical methods for obtaining large reductions in total domestic exposure, and (3) a clearer understanding of the anticipated clinical mechanisms and responses of different subjects to increases and decreases in exposure.

## Measuring allergen exposure

Despite 20 years of measuring allergen concentrations in different domestic sites (beds, floors, etc.), we know very little about how each contribute to our aeroallergen exposure. We are now starting to learn that personal aeroallergen exposure varies with the individual and at different times of the day.<sup>20</sup> Increases in exposure appear to be associated with increases in domestic activity, and the most important allergen sources are bedding and clothing. However, at present, we have no consistent model of the importance of carpet or other sources in determining aeroallergen exposure. This is sobering in light of the frequency of advice to remove carpets.<sup>21</sup> Logic and anecdote tell us they are important; the evidence for this has not been established.

Very few intervention studies have attempted to measure changes in aeroallergen exposure (although it might seem intuitively obvious to do so). Instead, exposure (if measured at all) has been measured using changes in concentrations of allergens in dust reservoirs (i.e.  $\mu\text{g}$  allergen/g dust) as a proxy, which has consistently failed to correlate with airborne exposure.<sup>22-25</sup>

Allergen exposure can be measured by collecting air samples with filters and mechanical air pumps or with personal nasal air samplers followed by measurement of allergen with specific immunoassays of sufficient sensitivity - either amplified enzyme-linked immunosorbent assays or halogen assays.<sup>26</sup>

Where systems to measure aeroallergens have been used, they have shown that while conventional interventions may sometimes produce large changes in reservoir measurements at individual sites, interventions produce much less effect on total aeroallergen exposure<sup>27</sup> - probably due to contributions from other adjacent untreated sites. This may partly explain why some avoidance studies did not achieve clinical improvements.

It is important that, if a strategy to understand and improve allergen avoidance is to be developed, it will need to be based on meaningful measurements of changes in chronic personal aeroallergen exposure.

## Physical methods of reducing exposure

There are numerous approaches to reducing exposure. At one end of the spectrum are methods addressing individual sites in houses with specific hygiene measures, while at the other end are techniques aimed at the whole dwelling. The former follow a structured approach of addressing allergen sources, reservoirs and, finally, aeroallergen, while the latter approach includes passive domestic design methods such as reducing humidity to levels at which mites perish.<sup>28</sup> Overlaps and combinations occur.

### Control of sources

Control of mite populations is focused on installing barriers (occlusive covers in beds),<sup>29</sup> removing niches (replacing carpets, furnishings), modifying microclimate (dehumidification),<sup>30</sup> extreme physical conditions (heat: steam,<sup>31</sup> sunlight;<sup>32</sup> or cold: freezing,<sup>21</sup> liquid nitrogen<sup>33</sup>) and acaricidal chemicals.<sup>34,35</sup> In general, overall effects are not great. For removing pet sources the challenges are social (i.e. pet as family member), and for cockroaches the challenges may be social and economic as effective insecticides are available.

The general shortcomings with all approaches that focus on the control of sources are that accumulated allergen may remain, the effects of treatment may be temporary, and repetition is required. Such approaches are partially effective at best.

### Control of reservoirs

#### *Bedding.*

Encase mattresses and pillows in allergen- and mite-occlusive fabrics, and either wash all bedding (blankets, duvets) approximately each 6 weeks or use occlusive covers on upper bedding as well.<sup>36</sup> Issues include: is encasing a mattress three sides sufficient?; optimising encasing materials; use of 'built-in' mattress treatments (acaricides); and is feather bedding less allergy 'risk' than synthetic bedding?<sup>37-39</sup>

#### *Clothing.*

The importance of clothing may have been underestimated previously. Clothes can have high allergen amounts, especially after storage, and personal exposure varies with type of materials,<sup>40</sup> which is probably a proxy for frequency of laundry. Clothing may accumulate ambient aeroallergen quickly and be an important non-domestic source and carrier of allergens to homes.

#### *Furnishing.*

Similar to beds in that it can contain high amounts/concentrations of usual domestic allergens that are easily disturbed and are in close proximity to the subject. Furnishing is more difficult to control;

options include replacement and cleaning (vacuum and steam largely untested).<sup>41</sup> Studies using acaricides are not encouraging, opportunities for use of occlusive surface fabrics and in non-surface layers.

#### *Carpets.*

Carpets can probably constitute the largest reservoir of total allergen in house if there is a large amount of carpet in the house. The amount and concentration of allergen in carpets is much greater than that in than hard floors. The role in contributing to aeroallergen is insufficiently researched – partly determined by the structure of carpet and the type of fibre.<sup>42</sup> Some control over allergen can be exercised by superheated steam treatment,<sup>31</sup> much greater than long-term use of acaricides<sup>43</sup> that itself is greater than routine dry vacuuming or treatment with allergen denaturants.<sup>44</sup> Generally suggested is to avoid/remove carpets if possible.

#### *Other sites.*

If allergen occurs in the aforementioned major sites, more allergen will also be detected ubiquitously distributed throughout the house – on walls and other surfaces if sensitive methods used. While the size of this pool is smaller, it may have a significant contribution to the circulating aeroallergen pool and thus requires removal for effective allergen avoidance. Removal by vacuuming, washing and use of dry electrostatic cleaning cloths are advocated (all these are applicable to hard floors too).

### Control of aeroallergen

Direct control of aeroallergen needs much more study. Initial observations are that attempts to remove aeroallergen by operation of an isolated air filter unit or ionisers has little clinical effect (despite logic of approach).<sup>45</sup> There is lack of data on the effect of these approaches on total personal aeroallergen exposure. The lack of supportive clinical data has not stopped widespread commercial promotion.

### Holistic approaches

It has been possible in North American and European studies to adopt design or dehumidification approaches to enable houses to be dehumidified sufficiently that mite populations do not survive and allergen gradually declines.<sup>28,46</sup> However, several other attempts to do this have not been successful.

Within communities, allergen concentrations vary massively between houses,<sup>47</sup> suggesting local design issues or lifestyles could allow houses to be built that provide low exposure. So far, regression analysis of allergen concentration as a function of housing factors has not provided a strong tool to explore this.

Numerous approaches to reducing allergens are feasible – they need to be used in combinations dictated by the occurrence of allergens, the economics and the opportunities for intervention. The aim should be to massively reduce the total personal exposure to aeroallergen.

### Effect on symptoms

Concepts of dose ‘thresholds’ and ‘safe levels’ for asthma are currently not supported and we have little information about how real domestic exposure to allergens actually creates acute and chronic clinical outcomes. It is probable that there are a number of different mechanisms. Without this information, it is difficult to rationally develop strategies for avoidance.

For example, the size of the particles carrying allergens may be very important. It is known from examples of ‘thunderstorm asthma’, associated with exposure to starch granules from fragmented pollen, that it can have both profound acute and chronic effects,<sup>48</sup> whereas exposure to pollen grains itself has a negligible effect. On this basis, do we need to pay more attention to that subfraction of exposure associated with small particles and not to larger particles? If this was the case, aspects such as air exchange rates in buildings, flushing out continuously suspended small particles, may be important.

Conversely, it has been postulated that occasional low-level exposure to domestic allergen carried on large particles might have a cumulative effect, principally on bronchial hyperreactivity and not acute symptoms. This would suggest avoiding specific episodes of high exposure, such as generated during cleaning, was important.

Finally, we currently cannot define the asthma phenotype that benefits most from reducing exposure. In a classic study of long-term avoidance in a clean hospital setting, different rates of improvement were observed in the majority of, but not in all, subjects.<sup>49</sup> The basis of this was not known.

Understanding the occurrence of normal domestic exposure and relating this to the clinical effects of such exposure are critical in determining how to design effective strategies for allergen avoidance.

### Conclusion

Exposure to common domestic allergens is casually linked to sensitisation and at times to the severity of asthma symptoms. Minimising exposure is an important component of disease management. However, the strategies and benefits of avoidance are poorly defined as meaningful measurements of avoidance have not been sufficiently employed, and to many it is unclear whether some methods actually reduce exposure and by how much. Recent advances in allergen

sampling and measurement will allow progress in development of methods to minimise personal exposure to aeroallergen.

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## Role of house-dust endotoxin exposure in aetiology of allergy and asthma

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Endotoxin and its purified derivative lipopolysaccharide (LPS) are Gram-negative bacterial potent pro-inflammatory constituents continuously shed into the environment.<sup>1</sup> A number of different Gram-negative bacteria inhabits the normal body surfaces including the skin, oral cavity, respiratory tract, gastrointestinal tract, vagina and urinary tract. Humans can be exposed to endotoxin via several ways. In addition to the septic shock frequently



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