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Review Article

House Dust Mite Allergy

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INTRODUCTION

House dust

House dust (HD) allergy was recognized as early as the 1920s when dust extracts from vacuum cleaners, certain types of pillows, and mattresses were found to give relevant positive reactions in skin tests on asthmatics (26, 44, 53). Even though allergy to HD as judged by skin testing is one of the most prevalent (93), a long period of time should elapse before the major origin of the HD allergen(s) was elucidated. Constituents such as substances which manifest in humid indoor climate (53), fungi, textile fibres, human and animal dander and feathers were each in term reported to be of major allergenic importance (reviewed in 9). Apart from the prevalent animal dander (1, 21) most of these identified components are now shown to be of less clinical significance (9, 85).

Mites

Since 1964 an increasing number of observations have incriminated mites of the genus Dermatophagoides as a major pathogenic (68) or, more precisely, allergenic (86) source in HD. In the early studies the majority of HD-sensitive patients showed positive skin prick tests to *Dermatophagoides farinae* (Df) (52) or to *Dermatophagoides pteronyssinus* (Dp) and a good correlation was found between the allergenicity of HD extracts in skin tests and their contents of Dp (58, 85, 86). Similarly, the seasonal variation in allergenicity of HD, as well as in the number of patients with HD atopy referred for investigation, parallelled the variation in size of the mite population (85).

Subsequently, several challenge and *in vitro* tests have confirmed mites as important allergens in HD (11, 61, 65, 72).

BIOLOGY

Zoologically, mites are more closely related to spiders and scorpions than to insects. They have eight legs in the adult stage and body segmentation is lacking.

Species

A variety of mite species has been identified in HD, but only a few of these have proved to be of significance to inhalant allergy. The primary house dust mites (HDM) are *D. pteronyssinus* (Dp), *D. farinae* (Df) and *Euroglyphus maynei,* all belonging to the Pyroglyphidae family. The Dermatophagoides species with their worldwide distribution are the most intensively investigated. This review will concentrate on these species.

Even though the prevalence of the different mites is related to climate rather than geo-

graphic conditions, Dp is considered a marine specie, predominating in northern Europe, New Zealand and Australia (3, 15, 22, 48, 58, 79, 80), whereas Df is regarded as continental, mostly distributed in North America and central Europe (7, 32). At higher altitudes *E. maynei* may be the major species of mite fauna (84).

The closely related storage mites (*Glycyphagus, Tyrophagus* and *Acarus*), predator mites and other mites, such as *Tarsonemus,* have been found in minor proportions (19, 22, 41, 48, 58), but their role in HD allergy is not fully elucidated.

Changes in heating, ventilation, and cleaning procedures could have brought about a change in mite fauna, with an increase in numbers of Dermatophagoides up to their recognition in the 1960s. Alternatively, other methods of dust collection and examination could explain why these mites had hitherto been overlooked (91).

Life cycle

Under optimum conditions the female Dp produces 20–40 eggs once or twice during life. They are hatched after 6 days and the total immature life lasts about 25 days with three further stages. Under the same conditions the adults live about 2–3½ months (85). The life cycle of Df is parallel (52).

Sources

In the laboratory HDMs are normally grown on proteins (e.g. human hair, scales or contents from electric razors, etc.) and a small proportion of yeast (91). In dwellings, beds are the preferential breeding grounds. Here sufficient food is supplied in the form of human scales and the temperature seems ideal (32, 46). The most important habitat is the mattress (58) from which source the bedclothes are repopulated after laundry. Also dust from overstuffed furniture, carpets (3, 7, 80, 82), and unlaundered clothing (41) can contain high numbers of HDMs, but since these sources are not in such close contact with the eyes, nose or mouth as bedding, they probably play a less important role with respect to allergy.

Climate factors

Laboratory studies have shown that HDM cultures require certain temperatures and a moist environment in order to grow. For Dp the optimum conditions are 25°C and 70–80% relative humidity (RH) (31, 46, 85). Under these circumstances egg production is maximum, mortality minimal during the immature stages and the life cycle fairly short. The life of the adult mites could be increased from about 4–5 weeks to 3–4 months by lowering the temperature to 10°C, but this would stop perpetuation entirely (31). At higher temperatures (51°C, and 60% RH for 6 h) Dp will not survive (45).

For Df 25–30°C and 50–60% RH seems ideal (31). In a temperate climate this could only be accomplished for longer periods in such locations as chairs or beds (46). It requires a temperature of −18°C for 48 h to kill Df (69). This can also be accomplished by exposure to 40–50% RH at 25–34°C for 4–11 days (12).

A large number of field studies have confirmed this information. Mites are more abundant in humid homes (19, 27, 48, 82), and in temperate climates the number of HDMs increases during the humid summer months whereas during the heating season, when the indoor RH is low, mite numbers decline (7, 32, 84, 85). This low humidity during winter seems to be a critical factor in the survival of the mite population (48). Likewise, the low number of mites at high altitudes (84) could possibly be related to a low indoor RH in the regions investigated.

CLINICAL IMPORTANCE

The only role of HDMs in human medicine seems to be related to their allergenic properties. There is no reliable information about these mites actings as vectors of diseases or giving rise to symptoms on infestation (like the related scabies mite).

Prevalence of allergy

Allergy to mites and especially to HDMs is fairly common. Among suspected HD-allergic patients positive prick tests with extracts from Dermatophagoides species were much more frequent than with storage mite extracts (16, 92). In a study including patients referred for possible allergic diseases, positive skin prick test to HD and Dermatophagoides could be demonstrated in 21% and 16% respectively. Frequencies were equivalent to reactions to animal dander, higher than for tree or herb pollens, or mould fungi, and only slightly lower than the frequency for positive reactions to grass pollen (24%) (93). The prevalence of asthma among adults in the same region is one new case/year/200 persons (90). Combined, these figures would give one new HDM-allergic asthmatic/year/1,250 persons. The true figure is probably slightly higher, since asthmatics with minor suspicion of allergy would be less likely referred for allergy examination.

Allergens

By means of crossed radioimmunoelectrophoresis, in sera from allergic patients antibodies have been demonstrated against up to 29 different components in purified bodies of Dp (55). Forty-four to 72% of the IgE against Dp has been found directed against a glycoprotein designated Dp-antigen P_1 (23). This is identical to the antigens termed Dp-42 and Dpt 12 (25). The most important allergenic components seem to be in the excreta of mites. More than 80% of the airborne major antigen P_1 is associated with particles with the appearance of mite faeces (80). A corresponding major allergen (Ag 11) has been demonstrated in Df mites (28).

A very close, but not total, identity has been demonstrated between Dp and Df by immunochemical analyses (11) and skin prick tests (70), whereas the storage mites seem to contain different allergens (5, 92).

Sensitization

A dose response relationship between the number of HDMs in mattresses and the occurrence of mite-allergic asthma has been demonstrated (47). The importance of diminishing the HDM exposure in early childhood is underlined by the observation that HDM allergics are born more frequently in the summer and autumn (88). The relative risk of developing HDM allergy when born in these months was 1.44 (50).

Even though no common antigens are to be expected there seems to be some co-occurrence between allergy to animals and to HDMs, since problems after contact with dog were reported more than twice as often (31%) in mite allergics with nose symptoms than in a corresponding group of non-mite allergics (30).

CLINICAL SYMPTOMS

In a large sample of patients sent for allergological examination where skin tests to HDMs were shown to be positive, 45% had asthma, 34% rhinitis, 7% atopic dermatitis, and only 4% urticaria as the main diagnosis. The distribution was similar to that of animal and mould allergens. In contrast, rhinitis predominated among pollen allergics (49–63%) (93). The explanation for these different clinical pictures could be that pollens, due to their large size, are predominantly deposited in the upper airways. However, this does not support the hypothesis (80) that faecal pellets of pollen size are the main allergens of HDM – unless these particles would have a tendency to break down to fragments before entering the airways.

In contrast to many other allergies it is difficult to diagnose HDM allergy from the case history alone. Characteristically, only 62–65% with positive tests for Dp and Df (in children only 52% (88)) had noticed a worsening in lung or nose symptoms when previously exposed to house dust. On the other hand, as many as 34–37% of patients with other allergies, but no reaction to mites (in tests), were bothered by house dust (30). The reason could be an un-

specific irritative effect or it could be the contents of other allergens in the dust.

Asthma and rhinitis

Because HDMs are more or less ubiquitous one would expect HDM allergy to have a more unfavourable course than other allergies where allergens have a limited season or can be avoided. In this context it is important that an earlier onset of the disease has been demonstrated among HDM-allergic asthmatics compared to other adult asthmatics (58% versus 18% with debut before the age of 11) (30).

Even though the number of live mites increases during and following warm and humid seasons, asthmatics allergic primarily to HDMs have more symptoms during the subsequent cold months (64, 65) when some of the mites have disintegrated (and people spend more time indoors). Although aggravation has been reported to occur at night in bed (75, 88), where allergen exposure is high, this is not a universal finding. Nevertheless, nightly bronchoconstriction seems to be a general phenomenon in many asthmatics, with factors other than allergy playing a role (6).

Itching eyes and tears seem to be more frequent in rhinitis caused by HDM than by other allergens (30), the reason for this is uncertain.

Skin symptoms

HDM allergens certainly play their most important role as inhalants, but there is some evidence that they play a pathogenic role in chronic allergic skin diseases too. Patch test with Dp-allergen P_1 can produce delayed hypersensitivity response (excematous reactions) in some patients with atopic dermatitis and positive immediate skin reactions to the same allergen (62). This is in accordance with the finding that eczema is more common in patients with positive skin prick test to HDMs than in other allergics (9–16% versus 5%) (4). Immediate skin reactions to HDM or HD have been demonstrated in nearly half the patients with atopic dermatitis (4), and Dp could in fact be demonstrated more often in the clothes of patients with chronic dermatoses (41). On the other hand, in skin reactions of immediate type (recurrent urticaria) dust was only suspected as a worsening factor in 2% (42).

Other diseases

A high prevalence of specific IgE against Dp has been demonstrated in cases of sudden infant death syndrome (81) and in scabies (35), but here the clinical significance has to be demonstrated.

ALLERGEN AVOIDANCE

Temperature

Killing of mites in dwellings by temperature alone is seldom feasible, at least in temperate climates. Only in colder regions is it possible to expose mattresses, blankets, pillows and eiderdowns to the necessary −18°C for 2 days (Df) (69). The same effect could be accomplished by heating to more than 45°C for 2 h (Dp) (45). However, if the mites were exposed to low relative humidity at the same time, less extreme temperatures would probably be sufficient.

Humidity

Repeated ventilation in the cold season is not enough to reduce indoor humidity to a degree that could influence mite counts (49). On the other hand, theoretically, humidifiers in bedrooms, as well as beds with no ventilation beneath the mattress, should be avoided in the homes of HDM-allergic patients.

Dwellings and furniture

Bad housing construction seems to be a major reason for mite growth. In old houses water from either the air or the ground gains entry and in new houses the humidity produced inside is not always allowed to escape, thereby creating an ideal indoor climate for HDM. In this respect wooden (Japanese) houses seem better than concrete (82).

Materials which hide mites and prevent cleaning are obviously more heavily infested. This has been shown for carpets compared with plain floors (7, 63) and for mattresses with inner springs or capok compared with foam mattresses (3). HDMs can be found in new houses as soon as they become inhabited (15), and some investigators have found that the older the house (64) or mattress (15) the greater the number of mites, whereas others could show no such correlation with respect to carpets or mattresses (7, 48).

Cleaning

This factor seems to be of much less importance than that mentioned above. Dust load is generally not related to mite numbers (7, 47), and cleaning measures in most studies have been disappointing. Repeated vaccuuming does not remove mites completely from carpeting, this can only be done on hard-surface flooring (63). Vigorous vacuuming of bedding (15 min/bed/day) would only decrease the number of mites two-fold after the first week (22). The difficulties are illustrated by the fact that even a powerful industrial cleaner is not able to remove significantly more mites or dust from a mattress than a household cleaner (22).

In theory, the cleaning of mattresses should be facilitated by the use of plastic covers, but even though uncontrolled studies did show good preventive effect in this and similar antigen avoidance measures (15, 71, 73), no real clinical effect could be demonstrated in controlled trials (18, 19, 20). Likewise, an extensive scheme for cleaning and prevention was not able to improve lung function or medicine consumption, even though some subjective effect was reported (49).

Chemical agents

Mites are highly resistant to germicides. Of seven acaricides, nine insecticides, and 13 disinfectants, Lindane (gamma benzene-hexachloride) was the only product which killed the mature Dp. In a 2-h test it had to be used in a 1% concentration (5–10 times the concentration recommended in agriculture) (54). Other insecticides could be effective following longer exposure (12), but serious concerns could be raised as to the side effects of such insecticides when used in bedrooms. Furthermore, frequent treatment would be necessary since HDMs present in our clothes or elsewhere could rapidly re-infest the treated area. Natamycin, a fungicide with less toxicity, has shown some effect on symptoms in an uncontrolled clinical trial (56). It acts on fungi which are important for the growth of *Dermatophagoides*.

In the future such chemicals may prove to be useful adjuvants in controlling mite growth.

IMMUNOTHERAPY

As long as the above mentioned measures for primary and secondary prevention in HDM allergy are insufficient, other forms of therapy will be needed. Immunotherapy may be appropriate here, but even though a promising effect in pollen allergy was described as early as 1911 (37, 67), several years have elapsed before controlled studies with HD/HDM appeared.

Controlled studies

From 1949 to 1983 reports have been presented in international publications of 15 placebo-controlled, and mostly blinded studies of the effect of injection-immunotherapy on HDM or HD allergy (Table 1). Only two of these studies showed immunotherapy to have no effect at all (14, 39). The rest showed effects varying from clinical improvement without immunological changes (29, 87, 89) to effects on both immunological parameters and symptoms/bronchial reactivity (24, 33, 36, 38, 51, 77). Even isolated changes in antibodes with no clinical change was observed (13). Half of the studies gave no information on immunological examination. Although most studies did show a statistically significant effect on one or more points, other parameters – thought to be equally important – were not affected by the therapy. There seem to be several reasons for this lack of impressive effect. The most important of these are the selection of patients, the allergen doses admini-

Table 1

Placebo-controlled studies describing the effect of immunotherapy with house dust or house dust mites

Author (reference)	Age	Diagnosis	Allergen	Type of extract	Duration of treatment (months)	Effect as evaluated by									
						Double blind design	Allergen challenge	Lung function	Skin test	Symptom score	Medicine score	Specific IgE	Specific IgG	Histamine release	Other parameters
Bruun (17)	adults	asthma	house dust	aqueous	18	(single blind)									yes (clinical assessment)
Br. Tuberc. Assoc. (14)	adults (+ children)	asthma	house dust	aqueous	4	yes		no		no	no				
Smith (74)	children + adults	asthma	*D. pteronyssinus*	aqueous	4	yes		no		yes	yes				yes (overall assessment)
Aas (2)	children	asthma	house dust	aqueous	30–36	yes		yes							yes (parents' assessment)
Maunsel et al. (59)	adults	asthma	*D. farinae* (house dust as control)	aqueous(?)	6–9	yes									yes (overall assessment)
D'Souza et al. (77)	adults	asthma/ rhinitis	*D. pteronyssinus*	aqueous	3	yes	yes		no	(yes)	(no)	yes	yes	yes	yes (overall assessment)
Taylor et al. (78)	children	asthma	house dust *D. farinae*	?	2	yes		no							yes (growth parameter)
Gaddie et al. (39)	adults (+ children)	asthma	*D. pteronyssinus*	tyrosine adsorbed	12	yes	no	no	no	no	no				
Gabriel et al. (24, 38)	children + adults	rhinitis	*D. pteronyssinus*	aqueous	16–17	yes	no		no	yes		no	yes		
Warner et al. (87, 89)	children	asthma (+ rhinitis)	*D. pteronyssinus*	tyrosine adsorbed	12–24	yes	yes (late reactions)	yes	no	yes	yes	no	no		
Marques et al. (57)	adults (+ children)	asthma	*D. pteronyssinus*	tyrosine adsorbed	1½–8	yes				(yes)					yes (overall assessment)
Newton et al. (66)	adults	asthma	*D. farinae*	alum precipitated	12	yes	yes	no	no						
Br. Thorac. Assoc. (13)	adults	asthma	*D. pteronyssinus*	aqueous	4–18	(yes)		no	no	no	no	yes	yes		no (overall assessment)
Davies et al. (29)	adults	rhinitis	*D. pteronyssinus*	tyrosine adsorbed	12	yes	yes		no	yes		no			
Formgren et al. (33, 36, 51)	?	asthma/ rhinitis	*D. farinae*	?	12	yes	yes		yes			no	yes	no	no (histamine challenge)

stered, the duration of treatment, and the reliability (objectivity) of the parameters for assessment.

Extracts

Even though HDM is known to be a common and major component of HD in relation to allergy, the results of comparative studies including HD and HDM are contradictory (10, 59, 76). The explanation could very well be different contents of HDM allergens in the extracts used.

Alternative regimens in immunotherapy have been tried. An early study reported HD therapy to be more effective by inhalation than by injection, although the effect was of short duration (60). No effect of oral immunotherapy with HDM could be demonstrated (83), and no clear-cut relationship was found between the use of tyrosine-adsorbed extracts and the success of the trials (39, 57, 87, 89).

Patient selection

Immunotherapy is a specific treatment and the outcome is dependent on choosing the right allergens for the right patient. Although skin testing is a reliable diagnostic method, allergen provocation adds further information when selecting the patients and evaluating the therapeutic results. It is interesting that clinical effect was found in all seven of the above described studies using allergen challenge of the relevant organ in the selection of patients (2, 29, 36, 38, 66, 77, 89). Late reaction to allergen challenge may imply more favourable results of subsequent therapy (89).

It seems that the outcome of immunotherapy is also age- and symptom-dependent, since all studies showing no clinical, therapeutic effect included adult asthmatics (13, 14, 39). Spontaneous cure is more frequent in the lower age group, therefore it is important to ensure proper age-matching, especially in childhood studies.

Allergen doses

In immunotherapy failure will result when insufficient amounts of allergen are administered (40). Because of differences in allergenic standardization it is generally difficult to evaluate whether high or low doses are used in the trials, and whether maximum tolerated doses are aimed at or not. By looking at the adverse effects described, it is possible to get an impression of the allergenic potential of the acquired doses, although the modified allergens may not be comparable in this respect. In the studies presenting immunological changes, adverse reactions have been most pronounced during active treatment (13, 24, 38, 57, 77), whereas there have been no immunological changes in studies using allergen doses insufficient to cause any adverse reactions that are different from those produced by placebo (29, 87, 89).

Duration of treatment

In several of the studies referred to above immunotherapy was only performed during a phase of dose increase (i.e. 2–4 months). This could be one of the reasons for the modest results, since the effect of immunotherapy with HD or HDM is not necessarily apparent just after the initial phase. Improvements in either allergen challenge threshold, or symptom + medication score, could be monitored at intervals of 1 month (29), 3 months (77), 4 months (38, 89) or 6 months (57) after the phase of dose increase. This in contrast to the immunological changes which would be measurable at an earlier stage. Even though this is not proof against a pathogenetic role of the immunological parameters measured, it seems to imply that other still unknown factors may also play an important role.

The persistence of the acquired effect after the termination of maintenance therapy is still an open question. In one study half of the patients relapsed within 10 months, but here the treatment period had been short (16 weeks) (74).

Evaluation of effect

The fact that allergy to HDM is often associated with other allergies (65), and the many non-allergic factors influencing especially the asthmatic symptoms, make it difficult to assess the specific effect of immunotherapy on HDM by means of clinical scoring systems.

Although the effect of immunotherapy seems to have allergenic specificity (43), it could be hoped that a beneficial effect on the relevant allergy could in some way improve the accompanying unspecific hyperreactivity as well. This would be important since irritants in many cases seem to be of great clinical significance and the overall clinical improvement is most relevant from the patients' point of view.

Symptom and medication scores are widely used, but involve several difficulties. Even when the treated groups are matched primarily, the use of a small number of patients would demand the regulation and control of several factors, such as medication, antigenic load, irritants, infections, etc. in order to validate the scores. Since this is seldom feasible only very impressive effects would be expected to show. With challenge tests this problem can to some extent be overcome and, with the exception of two studies (38, 39), immunotherapy seems to have a beneficial effect on this parameter (2, 39, 36, 51, 66, 77, 89). In addition, (bronchial) histamine challenge has been introduced in order to evaluate the effect on the unspecific reactivity. However, no such effect could be demonstrated in a recent study (36).

Clinical assessment would seem to be a fairly subjective parameter and the results evaluated in this way are conflicting. Objective measurements, such as lung function tests performed at the clinic, reveal only modest or no effect (13, 39, 74, 78), as could be expected from the fluctuating nature of the asthma disease.

Immunological parameters

Decrease in skin test sensitivity following immunotherapy with HDM has been reported in only one (51) of seven trials, whereas four of five studies could show an increase in specific IgG during treatment. In other types of allergy certain amounts of specific IgG have been indicative of successful treatment (40), and preliminary observations have disclosed the highest IgG_4/IgE ratio in a group where immunotherapy with HD had been successful (34). Interestingly enough, in the HDM study in which no change in IgG was demonstrated, the patients did in fact show clinical effects on several parameters (87, 89), whereas no clinical improvement could be demonstrated in another therapeutic trial giving rise to an increase in specific IgG (13).

Immunotherapy had variable effect on the specific IgE level. Although in most cases a clinical effect without IgE change was reported (29, 33, 38, 89), immunological changes without therapeutic effect could also be demonstrated (13).

Other studies

The effect of immunotherapy with HD(M) has also been investigated in several studies differing from those above in that they were not placebo controlled. An improvement could be measured by challenge test when this was applied (8, 10, 60).

CONCLUSIONS

The two closely related HDMs, Dp and Df, seem to be of major allergenic importance in HD. The faeces particles, in particular, contain allergenic material in a concentrated form. Practicable control measures, such as chemicals, cleaning, ventilation, and temperature regulation, have only been able to reduce the number of mites in houses to some extent, and, in general, the clinical effect has been disappointing. Therefore immunotherapy could be appropriate for this type of allergy, and, in fact, in some studies such treatment has proved to be effective. The more unfavourable results in other studies stress the importance of such factors as patient selection, sufficient allergen amounts, and appropriate duration of treatment.

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