

HOUSE-DUST MITES, THE ATOPY PATCH TEST AND CARING FOR THE PATIENT WITH ATOPIC DERMATITIS

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ABSTRACT

Atopic dermatitis (AD) is a common and much studied affliction, yet the role of aeroallergens in either its causation or the propagation of symptoms remains unclear. This article looks at the evidence surrounding the possible role of house-dust mite (HDM) as a cause of AD. The role of the atopy patch test in identifying those who are HDM sensitised or those who may benefit from HDM avoidance measures is also examined. Finally, the evidence surrounding HDM avoidance measures is reviewed and the possible role of primary carers and allergy specialists is considered.

As the incidence of allergic diseases, including atopic dermatitis (AD),¹ increases, there is continuing interest about the underlying cause of these conditions. There is little question that the causes of AD are multifactorial and include allergy, genetics, infection, and climatic and emotional influences.² The degree to which each of these components has a role in the causation of AD is controversial. The role of aeroallergen sensitivity, particularly to house-dust mite (HDM), remains a topic for debate.

The atopy patch test (APT) has been used by many as a model to study the role of aeroallergens such as HDM in AD.³ Unlike skin-prick testing (SPT), which is effectively a measure of IgE sensitivity to HDM, the APT elicits a delayed-type response involving allergen-specific CD4+ cells, which clinically resembles eczema in those with AD. There is increasing evidence that this reaction is due to a specific cellular response, probably mediated by IgE.⁴ The patch test reaction to aeroallergens is specific to sensitised AD patients and does not occur in healthy patients,⁵ although its clinical relevance remains unclear. The outcome of APT testing of AD patients shows wide variability from 15% to 100%.⁶ This wide range could be attributed to the variation in patient selection and perhaps, more importantly, the methodology of these studies.⁷ Without consistency of APT allergen, vehicle, test site, reading time and skin condition (i.e. skin stripped or not) it is difficult to compare studies. Fortunately, more recently, there has been greater standardisation of methodology.⁸ However, the relationship between SPT and APT to HDM remains unclear.¹ Although positive APTs are found more commonly in the presence of high IgE levels, they may also be absent despite them, and therefore these tests can be dissociated.⁹

Regardless of the percentage of AD patients who test positive to APT for HDM, the test is only of relevance if it tells us something about the disease or its causation. If HDM sensitisation is a possible cause of AD, then it could

be postulated that in those cases where it was important, certain patterns might be recognisable or the disease may be sensitive to avoidance of the offending HDM allergen. Much of the work around APT has focused on the value of the test in identifying such cases.

Some workers have therefore explored the utility of APT by considering its association with the observed pattern of clinical disease. Darsow *et al.*⁸ found a relationship between APT positivity and distribution of eczema. APT was much more likely to be positive among those whose eczema was predominantly on exposed parts of the skin (69% versus 39% in those with AD not in this pattern). Imayama *et al.*¹⁰ were able to classify AD patients into groups depending on morphology and compare them according to allergometric testing. They found high HDM sensitisation among those with extensive erythematous skin lesions especially involving the face. Unfortunately, the value of these observations has been limited by their lack of reproducibility in later studies.¹¹

Further research has focused on whether APT testing can tell us something about the ongoing role of HDM in clinical disease. Ricci *et al.*¹² showed that the higher the exposure to HDM allergen, the more likely a child with AD would be sensitised to HDM, reflected in positive APT, and thus possibly suggesting causation. However, although there is evidence that HDM avoidance may or may not¹³ influence disease severity, even in the randomised controlled trials of HDM avoidance that did show improvements in disease severity,¹⁴ this improvement was not found to be specific to those with positive allergy tests to HDM. Indeed, Davis *et al.*¹⁵ reported on a cohort of 662 AD patients who had APT to HDM and although confirming high rates of reactivity (55%), these reactions were seldom of any relevance (6.7%). Further to this, Gutgesell *et al.*⁹ found no correlation between SCORAD of 92 AD patients, their der p1 exposure and HDM sensitisation. Rather confusingly, they found that those with the highest HDM exposure seemed to have least APT positivity and therefore concluded that APT positivity should not be used alone as an indication to instigate HDM avoidance measures. Perhaps, rather than relying on positive APT to HDM to recommend HDM avoidance measures, it could be argued that most AD sufferers would benefit from reducing HDM in the environment given the high proportion who will develop HDM-induced respiratory symptoms.¹⁶

The role of HDM as a cause of AD may be reflected in the pattern of disease it causes or in a beneficial response to avoidance, but as outlined above, the role of APT remains unclear. However, APT to HDM may serve other roles in patients with AD such as a predictor of disease persistence¹⁷ or diagnosis of respiratory allergy to HDM.¹⁸

ARE DUST MITES IMPORTANT IN THE CAUSATION OF ATOPIC ECZEMA?

As mentioned above, many factors appear to have a role in the causation and exacerbation of AD. One of these factors is aeroallergens. Given the ubiquity of

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HDMs in the environment and their recognised allergenicity to the atopic population, it is unsurprising that there is considerable volume of work investigating any association with AD. Despite this, there has been no clear consensus that aeroallergens are important in the pathogenesis of AD¹⁶ and this area remains both controversial and the subject of considerable research interest.

Evidence in favour of a role for HDM in AD includes:

- The presence of immune sensitisation to HDM, as demonstrated by SPT or APT, can be detected in the majority of AD patients, under certain conditions. The response to APT in AD patients is an eczematous lesion which resembles naturally occurring disease.¹⁹
- The avoidance of exposure and thus sensitisation to HDM antigen in early life appears to be associated with less atopic disease in later childhood.²⁰
- The homes of patients with AD have a higher level of exposure to HDM than those of controls¹³ and a dose-response curve has been demonstrated between AD disease activity and exposure to HDM in patients' beds.²¹
- Randomised controlled trials have demonstrated that decreased exposure to HDM will improve the severity of disease in AD patients.¹⁴
- Although the role of IgE allergens in AD remains uncertain, HDM has been shown to worsen skin disease not only when in contact with the compromised skin of atopic patients but also when inhaled.²²

Conversely, there is also evidence that suggests that HDM may play only a minor role in most AD:

- Much of the evidence that suggests that HDM sensitisation is important in AD is based on indirect, immunological findings including antigen-specific T cells and IgE, detected often in patients with AD. Control populations are seldom included in such studies. Indeed, there is evidence that non-specific positive APT to HDM occur in a high proportion of non-atopic patients referred to a patch test clinic.²³
- There is a bias among supporters of the role of HDM in AD to focus in on the studies which have shown evidence of clinical improvement on HDM avoidance while not mentioning the many studies that failed to reproduce this effect.²⁴ In fact, even in the studies where a role for avoidance was suggested, the clinical improvement did not correlate to HDM sensitisation¹⁴ and other work has shown no correlation between der p1 levels in mattresses and AD severity.⁹
- Although worsening of AD was demonstrated by inhalation of HDM allergen, this study²² was limited by the fact that the patient's experience of dyspnoea effectively unblinded the study.
- It is a well-recognised phenomenon that most AD patients improve in hot humid climates, where HDM levels are higher, yet AD prevalence is highest in dry areas, where HDM levels are lowest.²⁵

In short, the role of aeroallergens such as HDM as a cause of AD remains unclear.

THE IMPACT OF BEING ALLERGIC TO DUST MITES – ARE CHANGES IN LIFESTYLE HELPFUL?

On the balance of evidence, it seems likely that aeroallergens play a major role in the pathogenesis of allergic disease. Indoor allergens, especially dust mites, are of particular importance in atopic eczema. There is clear evidence from randomised controlled trials that not only can an individual's HDM exposure be effectively limited but that this can greatly reduce the activity of atopic eczema.¹⁴ Similarly, decreased exposure to mite

allergen can also improve the symptoms of asthma²⁶ although conflicting evidence remains.²⁷

Being allergic to dust mites, with eczema that responds to avoidance, will have significant impact on the sufferer's life. Considerable changes may be required to the patient's environment to reduce allergen exposure. Such changes may range from the extreme, such as moving to a location at higher altitude,²⁸ to simple avoidance measures in the home. However, a complete regimen has implications with regard to cost, both in terms of time and money. Furthermore, eczema highly sensitive to dust mite exposure may require modification of travel plans and day-to-day activities to avoid contact with excessive allergen.

There remains a degree of uncertainty as to which measures will be helpful and which may be unhelpful. Considerable research interest has surrounded investigation as to which interventions are effective at reducing mite exposure adequately to achieve clinical effects. Similarly, expensive measures of unproven and questionable value are widely marketed.

Before considering which of these measures may or may not be helpful, it is worth noting that advice to parents on mite avoidance needs to be individualised. There is little value in recommending expensive measures to those who cannot afford them or time-consuming ones to those with little motivation. To this end, I have tried to consider environmental control measures in terms of necessity and cost effectiveness.²⁹

Changes in lifestyle which are effective but relatively inexpensive

These are relatively simple measures that are highly effective at reducing the amount of der p1 in the patient's environment and therefore justify the cost they may incur:

- Mattress and pillow covers – impermeable plastic covers for mattresses and pillows may not be comfortable but can reduce dust-mite levels to only 1% of those of normal mattresses.³⁰ Tightly woven fabrics offer similar protection but are more comfortable. These covers offer the most cost-effective measure to reduce allergen exposure and there is clear evidence of their effectiveness in this regard³¹ although the actual clinical significance of this reduction remains subject to debate.³²
- Vacuuming carpets – regular vacuuming is an effective way of reducing der p1 levels on carpets. Numerous studies have looked into the value of different approaches to carpet cleaning such as shampooing³³ or wet vacuuming³⁴ but the evidence seems to show that a simple modern vacuum cleaner is just as good as the combination of a high-power, high-filtration vacuum cleaner plus an acaricidal spray.¹⁹
- Removing stuffed toys – these are ideal environments for dust-mite growth. Soft toys in a child's bedroom provide a considerable source of allergen. If not removed, these may be washed or even frozen³⁵ to kill mites.
- Washing bed linen in hot water – washing at high temperatures is an effective way to kill dust mites and remove allergen. Lower temperatures may only achieve the latter.³⁶
- Regular damp dusting of hard surfaces.
- Reducing relative indoor humidity – because dust mites thrive only in more humid environments, reducing humidity can make an environment more hostile to them. This in turn reduces their numbers.³⁷

Changes in lifestyle which are effective but not cheap

These measures follow the principles above, but because of their more extreme nature, can only be justified if eczema is severe, very sensitive to mites or the patient is highly motivated:

- Remove carpets, especially from bedroom.
- Remove upholstered furniture.
- Avoid living in basements.

Changes in lifestyle which may be of little benefit

These measures are commonly marketed to help with HDM reduction but studies have not been able to show any benefit proportional to the effort required:

- Acaricides – shown to kill mites but populations soon recover, thus necessitating regular applications.³⁸ No substitute for removing the carpet.
- Tannic acid – despite promising laboratory data, this has not been shown to be as effective in practice.³⁹
- Air cleaners – there is little evidence to support their use⁴⁰ which is unsurprising given that dust-mite allergen does not remain airborne for long.

In summary, it seems likely that changes in lifestyle that effectively reduce HDM exposure will be helpful in many of those who have eczema. However, some measures may be expensive or time-consuming yet may do little to actually reduce allergen levels. Advice on such lifestyle changes needs to be carefully individualised for each patient.

WHAT ADVICE CAN THE PRIMARY CARER OFFER?

A wide range of treatments are available for atopic eczema. The treatment or degree of lifestyle change to be recommended will depend very much on the severity of the disease, how much it is affecting quality of life and the motivation of the patient. There is little value in recommending expensive and intrusive HDM avoidance measures in the unmotivated patient with mild disease.

Initial advice would revolve around simple non-pharmacological measures such as wearing light cotton clothing,⁴¹ avoiding overheating and irritants such as cigarette smoke or soaps which dry the skin. Bathing once a day, to decrease the load of staphylococcus on the skin, is also worthwhile.

As discussed in the section above, advice on allergen avoidance must be tailored to the individual circumstances. Similarly, if there is evidence of allergy to pets, avoidance should be recommended.

Further advice involves topical medication. This includes regular use of emollients, ideally ointments, applied regularly and often. Patients may not tolerate these or adhere to recommended use and therefore advice regarding less greasy preparations should also be given. Bath oils and soap substitutes should also be recommended to help keep the skin hydrated.

Immunosuppressive topical agents such as steroids should be recommended for active eczema, as appropriate for age and severity. Patients should also be advised about how much of the preparation to apply, as well as when to apply it relative to use of emollients. Lack of such explanation is a common cause of treatment failure. The patient should be advised that once the disease is under control, the skin should be monitored for any emerging inflammation to allow early intervention.

Many GPs recommend antihistamines, especially for children, although there is still no convincing evidence of their value.⁴² Sedating antihistamines may be useful in helping itchy children sleep.

Other useful advice includes involvement of nurse education, especially in the management of children⁴³ and information about support groups. If there is a strong psychological or emotional element underlying the eczema then behavioural techniques to break the itch-scratch cycle may be of value.⁴⁴

There are numerous other potential treatments including calcineurin inhibitors and, in children, dietary manipulation, but these methods are best dealt with by specialists with a particular expertise, rather than primary carers. There are numerous other treatments which have little evidence base to support their use,⁴² such as complimentary medicine, but may be found useful on an individual basis.

WHAT COULD AN ALLERGIST CONTRIBUTE TO THE MANAGEMENT OF THE PATIENT?

In some countries there is very limited access for patients to consult allergists, e.g. within the UK National Health Service.⁴⁵ As a result, many of those who suffer from allergic disease do not get the expert input required to optimise their holistic care. Where referral to allergists is possible, there are a number of ways that an allergist could enhance the quality of care, above and beyond that offered by a general practitioner.

Confirming diagnosis

Atopic eczema is a clinical diagnosis and in rare cases, can be mimicked by other, potentially dangerous conditions. It may take a doctor with a particular interest in eczema to be able to differentiate it from the dermatitis seen in Wiskott-Aldrich syndrome or Langerhan's cell histiocytosis.

Optimising pharmacological therapies

An allergist will be able to systematically go through all the current eczema treatments that the patient uses in order to ensure that they are appropriate. Specialist treatments include wet wrapping (which would usually require the support of a specialist nurse) and more recent topical treatments such as the calcineurin inhibitors. Topical tacrolimus and pimecrolimus have clear benefits in patients with atopic eczema but are recommended only for prescription by specialists.⁴⁶

In selected cases, there may also be a role for dietary manipulation if it is thought that food allergens are driving eczema. Again, some treatment should be kept in specialist hands because of the risk of nutritional compromise and unnecessary exclusions.⁴⁷

Allergy testing

In vitro allergy testing is limited within the general practice setting. Although the importance of sensitivity to dust mites has been discussed above, other environmental allergens may also be relevant to the disease process. SPT for dog, cat and other animals may also lead to appropriate avoidance and improvement of eczema.

Diagnosis and treatment of co-morbid allergic disease

Atopic eczema forms part of the allergic march and has a close association with other atopic disorders. Children who are sensitised to HDM are at particularly

high risk of later development of allergic airways disease.⁴⁸ This increases the necessity of the involvement of an allergist to monitor any symptoms of asthma, ensuring that they are adequately controlled. Uncontrolled asthma is an important risk factor for life-threatening allergic reactions to food – another important association with eczema.

An allergist can assess the patient for rhinitis and food allergies and institute appropriate treatment. This avoids fragmented care for many sufferers of atopic disorders, who may otherwise see numerous different systems specialists rather than having their allergies holistically managed.

Disease prevention

Further to recognition and management of concurrent disease, there is controversial evidence suggesting that, in selected patients, the development of future allergic disease may be preventable. A recent study has suggested that the development of asthma may be reduced by the use of antihistamines. The Early Treatment of the Atopic Child study⁴⁹ was a double-blinded, parallel-group, randomised trial of cetirizine administered twice daily compared with placebo given to infants between 1 and 2 years of age with AD. The trial sought to establish whether the use of cetirizine compared with placebo for 18 months in infants with AD suppressed or truly delayed the onset of asthma, even after cessation of therapy. Results showed that those infants with evidence of sensitivity to HDM, grass pollen, or both, who were treated with cetirizine were significantly less likely to have asthma compared with those treated with placebo over the 18 months of treatment ($p = 0.005$ and 0.002 , respectively), although this effect diminished in the HDM-sensitised group over time.

Advice on allergy prevention in children/siblings

Allergists are commonly asked for advice on allergy prevention for 'high-risk' infants, either children of an adult sufferer or future siblings of a child. A review of different strategies is beyond the scope of this essay. However, there is good evidence⁵⁰ for the value of prolonged breastfeeding and delayed introduction of solid foods in the prevention of future allergic disease in such infants. The fact that up-to-date, evidence-based advice may prevent future disease would justify the involvement of an allergist.

Support and information

The allergist is better placed than a primary carer to answer questions about the patient's atopic eczema and allergen avoidance. Many allergy clinics also have specialist nurses who can spend more time going through treatments and allergen avoidance strategies with the patient. They can also put the patient in touch with support groups and direct them to useful websites (such as www.housedustmite.org).

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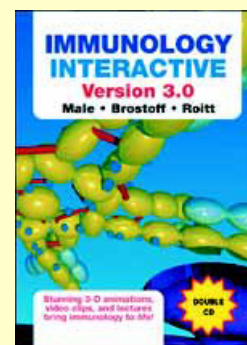
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