

## Practice Parameter

## Environmental assessment and exposure control of dust mites: a practice parameter

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## Classification of recommendations and evidence

There may be a separation between the strength of recommendation and the quality of evidence.

### Recommendation rating scale

Statement	Definition	Implication
Strong recommendation	A strong recommendation means the benefits of the recommended approach clearly exceed the harms (or that the harms clearly exceed the benefits in the case of a strong negative recommendation) and that the quality of the supporting evidence is excellent (grade A or B). In some clearly identified circumstances, strong recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits strongly outweigh the harms.	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
Moderate recommendation	A moderate recommendation means the benefits exceed the harms (or that the harms clearly exceed the benefits in the case of a negative recommendation), but the quality of evidence is not as strong (grade B or C). In some clearly identified circumstances, recommendations may be made based on lesser evidence when high-quality evidence is impossible to obtain and the anticipated benefits outweigh the harms.	Clinicians also should generally follow a moderate recommendation but should remain alert to new information and sensitive to patient values and preferences.
Weak recommendation	A weak recommendation means that the quality of evidence that exists is suspect (grade D) or that well-done studies (grade A, B, or C) show little clear advantage to one approach vs another.	Clinicians should be flexible in their decision making regarding appropriate practice, although they may set bounds on alternatives; patient values and preferences should have a substantial influencing role.
No recommendation	No recommendation means there is a lack of pertinent evidence (grade D) and an unclear balance between benefits and harms.	Clinicians should feel little constraint in their decision making and be alert to new published evidence that clarifies the balance of benefit vs harm; patient preferences and values should have a substantial influencing role.

### Category of evidence

- Ia Evidence from meta-analysis of randomized controlled trials
- Ib Evidence from at least 1 well-designed randomized controlled trial
- Ic Evidence from at least 1 randomized controlled trial that was not very well designed
- IIa Evidence from at least 1 controlled study without randomization
- IIb Evidence from at least 1 other type of quasi-experimental study
- IIc Evidence from 1 of the above that was not very well designed
- IIIa Evidence from well-designed nonexperimental descriptive studies, such as comparative studies
- IIIb Evidence from nonexperimental descriptive studies, such as comparative studies that were not very well designed
- IVa Evidence from expert committee reports or opinions or clinical experience of respected authorities or both

### Strength of evidence

- A Directly based on category I evidence that is well designed
- B Directly based on category II evidence or recommendation from category I evidence that is not well designed
- C Directly based on category III evidence or recommendation from category II evidence that is not well designed
- D Directly based on category IV or recommendation from category III evidence that is not well designed
- LB Laboratory based
- NR Not rated

### Summary of conflict-of-interest disclosures

The following table is a summary of interests disclosed on Work Group Members' Conflict-of-Interest Disclosure Statements (not including information concerning family member interests). Completed Conflict-of-Interest Disclosure Statements are available upon request.

Work Group Member	Disclosures
James Sublett, MD (co-chair)	Owner: AllergyZone
Kevin Kennedy, MPH (co-chair)	None
Jay Portnoy, MD (Joint Taskforce liaison)	Speaker: ThermoFisher
Charles Barnes, PhD	Consultant, research grant: Clorox Corp
Ginger L. Chew, ScD	None
Carl Grimes, CIEC	Owner: Healthy Habitats LLC
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Jeffrey D. Miller, MD	Owner: Mission: Allergy, Inc
J. David Miller, PhD	None
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P. Brock Williams, PhD	None
Fares Zaitoun, MD	None

### Resolution of potential conflicts of interest

The Joint Taskforce (JTF) recognizes that experts in a field are likely to have interests that could come into conflict with the development of a completely unbiased and objective practice parameter. To take advantage of that expertise, a process has been

developed to prevent potential conflicts from influencing the final document in a negative way.

At the workgroup level, members who have a potential conflict of interest do not participate in discussions concerning topics related to the potential conflict; or, if they do write a section on that topic, the workgroup completely rewrites it without their involvement to remove potential bias. In addition, the entire document is reviewed by the JTF and any apparent bias is removed at that level. The practice parameter is sent for review by invited reviewers and by anyone with an interest in the topic by posting the document on the Web sites of the American College of Allergy, Asthma, and Immunology (ACAAI) and the American Academy of Allergy, Asthma, and Immunology (AAAAI).

For example, Jeffrey D. Miller, MD, owns a company that sells a product discussed in this practice parameter. Dr Miller wrote a section on mattress encasings. This section was rewritten by other members of the workgroup without his participation. He did not provide subsequent input into that section.

## How this practice parameter was developed

### The JTF on Practice Parameters

The JTF on Practice Parameters is a 13-member taskforce consisting of 6 representatives of the AAAAI, 6 of the ACAAI, and 1 of the Joint Council of Allergy and Immunology. This taskforce oversees the development of practice parameters; selects the workgroup chair(s); and reviews drafts of the parameters for accuracy, practicality, clarity, and broad utility of the recommendations for clinical practice.

### The Environment Practice Parameter Workgroup

The Environment Practice Parameter Workgroup was commissioned by the JTF to develop practice parameters that address environmental assessment and remediation. The co-chairs (James Sublett, MD, and Kevin Kennedy, MPH) invited workgroup members to participate in the parameter development who are considered experts in the field of environmental assessment and contaminant reduction. Workgroup members have been vetted for financial conflicts of interest by the JTF and their conflicts of interest have been listed in this document and are posted on the JTF Web site (<http://www.allergyparameters.org>). Where a potential conflict of interest is present, the potentially conflicted workgroup member was excluded from discussing relevant issues.

The charge to the workgroup was to use a systematic literature review, in conjunction with consensus expert opinion and workgroup-identified supplementary documents, to develop practice parameters that provide a comprehensive approach for identifying and managing environmental exposures and their health effects based on the current state of the science.

### Protocol for finding evidence for this practice parameter

A search of the medical literature was performed for different terms that were considered relevant to this practice parameter. Literature searches were performed on PubMed and the Cochrane Database of Systematic Reviews. Figure 1 shows the number of references from 1960 to the present for the terms *dust mite*, *Dermatophagoides*, *pteronysinus*, or *farinae* (designated as *mite* in the figure). The search was narrowed by adding the terms *allergy* or *asthma*, designated as *Combo* in the figure. This document includes references from 1970 through early 2013. All reference types were included in the results. References identified as being relevant were searched for additional references and these also were searched for citable references. In addition, members of the workgroup were asked for references that were missed by this initial search. Although the ideal type of reference would consist of a randomized, double-blinded, placebo-controlled study, the topic of this practice parameter is represented by very few such studies. In consequence, it also was necessary to include observational studies, basic laboratory reports, and regulatory requirements to develop a document that addresses most of the issues discussed in this practice parameter.

## Glossary

**Condensation:** The conversion of water vapor to liquid phase when cooled below its dew point.

**Dew point:** The temperature below which water vapor in a volume of humid air at a constant barometric pressure will condense into liquid water. Condensed water is called *dew* when it forms on a solid surface.

**Hygroscopic:** A substance that is prone to absorbing moisture in damp environments, such as salt or sugar.

**Hygrometer:** A device that is used to measure RH in an environment.

**Relative humidity:** The ratio of the partial pressure of water vapor in an air–water mixture to the saturated vapor pressure of water at a prescribed temperature.

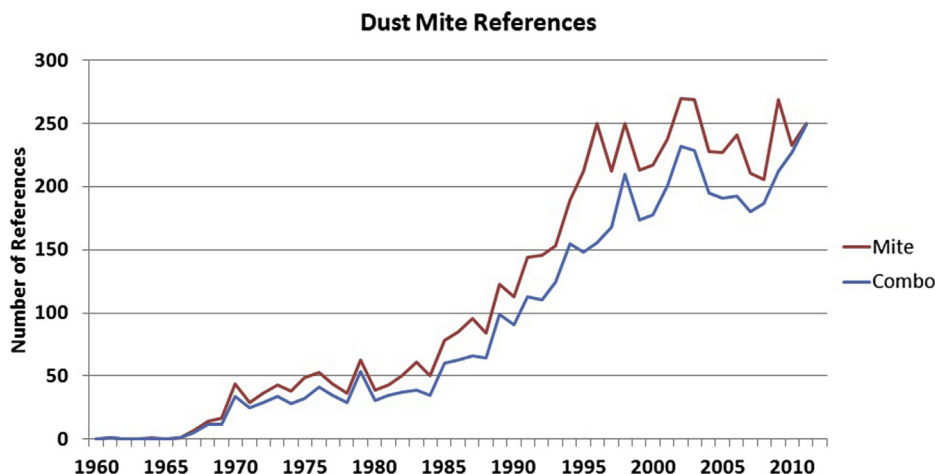


Figure 1. Number of references per year. Combo, mite and allergy; Mite, search for dust mite or *Dermatophagoides* species.

## Summary statements

1. Advise patients to minimize exposure of susceptible children to dust mite allergens to decrease their risk of developing mite-specific IgE. Because intermittent exposure to mite allergens can lead to sensitization, primary prevention might not be possible to achieve in regions where mite exposure is prevalent. (Strength of recommendation: strong, A evidence)

2. Advise patients to minimize exposure of dust mite-sensitized children to dust mite allergens to decrease their risk of developing asthma and possibly rhinitis. (Strength of recommendation: strong, A evidence)

3. Advise dust mite-sensitized patients with asthma or rhinitis to minimize exposure to dust mite allergens in addition to avoiding other relevant allergens to which they are sensitized and avoiding irritants, to decrease their risk of developing symptoms. (Strength of recommendation: strong, B evidence for asthma; strength of recommendation: strong, C evidence for rhinitis)

4. Advise patients to minimize exposure of dust mite-sensitized children with atopic dermatitis to dust mite allergens, to decrease the symptoms of atopic dermatitis. (Strength of recommendation: moderate, C evidence)

5. Although 5% to 15% of patients who are highly sensitized to dust mite also are sensitized to crustaceans, the clinical significance of this is unknown. For that reason, no recommendation can be made regarding the need to advise crustacean-naïve patients about their risk of ingestion. (Strength of recommendation: none, D evidence)

6. Evaluate patients who complain of oral symptoms or symptoms consistent with an IgE-mediated reaction after ingestion of grain flour for dust mite sensitization regardless of whether they have wheat-specific IgE. (Strength of recommendation: moderate, C evidence)

7. Test patients with suspected dust mite allergy for the presence of dust mite-specific IgE using a skin prick test or in vitro test for specific IgE. (Strength of recommendation: strong, B evidence)

8. Currently there is no evidence supporting routine measurement of specific IgE to dust mite components, although such measurements may be considered when necessary, such as for patients with potential Der p 10 (tropomyosin as found in cockroach and crustaceans) sensitivity. (Strength of recommendation: weak, D evidence)

9. Encourage dust mite-allergic patients to obtain and use a hygrometer to measure humidity in their home. (Strength of recommendation: strong, D evidence)

10. Advise patients that relative humidity in the home should be kept at 35% to 50% to decrease the growth of dust mites. (Strength of recommendation: strong, B evidence)

11. Do not recommend the use of acaricides to eliminate mite populations because of their limited efficacy at lowering allergen levels and concerns about the use of chemical agents in the home. (Strength of recommendation: moderate, B evidence)

12. Tell patients that the use of physical measures to kill mites, such as heating, freezing, and desiccation, theoretically should be effective; however, controlled trials have not been performed to demonstrate clinical benefit when they are used. (Strength of recommendation: weak, D evidence)

13. Advise patients that bedding should be washed weekly to decrease dust mite numbers and mite allergen levels, and that high temperature is not necessary. Home hot water should be kept below the temperature (120°F) that causes a scalding risk to occupants. (Strength of recommendation: strong, B evidence)

14. Suggest postintervention measurement of mite allergens in settled dust for homes in which mite-sensitive people live if symptoms persist despite reasonable efforts to decrease mite exposure. (Strength of recommendation: weak, D evidence)

15. Measurement of airborne mite allergens offers no benefit over their measurement in settled dust and therefore should not be recommended. (Strength of recommendation: moderate, C evidence)

16. Recommend regular vacuuming using cleaners that have high-efficiency particulate air (HEPA) filtration or with a central vacuum with adequate filtration or that vents to the outside to decrease exposure to dust mite allergen-containing particles. (Strength of recommendation: strong, B evidence)

17. Recommend that patients should use mite allergen-proof mattress, box spring, and pillow encasings to decrease exposure to mite allergens. (Strength of recommendation: strong, B evidence)

18. Discourage members of families with an atopic background from sleeping in bunk beds. If bunk sleeping is necessary, the sensitized person ideally should sleep in the top bed and the top and bottom mattresses (and any fabric-covered “bunky-boards”) should be enclosed in allergen-impermeable encasings. (Strength of recommendation: moderate, B evidence)

19. Do not recommend tannic acid for decreasing mite allergens in carpet dust because it is only marginally effective. (Strength of recommendation: moderate, C evidence)

20. HEPA filtration alone is of uncertain benefit for patients with mite allergy, although it can decrease local exposure to airborne mite allergens and to some irritants. If used, recommend that HEPA cleaners should be placed in areas of mite contamination where air disturbance is likely to suspend particles so that they are available for removal. (Strength of recommendation: weak, C evidence)

21. Recommend a multifaceted approach for dust mite avoidance using a combination of techniques that includes repetitive and sequential interventions shown to decrease mite exposure, as described earlier, for patients with dust mite allergy who are at risk of mite exposure. (Strength of recommendation: moderate, A evidence)

22. Offer subcutaneous immunotherapy to dust mite-allergic patients with rhinitis or mild to moderate asthma if they meet the general criteria for receiving allergen immunotherapy (Strength of recommendation: strong, A evidence for asthma; strength of recommendation: moderate, B evidence for rhinitis)

23. Consider subcutaneous immunotherapy for dust mite-allergic patients with atopic dermatitis if they meet the general criteria for receiving allergen immunotherapy; however, possible exacerbation of the disease during the initial phase of immunotherapy should be discussed with the patient (Strength of recommendation: moderate, A evidence)

24. Patients receiving immunotherapy for dust mite ideally should receive a dose that delivers approximately 7 µg of Der p 1 per injection or 500 to 2,000 AU per injection to obtain an optimal balance between efficacy and safety. (Strength of recommendation: strong, A evidence)

25. US dust mite extracts can be mixed with pollen extracts, including grass and animal dander extracts. Also at maintenance immunotherapy concentration, US dust mite extracts can be mixed with fungal or cockroach extracts when glycerin content is kept at 10%. (Strength of recommendation: moderate, LB evidence)

26. Recommend 3 to 5 years of immunotherapy to obtain the maximum benefit from immunotherapy for dust mite-induced asthma and rhinitis. (Strength of recommendation: moderate, A evidence)

**27. Certain protocols and dosages of sublingual immunotherapy have been shown to be safe and effective for dust mite–allergic patients with rhinitis, mild to moderate asthma, and/or atopic dermatitis; however, because there currently is no Food and Drug Administration–approved product available in the United States, its use should not be recommended until such a product becomes available. (Strength of recommendation: moderate, A evidence)**

### Executive summary

Dust mites are 8-legged arthropods that live in the house dust of homes located in regions where they are prevalent. They have been recognized as the major source of allergens in house dust since 1967. The most common species found in homes in temperate regions of the United States are *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*. In addition, others, such as *Blomia tropicalis*, can be found in homes in tropical and subtropical regions.

Dust mites feed on organic materials, including skin scales, fungi, yeasts, and bacteria. Because they are composed of approximately 75% water by weight, they maintain their water balance through uptake of water vapor when RH is at least approximately 65%. They are susceptible to water loss when humidity decreases below 65% and have decreased survival and reproduction with an RH below 50%.

Mites produce and excrete numerous allergens into the environment, including cysteine proteases such as Der p 1 and Der f 1, serine proteases including Der p 3, 6 and 9, and proteases that can activate protease-activated receptor-2, which are proinflammatory in humans through a non-IgE-dependent mechanism. Mites also produce glycosidases and carbohydrate-binding proteins and muscle, cytoskeleton, and calcium-binding proteins. There is cross-reactivity among various mite species and between mites and other related families, such as crustaceans and cockroaches.

Tests for measurement of mite allergens from environmental samples are commercially available. Such tests have included measurement of guanine as a proxy for fecal material and of specific allergens using polyclonal and monoclonal antibodies. The most commonly used assays are for the measurement of Der p 1 and Der f 1. Assays for Der p 2, Der f 2, and Blo t 5 also are available. Recently, a new set of international standards for dust mite allergens that have been standardized using molecular techniques has led to a revision of the concentrations reported in earlier studies of mite exposure. This may require a reassessment of exposure thresholds associated with the development of sensitization, disease, and morbidity.

Although homes in arid regions of the world are virtually free of dust mites, it is estimated that 84% of US homes have detectable dust mite allergen and that half have concentrations of at least 2  $\mu\text{g}/\text{g}$  of dust. In Canada, the percentage of homes overall with house dust mite allergen concentrations higher than 2  $\mu\text{g}/\text{g}$  is somewhat smaller but similar in highly populated areas in central and eastern Canada and in British Columbia. Factors leading to increased mite concentrations include older, single-family homes with lower household income. Increased population density, the presence of carpeting, and lack of air conditioning also lead to increased dust mite exposure. The presence of moisture, cockroaches, and mold also is associated with increased mite populations. Homes in warm damp regions of the country, such as New Orleans and Florida, tend to have a more diverse population of dust mites.

There is up to a 20-fold variation in mite exposure in regions that have significant seasonal variation in temperature. Dust mite allergen levels tend to increase during the summer when humidity is high and remain elevated through the winter before decreasing during the late winter and spring.

Dust mite allergens are associated with particles that tend to have a large aerodynamic behavior, with most settling within 15 minutes of disturbance. Very little mite allergen can be found in the air of

undisturbed rooms. Mite allergens are found in settled dust in carpeting, bedding, and upholstered furniture but not on hard surfaces. Clothing also appears to be an important source of mite allergen exposure, particularly if the clothing is washed infrequently.

Primary prevention of IgE sensitization to mite allergens in susceptible children requires strict, continuous avoidance of exposure for long periods. Prevention of sensitization has been observed in arid regions where mites are absent; however, it is difficult to completely eliminate mite exposure in homes located in mite-prevalent regions. Even when exposure in a particular home is avoided, intermittent exposure to mite allergens when one travels to other indoor environments often leads to sensitization. In consequence, most attempts at primary prevention have been unsuccessful. Even so, there is a correlation between the amount of exposure and the degree of sensitization. For that reason, exposure to mite allergens should be minimized in susceptible children as much as is feasible.

The goal of secondary prevention is to decrease the risk of developing asthma and rhinitis in already mite-sensitized children, usually during the first year of life. Several prospective studies have found that mite avoidance lowers the risk of developing asthma in a dose-dependent manner. Specific thresholds for exposure have been proposed in several of these studies; however, such cutpoints are not used in this practice parameter because there does not appear to be a level of exposure that does not offer at least some risk of developing asthma or rhinitis. In addition, the relation between allergen exposure and disease development appears to be complicated by other factors, including exposure to other allergens and to irritants and pollutants.

The advisability of decreasing exposure to mite allergens in already sensitized individuals who have asthma or rhinitis has been accepted conventional wisdom since mite allergens were identified. Many controlled studies have shown the importance of allergen avoidance; however, to be most effective, other relevant allergens and irritants should be avoided. Avoidance of allergens can lead to decreased bronchial hyper-responsiveness, decreased morbidity, and decreased need for medications. This appears to be true even for patients with asthma who are not mite allergic because mite emanations have proinflammatory properties that do not necessarily act through an IgE mechanism.

Atopic dermatitis can be triggered by exposure to dust mites in sensitized individuals. Live mites have even been found on the skin of up to 35% of children with atopic dermatitis and on their clothing and bedding. Interventions leading to decreased mite exposure have been shown to lead to improvement in moderate to severe atopic dermatitis.

Because mites are members of the arthropod family, they contain tropomyosin (Der p 10), which cross-reacts with other arthropods, including crustaceans and cockroaches. As many as 5% to 15% of mite-sensitized individuals also are sensitized to crustaceans. A presumably small, but currently unknown, percentage of dust mite–allergic individuals may be at risk of a reaction after the ingestion of crustaceans. Because the extent of this risk is unknown, no recommendation is made regarding the need to advise crustacean-naïve patients about their risk of ingestion.

Dust mites can contaminate grain flour. Systemic reactions have been reported in dust mite–allergic individuals after the ingestion of grain flours, including beignets, wheat, pancakes, polenta, *okonomi-yaki*, and grits. Symptoms have ranged from erythema and urticaria to wheezing with dyspnea and even to anaphylaxis with loss of consciousness. Cooking apparently is not sufficient to completely denature mite allergens. Therefore, it is important to store such flour in sealed dust mite–impermeable bags, ideally in the freezer or refrigerator. Individuals with symptoms consistent with an allergic reaction to grain flour should be tested for sensitivity to dust mites.

The clinical evaluation of patients with suspected mite allergy begins with inquiries about a history of atopy, including a history of increased symptoms upon disturbance of dust as would occur with vacuuming and dusting. Because this type of history is neither sensitive nor specific, individuals who live in regions where mites are prevalent should undergo tests for mite-specific IgE, such as skin prick tests and/or *in vitro* tests. The performance characteristics of these types of tests have recently been evaluated and are similar to each other. These provide high sensitivity and specificity when appropriate criteria for a positive test result are used.

Extracts used for tests of dust mite sensitization have been standardized in the United States for total biologic potency; however, substantial differences are present between extracts in terms of individual constituents. In consequence, extracts from different sources are not considered interchangeable regardless of their total biologic activity. European extracts also can differ substantially, in potency and constituents, from those produced in the United States, making it difficult to compare the results of studies using the different extracts. Although tests for specific IgE to mite components are available, such tests are not recommended for routine use because their clinical value is not known.

Decreasing exposure to dust mites requires a multi-intervention approach that addresses facilitative factors, sources, reservoirs, and pathways to occupants. Although the most effective intervention is to live in a region where mites are not present or to duplicate such conditions in a home if it is located in a region in which they are prevalent, such complete control is often impractical. Ideally, indoor humidity must be kept low year-round regardless of outdoor conditions. Mattresses, pillows, and bedding must be made free of mite allergen emanations, and carpeting and other potential reservoirs should be removed completely.

The most important facilitative factor for mite growth is RH. Mites require RH higher than 65% to prevent water loss and to thrive. Once humidity decreases below 50%, mite proliferation decreases and survival is decreased. Depending on how dry the environment is kept, mites can survive for weeks before they die. If the humidity increases for as little as 1.5 hours per day, as could occur during cooking or bathing, the mites can survive. An elevated RH for as briefly as 3 hours per day permits mites to produce eggs. To determine the RH, patients are advised to obtain an inexpensive hygrometer, available from many outlets in the United States.

The difficulty of maintaining low RH in regions where moisture is increased has been demonstrated by numerous attempts to decrease mite exposure and improve health by using indoor dehumidification. The series of studies performed in Manchester, England used increasingly intense measures to remove moisture from homes, ranging from free-standing dehumidifiers (ineffective) to whole-house dehumidification (effective at decreasing mite allergens but not clinical symptoms). Studies in the United States that used even more extensive dehumidification measures were able to demonstrate significantly decreased live mites and mite allergen exposure. The lesson is that homes in which RH can be kept at 35% to 50% continuously will have lower concentrations of mite allergen than in homes in which RH is permitted to fluctuate.

Elimination of mites, the source of mite allergen, should lead to decreased exposure. Because there is a strong relation between mite allergen concentrations in dust and the number of live mites in an environment, it is not necessary to enumerate live mites to determine the mite load of an environment. Techniques to kill mites have included chemical acaricides; physical measures such as heating, freezing, and desiccation; and washing of bedding and clothing.

Acaricides can kill mites under laboratory conditions. They also kill surface mites when applied to carpeting and bedding; however, the duration of the benefit is short term so the application must be

repeated every 1 to 3 months. In addition, the decrease of mite allergen exposure is modest at best and is not likely to be clinically useful. In addition, there is a concern about the application of chemicals in the home and particularly on mattresses and furniture where contact with occupants is likely to occur. For these reasons, the use of acaricides is not recommended for killing mites.

Physical measures, such as freezing, heating, and desiccation, theoretically should be effective; however, there are no clinical trials that have demonstrated benefit from such interventions. Therefore, their use is considered optional. Regular washing of bedding and clothing has been shown to effectively remove mite allergens and to kill mites. Most mites that are killed in the washing process die by drowning. Although higher temperature kills slightly more mites, this comes with an increased risk of scalding if home hot water is kept at 130°F or higher. For this reason, it is recommended that home water temperatures be no higher than 120°F and that washing be performed at weekly intervals.

The most effective way to manage reservoirs of mite allergens is to remove them completely from the environment. That means removing carpets, drapes, and upholstered furniture and sealing mattresses, box springs, and pillows in mite-impermeable covers. Because many home occupants are unlikely to comply with such measures, partial interventions may be an appropriate beginning. If symptoms persist after dust mite decreasing interventions, it may help to determine whether such persistence is due to failure of the intervention to decrease exposure or to the presence of other exposures that have not been removed. For that reason, it may help to collect a preintervention dust sample so that it can be compared with a sample collected after the intervention. Many analytic laboratories can measure mite allergens to determine whether the intervention is successful. Such measurements should be performed on dust samples because they are more reliable than air samples and they provide the same type of information.

Methods for removing mite allergens from reservoirs include regular vacuuming with a high-efficiency vacuum and the use of mite-impermeable mattress, box spring, and pillow encasings. Use of tannic acid as a mite allergen denaturant is not effective and therefore not recommended. Regular (at least weekly) vacuuming is essential for preventing buildup of mite allergens in homes with carpets. To be effective, a vacuum needs to capture particles that carry mite allergens to prevent their dispersal. Although vacuuming does not remove all live mites, mite allergens in the form of fecal particles can be removed. Over time, the amount of exposure to mite allergens has been shown to decrease sufficiently for health benefits to be possible. Bedding and furniture also can be vacuumed to decrease mite allergen exposure from those reservoirs.

Mattresses, box springs, and pillows are major sources of mites and mite allergens. The most effective way to prevent mite colonization is to encase a mattress, box spring, or pillow in a mite allergen-impermeable encasing. Existing mattresses, box springs, and pillows can be kept if they are encased in allergen-impermeable covers to entrap already-present mites and mite allergens. There are several different types of mattress encasings, including woven microfiber encasings, which prevent mite allergen escape yet allow air and water vapor to pass freely through the fabric. Woven microfiber fabrics with a mean pore size smaller than 10  $\mu$  can effectively block passage of Der p 1, whereas a mean pore size smaller than 6  $\mu$  is necessary to block cat allergen Fel d 1. Nonwoven encasings are not recommended because they trap mite allergens and are not washable, leading to allergen accumulation. Although encasings effectively contain mite allergens, in many cases mite covers alone are unlikely to achieve a clinical benefit unless they are used as part of a more comprehensive multifaceted avoidance plan.

HEPA filtration is of uncertain benefit, although it can decrease local exposure to airborne mite allergens and to some irritants. If



used, HEPA cleaners should be placed in areas of mite contamination where air disturbance is likely to suspend particles so that they are available for removal. Laminar flow cleaners that remove particles from the breathing space of beds have been demonstrated to be of some benefit, although they may not be practical for routine use.

Overall, there is evidence that a multifaceted approach using a combination of techniques for dust mite avoidance that includes repetitive and sequential interventions can decrease mite exposure. Such interventions should be recommended for patients with dust mite allergy who are at risk of mite exposure. Therefore, combinations of interventions for mite avoidance should address facilitative factors, sources, and reservoirs. The most effective combination includes maintaining humidity at 35% to 50%, regular washing of bedding to remove mites and mite allergens, regular vacuuming with a high-efficiency vacuum, use of mattress and pillow encasings, and HEPA filtration if deemed necessary.

Allergen immunotherapy (subcutaneous and sublingual) with dust mite extract has been shown to be effective for treating asthma and rhinitis in mite-allergic individuals. In addition, there is some evidence that patients with atopic dermatitis may benefit from dust mite immunotherapy. To be useful for SCIT, an effective dose of mite allergen needs to be given (7 µg of Der p 1 per dose for European extracts and 500–2,000 AU per dose for US extracts). For SLIT, 4,200 AU containing approximately 70 µg of Der f 1 given daily has been shown to be effective. The frequency of administration in studies showing efficacy have ranged from weekly to monthly once maintenance is reached for SCIT and daily to 3 times per week for SLIT once a maintenance dose is achieved. There is no evidence to support giving lower doses more frequently or higher doses less frequently to obtain similar efficacy. Dust mite extracts are

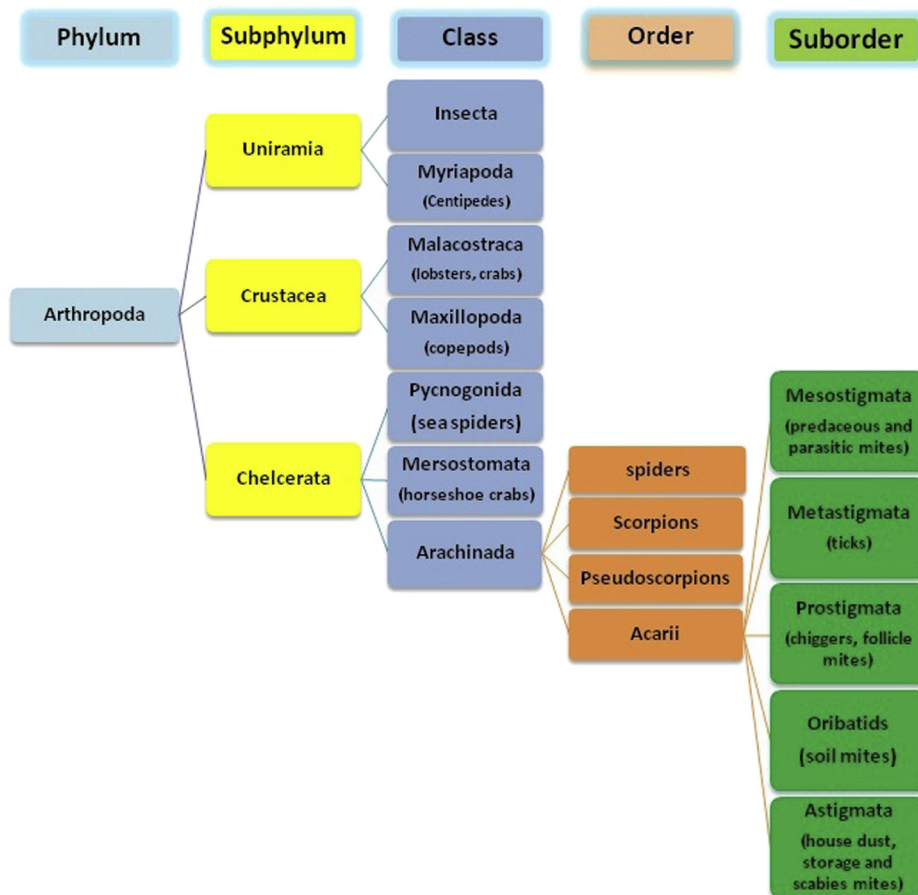
compatible with pollen and animal dander extracts and can be mixed with fungal and cockroach extracts provided they are kept in glycerin at a concentration of at least 10%. In general, 3 to 5 years of immunotherapy is sufficient to obtain maximum benefit from immunotherapy for dust mite–induced asthma and rhinitis.

**Overview of dust mites**

*Dust mite taxonomy*

Mites and ticks are 8-legged arthropods called *arachnids* that belong to the taxonomic order of Acari, which comprises tens of thousands of species grouped under several suborders, families, and genera. Most of these mites live freely in various biologic habitats, are very diverse in form and behavior, and function in the biologic recycling process as scavengers or saprophagous mites. Other mite species are plant parasites and major pests for crops, and still others can transmit diseases to humans (chiggers, ticks). However, relatively few species of mites, which belong to a particular taxon (Astigmata), have clearly been shown to produce allergens that induce IgE-mediated allergic reactions in susceptible individuals.

House dust mites were recognized as the major source of the allergens in house dust in 1967 when Voorhorst et al<sup>1</sup> in the Netherlands and Miyamoto et al<sup>2</sup> in Japan reported the identification of *D pteronyssinus* as a major dust mite in house dust. House dust mites belong to the phylum Arthropoda (ie, animals with external skeletons and jointed limbs), subphylum Chelicerata, class Arachnida, order Acari, and suborder Astigmata (Fig 2).<sup>3,4</sup> The term *house dust mites* has traditionally been used for members of the Pyroglyphidae family that live permanently and almost exclusively



**Figure 2.** Taxonomy of dust mites.

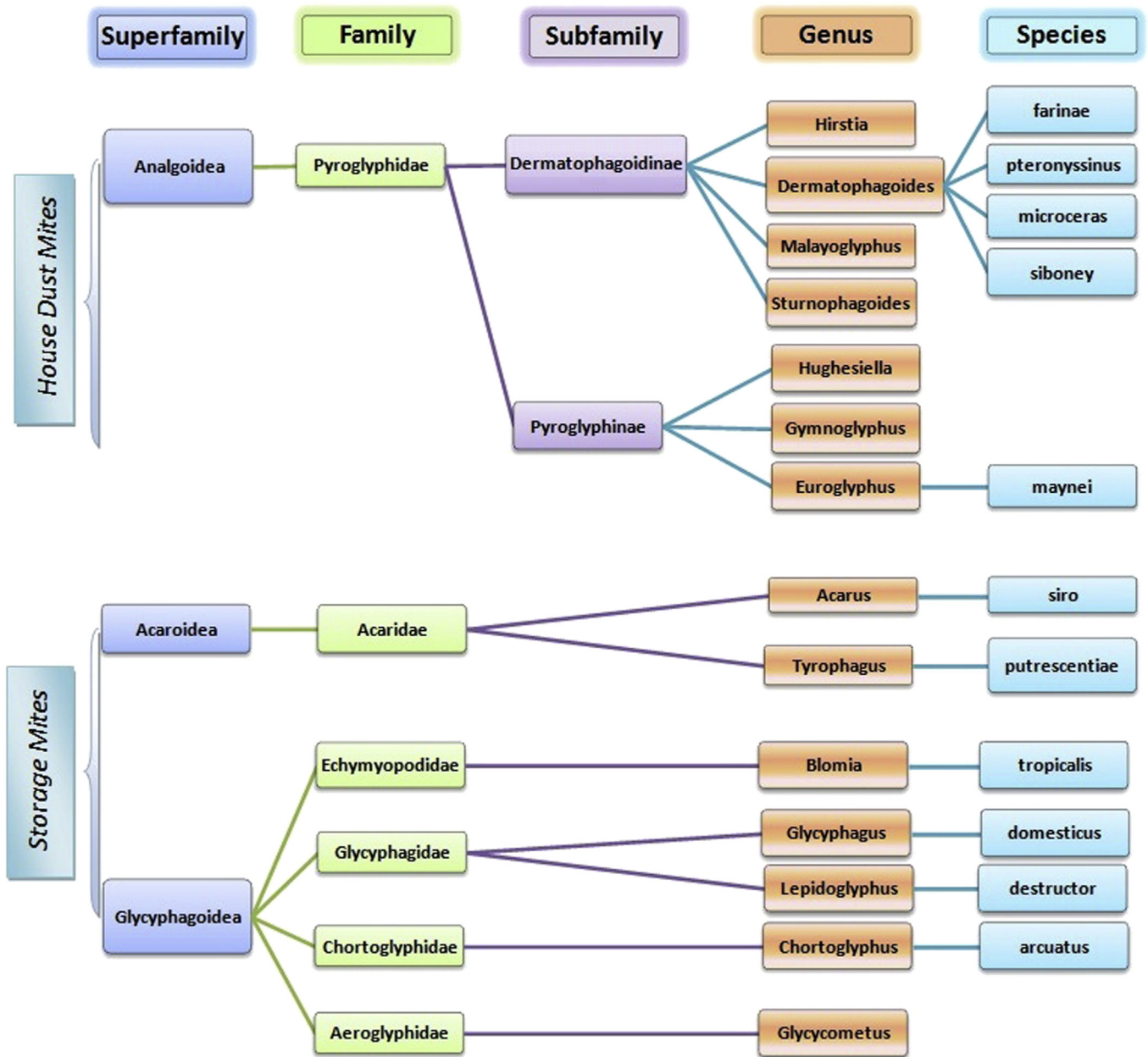


Figure 3. Taxonomy of dust mite species.

in house dust, although dust mites from other families have been found in house dust. The term *domestic mites* includes house dust mites of the Pyroglyphidae family and other Astigmatid mites traditionally referred to as *storage mites* or *stored-products mites*, which belong to different taxonomic families (Acaridae, Glycyphagidae, Echymyopodidae, and Chortoglyphidae; Fig 3).<sup>3</sup> Several species of storage mites are a potent source of allergens and can be found in house dust. Some other mite species of different taxonomic classes, which may be found in house dust, are predatory mites (Cheyletidae), parasitic mites of plants such as spider mites (Tetranychidae), and glistening mites (Tarsonemidae). Although their clinical importance is minor, several species of mites besides those found in house dust can induce allergic reactions, such as the citrus red mite (pest in apple orchards)<sup>5</sup> and the mite *Hemisarcoptes cooremani* (pests in orchards and gardens).<sup>6</sup>

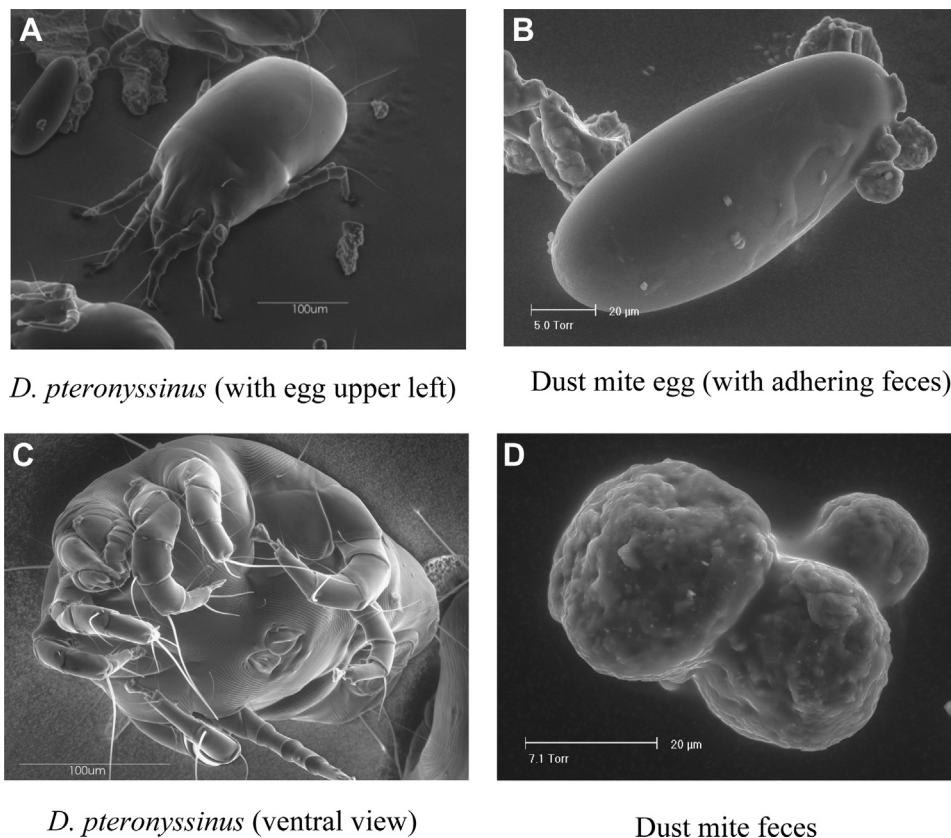
House dust mites are named according to a scientific system consisting of the genus name, such as *Dermatophagoides*, and a species

name, such as *farinae*. This binomial name is always written in italics. The family Pyroglyphidae is composed of about 16 genera and 46 species,<sup>7,8</sup> and at least 13 species have been found in house dust and recorded from locations throughout the world and across all continents.<sup>3</sup> However, 3 species, *D pteronyssinus*, *D farinae*, and *Euroglyphus maynei*, are most common, comprising 80% to 90% of house dust mite fauna.<sup>9</sup> *Blomia tropicalis*, a storage dust mite, is a common dust mite found in homes in tropical and subtropical regions.

#### Biology and physiology

Adult house dust mites have an oval shape and creamy to translucent white bodies that measure 0.2 to 0.4 mm and are barely visible to the naked eye.<sup>10</sup> Although electron microscopic images are widely available, such images may give the false impression that dust mites are so small as to require an electron microscope for visualization; in reality, they are easily seen under low power





**Figure 4.** Images of dust mites, eggs, and feces. Copyright © Mission: Allergy, Inc. Used with permission.

microscopy at  $\times 20$  to  $\times 80$  magnification (Fig 4). Dust mites feed mainly on organic detritus that accumulates in house dust, including desquamated human or pet skin scales, which are colonized by fungi, yeasts, and bacteria.<sup>11,12</sup>

There are several aspects of the biology and physiology of dust mites that are relevant to allergy, including food and water requirements, heat requirements, habitat, size, life cycle, and gastrointestinal allergen production. Water balance is critical to house dust mite survival. House dust mites are about 75% water by weight and do not drink or urinate. They obtain and maintain their water balance through uptake of water vapor when the RH is at least approximately 65%, and they experience water loss by evaporation when the surrounding RH decreases below approximately 55%.<sup>13</sup> The critical lowest humidity is temperature dependent and ranges from 55% to 75% RH over the temperature range of 15°C to 35°C<sup>20,21</sup> with *D pteronyssinus* and *D farinae* appearing to thrive best at 75% to 80% RH and 25°C to 30°C (77–86°F).<sup>10</sup> Although lacking eyes, dust mites are light sensitive and photophobic, and thus live deep within soft substrates, such as pillows, mattresses, and carpets, where moisture is retained and humidity fluctuations are minimized. Because they move away from light, dust mites do not live on hard exposed surfaces, although some temporarily migrate to the top of carpeting during the dark of night. It is not uncommon to find thousands of mites in a single gram of house dust.<sup>14</sup>

Dust mites are equipped with many biophysical mechanisms, including timely excretion of feces, which allow them to survive prolonged periods of drought.<sup>15</sup> They maintain internal water homeostasis by specialized organs, the supracoxal glands, located at the base of the first pair of legs. These glands concentrate sodium and potassium chloride, which act to osmotically absorb water vapor from the environment. However, these glands can maintain a positive water balance only at an ambient RH of at least 50%. This dependence on environmental factors of temperature and RH is

reflected in seasonal fluctuations in dust mite numbers and allergen levels in different parts of the world.<sup>16</sup>

Dust mites have a well-developed digestive tract, including an elaborate system of mouth parts (chelicerae and pedipalps), salivary glands, and a duct consisting of esophagus, midgut (food absorption), hindgut (water resorption), and slit-formed anus.<sup>17</sup> When a mite has eaten, cells from its gut containing digestive enzymes form a peritrophic membrane that adheres to the surface of the ingested food. In the posterior midgut, the peritrophic membrane-wrapped food balls coalesce to be excreted later as fecal pellets.<sup>18</sup> Fecal pellets are produced by house dust mites at a rate of 20 pellets per day, vary in size from 20 to 40 µm, and are considered a rich source of digestive enzyme-derived allergens.<sup>19,20</sup> The density of fecal pellets allows them to become airborne and easily inhaled when the substrate in which they were deposited is disturbed (eg, by making a bed, walking on a carpet, or moving on a pillow), followed by settling within 20 to 30 minutes.

In contrast to the gastrointestinal system, house dust mites have no organized respiratory structure or external openings for ventilation. They are aerobic and exchange oxygen and carbon dioxide by passive diffusion across their cuticle.

#### Reproduction

House dust mites reproduce sexually and adult male and female mites have complete and elaborate sexual organs, which are often helpful as identification characteristics.<sup>21</sup> Because temperatures and RH are not uniform in the various areas where house dust mites are found, the rate of reproduction, development, and mite population growth vary.<sup>8</sup> For example, mite populations in carpets over slab floors that remain cool develop more slowly than populations inhabiting mattresses or sofas.

The life cycle of the most commonly studied house dust mites, *D farinae*, *D pteronyssinus*, and *E maynei*, consists of 5 stages: an egg,

a 6-legged larva, two 8-legged nymphal stages (protonymph and tritonymph), and male or female adult.<sup>22</sup> Six-legged larvae hatch from the eggs and remain active for some time before shedding their integument and becoming 8-legged resting protonymphs. The protonymphs in turn shed their integument and become larger active tritonymphs. The tritonymphs undergo another shedding of skin, developing into active adult mites.<sup>23</sup> The shed integuments and exoskeletons are an important secondary source of mite allergens and immunomodulators, including chitin. The duration of this developmental stage varies from 19 to 33 days at favorable conditions of temperatures from 22°C to 32°C and approximately 75% humidity.<sup>22</sup> After reaching the adult stage, dust mites can live for about 4 to 6 weeks and mate 1 to 3 times, with the female mite laying about 1 to 2 eggs per day, for a total of 50 to 80 eggs in its lifetime.<sup>24,25</sup>

In total, the average life cycle of a house dust mite, starting from the hatched egg stage, ranges from approximately 60 to 120 days, depending on ambient RH and temperature.<sup>22,26</sup>

### Clinical assessment

Algorithm (Fig 5)

#### Annotations

#### 1. Patient with possible dust mite-related illness.

Patients generally present for evaluation if they have an illness such as eczema, rhinitis, or asthma. Rhinitis and asthma are respiratory illnesses that can be exacerbated by inhalation of dust mite allergen; eczema can be exacerbated by skin contact, given sensitization and sensitivity. Because exposure to dust mites also can trigger symptoms in nonsensitized individuals, sensitization per se is not the only criterion for possible morbidity from exposure.

This algorithm can be used to evaluate a patient's risk for morbidity from dust mite exposure regardless of his or her sensitization status. The purpose of this first algorithm is to determine which patients would most likely benefit from a more complete evaluation of their home environment for possible dust mite exposure. As such, this section should be used as a screening procedure. The 2 factors that determine whether further dust mite assessment is indicated include patient factors and environmental factors. The next 2 questions address each of these issues in turn.

#### 2. Increased risk for dust mite morbidity?

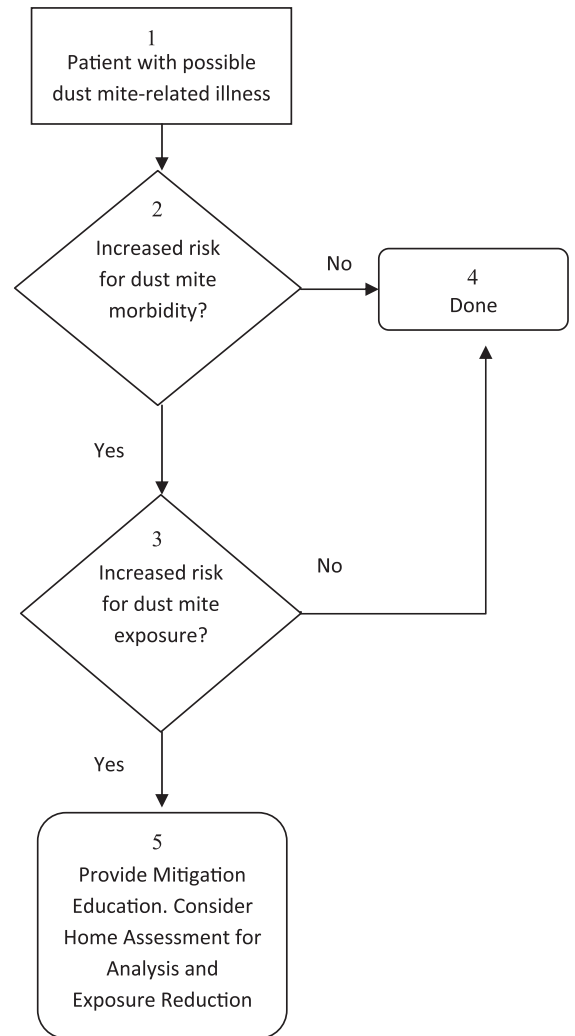
Patients who are not sensitized to dust mites but who are at increased risk to become sensitized ideally should be identified before the sensitization takes place and therefore deserve a greater degree of evaluation for dust mite exposure. Patients are at increased risk of dust mite sensitization if they have an elevated total IgE; if they are sensitized to other allergens (increased specific IgE or positive skin test reaction); if they have asthma, eczema, or allergic rhinitis; or if there is a strong family history of atopy. The latter criteria are particularly important in very young children because they might not yet have developed evidence of atopy.

There are some basic questions that can be used to assess the likelihood that a patient will experience morbidity from dust mite exposure:

- Does the patient have eczema, asthma, or rhinitis?
- Is there a positive family history for atopy?
- Does the patient have atopy? This could be manifested as an elevated total IgE or the presence of specific IgE antibodies.

#### 3. Increased risk for dust mite exposure?

This question can be used to determine whether a patient is at increased risk of exposure to elevated levels of dust mite allergens. Dust mites tend to be found in locations where there is warmth and moisture. They can survive in cold, dry climates by occupying human residences that are artificially heated. Home and location



This is an iterative process.

Exposure and associated risk factors can be time-varying

Figure 5. Algorithm 1.

factors associated with increased dust mite exposure are discussed in the following sections.

#### Facilitative factors

For dust mites, the most important facilitative factor is moisture, so questions to ask relate to this factor. In Appendix A, there is a detailed discussion of moisture and humidity. In Appendix B, there is a 3-step guide for clinicians use to assess whether their patients might be at increased risk for dust mite exposure. In summary, the following questions address facilitative factors.

- Does the patient live in a location with a warm, humid or damp climate? The Köppen climate classification ([http://webmap.ornl.gov/wcsdown/wcsdown.jsp?dg\\_id=10012\\_1](http://webmap.ornl.gov/wcsdown/wcsdown.jsp?dg_id=10012_1)) has maps with climate zones related to temperature and humidity for the United States that can be used to determine the answer to this question for a particular location. Microclimate also is important; general climatic information must be interpreted in the context of the patient's residence and work locations.
- What is the RH in the patient's home? In general, an RH greater than 50% facilitates mite growth, whereas air that is too dry (<25% RH) can serve as a respiratory irritant. Patients should be

encouraged to obtain a hygrometer to measure indoor RH and to make indoor climate adjustments as necessary to keep the RH at 35% to 50%. Because dust mite habitats, such as mattresses, upholstered furniture, and settled dust, are sensitive to changes in ambient RH, this should be sufficient to control mite populations.

- Does the patient's residence have microenvironments in which dust mites might thrive? Some building materials are more likely to absorb water than others, so it is important to understand what materials are in a patient's home and the mean humidity in house. Absorption of moisture is faster than desorption, so materials that bind water, such as house dust, tend to buffer the humidity. For that reason, moisture control must be consistent.

**Reservoirs**

- How old is the building in which the patient lives? Older buildings have had more time to become contaminated by dust mites and their allergens. Regardless of a building's age, low levels of humidity will lead to decreased mite contamination over time.
- How old are the pieces of upholstered furniture, mattresses, and carpeting? Older furniture and mattresses are likely to have larger numbers of dust mite and to have accumulated increased concentrations of dust mite allergen over time. If the furniture is imported from a different location where mite growth is supported, there could be mite allergen contamination although the current environment does not support mite growth.
- How frequently is bedding changed and how is it washed? What type of bedding does the patient sleep on? Bedding should be washed weekly to remove mite allergens and to decrease the mite population.
- If there is carpeting, how frequently is the home vacuumed? Ideally the carpeting should be vacuumed at least weekly or more frequently depending on traffic and use. Does the carpeting sit on a concrete slab that would tend to provide moisture through intrusion or condensation? The carpet backing can become damp, promoting mite growth, even if the pile remains dry.

Depending on the answers to these questions, it may be of value to offer the option of surveying a patient's home with a simple or advanced screening method. This could involve collecting a sample of dust from the home environment and testing the sample for dust mite allergen. Mite allergen measurement can be performed using dust from a used vacuum bag; however, dust collection by a trained technician is ideal and can help to pinpoint the main sources of exposure within a home. If a used vacuum bag from the resident's home is used, one should realize that it is the accumulation of many different locations within the home and represents a period that may or may not reflect current exposure in that home. The 2 dust mite allergens for which standardized measurements are available are Der p 1 and Der f 1. A rapid test is also available for use in the home to quickly identify dust mite products.

**4. Done**

Because the patient is not at increased risk for dust mite morbidity or exposure, it is not necessary to perform additional procedures. However, exposure and associated risk factors can change over time. Periodic re-evaluation of the risk for dust mite allergen exposure should occur depending on the clinical history.

**5. Provide mitigation education and consider home assessment for dust mite analysis and decreasing exposure.**

Based on the environmental history gathered in answer to questions 1, 2, and 3, the clinician can offer specific education regarding the mitigation of facilitative factors and abatement of reservoirs. These activities often can be carried out by patients and/or their families and result in a decrease of live mites and mite allergen. There are often other instances when homes with

elevated dust mite allergen levels in settled dust should be followed up with a more complete assessment by a professional service. Based on the physician's understanding of the patient's motivation and ability, the physician should recommend appropriate steps that are likely to lead to decreased exposure. Because this is often an iterative process, a combination of these 2 interventions may be appropriate for long-term decrease. When a professional is recommended, suggestions for selecting such a service are provided in [Appendix A](#) of the Rodent Practice Parameter.<sup>27</sup>

**Environmental assessment, mitigation, and abatement**

Algorithm (Fig 6)

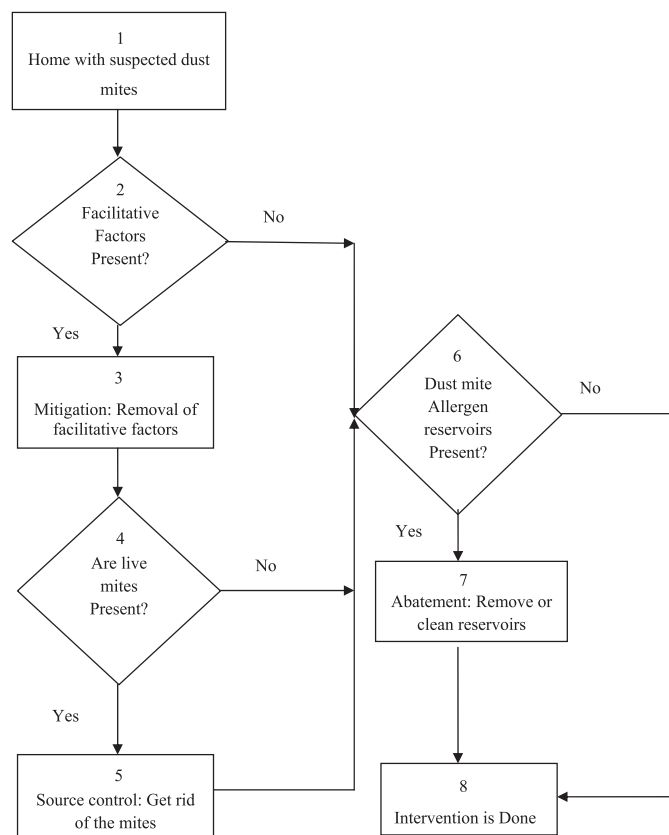
**Annotations**

**1. Home with suspected dust mites.**

Mite assessment and decreasing exposure are indicated when a building's occupants are at increased risk of morbidity from mite exposure (atopy, mite-specific IgE, family history) and the home has an increased likelihood of mite contamination (increased humidity/moisture, older building, upholstered furniture, carpeting, etc). If dust mite allergens have been measured in dust, increased concentrations of Der p 1 or Der f 1 also indicate a need for an environmental intervention.

**2. Are facilitative factors for dust mite present?**

Dust mites require moisture, warmth, and a source of food to survive. There can be seasonal variations in these factors that should be taken into account. For example, summer is warm and damp in some locations so mite populations expand, whereas winter is cold and dry so populations tend to decrease. If facilitative factors are present, then mites are likely to thrive and allergen removal alone is unlikely to succeed.



This is an iterative process. Exposure and associated risk factors can be time-varying.

**Figure 6.** Algorithm 2.

The tools necessary to identify facilitative factors are listed below.

- Hygrometer and thermometer to determine RH and dew point. This can be used by the occupant to determine whether decreasing humidity is needed.
- Moisture meter to measure available water within a material (usually performed by a professional when excessive moisture is suspected). This can be used to identify sources of moisture when they are not apparent.

### 3. Mitigation: remove facilitative factors.

Once excessive moisture is identified, it is important to remove it. Condensation can be decreased by keeping the RH below 50% using a dehumidifier and/or air conditioning. If used, the dehumidifier needs to be emptied regularly or set to drain continuously, and it should be located in areas where dampness is likely to occur. Air conditioners need to run long enough to remove sufficient moisture from the air to decrease RH. If the air cools too quickly, as could occur with an oversized unit, adequate dehumidification might not be achieved.

Sources of intrusion or leakage should be identified, repaired, and/or sealed. Surfaces on which condensation can occur should be appropriately insulated and sealed with special attention to proper placement of vapor barriers. Cold water pipes may need to be insulated to prevent condensation.

### 4. Are live mites present in the home?

Once facilitative factors have been removed, or if they are not present, it is unlikely that live mites can continue to live in the house and it may not be necessary to test for their presence. Homes with a history of RH above 50% or microenvironments in which mites can grow are likely to have live mites present. For mites to survive, the RH in a house needs only to exceed 50% for 1 hour per day, and 2 to 3 hours per day is necessary for mites to reproduce.

Although moisture is a limiting facilitative factor, food generally is plentiful and does not limit mite survival or growth. Mites also prefer cool, dark locations as is found in a box spring or carpet pad, although it is not usually feasible to remove these factors short of removing carpeting completely. Although it is possible to identify

live mites in dust samples microscopically, it is easier to simply assume that mites are present if facilitative factors for their growth are present.

### 5. Source control: get rid of the mites.

The presence of live, allergen-producing dust mites continuously replenishes mite allergens in the environment. Ideally, mite populations should be eliminated or at least significantly decreased or else it is unlikely that exposure can be decreased sufficiently to improve health. The most effective method to eliminate mites is to decrease their access to moisture by maintaining the indoor RH below 50% for sustained periods. Mattress, box spring, and pillow encasings also may be used to separate live mites and their allergens from building occupants. Owing to their lack of effectiveness, the use of acaricides is not recommended.

### 6. Are dust mite allergen reservoirs present?

Dust mite reservoirs include carpeting, upholstered furniture, mattresses, bedding, and settled dust. The presence of these reservoirs generally is obvious by history and visual inspection. The presence of mite allergens can be confirmed by measuring Der p 1 and/or Der f 1 in dust samples. Because the 2 species are not always correlated, measurement of allergens from these species (or a cross-reactive allergen) is ideal if allergen measurement is performed.

### 7. Abatement: remove or clean reservoirs?

Abatement, or removal and cleaning, of dust mite reservoirs is necessary because mite allergens are highly stable for long periods.<sup>28</sup> This means that even if the mites are killed, occupants will continue to have exposure to mite allergens and other immunomodulators such as chitin from their exoskeletons. The most effective way to remove reservoirs is to eliminate carpeting, furniture, and mattresses from the home. In many cases, this is impractical. For that reason, regular vacuuming with a HEPA or cyclonic vacuum is necessary because it removes dust mite-containing particles from carpeting and furniture. Mattress, box spring, and pillow encasings can serve as a barrier between sleepers and mite allergens contained in those substrates. Bedding should be washed regularly as discussed in the washing section of this parameter. Owing to the intermittent nature of airborne mite exposure, HEPA filters have not been shown to be effective for

**Table 1**  
Cross-reactivity patterns among dust mite allergens

Number	Function	MW (kDa)	Der p	Der f	Blo t	Aca s	Gly d	Lep d	Tyr p	Ale o	% + sIgE <sup>a</sup>
1	cysteine protease	27	yes	yes	yes	?	?	?	yes	yes	87
2	NPC2 family	15	yes	yes	yes	?	yes	yes	yes	?	98
3	trypsin	29	yes	yes	yes	yes	?	yes	yes	yes	16
4	A-amylase	56	yes	yes	yes	yes	?	yes	yes	yes	25
5	?	14	yes	yes	yes	?	?	yes	?	?	37
6	chymotrypsin	25	yes	yes	yes	yes	?	yes	yes	yes	41
7	?	24	yes	yes	?	?	?	yes	?	?	46
8	GST	27	yes	yes	?	?	?	?	?	?	40
9	collagenase	29	yes	yes	?	yes	?	yes	yes	yes	92
10	tropomyosin	37	yes	yes	yes	?	?	yes	yes	?	81
11	paramyosin	98	yes	yes	yes	?	?	?	?	?	87
12	?	14	?	yes	yes	?	?	?	?	?	?
13	FA binding Protein	?	?	yes	yes	yes	?	yes	yes	?	?
14	apolipoprotein	177	yes	yes	?	?	?	?	?	?	84
15	chitinase	98	yes	yes	?	?	?	?	?	?	70
16	gelsolin/villin	53	yes	yes	?	?	?	?	?	?	47
17	Ca <sup>2+</sup> binding protein	53	yes	yes	?	?	?	?	?	?	35
18	chitinase	60	yes	yes	?	?	?	?	?	?	54
19	antimicrobial protein	?	?	?	yes	?	?	?	?	?	?
20	arginine kinase	20	yes	yes	?	?	?	?	?	?	?
21	?	?	yes	yes	yes	?	?	?	?	?	?
22	?	14	yes	yes	?	?	?	?	?	?	?
23	?	14	yes	?	?	?	?	?	?	?	?
24	troponin C	18	yes	yes	?	?	?	?	yes	?	?

Abbreviations: Aca s, *Acarus siro*; Ale o, *Aleuroglyphus ovatus*; Blo t, *Blomia tropicalis*; Der f, *Dermatophagoides farinae*; Der p, *Dermatophagoides pteronyssinus*; FA, fatty acid; GST, glutathione S-transferase; Gly d, *Glyciphagus domesticus*; Lep d, *Lepidoglyphus destructor*; MW, molecular weight; sIgE, specific IgE; Tyr p, *Tyrophagus putrescentiae*.

<sup>a</sup>For Der p proteins, dependent on population studied.



decreasing mite allergen exposure, although they may be useful under specific circumstances.

### 8. Intervention is done.

Once facilitative factors are removed, the dust mites are killed, and reservoirs are cleaned, the intervention is completed. It is still desirable to maintain an ongoing program of humidity control, mite allergen containment, and reservoir cleaning, but otherwise the occupant is no longer at increased risk of morbidity from dust mite exposure.

## Functional overview of mite allergens

### General considerations

Many mite allergens from *D pteronyssinus* and *D farinae* show significant homology. A discussion of such allergens with a brief description of their known properties is presented in Appendix C. A list of mite allergens from various mites is presented in Table 1. The functional effects ascribed to most of these proteins involve, in one way or another, the activation of innate immune mechanisms, many of which seem to favor T-helper cell type 2 (T<sub>H</sub>2) responses. Although any of these proteins might induce IgE responses, collectively they seem to complement each other in this respect through bystander immunologic effects.

Allergens from mites include commonly encountered functions of allergens from a wide variety of sources, such as proteases (Der p 1, 3, 6, 9, 20), lipid-binding proteins (Der p 2, 7, 13, 14), contractile proteins (Der p 10, 11, 16, 17, 24), glycosidases and carbohydrate-binding proteins (Der f 4, 12, 15, 18, 23), and glutathione S-transferase (Der p 8). Other functions of mite allergens include heat shock protein-70. In addition, many allergens, including Der p 5, 19, 21, and 22, are unidentified as to function.

### Proteases

Der p 1 and Der f 1 are glycoproteins of the papain family with cysteine protease activity similar to that of some plant allergens (kiwi Act d 1, actinidin, pineapple Ana c 2, bromelain, fig ficin, papaya Car p 1, papain, soybean Gly m Bd30K, and mammalian enzymes such as cathepsins H and B). These mite allergens originate from the intestinal tract of the mite. Der p 1 can cleave the CD23 IgE receptor from human B-cell membranes, thus ablating the feedback inhibitory mechanism that normally limits IgE synthesis.<sup>29</sup> Der p 1 also can cleave the CD25 subunit of the T-cell interleukin-2 receptor, which can promote T<sub>H</sub>2 responses. In addition, Der p 1, 3, 6, 9, and 20 can proteolytically degrade tight junctions in lung epithelium and cause the release of proinflammatory cytokines from bronchial epithelial cells, mast cells, eosinophils, and basophils. These synergistic effects can promote IgE synthesis and have direct inflammatory effects on lung epithelium, which in turn could explain why mite allergens are closely associated with asthma. More than 50% of allergic patients and up to 80% of children with asthma are sensitized to Der p 1. Der p 1 appears to be sufficient to diagnose up to 97% of dust mite–allergic patients.<sup>30</sup>

Der p 3, 6, and 9 are serine proteases. Der p 3 is a trypsin-like enzyme and is a major constituent of mite feces. It is quite similar to the cockroach Bla g 10. Der p 6 is chymotryptic and with Der p 9 exhibits collagenase activity. Trypsin-like enzymes also are found in insect venoms. Trypsin can trigger protease-activated receptor-2, whose cleavage results in the initiation of multiple G-protein–coupled signaling cascades. These cascades result in many events that promote T<sub>H</sub>2 skewing and inflammation, such as the production of thymic stromal lymphopoietin and interleukins 4, 5, 13, 21, 25, and 31.

House dust mites have proteases that can activate protease-activated receptor-2. Exposure to dust mites has been shown to increase the secretion rate and number of responding glands in

patients with allergic rhinitis even if they are not mite sensitive, suggesting a nonspecific proinflammatory mechanism that is not dependent on specific IgE.<sup>31</sup>

### Glycosidases and carbohydrate-binding proteins

Der p 4, 15, 18, and 23 are proteins that interact with carbohydrate moieties. Der p 4 is an  $\alpha$ -amylase and Der p 15 and 18 are chitinases. Der p 20 is an arginine kinase that also binds chitin. These proteins are widely distributed throughout nature and for unknown reasons can be potent allergens from many different sources. Alpha-amylases from the storage mite (*Acarus siro*) and fungal amylases in flours and some grasses are responsible for some types of occupational asthma. The amylase activity of dust samples correlates with counts of live mites and with concentrations of Der p 1. Der p 4 and Eur m 4 sequences are 90% identical and 50% identical, respectively, to other insect and mammalian  $\alpha$ -amylases.<sup>32</sup> Der p 15 and 18 are chitinases related to pathogen resistance (fungal, worm, and other arthropods). The chitinases seem to be very important in dog allergic reactions but somewhat less so for humans. From a functional point of view, sensitization to chitinases from other sources has been identified as being responsible for the latex fruit syndrome. In addition, chitin fragments are immunomodulatory and the chitinases may facilitate their production from plants, fungi, and insects, helping to induce T<sub>H</sub>2 responses.

### Muscle, cytoskeleton, and Ca<sup>2+</sup>-binding proteins

Der f 10, 11, 16, 17, and 24 are tropomyosin, paramyosin, gelsolin, Ca<sup>2+</sup>-binding protein, and troponin C, respectively. These proteins are involved in the structural aspects of cells, in addition to cytoskeleton organization, membrane trafficking, and lipid signaling, such as the regulation of diacylglycerol and phosphatidylinositol 4,5-bisphosphate signaling pathways. Der f 10 tropomyosin is a highly conserved protein throughout insects, shell fish, and parasites and as such represents a cross-reactive and possible cross-sensitizing allergen. Two studies have indicated that 5.6% to 15.2% of dust mite–allergic patients have IgE to Der p 10.<sup>33,34</sup>

### Lipid-binding proteins

Der p 2, 7, 13, and 14 are lipid-transfer or lipid-carrying proteins. These also are commonly found as allergens from different sources, including plants. Der p 2 is closely related to lymphocyte antigen 96 (MD-2 protein) that allows toll-like receptor 4 to bind to endotoxin. Thus, Der p 2 seems to be related to the activation of innate immunologic mechanisms, many of which seem to favor T<sub>H</sub>2 immunologic responses. Lipid-binding proteins participate in signaling pathways that affect the distribution and activity of lipid-metabolizing enzymes and protein kinases that regulate the activity of many of these enzymes. Lipid-transfer proteins from different sources seem to be potent allergens.

### Others

Cross-reactivity has been observed between ascaris and dust mites species *B tropicalis*, *D pteronyssinus*, and *D farinae*. Among allergic subjects, 70% exhibited ascaris-specific IgE, whereas 20% to 28% of ascaris-allergic subjects showed dust mite–specific positive IgE. Ascaris antigens inhibited up to 92% of dust mite–specific IgE in mite allergic subjects and up to 54% of ascaris-specific IgE was inhibited by dust mite allergens.<sup>35</sup>

In 1 study, commercial dust mite extracts were analyzed for endotoxin levels, protease and chitinase activities, and effects on transepithelial resistance, junctional proteins, and proinflammatory cytokine release in human bronchial cells. These extracts varied extensively in serine protease activity, including the ability to induce dust mite–specific IgE, goblet cell hyperplasia,



eosinophilic inflammation, and airway hyper-reactivity independent of protease activity.<sup>36</sup>

### Measurement of dust mite allergens

Efforts to measure the number of mites and the allergenic protein products they produce in house dust have been ongoing since dust mites were recognized as major allergenic species.<sup>2,37</sup> Early mite enumeration involved microscopic examination of house dust and vacuum samples of bedding, including counts of observable mite bodies.<sup>38</sup> Because house dust mites excrete guanine, the measurement of guanine in house dust has been used to estimate mite presence.<sup>39,40</sup> The first commercial test detected guanine in the dust based on the assumption that most guanine in dust comes from mite fecal pellets. The test used a dipstick that was inserted into a suspension of dust, leading to a color change that could be compared with an included color chart card to provide an interpretation. This test correlated well with dust mite allergen, although this test is no longer available.<sup>41</sup>

The earliest reported immunologically based assay for dust mite antigens found in a PubMed search of *dust mite* and *allergy* was in 1979.<sup>42</sup> This assay used polyclonal antibodies raised in rabbit as part of a counterimmunoelectrophoresis method. These investigators reported that mite antigens were detected in 64% of 105 dust samples tested and there was good correlation with microscopic visual observation methods. In 1981, a 24-kDa protein isolated from dust mite feces was identified that bound a large percentage of dust mite–directed human IgE. An inhibition radioimmunoassay method for quantification of this protein also was described.<sup>19</sup> The development of monoclonal antibodies to mite allergen protein and the identification of individual epitopes<sup>43</sup> accompanied the development of a specific assay for *D pteronyssinus* antigen P1 (Der p 1) in 1984. Subsequently, 4 IgE-targeted proteins were identified from *D farinae*,<sup>44</sup> and the field of quantification of mite-specific allergenic material in house dust was developed. These early identified allergens eventually were renamed Der f 1, Der p 2, etc; subsequently, through the efforts of many researchers, the groups of mite-related proteins listed above were identified.

Because an assay theoretically can be developed for each mite allergenic protein, a large number of assays could be available. Practically, assays for whole dust mite, Der f 1, Der p 1, Der f 2, and Der p 2, are most frequently used and reported in the literature.<sup>45</sup> These assays are constructed from 2 monoclonal antibodies, each binding to a different site on the protein molecule; from 1 monoclonal antibody and 1 polyclonal antibody; or from polyclonal antibodies usually in an inhibition format. Assays based on these configurations have been reported that use radioimmunoassay, enzyme-linked immunoassay, and fluorescent immunoassay methods.

The most commonly available mite assays are available in a monoclonal antibody immunoassay format for Der f 1, Der p 1, Der f 2, mite group 2, and Blo t 5 (<http://inbio.com/US/Products/>). Assays for dust mite allergen proteins also are available in a multiplex format in combination with allergenic proteins from up to 5 other allergenic species,<sup>46</sup> in a chip format for general mite species present in food,<sup>47</sup> and in a screening format (<http://inbio.com/US/Products/Rapid-Test-and-Dust-Collection>), although this method has some limitations in that it measures proteins in mites and not just dust mites, including *Aleuroglyphus ovatus*, *A siro*, *Lepidoglyphus destructor*, *Tyrophagus putrescentiae*, and *Tribolium castaneum*. In addition, the test is in the research phase and currently not commercially available. At least 2 “in-home” assays are available through the Internet. One is in a dipstick format (Aclostest; Lofarma, Milan, Italy) and the other is a diffusion/migration format kit (Ventia Rapid Allergen Test; Indoor Biotechnologies, Charlottesville, Virginia). In-home dust collection kits also are available, with the dust sample then sent to a laboratory for allergen immunoassay

(MARIA Multiplex Test for Indoor Allergens; Indoor Biotechnologies; and Dust Mite Screen Check, Environmental Diagnostics Laboratory, Clearwater, Florida).

The performance of individual dust mite assays depends on the format, the test, and the experience of the laboratory performing the test. Published performance for the polyclonal whole mite assay indicates the lower limit of detection to be 100 ng/g of dust, with a sensitivity of 50 ng/g of dust.<sup>48</sup> For the monoclonal Der f 1, Der p 1, and Der p 2 assays, the lower limit of detection is reported at 2.0 ng/mL, with a sensitivity of 0.5 ng/mL; for the mite group 2 assay, the lower limit of detection is reported at 0.8 ng/mL, with a sensitivity of 0.2 ng/mL; and for the Blo t 5 assay, the lower limit of detection is reported at 2.0 ng/mL, with a sensitivity of 0.5 ng/mL (<http://www.inbio.com/UK/Products/ELISA-Kits/House-Dust-Mite>). The monoclonal assays have been shown to have good agreement with mite counts in house dust collections.<sup>49</sup> In addition to the laboratory-based immunoassays, 2 low complexity tests for the evaluation of mite presence in house dust or bed vacuum samples are available. These tests are qualitative in nature with typically 3 levels of detection (low, medium, and high). The amount of dust used for the assay contributes to the variability of test results. Therefore, it is important that sampling methodologies be standardized so that sample sizes are consistent.

The results of tests for mite allergen concentrations are highly dependent on the standards used to calibrate them. Enzyme-linked immunosorbent assay (ELISA) standards used for dust mite measurements in studies that established thresholds of exposure were recently compared with World Health Organization/International Union of Immunological Societies standards that were subjected to extensive analysis to determine their actual concentration.<sup>50</sup> Then, dose–response curves were compared with previous individual ELISA standards and allergen measurements of house dust extracts to obtain correction factors. For dust mite allergens, conversion factors were 1.7 for Der p 1 and 12.7 for Der f 1. This means that a concentration of 2  $\mu\text{g/g}$  of dust measured with the newer universal standard would be equivalent to 3.4  $\mu\text{g/g}$  for Der p 1 and 25.4  $\mu\text{g/g}$  for Der f 1 using the older standard for ELISAs. Threshold values for the old and new standards are listed in Table 2. In other words, even if patients can decrease dust mite allergen levels to 2  $\mu\text{g/g}$ , this is still a very high level of Der f 1. Patients should try to obtain more extensive allergen avoidance and not stop there.

### Exposure to dust mite allergens

Dust mites are found in geographic areas and climates with sufficient humidity to elevate moisture inside buildings and in buildings where humidity levels are raised artificially. Arid areas and high elevations generally do not support dust mite colonies indoors. It is estimated that 84% of US homes have detectable dust mite allergen. Higher concentrations of dust mite allergen tend to be found in older, single-family homes with lower household

**Table 2**

Comparison of Der f 1 and Der p 1 concentrations with previously published thresholds or cutpoints

Older value (using older standard)	Value compared with newer literature	
	Der p 1 ( $\mu\text{g/g}$ )	Der f 1 ( $\mu\text{g/g}$ )
2 $\mu\text{g/g}$	1.2	0.2
10 $\mu\text{g/g}$	5.9	0.8
Current value (using newer universal standard)	Value compared with older literature	
	Der p 1 ( $\mu\text{g/g}$ )	Der f 1 ( $\mu\text{g/g}$ )
2 $\mu\text{g/g}$	3.4	25.4
10 $\mu\text{g/g}$	17.0	127.0

Conversion factors were applied from old to new units (top) and from new units to older units (bottom).

income, musty or mildew odor, and higher bedroom humidity.<sup>51</sup> Air and dust concentrations of Der p 1 and Der f 1 also are related to the size of the family living in the home.<sup>52</sup> The concentration of mite and cockroach allergens in dust are associated with lower socioeconomic factors and increased population density.<sup>53</sup> Der p 1 allergen concentrations tend to be higher in homes with carpets.<sup>54</sup> Other factors that are associated with increased dust mite allergen exposure include absence of air conditioning and the presence of mold or mildew.<sup>55</sup>

In a survey of dust mites over a 5-year-period in 8 geographic areas of the United States, the most common dust mites were *D farinae*, *D pteronyssinus*, *E maynei*, and *B tropicalis*. All homes contained *Dermatophagoides* species mites, and most were coinhabited by *D farinae* and *D pteronyssinus*. *Euroglyphus maynei* was found in New Orleans, Memphis, Galveston, Delray Beach, and San Diego. *Blomia tropicalis* also was found in these same cities. Most homes had mite densities of at least 500 mites per gram of dust.<sup>14</sup>

Very few mites can grow if the indoor RH is lower than 45% with an indoor temperature of 22°C.<sup>56</sup> The concentration of dust mite allergens in air and dust varies within and between homes. In the United States, peak concentrations typically are found in the autumn. Dust mite allergens can display as much as a 20-fold seasonal variation that is not restricted to the houses of allergic patients. Dust from certain reservoirs such as sofas tend to remain consistently high, showing less seasonal variation than dust from other sites. Allergen levels tend to increase in July and remain elevated through December. Before this increase, mite numbers increase in June and July and decrease in September, when humidity decreases.<sup>57</sup>

In a survey of 158 houses, mean concentrations of Der p 1 were 1.9 µg/g in dust from living rooms, 1.7 µg/g from bedrooms, and 2.0 µg/g from mattresses. Der p 1 concentrations higher than 10 µg/g were found in 25% of living rooms and mattresses and in more than 30% of bedrooms. Bed and floor dust contained a wide range of Der p 1, ranging from 0.1 to 100 µg/g of dust, and this concentration correlated well with the number of mite bodies.<sup>58</sup> Der p 1 levels also were associated with window condensation, open fires, vacuum cleaner type, smokers in the house, the age of house, the use of blankets, and the temperature at which bedding is washed.<sup>59</sup>

There is still some uncertainty regarding the aerodynamic behavior of particles carrying dust mite allergens, their aerosolization, and removal from surfaces.<sup>60</sup> For example, very little dust mite allergen can be detected in the air of an undisturbed room. During domestic activities that disturb dust, 1 to 30 ng can be detected.<sup>58</sup> Allergens from dust mites tend to become airborne during disturbance and then fall rapidly, mainly because many of them are carried on fecal pellets. Dust mites produce about 20 pellets per day, each measuring 10 to 24 µ in diameter. Der p 2 and Der f 2 have molecular weights of 14,000 kDa and are associated with mite bodies. Other smaller allergens become airborne with disturbance, most of them settle within 15 minutes because of their size and weight,<sup>61</sup> and they are carried on particles that are distinct from fecal pellets. Even so, more than 95% of the allergen accumulating in mite cultures is associated with fecal particles.<sup>19</sup> In samples with more than 10 mites per 100 mg of dust, Der p 1:Der f 1 concentrations closely correlated with the number of mites counted by microscopy.<sup>49</sup>

Mite allergens generally are not found on hard surfaces.<sup>62</sup> *Dermatophagoides farinae* allergens can be detected in settled dust samples of most homes; however, it can be detected in only 20% of samples obtained by wiping walls.<sup>63</sup> Dust mites rarely survive in forced-air systems and the fecal pellets are generally too heavy to stay airborne even if expelled through a supply vent. A study of airborne and surface dust mite exposures in hospitals found low levels of mite allergen that were unlikely to be of clinical significance to mite-sensitive patients with asthma.<sup>64</sup>

Nasal air sampling has been used to measure personal Der p 1 and Der p 2 exposure in volunteers who wore nasal samplers to bed. In 1 study, Der p 1 and/or Der p particle numbers correlated significantly with mattress allergen concentrations.<sup>65</sup>

In another study from Brazil, 240 dust samples collected from 60 houses during March and July found *D pteronyssinus* as the most frequent species followed by *D farinae* and *E maynei*. *Blomia tropicalis* was found less frequently. The highest levels of Der f 1 and Der p 1 were found in bedding, with Der f 1 levels significantly higher than Der p 1 levels. There was a significant correlation between the number of mites and the corresponding allergen levels.<sup>66</sup>

Dust mites and their fecal pellets tend to be found in microenvironments where there is a food source such as human skin cells and micro-organisms plus sufficient dampness. This includes surfaces where humans sit or lie for extended periods, such as bedding and upholstered furniture. Microenvironments with those characteristics include bedding and furniture with porous surfaces and carpets. Higher dust mite allergen levels are associated with wool bedding and inner-spring mattresses.<sup>67</sup> Although mattresses are major reservoirs of mite allergen, studies have shown significantly higher levels of mite allergen<sup>68,69</sup> and mite bodies<sup>70,71</sup> in mattress bases (box springs) than in mattresses.

Personal clothing appears to be an important source of mite allergen exposure. This is particularly true of clothing that is washed less frequently. Such items tend to carry more allergen than regularly washed items and this corresponds to the amount of allergen inhaled.<sup>72</sup>

## Health effects

The health effects that can occur from exposure to dust mites can be divided into sensitization; development of a disease, such as asthma, rhinitis, or atopic dermatitis; and induction of symptoms in sensitized individuals who have developed a disease. Each of these is considered separately.

### Sensitization to dust mite

**1. Advise patients to minimize exposure of susceptible children to dust mite allergens to decrease their risk of developing mite-specific IgE. Because intermittent exposure to mite allergens can lead to sensitization, primary prevention may not be possible to achieve in regions where mite exposure is prevalent. (Strength of recommendation: strong, A evidence)**

Prevention of dust mite sensitization is important given the abundant evidence that sensitization is a risk factor for developing asthma. This evidence includes a prospective birth cohort study in which whole-body plethysmography was used to show that children of atopic parents and those with personal atopy have impaired lung function in early life.<sup>73</sup> The importance of dust mite-specific sensitization was demonstrated in a study of school children in central Virginia. The investigators used multiple regression analysis of exposure and sensitization to several aeroallergens to identify dust mite sensitization as the only factor independently associated with developing asthma. Although a relation between dust concentration in the child's home and development of asthma could not be identified, most houses were noted to contain high concentrations of dust mite allergen, so that sensitization became the dominant risk factor for asthma.<sup>74</sup> Similar results were found in a study of children living in New Zealand in which IgE to dust mite was associated with a greater than 5-fold increase in the odds of wheezing.<sup>75</sup> In another study, the amount of specific IgE to dust mite was shown to be associated with increased risk of decreased lung function.<sup>76</sup>

Early sensitization to dust mite does seem to predict later development of asthma. In 1 study, a positive skin prick test reaction to dust mite at 1 or 2 years of age predicted wheeze at 12 years

of age. In addition, mite-sensitized children with eczema were even more likely to develop asthma.<sup>77</sup> These findings were confirmed in another study that found a significant association between a positive skin prick test reaction for dust mites during the preschool years and persistence of asthma after 4 to 9 years.<sup>78</sup>

The evidence for a relation between sensitization and dust mite exposure is based largely on epidemiologic observations that people who live in intrinsically low-dust mite environments, such as cold or dry locations, tend to not become sensitized to dust mites. This is most likely due to lack of exposure to dust mites. Individuals who have been exposed to dust mites and who already have become sensitized may benefit by moving to a dust mite-free environment, although prevention of sensitization is no longer a goal.<sup>4</sup> For example, despite moving to New York City homes with extremely low dust mite exposure, 31% of Puerto Rican women who were born in Puerto Rico were sensitized to dust mites.<sup>79</sup> In fact, almost 35% of children from 8 inner-city areas in the United States had skin reactive to dust mite allergen, and this percentage did not vary much depending on living in low vs high dust mite level areas.<sup>80</sup> What is known about sensitization is that susceptible children are those who have parents with a history of atopy. Furthermore, the assessment of biologically relevant timing of exposure required for sensitization is complicated.

The relation between exposure to dust mites and sensitivity has been evaluated by comparing children living in the Alps with low exposure against those living at sea level where exposure is higher. Subjects enrolled in the study underwent skin testing for mite sensitization. In addition, mite levels from mattress dust samples were measured. As expected, dust mite levels were significantly lower in mattresses from the Alps than in those from sea level. In addition, the prevalence of positive skin test reactions to dust mites was significantly lower in mountain schoolchildren than in those living at sea level, confirming a relation between exposure and sensitization to dust mites.<sup>81</sup>

In another similar study, 3 case-control studies of asthma in 332 children (157 with asthmatic symptoms and 175 controls) attending schools in Los Alamos, New Mexico and central Virginia were combined. Skin prick tests, histamine bronchial hyper-reactivity, and concentrations of dust mite, cat, and cockroach allergens were measured. The prevalence and degree of sensitization to dust mite and to cockroach was strongly associated with the amount of exposure to the respective allergen.<sup>82</sup>

A study of 567 children attending a Los Alamos middle school compared results of skin testing and specific IgE for dust mite, cat, and dog. Concentrations of mite allergen were very low (mean 0.18  $\mu\text{g/g}$  of Der p 1), and rates of mite sensitization were equally low despite a high rate of sensitization to cat. This indicates that the children tend not to become sensitized to allergens to which they are not exposed.<sup>83</sup>

There is preliminary evidence that sensitization to dust mites may begin prenatally depending on maternal allergen exposure during pregnancy. In the Asthma Coalition on Community, Environment, and Social Stress (ACCESS) project, prenatal dust mite exposure to higher than 0.2  $\mu\text{g/g}$  was associated with a 29% increase in cord blood total IgE and a significant nonlinear increase in mite-specific IgE.<sup>84</sup>

An important and to date unanswered question is whether a dust mite-laden environment that undergoes interventions to decrease exposure would have the same salutary effect on sensitization as an environment that is intrinsically free of dust mite allergen. One study that compared levels of mite-specific IgE with exposure to mite allergen in mattresses found a highly significant correlation between the 2 variables, with higher exposures being associated with higher levels of specific IgE.<sup>85</sup>

Another study in 6 large random samples of children in different regions of New South Wales, Australia found that more children

were sensitized to house dust mites in regions where Der p 1 levels were high.<sup>86</sup> In another study, 1,812 children underwent 3 skin prick tests at 12-month intervals for *D pteronyssinus* and 6 other allergens and had dust mite allergen from their mattresses measured. Der p 1 exposures were correlated with rates of sensitization starting at 2  $\mu\text{g/g}$ . The investigators suggested that this is a minimal avoidance level for primary prevention in children with sensitization to other allergens.<sup>87</sup>

In a systematic review, the Institute of Medicine noted that in areas where most houses have higher than 2  $\mu\text{g}$  of mite allergen per gram of dust, sensitization has consistently been found in a large proportion of children with asthma. The report also emphasized that such a threshold is not absolute in that highly sensitive individuals may become sensitized at lower concentrations of exposure, whereas nonatopic individuals are unlikely to become sensitized even at substantially higher exposures.<sup>88</sup> In addition, it is important to remember that the cutpoints mentioned here refer to the old standards for dust mite allergens. A comparison of these older values with values obtained using the new standard is presented in Table 2.

In another attempt to determine whether early exposure to dust mite allergens causes primary sensitization, the Manchester Asthma and Allergy Study was a prospective study that recruited subjects in utero by screening parents using skin prick testing and an allergy questionnaire.<sup>89</sup> Then, subjects were randomly allocated to full mite allergen avoidance or to a normal regimen. The interventions included mattress encasings, use of HEPA vacuum cleaners, vinyl flooring in the infant's bedroom, a new crib and mattresses encased in mite-proof material, application of benzyl benzoate on carpets and soft furniture, and weekly washing of bedding and washable soft toys. Using this combination of interventions, Der p 1 from mattresses was decreased by 97% during the second and third trimesters of pregnancy and for 12 months after birth in the active but not in the control group. Der p 1 levels from the crib mattress and nursery floor in the active group also remained extremely low in the active vs control group.<sup>90,91</sup>

The difference between this study and the observational studies is that these subjects lived in an area that is intrinsically high in dust mites and an intervention was used to decrease exposure. Two thirds of homes contained Der p 1 levels higher than 2  $\mu\text{g/g}$ , and 40% had Der p 1 levels higher than 10  $\mu\text{g/g}$ . In addition, dampness and condensation were common findings in these homes. It is likely that subjects were exposed to elevated dust mite levels when visiting other homes. Failure to prevent sensitization with extensive dust mite avoidance in this study therefore may have been due to exposures to outside sources of dust mite allergens.<sup>92</sup>

There is evidence that even a single bronchial allergen challenge with dust mite allergen can lead to increased production of mite-specific IgE that is detectable 5 weeks after the challenge.<sup>93</sup> Upholstered seats in public buildings and public transport, for example, can serve as reservoirs that could compromise the beneficial effects of allergen-avoidance interventions used at home. In 1 study, dust samples from 5 schools, 6 hotels, 4 cinemas, 6 pubs, 3 buses, 2 trains, and 12 domestic households were assayed for Der p 1. Mite allergen levels were higher in private homes than in public places except for cinema seats. High levels of Der p 1 were found in 30% of upholstered seats, with 9% having a concentration higher than 10  $\mu\text{g/g}$ .<sup>94</sup>

#### *Development of asthma and rhinitis*

### **2. Advise patients to minimize exposure of dust mite-sensitized children to dust mite allergens to decrease their risk of developing asthma and possibly rhinitis. (Strength of recommendation: strong, A evidence)**

The relation between dust mite exposure and the risk of developing asthma has been evaluated extensively.<sup>95</sup> The effect of

environmental modification in the first 12 months of life on the prevalence of asthma in high-risk individuals was evaluated by providing children with a low allergen diet and decreased dust mite exposure or standard care. By 18 years of age, there was a significantly lower prevalence of asthma in the prevention group compared with the control group. This effect occurred early and persisted into adulthood.<sup>96</sup>

Dust mite exposure and the risk of developing asthma by 6 to 7 years of age also has been evaluated in some prospective studies.<sup>97,98</sup> In 1 study, exposure to more than 2  $\mu\text{g}$  of dust mite allergen per gram of dust increased the risk for the development of IgE and asthma in susceptible children.<sup>99</sup> In another study in the United Kingdom, exposure in early childhood to house dust mite allergens was found to increase the risk for the subsequent development of asthma.<sup>100</sup> In addition, the higher the level of dust mite exposure at 1 year, the sooner the first episode of wheezing occurred. The relative risk of asthma was almost 5 times greater in the subjects who were exposed to high levels of dust mite allergen ( $>10 \mu\text{g/g}$ ) than in those exposed to lower levels. These findings were confirmed in a Boston study of 440 children with a parental history of atopy in which early exposure to house dust mite was associated with an increased risk of asthma and late-onset wheezing.<sup>101</sup> Children exposed to high levels of dust mite allergen in their bed at 2 to 3 months old had a 3-fold increase in the odds of asthma at 7 years old compared with those exposed to low levels of dust mite allergen.

Although thresholds of exposure, such as 2  $\mu\text{g/g}$ , have been mentioned in many studies, one would expect that if dust mite exposure were a cause of asthma, then there would be a direct relation between the amount of exposure and the prevalence of asthma. This was evaluated in children living in 6 different regions of New South Wales, Australia. After adjusting for sensitization to other allergens, the investigators found that the risk of developing asthma in house dust mite–sensitized children was linearly related to Der p 1 exposure.<sup>86</sup> Because there was no specific cutoff or threshold for mite exposure, this study result suggests that to decrease the risk of developing asthma in sensitized children, exposure should be minimized as much as possible rather than pursuing a specific cutoff value.

Obviously, the relation between allergen exposure and disease development can be complicated by other factors, including exposure to other allergens and to irritants and pollutants.<sup>102</sup> For example, in the National Asthma Campaign Manchester Asthma and Allergy Study, the odds of developing asthma increased with the number of positive skin test reactions to common aero-allergens, including dust mites.<sup>103</sup>

A review of 6 primary prevention studies using environmental modifications to prevent the development of asthma in sensitized children consistently identified decreases in asthma and in some cases rhinitis and atopic dermatitis in response to decreased exposure to dust mites.<sup>104</sup> In the Isle of Wight study using mite and food avoidance for 9 months, researchers found that at 8 years of age the active group had less wheeze, less bronchial hyper-responsiveness, and less atopy. The Canadian Primary Prevention Study used inhalant and food avoidance, which led to a decrease in asthma and rhinitis in the active group at 1 year of age. The Study on the Prevention of Allergy in Children in Europe also used inhalant and food avoidance and found less atopy and sensitization to mites in the active group. The Childhood Asthma Prevention Study used mite avoidance and supplemental  $\omega$ -3 fatty acids and found that eczema was more common in children with mite avoidance and  $\omega$ -3 supplementation, although wheezing at 18 months of age was decreased in that group. The Prevention and Incidence of Asthma and Mite Allergy Study found a small decrease in nocturnal cough in the mite-avoidance group. The Manchester Asthma and Allergy Study found that prescribed medication for

wheeze and wheeze with shortness of breath were less common in the active group.

#### *Morbidity from exposure*

**3. Advise dust mite–sensitized patients with asthma or rhinitis to minimize exposure to dust mite allergens in addition to avoiding other relevant allergens to which they are sensitized and avoiding irritants, to decrease their risk of developing symptoms. (Strength of recommendation: strong, B evidence for asthma; strength of recommendation: strong, C evidence for rhinitis)**

The conventional wisdom is that individuals with asthma who are exposed to an allergen to which they are sensitized are more likely to develop symptoms than if they are not exposed. This can be supported with different approaches, including a demonstration that sensitized patients with asthma and greater exposure are more likely to develop symptoms, and that decrease of the exposure leads to fewer symptoms. In addition, bronchial challenges with dust mite extract have been performed in sensitized individuals demonstrating objectively that mite exposure can cause asthma symptoms.<sup>105</sup>

In 1 study of adult patients with asthma sensitized to dust mite, Der p 1 exposure was greater in patients with severe asthma than in those with mild asthma, supporting an association between the degree of allergen exposure and asthma severity.<sup>106</sup> Total Der p 1 plus Der f 1 exposure also correlates with the amount of  $\beta$ 2 agonists, long-term treatment, and the number of asthma attacks in patients with dust mite allergy and asthma.<sup>107</sup>

Bronchial hyper-responsiveness can be increased by allergen exposure and there is a relation between immediate hypersensitivity to dust mites and asthma. In addition, natural exposure to dust mite allergens is different from bronchial provocation. Indoor allergens play a major role in causing bronchial inflammation, with consequent bronchial reactivity, and this is usually not apparent to the patient.<sup>108</sup> In allergic patients with asthma, airway hyper-responsiveness increases during autumn, depending on sensitization to dust mite and an increase of exposure to dust mite allergen.<sup>109</sup>

Another study of nonsmoking adults with asthma found that mite-sensitive patients who reacted to methacholine also were exposed to significantly higher concentrations of Der p 1 in their beds than nonreactors. In addition, Der p 1 and Der p 2 in beds significantly correlated with bronchial hyper-responsiveness.<sup>110</sup> A similar association between sensitization and exposure to dust mite in the home was found for pulmonary function, exhaled nitric oxide, and airway hyper-responsiveness in another study of patients with asthma. Subjects who were sensitized and exposed to high levels of dust mite had lower forced expiration in 1 second, higher forced exhaled nitric oxide, and more severe airway hyper-responsiveness than subjects who were not sensitized and exposed to dust mites.<sup>111</sup>

Although dust mite exposure is an important trigger of asthma, its contribution to rhinitis symptoms is less well studied. One study of adults with perennial rhinitis sensitized only to dust mites showed evidence of persistent inflammation even when rhinitis symptoms were not present. In addition, expression of intercellular adhesion molecule-1 (CD54) was increased on conjunctival and nasal epithelial tissue in those patients compared with nonallergic adults who had the same mite allergen exposure.<sup>112</sup>

The long-term effects of dust mite exposure were demonstrated in a 4-year prospective cohort of persons with asthma in which exposure to high levels of dust mite allergens at baseline was associated with a subsequent increase in bronchial hyper-responsiveness. Bronchial hyper-responsiveness increased in those who were exposed to high mite allergen levels and not in those who were not exposed.<sup>113</sup>



Similar results have been found in children. A study of children living in Vancouver or Winnipeg found that in children with positive skin test reactions to dust mite, allergen exposure correlated with mean daily asthma symptom scores and negatively with daily peak expiratory flow rate.<sup>114</sup> Furthermore, in a study of 82 children admitted to the hospital for asthma, 75% had been exposed to more than 10 µg/g of Der p 1 before admission, 82% were sensitive to house dust mite, and 60% were exposed and sensitive as opposed to 23% of controls.<sup>115</sup>

Asthma exacerbations are even more common in children who are sensitized and exposed to dust mite and who have a concurrent viral infection<sup>116</sup> and in adults in whom the combination of sensitization, high exposure to dust mites, and viral infection increased the risk of being admitted for asthma.<sup>117</sup>

There is evidence that exposure alone is associated with asthma symptoms regardless of sensitization. This was shown in a study of patients with atopy and asthma who were not sensitized to dust mite but who were exposed to high levels of mite allergen. Significantly more severe bronchial hyper-responsiveness was identified in those with high exposure than in subjects not exposed to high levels of dust mite.<sup>118</sup> Although early exposure to high levels of dust mite allergen may be associated with the development of asthma; this may be augmented by exposure to endotoxin at the same time. This suggests that early endotoxin exposure and dust mite allergy exposure may increase the risk for development of asthma.<sup>101</sup>

Exposure to 10 µg of Der p 1 and Der f 1 per gram of house dust exposure has been suggested as an exposure threshold for the development of asthma symptoms in already sensitized children.<sup>56,119</sup> Another study, using data from the Childhood Asthma Management Program, evaluated home dust allergen exposure and the number of other positive allergy skin test responses. Positive allergy skin test responses to dust mites were more likely in those exposed to mite levels higher than 10.0 µg/g of dust.<sup>120</sup> The same caveat applies as before because the relation between exposure and development of symptoms does not support a single level below which symptoms do not occur. In addition, the levels listed here need to be converted from the old standards to the new ones to compare results from previous studies with those of more current studies (Table 2 presents conversion information).

Dust mite sensitization appears to increase the risk of wheezing regardless of exposure. In 1 study, children with elevated dust mite-specific IgE were found to have an increased risk of wheezing when they were infected with rhinovirus. This was true regardless of exposure to mite allergens.<sup>121</sup> Because exposure to dust mites can trigger symptoms in nonsensitized individuals,<sup>122</sup> sensitization per se is not the only criterion for possible morbidity from exposure. Proposed mechanisms for this effect include inhibition of cyclo-oxygenase-1, an interaction between glycan-dectin and bone marrow mast cells,<sup>123</sup> stimulation of toll-like receptor 4 by Der p 2 and Der p 7, and protease (Der p 1, 3, 6, 9) activation of eosinophils and dendritic cells. Other proposed mechanisms include epigenetic changes through miRNA16 to miRNA21 and miRNA126, which can inhibit GATA-3 (Trans-acting T-cell-specific transcription factor) and induce T<sub>H</sub>2 responses and stimulation of epithelial cells to produce vascular endothelial growth factor secretion. In addition, Der p extracts can induce apoptosis in A549 cells. It is also possible that chitin could cause problems in individuals with acidic mammalian chitinase deficiency.

#### Atopic dermatitis

**4. Advise patients to minimize exposure of dust mite-sensitized children with atopic dermatitis to dust mite allergens, to decrease the symptoms of atopic dermatitis. (Strength of recommendation: moderate, C evidence)**

The likelihood of developing symptoms of atopic dermatitis can be increased as a result of exposure to dust mite allergen. In 1 study, a significant increase in transepidermal water loss was observed after exposure to volatile organic compounds in patients who also had prior exposure to Der p 1. Such patients also developed an increase in dermal blood flow and increased atopy patch test reactions to dust mite allergen.<sup>124</sup>

Children with atopic dermatitis have a higher prevalence of mites on their skin than healthy children. In addition, such children often are sensitized to dust mite allergens. In 1 study, dust mites were found on the skin of 35% of children with atopic dermatitis as opposed to 7.9% of healthy controls. No correlation was found between the number of mites on the skin and on clothes and the bedding of those same patients.<sup>72</sup>

Molecules from dust mites have been shown to induce the release of proinflammatory cytokines and chemokines from epidermal keratinocytes and dermal fibroblasts in vitro. This suggests a mechanism for dust mite-induced atopic dermatitis and suggests that avoiding skin contact with house dust mites may decrease mite-induced inflammation.<sup>125</sup>

The importance of dust mite exposure in atopic dermatitis was further demonstrated in patients who showed improvement when dust mite exposure was decreased. In 1 study, the homes of patients with eczema and dust mite sensitivity received allergen-impermeable bedcovers or cotton covers, benzyl tannate spray or water, and a high-filtration vacuum cleaner or a conventional domestic vacuum cleaner. The severity of eczema decreased in the 2 groups, but the active group showed significantly greater improvements in severity score. Most of this was due to a decrease in mattress dust and carpet levels of Der p 1.<sup>126</sup>

Moderate to severe atopic dermatitis is strongly associated with sensitization to dust mite, suggesting that dust mites contribute to the severity of disease and that mite avoidance may be beneficial for the treatment of these patients.<sup>127</sup>

#### Dust mites and food

**5. Although 5% to 15% of patients who are highly sensitized to dust mite also are sensitized to crustaceans, the clinical significance of this is unknown. For that reason, no recommendation can be made regarding the need to advise crustacean-naive patients about their risk of ingestion. (Strength of recommendation: none, D evidence).**

Although 5% to 15% of patients who are highly sensitized to dust mite also are sensitized to crustaceans, the clinical significance of this is unknown.<sup>33,34</sup> Cross-reactive IgE-binding epitopes have been described between shrimp, cockroach, and house dust mite tropomyosin. Inhibition tests have demonstrated that mite allergen cross-reacts with shrimp, crab, and cockroach allergen.<sup>128</sup> This is believed to account for the presence of detectable IgE to crustaceans such as shrimp in patients with cockroach and dust mite allergies who may not have had prior seafood exposure. Analysis of 504 serum samples from the National Cooperative Inner-City Asthma Study found a strong correlation among shrimp, cockroach, and dust mite IgE levels. In particular, high exposure to cockroach correlated with the development of shrimp and cockroach IgE. In contrast, exposure to dust mite alone was highly correlated with IgE to *D. farinae* but not with shrimp.<sup>129</sup>

Allergic reactions to this Der p 10 cross-reactive binding have been reported for different crustaceans, including limpets,<sup>130</sup> snails,<sup>131</sup> shrimp, and crab.<sup>128</sup> Lobster tropomyosin has the greatest and cockroach the least amino acid sequence similarity with shrimp.<sup>132</sup>

**6. Evaluate patients who complain of oral symptoms or symptoms consistent with an IgE-mediated reaction after ingestion of grain flour for dust mite sensitization regardless of whether**



### they have wheat-specific IgE. (Strength of recommendation: moderate, C evidence)

Although mite allergens generally cause symptoms by inhalation, more than 100 cases have been reported of generalized allergic symptoms after the ingestion of mites as contaminants of food products. Mite-infested foods that have provoked symptoms include beignets,<sup>133</sup> wheat flour,<sup>134–136</sup> pancakes,<sup>137–139</sup> polenta (corn flour),<sup>140</sup> *okonomi-yaki* (flour-covered scallops, bonito, and mackerel),<sup>141</sup> and grits.<sup>142</sup>

Symptoms have ranged from erythema and urticaria to wheezing with dyspnea to anaphylaxis with loss of consciousness and have occurred in children<sup>143</sup> and adults. One patient developed food-related exercise-induced anaphylaxis.<sup>138</sup> All reported patients had a history of atopic disease. For reasons that are not clear, many patients have coexisting aspirin sensitivity,<sup>135,140,144</sup> with a recent review counting 59 of the 135 (43.7%) of the total reported patients as being sensitive to nonsteroidal anti-inflammatory drugs.<sup>145</sup> Skin and *in vitro* testing have shown reactivity to mites and to the contaminated food substance, but not to wheat or to the contents of uncontaminated packages of the same food.

Microscopic examination of the food products in question generally showed obvious mites, and immunoassays showed high levels of mite allergen. Given its name (*farinae* = “wheat”), it is perhaps not surprising that the most commonly implicated species has been *D farinae*.<sup>133,135,139,141,144</sup> Other responsible mite species have included the domestic mites *D pteronyssinus*,<sup>140</sup> and *B tropicalis*<sup>146</sup> and the storage mites *Suidasia medinensis*,<sup>136,138</sup> *Tyrophagus putrescentiae*,<sup>134,141,140</sup> *Tyrophagus entomophagous*,<sup>135,147</sup> and *Blomia freeman*.<sup>137</sup> Because symptoms were produced by cooked foods, it is likely that the heat-stable group 2 allergens, rather than the heat-labile group 1 allergens, are the primary inducers of the reactions.

In most cases, the infestation of the food product has apparently occurred in the home, with contamination found in products that had been left open for periods before the provoking use.<sup>139,148</sup> Examination of unopened food packages have generally not showed contamination,<sup>133,140,141</sup> although a survey of grain stores in Greece showed the frequent presence of storage mites.<sup>149</sup> Cases are more common in tropical or semitropical areas, where the high humidity supports mite growth,<sup>150</sup> but cases have occurred throughout the world, including the northeastern United States.<sup>145,139</sup>

Freezing kills dust mites and refrigeration makes them immobile, preventing their reproduction. Therefore, it is prudent for mite-allergic patients to store opened pancake mix, flour, and other similar food products in the freezer or refrigerator.

Cooking may decrease the amount of biologically active dust mite allergen in grain flour by denaturing it. It is known that dry heat can effectively denature mite allergens. Der p 1 denatures within 30 minutes at 120°C, whereas Der p 2 is more heat stable, requiring 140°C for 30 to 60 minutes to denature.<sup>151</sup> Thus, although cooking does expose mite allergens to moist heat for a sufficient time to bake food, the center of the food may be exposed to lower temperatures for much of that baking time. Therefore, full denaturation of mite allergens by baking might not occur reliably.

To prevent contamination of food products, sealable plastic bags can be used. In 1 study, dust and dry pet food stored in paper bags, sealable plastic bags, and sealable plastic boxes were analyzed for 90 days using tests for guanine as an indirect indicator of mite levels (Axarex; Dyn'R, Aix en Provence, France), a Der p 1 ELISA, and mite flotation to count the number of live mites present. Guanine test results were negative in all food samples but positive in all house dust samples. The Der p 1 levels and mite numbers significantly increased in food from paper bags but not from plastic bags or boxes. In addition, mite numbers and Der p 1 levels were 10 to 1,000 times higher in house dust than in the corresponding food samples.<sup>152</sup>

### Clinical evaluation

It has been suggested that a positive history of house dust or house dust mite allergy in patients with asthma is one in which respiratory symptoms become worse during activity that disturbs house dust, such as vacuuming, dusting, sweeping, making the bed, or shaking out blankets, or in which symptoms are alleviated when going outdoors. Seasonal variation and other features of the history are of little value in distinguishing mite-sensitive patients with asthma. In addition, although often asked about, worsening asthma at night in bed or in the morning was not predictive of dust mite sensitization.<sup>95</sup>

One study evaluated the ability of history and physical examination alone to determine allergists' ability to predict sensitization to 7 common allergens in 152 children at 2 different allergy centers. Diagnosis of dust mite sensitivity based on history correlated poorly with skin prick testing and levels of mite-specific IgE. Allergists tended to overdiagnose dust mite allergy in that 22% of patients with a positive history reacted negatively to dust mite and 76% of indeterminate results were negative. This suggests that the diagnosis of dust mite allergy by history alone is not consistent and that discrepancies are dependent on the allergen and on the allergist.<sup>153</sup>

Because a clinical history of dust mite allergy is an unreliable predictor of sensitization, patients should be suspected of having dust mite allergy if they live in a location where dust mites are prevalent, if there is a family or personal history of atopy, or if there is a personal history of asthma, rhinitis, or atopic dermatitis.

#### Tests for dust mite sensitization

### 7. Test patients with suspected dust mite allergy for the presence of dust mite–specific IgE using a skin prick test or *in vitro* test for specific IgE. (Strength of recommendation: strong, B evidence)

Patients with suspected dust mite allergy ideally should be tested for sensitivity to dust mite allergens. The gold standard for this type of evaluation is with nasal, ocular, or bronchoprovocation with extracts containing relevant dust mite allergens.<sup>154,155</sup> Although such tests can demonstrate sensitivity to dust mite allergens, they do not confirm that any observed reaction is mediated by the presence of specific IgE antibodies. In addition, these tests are inconvenient, expensive, and not widely available and there is a risk of adverse effects from the test, including anaphylaxis. For that reason, diagnostic tests are generally used as proxies for these gold standard tests. Such tests include an appropriate history followed by percutaneous (prick) and/or intracutaneous tests and *in vitro* blood tests for the presence of dust mite–specific IgE antibodies.<sup>156</sup> The goal of diagnostic testing is to determine a patient's sensitization status and minimize unnecessary testing and medications. This can allow a patient to avoid the allergen and to determine whether he or she is a candidate for allergen immunotherapy.

#### Dust mite extracts

Tests for dust mite sensitivity are performed using extracts that are commercially available from different sources. Dust mite extracts consist of complex heterogeneous mixtures of allergenic and nonallergenic proteins, glycoproteins, and polysaccharides. They are derived from cultures of dust mites.

Commercially available dust mite extracts have been standardized relative to reference preparations and have potencies that are expressed as allergy units (AU) per milliliter. The goal of allergen standardization is to produce well-characterized extracts of known biologic potency and composition.<sup>157</sup> The World Health Organization established an international standard

for *D pteronyssinus* extract with an assigned unitage of 100,000 IU per ampule. These units refer to the total allergenic activity of the ampule but also take into account individual major allergens, including Der p 1.<sup>158</sup>

It is important to remember that standardization of dust mite extracts is based on total biologic potency, whereas the individual components of standardized extracts may vary. This was demonstrated in 1 study in which absolute and relative quantities of Der p 1 and Der p 2 were compared in 6 different commercial standardized extracts of *D pteronyssinus*. Ratios of Der p 1 to Der p 2 ranged from 1.1:1 to 6:1. This variation in the proportion of Der p 1 and Der p 2 among different *D pteronyssinus* extracts may influence their biological effectiveness. Patients with reactivity against only Der p 1 or Der p 2, who were found to comprise approximately one third of the mite-allergic population, may not respond optimally to extracts containing relatively low levels of the allergen to which they are sensitive.<sup>159</sup>

Extracts currently available in the United States include *D farinae*, *D pteronyssinus*, and mite mix with equal parts of *D farinae* and *D pteronyssinus*. Dust mite extracts come in concentrations of 3,000, 5,000, 10,000, and 30,000 AU/mL.<sup>160</sup> Although the use of the mite mix in selected individuals may decrease the number of tests by a nominal amount, there is no information about how this would affect the performance characteristics of the tester or the efficacy of treatment if immunotherapy were given.

Allergenic extracts for the diagnosis and treatment of dust mite are produced from cultures of dust mites. The growth phase at which the extract is produced can affect its contents. In 1 study, 3 different growth phases were evaluated: the latency phase (F1), the growth phase (F2), and the death phase (F3). Extracts produced from the growth phase yielded in vitro and in vivo results that were 3 times more potent than those from the other phases, suggesting that the maximum growth phase (F2) is the best for producing extracts.<sup>161</sup> This was confirmed in a follow-up study in which extracts produced from the growth phase had 6 times more relative allergenic activity in in vivo studies than extracts from the latency and death phases.<sup>162</sup>

To determine how extracts from different countries compare, total protein, specific IgE binding, and major allergen content of diagnostic extracts from Europe, the United States, and Mexico were compared with the Food and Drug Administration's Center for Biologics Evaluation and Research reference extracts for *D pteronyssinus*. The total protein content of US reference extracts was higher than all other extracts. European dust mite extracts had 3,300 to 4,400 AU/mL compared with 10,000 AU/mL in US extracts. This suggests that European and Mexican extracts have a relative potency less than 50% that of US extracts.<sup>163</sup> In addition, although extracts produced in Europe, South America, and Australia appeared to provide similar skin test reactivity when tested in a group of mite-sensitive adults, IgE inhibition found that 2 of the extracts were very similar, whereas the third differed quantitatively and qualitatively when subjected to western blot analysis.<sup>164</sup> This means that extracts from different countries should not be interchanged even if they are labeled with the same potency in allergy units per milliliter.

The importance of high-quality extracts was illustrated in 1 study in which a high frequency of positive skin prick test reactions to dog dander was found in patients who did not have detectable dog-specific IgE by in vitro test. The dog extract turned out to be contaminated with the major allergens (Der p 1 and Der p 2) of the dust mite, causing false-positive responses in patients sensitized to dust mite.<sup>165</sup> The stability of diluted *D farinae* extracts also was evaluated in various diluents, including phenol–saline with and without human serum albumin. The phenol–saline extract lost 90% of its activity within 1 week, whereas extracts with serum albumin were stable for at least 8 months after reconstitution.<sup>166</sup>

### Which mite to test for?

Although *D pteronyssinus* and *D farinae* have some species-specific allergens, cross-reactivity between homologous allergens from *Dermatophagoides* species is high and ELISA cross-inhibition studies have shown *D farinae* to be a strong inhibitor of *D pteronyssinus* IgE binding.<sup>167,168</sup> Moreover, other mites with less *Dermatophagoides* species cross-reactivity might be of importance in areas where there is clear dominance of other genera.<sup>169</sup> Therefore, in areas where *D pteronyssinus* and *D farinae* are predominant, it is reasonable to test with a mixture of the 2. In other regions, it might make sense to test for *E maynei* or *B tropicalis* in addition to *Dermatophagoides* species.

### Percutaneous (skin prick) and in vitro tests for mite-specific IgE

The performance characteristics found in 4 studies of percutaneous tests and in vitro tests for dust mite–specific IgE are listed in Table 3. In 1 study of *D pteronyssinus* extracts evaluated relative to more than 1,000 nasal challenges in patients with allergic rhinitis and suspected dust mite sensitivity, the sensitivity of skin and radioallergosorbent tests were comparable, although the specificity was low for the blood test.<sup>170</sup> Another study that compared challenges with ImmunoCAP (Thermo Fisher Scientific Inc, Kalamazoo, Michigan) found a positive likelihood ratio of 6.33 and a negative likelihood ratio of 0.84, for a sensitivity of 19 and specificity of 97.<sup>171</sup>

A study of 43 adults with asthma examined percutaneous tests and *D farinae*–specific IgE with bronchoprovocation. The sensitivity of the skin test was 81% and that of the IgE test was 67%. The specificity of the skin test was 52% and that of the IgE test was 71%. In this study, the skin test was believed to be more sensitive, whereas the IgE test was more specific.<sup>172</sup> It is important to recognize that the studies are from 25 and 21 years ago and that the third Korean study used European extracts.

More recently, a study using American extracts evaluated the ability of percutaneous skin testing and measurement of *D pteronyssinus*–specific IgE to predict a nasal challenge in 20 younger and 28 older adults. Neither test predicted positive challenge results in adults older than 60 years, whereas the 2 tests had excellent performance characteristics in younger adults. Skin test reactions with a wheal larger than 5 mm yielded 100% sensitivity and 90% specificity, whereas IgE higher than 0.35 yielded sensitivity and specificity of 100%.<sup>173</sup>

### Atopy patch test

The atopy patch test has been proposed for the diagnosis of atopic dermatitis. In 1 study, the atopy patch test reaction was more

**Table 3**

Performance characteristics of skin prick tests and in vitro tests for dust mite sensitization

	Sens	Spec	LR+	LR–	PPV	NPV
Reference 170						
Skin	97%	76%	4.06	0.03		
RAST	88%	26%	1.19	0.46		
Reference 171						
IgE	19%	97%	6.33	0.84		
Reference 172						
Skin	81%	52%	1.69	0.37		
IgE	67%	71%	2.31	0.46		
Reference 173						
Wheal >3 mm	70%	100%	ND	0.3	77%	100%
Wheal >5 mm	100%	90%	10	0.0	91%	100%
IgE >0.35 Ku/L	100%	100%	ND	0.0	100%	100%

Abbreviations: LR–, negative likelihood ratio; LR+, positive likelihood ratio; ND, not defined; NPV, negative predictive value; PPV, positive predictive value; RAST, radioallergosorbent test; Sens, sensitivity; Spec, specificity.

frequently positive in patients with atopic dermatitis than in the control group, whereas skin prick test and specific IgE results were more frequently positive in a control group with rhinitis or asthma but not atopic dermatitis.<sup>174</sup> Although these results are promising, they have not been adopted into standard allergy practice at this time.

#### Specific IgE for mite components

**8. Currently there is no evidence supporting routine measurement of specific IgE to dust mite components, although such measurements may be considered when necessary, such as for patients with potential Der p 10 (tropomyosin as found in cockroach and crustaceans) sensitivity. (Strength of recommendation: weak, D evidence)**

Commercially available tests for dust mite component-specific IgE include Der p 1, Der p 2, and Der p 10. The prevalences of serum IgE to commercial components in 1 study were 93% for Der p 1, 77% for Der p 2, and 28% for Der p 10. Total *D pteronyssinus*-specific IgE strongly correlated with specific IgE to Der p 1 and Der p 2 but not to Der p 10. No clinical implication for the prevalence, levels, or molecular IgE reactivity profile to house dust mite components has been determined. Der p 10 prevalence suggests different patterns in food and mite-related tropomyosin sensitization.<sup>175</sup> Similar results were found in another study of diagnostic tests for dust mite sensitization in Chinese patients with allergic rhinitis.<sup>176</sup>

#### Exposure assessment and decrease

The efficacy of allergen avoidance in mite-sensitive patients has been demonstrated by the decrease in bronchial hyper-reactivity and other indices of airway inflammation after moving to mite-free environments, such as high altitudes<sup>177,178</sup> and hospital rooms.<sup>179</sup> At high altitudes, the RH is generally too low to support dust mite growth; in hospital rooms, where the environment has been created for infection control purposes, all surfaces are washable, the mattress and pillows are covered in plastic, and all bedding is washed in hot water—all of which prevent mite growth or mite allergen accumulation.

Although the clinical benefits of living in a completely dust-mite-free environment are clear, the benefits of mite-allergen avoidance for homes in regions where mites are prevalent are less clear. The model of this series of practice parameters is to consider facilitative factors (ie, factors that contribute to growth of sources), sources that produce the allergens (in this case, mites), and reservoirs (ie, places where mite allergens can accumulate and expose occupants to allergens long after sources are gone). The best way to reproduce the situation of a home in a dust-mite-free region is to completely remove these 3 sources of exposure. Therefore, ideal interventions would ensure that indoor humidity remains low year-round regardless of outdoor conditions; mattresses, box springs, and pillows are impermeable to mites and allergens; bedding is washed regularly and thoroughly dried; and all carpeting, upholstered furniture, and draperies are removed to eliminate reservoirs. Although these interventions may be ideal, the practical aspects of environmental control are that patients are unlikely to do these things. For that reason, a more detailed discussion of interventions that are feasible follows.

#### Facilitative factors

Facilitative factors consist of environmental conditions that enable the growth of the source of a contaminant. The source of dust mite allergens is the dust mites. Dust mites can grow and reproduce only when they have access to environmental conditions compatible with their survival. Facilitative factors for dust mites include adequate moisture, moderate temperatures, and a source of food that usually consists of skin cells, fungi, and other

micro-organisms. Assessment of a home for the presence of these factors and their removal, when present, is the topic of this section.

#### Moisture

##### Assessment

**9. Encourage dust mite-allergic patients to obtain and use a hygrometer to measure humidity in their home. (Strength of recommendation: strong, D evidence)**

The most important facilitative factor for dust mites is moisture. An assessment of the amount of moisture available to dust mites in a home can be performed using an inexpensive device called a *hygrometer*.

A hygrometer is an instrument that is used for measuring the RH of the air. RH is the amount of water vapor in the air, expressed as a percentage of the maximum possible water vapor that can be held by air at that temperature. The dew point is the temperature below which the water vapor in a volume of air at a constant barometric pressure will condense into liquid water. Condensed water is called *dew* when it forms on a solid surface. Water activity ( $a_w$ ) is defined as the vapor pressure of water in a material divided by that of pure water at the same temperature. Appendix A presents a more detailed discussion of humidity and its measurement.

Because dust mites can survive only if there is sufficient water on the substrate in which they live, it is important for the homeowner to measure indoor humidity. In general, an RH lower than 50% is associated with water activity in upholstered furniture and bedding that is below that which dust mites require for survival. If the humidity is higher than 50%, abatement should be performed to decrease the amount of water that is available to dust mites.

In addition to measuring indoor humidity, it may help to ask questions related to moisture (Appendix B presents details on exposure assessment). For example, does the patient's residence have microenvironments in which dust mites might thrive? This depends on the water activity in walls, floors, carpeting, and so on. Some building materials are more likely to absorb water than others, so it is important to understand what materials are in a patient's home and how they absorb moisture. In general, the moisture content of materials that are not in contact with an outdoor surface is determined by the mean humidity in the house. For some materials that bind water, such as dust, absorption of moisture is faster than desorption. As a result, such materials tend to buffer the humidity.

Solid surfaces such as sheetrock and concrete slabs may have greater moisture content owing to condensation on cool surfaces and therefore could support mite growth in a home with lower RH.

##### Abatement

**10. Advise patients that relative humidity in the home should be kept between 35% and 50% to decrease the growth of dust mites. (Strength of recommendation: strong, B evidence)**

Mite bodies contain 70% to 75% water by weight, which they maintain to reproduce. They can extract water vapor directly from unsaturated air. Mites survive extended dry periods by forming a desiccation-resistant protonymph stage.<sup>180</sup>

Dust mites absorb moisture from the air, but only if the RH is sufficiently high. The minimum RH that is required to survive has been called the *critical equilibrium humidity*. Mites slowly lose water when the RH is less than the critical equilibrium humidity, although they may survive for weeks before they die.<sup>181</sup> A dehydrated mite can regain water within a few hours if the RH increases above the critical equilibrium humidity, even if only for a short time. Houses which are kept dry most of the time can still harbor living dust mites if the RH increases for as few as 1.5 hours per day, as would occur during cooking. As few as 3 hours per day of elevated humidity enables dust mites to produce eggs. *Dermatophagoides*



*farinae* is particularly resistant to desiccation and can survive for many months in low humidity conditions.<sup>182</sup>

In theory, humidity control should be an effective means of controlling mite populations. Because arid locations intrinsically have low mite populations, it makes sense that homes that can duplicate that low humidity should have equally low mite populations. Because homes in temperate climates have low humidity during the winter months, decreasing humidity is more important during the summer months owing to increased RH.<sup>183</sup> Even so, studies of humidity control using portable and central dehumidifiers have failed to decrease mite exposure, in part because of the difficulty in obtaining adequate humidity decreases and because even brief periods of elevated humidity are sufficient to sustain mite populations.

Because mites feed more, multiply faster, and produce more fecal matter at higher humidity levels,<sup>180</sup> it would seem reasonable that even moderate decreases in humidity should at least slow production of mite allergens. In 1 study, when daily humidity was maintained below 50%, even with brief increases above 50% for 2 to 8 hours daily, mite growth and the production of allergen were decreased. To completely prevent the growth of *D farinae*, however, the RH had to be maintained below 35% for at least 22 hours per day.<sup>184</sup> This was confirmed in another study in which *D farinae* was able to complete development when given short periods of moist air daily, but the rate of development was slower than when the RH was consistently elevated.<sup>185</sup>

In 1 study, portable dehumidifiers were placed in 6 homes in northwest England, and 6 other homes served as controls. Unfortunately, humidity did not decrease enough to retard mite growth. As a result, there was no difference in mite counts and Der p 1 levels measured before and at 1, 2, and 3 months after the installment of dehumidifiers.<sup>186</sup>

Because a single portable dehumidifier placed centrally in a house was not able to remove enough moisture to control dust mite populations, another study was performed to evaluate whole-house dehumidification using mechanical ventilation heat-recovery units. For this study, mite counts and Der p 1 levels were measured at 3-month intervals over a period of 1 year in 18 houses. No differences in Der p 1 concentrations or mite counts were found in any of the sampling sites. The whole-house unit also did not decrease indoor humidity to levels capable of retarding mite growth.<sup>187</sup>

Another study by the same group used enhanced central dehumidification in 10 houses and 10 control houses and demonstrated a winter humidity decrease from 50% to 37%. The humidity remained below the study target humidity of 45%, although there were transient increases in humidity. As a result, this system also failed to decrease mite exposure despite apparently adequate humidity control.<sup>188</sup>

In contrast to the studies performed in England, another study also performed in a humid temperate climate showed that it is practical to maintain an indoor humidity lower than 51% during the humid summer season, and that this resulted in significant decreases in mite and allergen levels. One group of homes used high-efficiency dehumidifiers and air conditioning, a second group used air conditioning alone, and a third group controlled climate by opening windows and had humidity higher than 51%. The low humidity homes started with 401 live mites and 17  $\mu\text{g}$  of Der 1 per gram of dust. These values decreased to 8 live mites per gram and 4  $\mu\text{g}$  of Der 1 per gram of dust after 17 months of maintaining humidity lower than 51%. The control homes did not show a decrease in live mites or allergen concentrations.<sup>189</sup> Although this study showed the validity of dehumidification for dust mite control, the difficulty in using dehumidification alone in damp environments to decrease dust mite antigen exposure was described in a recent Cochrane review.<sup>190</sup>

Because beds are a major site of mites and mite allergen exposure, the influence of overnight occupation of beds on the humidity in the mattress must be considered because elevated humidity might permit mites to survive despite adequate home dehumidification. Investigators in 1 study demonstrated that humidity inside beds did not increase when the beds were occupied because the temperature increased at the same time. Therefore, whole-house humidity control also may be effective to control dust mites in beds.<sup>191</sup>

Although it has been difficult to demonstrate decreased mite exposure with dehumidification, increased mite exposure with humidification has been observed. In 1 study, Der f 1 concentrations were measured to determine whether highly insulated windows and central heating systems would encourage mite growth. Temperature and absolute humidity increased and Der f 1 concentrations increased.<sup>192</sup> In another study of evaporative (swamp) coolers, which are used to cool homes in arid environments, significantly more positive skin test reactions to dust mites were found in children who lived in such homes.<sup>193</sup>

### Sources

The source of dust mite allergen is, of course, the dust mites. Dust mites can be found in virtually all homes that are in locations not too arid for their growth. If the mites are eliminated, further production of mite allergens will cease, leaving only allergen reservoirs as a source of continued exposure.

### Assessment

There is a direct correlation between the number of mites and the amount of mite allergen exposure. In 1 study of 31 dust samples, allergen concentrations measured by ELISA correlated well with the number of mite bodies counted by microscopy.<sup>194</sup> In another study, Der p 1 levels in bed and floor dust samples correlated with the number of mite bodies.<sup>58</sup> In a survey of apartments in Moscow, 73% of children with asthma who were sensitized to *D pteronyssinus* allergens had apartments that were infested with *D pteronyssinus* and *D farinae*. The number of mites varied from 0 to 162 mites per gram of dust for the 2 species. A strong correlation was found between the number of mites and the concentrations of Der p 1 and Der f 1.<sup>195</sup>

This relation between allergen exposure and the number of mites present is illustrated by the observation of a seasonal pattern to temperature and RH in the indoor environment. In 1 study, winters were associated with lower indoor temperatures in apartments and houses, with lower temperatures occurring in houses. RH also was lower during the winter, with apartments having the lowest humidity levels. Der f 1 and Der p 1 levels increased from August to peak in September and October and then decreased through June, when temperature and humidity were at their lowest. Adjusting for correlations within homes, dust mite allergen levels in beds were 1.8 to 2.2 times higher in the fall than in the spring and a similar correlation was found for floor dust. Dust mite allergen concentrations in beds were 19 times higher in houses than in apartments.<sup>196</sup>

To determine whether live mites are present in dust, it is possible to directly view them under a microscope. The procedure is of uncertain value, however, because mites may not be present in the sample that is obtained (they migrate away from sources of light and heat) and they may not survive long enough to be viewed under a microscope as live mites. In addition, it is difficult to enumerate the number mites per unit of dust. For all these reasons and the fact that allergen concentrations correlate well with the number of live mites, measurement of dust mite allergens in dust has become a de facto standard surrogate measurement for the number of mites.

### Source control

Source control for dust mites involves killing the mites. Mites most commonly live in upholstered furniture, carpeted floors, and bedrooms, although clothing also is an important niche for mites. There is no correlation between mite abundance and frequency or thoroughness of cleaning, the amount of dust on surfaces, and the age of furnishings. In addition, frequent vacuuming does not significantly decrease mite abundance.<sup>197</sup> Because of this, elimination of mites requires the use of chemical agents or physical means such as the use of heat to scald them, desiccation to dry them out, water to drown them, or low temperatures to freeze them. The intended result is that mite populations are eliminated or decreased and the production of mite allergens ceases or is substantially attenuated.

### Acaricides

#### **11. Do not recommend the use of acaricides to eliminate mite populations owing to their limited efficacy at decreasing allergen levels and concerns about the use of chemical agents in the home. (Strength of recommendation: moderate, B evidence)**

Acaricides such as benzyl benzoate (eg, Acarosol; Bissell, Grand Rapids, Michigan) are chemical agents that kill mites. These agents usually are applied to materials in which mites reside, such as carpeting, upholstered furniture, and bedding. The latter applications should be performed sparingly because of the risk of human exposure in such locations.

Benzyl benzoate has been evaluated for use as a moist powder and as foam. The active powder kills 90% of mites in culture within 12 hours and 100% in 24 hours.<sup>198</sup> The effects do not last for long and therefore it needs to be reapplied at 2- to 3-month intervals.<sup>199</sup> Although benzyl benzoate will kill dust mites, it is not clear whether this leads to alleviation of allergy symptoms. In 1 study, carpet treatment with benzyl benzoate was shown to decrease airborne and carpet dust mite allergen concentrations by more than 64%, although this degree of decrease was not shown to be clinically beneficial.

In a randomized, double-blinded, placebo-controlled study, the effect of benzyl benzoate was compared with baking soda (a control) in 12 adult patients with asthma at 0, 3, 6, 9, and 12 months. There were no significant differences in mean allergen levels between the 2 groups and no significant changes in lung function or medication use for either group.<sup>200</sup>

Disodium octaborate tetrahydrate (2 cups per 2 gallons of H<sub>2</sub>O per 100 square feet) applied to carpets with a carpet-cleaning machine decreased survival and population growth of *D farinae* and *D pteronyssinus* by 98% compared with water-cleaned and uncleaned carpets at 8 weeks after cleaning.<sup>201</sup>

Another acaricide, tri-*n*-butyl tin maleate, is applied industrially on samples of carpets, mattress foam, and fabrics. A laboratory test showed that after 1 day of incubation at 25°C and 75% RH, the acaricide killed all the mites.<sup>202</sup> Its use in residential settings has not been evaluated.

Another acaricide, pirimiphos methyl, also has been shown to decrease the levels of *D pteronyssinus* allergens in homes after a single application on upholstered furniture. Serial sampling showed a decrease of Der p 1 by greater than 90% compared with control furniture that lasted for 6 weeks.<sup>203</sup>

It has been suggested that application of an acaricide on mattresses and on textile floor coverings in living rooms and bedrooms can contribute to improvement in lung function and airway hyper-responsiveness; however, Der p 1 levels decrease more if mattresses are encased than if they are treated with acaricide.<sup>204</sup> Therefore, acaricides are not recommended for use on mattresses, particularly given the likelihood of exposure to the chemical when it is used in that location.

Another strategy to decrease mite numbers involves the use of plant-derived acaricides such as *Asarum heterotropoides* (*Asarum sieboldii* Miquel), which is a mixture of essential oils. One study evaluated 10 constituents. After 2.5 hours of exposure in a vapor phase mortality bioassay, methyl eugenol and *A sieboldii* Miquel essential oil resulted in 100% mortality in closed containers but only 4% to 8% mortality in open containers, suggesting that this approach is unlikely to be effective for home use.<sup>205</sup>

### Physical measures

#### **12. Tell patients that the use of physical measures to kill mites, such as heating, freezing, and desiccation, theoretically should be effective; however, controlled trials have not been performed to demonstrate clinical benefit when they are used. (Strength of recommendation: weak, D evidence)**

In addition to chemical acaricides, physical measures have been used to kill mites. Because mites are composed largely of water, they are susceptible to heating and to freezing. Dust mite eggs are harder to kill than live mites. The effect of temperature and humidity on hatching of *D pteronyssinus* eggs was investigated in 1 study. At 40°C, approximately 80% of eggs survived, whereas exposure to direct sunlight and dry heat at 50°C caused death after 3 to 5 hours. Mite eggs exposed to 60°C died instantaneously. For cold conditions, only the deep freezer at –70°C was effective in preventing hatching, suggesting that mite eggs are highly resistant to cold.<sup>206</sup>

Because dust mites are sensitive to heat, it seems reasonable that combined steam and heat treatment of home furnishings would decrease dust mite exposure, leading to decreased asthma symptoms. In 1 study, active heat and steam treatment of homes led to a sustained decrease of Der p 1 and Der p 2 for up to 12 months and alleviated the bronchial hyper-responsiveness of patients with asthma living there.<sup>207</sup>

In 1 study, used rugs were vacuumed, “wet cleaned,” “shampooed,” or heated in an autoclave to determine which intervention would be most effective for eliminating live mites and their allergens. Autoclaving was most effective for killing mites and for eliminating allergens. The other cleaning methods did not kill the mites, although they did remove mite allergens.<sup>208</sup>

A decrease in house dust mite populations in mattresses can be achieved with regular use of electric blankets when the beds are not being slept in. In addition, house dust mites in the heated portions of the mattress tend to migrate deeper inside the mattress.<sup>209</sup> In 1 study, the temperature on mattress surfaces increased by 26°C and the RH decreased by 24% within 3 hours when an electric blanket was left on while the bed was not slept in. This led to a decreased concentration of house dust mites on mattress surfaces.<sup>210</sup>

Another way to kill mites is by dehydrating them. This can be done by raising the temperature and decreasing airborne moisture to keep the humidity below the critical equilibrium humidity, which is the level required for mite growth and reproduction. This leads to loss of body water and eventual dust mite death. One study found that 16 houses with subfloor heating had fewer live mites than 21 homes without subfloor heating. In addition to mites in settled dust, mite numbers were smaller in upholstered furniture. Because moisture levels are lower during the winter, decreasing humidity is more effective if done during the summer.<sup>211</sup>

To summarize:

- Freezing mites kills them but does not get rid of the allergen.
- Dry heat to 60°C kills mites and their eggs.
- Dehydration with elevated temperature and low humidity can kill mites.



### Washing

**13. Advise patients that bedding should be washed weekly to decrease dust mite numbers and mite allergen levels, and that high temperature is not necessary. Home hot water should be kept below the temperature (120°F) that causes a scalding risk to occupants. (Strength of recommendation: strong, B evidence)**

Clothing is an important and probably under-rated source of mite allergen exposure.<sup>212</sup> Furthermore, although proper encasings prevent the escape of mite allergen from pillows, mattresses, and box springs, the blankets, sheets, and pillowcases remain a potential source of exposure. When considering techniques for the washing and drying of blankets, clothing, or other substrates that harbor dust mites, it is important to keep in mind the distinction between removing mites and removing their allergens. In addition, it is important to weigh the benefits of higher temperatures against the risk of scalding should someone accidentally become immersed in the hot water.

Regarding mites, the frequent recommendation to wash items in 55°C (130°F) water to kill mites is based not on washing blankets or clothing but on immersing mites placed in permeable capsules into water of different temperatures to determine the temperature needed to scald the mites to death.<sup>213</sup> However, when washing an item, as long as the mites are removed, it is immaterial whether the mites are scalded to death, drowned, or simply washed down the drain still alive, and there is evidence that temperatures lower than 130°F are adequate. Mite cultures in dialysis bags subjected to a 17-minute simulated wash cycle had 96% to 100% mortality at 50°C (122°F), 88% to 96% mortality at 40°C (104°F), and 90% to 98% mortality in cold water, indicating that most mites died by drowning.<sup>214</sup> A study of mixed laundry loads showed approximately 80% mite removal by cold water washing followed by line drying,<sup>215</sup> and a study of mite-inoculated blanket sections put through a normal wash cycle and then dried in a clothes dryer showed removal of 93% of mites with cold water washing.<sup>216</sup>

The dry heat of a clothes dryer also can be used to kill dust mites. All mites seeded into blankets were killed when the blankets were dried in a clothes dryer for 10 minutes<sup>217</sup>; 99% of mites naturally present in used duvets (“comforters”) were killed after 1 hour in a clothes dryer.<sup>218</sup>

Regarding mite allergen, 1 study showed that warm (37°C = 99°F) water washing removed a mean of 84% of the allergen in household laundry items (range 46% to 100% for specific items), with or without detergent, and removed 99% of allergen with the addition of bleach.<sup>215</sup> Another study showed that washing in warm (104°F) water removed 98% of mite allergen from sheets,<sup>219</sup> and yet another study showed that cold water washing with detergent removed 95% of mite allergen from duvets, blankets, and sleeping bags.<sup>213</sup> There is no indication that particular detergents vary in their ability to extract mite allergen, because a study (which did not do actual laundering, but rather placed samples of extracted dust in 11 different detergents) did not find any differences among detergents, with all extracting all the mite allergen in 5 minutes in cold water.<sup>220</sup>

The effects of dry cleaning with perchloroethylene on mite allergen are less clear. Although 1 study found no decrease in mite allergen concentration,<sup>213</sup> another study, of wool blankets with high levels of mite allergen, found a 78% decrease in group 1 mite allergen concentration.<sup>221</sup> However, because the total amount of dust (as distinct from allergen) was greatly decreased by dry cleaning, group 1 allergen decreased by 98% when expressed as allergen per square meter of blanket.

The role of additives in washing is unclear. Immersing mites for 4 hours at 35°C (95°F) in the recommended 0.35% concentration of bleach killed 100% of *D farinae* but only 32% of *D pteronyssinus*, whereas 10% bleach killed 100% of the 2 species.<sup>222</sup> However, studies of children<sup>223</sup> and adults<sup>224</sup> have suggested that the regular

use of household bleach, although associated with less atopy and asthma, is associated with more bronchitis and lower respiratory symptoms, although in neither case was the type of use specified. Short-term use of a dilute bleach solution on surfaces was associated with decreased allergic respiratory symptoms,<sup>225</sup> but it is unlikely that such dilute solutions would be effective in laundry.

Plants have evolved chemical defenses against mites, and many plant derivatives are effective miticides. Agents that have shown activity in laundry include benzyl benzoate, citronella, tea tree, eucalyptus, wintergreen (methyl salicylate), and spearmint oils.<sup>226–228</sup> However, despite being “natural,” these oils are not without potential toxicity from transcutaneous absorption or accidental or intentional ingestion.<sup>229,230</sup>

In addition to the effectiveness of killing dust mites and removing allergens, it is important to consider the risk of scalding with elevated water temperatures. The risk of developing a second- or third-degree thermal burn depends on the water temperature and duration of immersion. Exposure to the usual recommended upper limit for residential water temperature of 120°F (49°C) will lead to a second-degree burn within 8 minutes and a third-degree burn after 10 minutes. Exposure to water temperature of 131°F will lead to a second-degree burn within 17 seconds and a third-degree burn in 30 seconds. For that reason, the US Consumer Product Safety Commission has recommended that domestic hot water be set at 120°F. As an alternative to raising the temperature of the hot water for the entire home, several companies manufacture washing machines that boost the temperature of the water within the machine to at least 131°F for 3 minutes to kill mites (NSF Protocol P351—Allergen Reduction Performance of Residential and Commercial, Family-sized Clothes Washers; NSF International, Ann Arbor, Michigan). Such machines are another option for families with dust mite-sensitive members if they plan to purchase a new washing machine.

Another consideration, in addition to avoiding the scalding risk from hot water, comes from a White House report on harmonizing messages across government agencies. This report concluded that hot water washing is in conflict with the interagency climate change adaptation task force because it is wasteful of energy.<sup>231</sup>

Because hot water in the home presents a scalding danger to children,<sup>232</sup> and because allergen removed from blankets by washing generally reappears within 1 month,<sup>233</sup> a reasonable approach to controlling dust mite exposure would be to wash bedding weekly in warm water, without aiming for a specific and potentially dangerous temperature. This will remove most, not all, mites and mite allergens. Clothing also should be washed after use. With clothing and bedding, the usual amounts of bleach should be added to white loads, but the appropriateness of other additives is doubtful. For items such as blankets, a reasonable step would be to dry them in a clothes dryer for at least 10 minutes before washing. Comforters require 1 hour in a dryer to kill all mites; an alternative would be to encase the comforter or replace it with a comforter made with a barrier fabric. Dry cleaned items, such as woolen sweaters, should be kept in separate plastic bags after cleaning to prevent recontamination with mites from other items of clothing.

### Reservoirs

Once the facilitative factors that enable mites to grow have been abated and the live mites have been killed, residual dust mite allergens can lead to intermittent or even continuous exposure, causing health effects. Mite allergens can be extremely stable under normal indoor conditions. In 1 study, the speed of decay in 9 combinations of temperature (15°C, 20°C, and 25°C) and RH (33%, 55%, and 75%) was determined over 6, 12, or 18 months. No significant changes in the levels of Der p 1 and Der p 2 plus Der f 2 were detected for any of these combinations, even after 18 months

at a high temperature and humidity.<sup>28</sup> Therefore, to completely eliminate this exposure, it is necessary to identify reservoirs and to clean or mitigate them.

#### Assessment

The effectiveness of allergen removal from a contaminated environment can be determined by the measurement of dust mite allergens with appropriate immunoassays in house dust samples before and after allergen elimination.<sup>234</sup>

#### Measurement of mite allergens in settled dust

**14. Suggest postintervention measurement of mite allergens in settled dust for homes in which mite-sensitive people live if symptoms persist despite reasonable efforts to decrease mite exposure. (Strength of recommendation: weak, D evidence)**

The methods for measuring mite allergens (Der p 1, Der p 2, Der f 1, and Der f 2) are well defined and readily available in analytical laboratories across the country. Measurement of mite allergens has been useful in comparing extracts for skin testing and immunotherapy<sup>235</sup> and has been extremely valuable as a research tool.<sup>236</sup> A discussion of the accreditation of laboratories that perform environmental assays can be found in the Practice Parameter on Cockroach Allergy.<sup>237</sup> Methods for collecting dust samples for assay were described in the Practice Parameter on Rodent Allergy<sup>27</sup> and elsewhere.<sup>38</sup> The actual health benefits from decreasing mites are covered elsewhere in this practice parameter.

In theory, allergen level monitoring in patients' houses should improve their understanding of the role of allergens in their asthma and improve compliance with avoidance measures.<sup>238</sup> Measurement of mite allergens can help convince sensitized persons about the need for allergen removal efforts and environmental control to decrease mite populations.<sup>59</sup> Earlier recommendations to minimize mite allergen exposure to decrease the risk of sensitization and development of disease can be guided by actual measurements of mite allergen exposure. Even so, there have not been any controlled trials proving that such measurements in clinical practice are beneficial.

Measurement of mite allergens also can serve as a guide to the success of allergen removal. The earlier recommendation that dust mite allergen exposure be minimized to decrease morbidity is well established. Should symptoms persist despite appropriate interventions, it is reasonable to determine whether it is due to inadequately decreased exposure or to some other factor. Ultimately, there is no value in measuring mite allergens unless such measurements change the implementation of avoidance measures.

For homeowners to collect samples for measurement of dust mite allergen levels, simple and inexpensive methods of sampling are needed. It appears that a single sample from a vacuum cleaner is sufficient to represent overall exposure to mite allergens in the home.<sup>239</sup> In 1 study, 4 different devices were used to collect dust samples from carpets. Depending on how the results were expressed, 3 of the devices yielded results consistent with the reference method but not with each other.<sup>240</sup>

#### Measurement of airborne mite allergens

**15. Measurement of airborne mite allergens offers no benefit over their measurement in settled dust and therefore should not be recommended. (Strength of recommendation: moderate, C evidence)**

There is little correlation between air and dust concentrations of mite allergens.<sup>241</sup> Most studies of dust samples and air samples taken from the same room have found no measurable airborne Der p 1 even when reservoir dust levels were as high as 127  $\mu\text{g/g}$ .<sup>242</sup> The reason airborne measurements are low is that airborne mite allergen concentrations are absent without vigorous disturbance. One study using a multistage cascade

impactor found that almost 80% of airborne Der p 2 was carried on particles larger than 4.7  $\mu$  in diameter. In contrast, 20% was associated with particles 1.1 to 4.7  $\mu$ .<sup>243</sup>

Although most detectable dust mite allergens in air samples are associated with large particles, smaller fragments also are present. In 1 study at an animal facility, the number or size of particles carrying airborne mite allergens was measured in allergens collected with a filter or on the stages of a cascade impactor. During the disturbance of rat litter, approximately 46% of particles had a mean size of approximately 7  $\mu$  in diameter. After 15 to 35 minutes, 16% of these medium-sized particles were still airborne. Disturbance of house dust was associated with about 80% of Der p 1—carrying particles, with a diameter larger than 10  $\mu$  and very few remaining airborne after 15 to 35 minutes.<sup>244</sup> These results were further confirmed in another study in which neither Der p 1 nor Der f 1 was detected unless the air was disturbed.<sup>245</sup>

Assessment of personal exposure to dust mite has always been difficult, usually relying on proxy measurements such as air or settled dust concentrations. The reason to measure airborne dust mite allergen levels is to obtain an estimate of personal exposure that takes place in a patient's breathing zone. One study found similar Der p 1 and Der p 2 concentrations in air collected with nasal samplers and in mattress dust, suggesting that the dust measurements are a good proxy for personal exposure.<sup>65</sup> Another study found that nasal air samplers offered no advantage over settled dust for measuring personal dust mite exposure.<sup>246</sup>

Although most detectable dust mite allergens in air samples are associated with large particles, this is not to say that exposure to smaller fragments does not occur. To date, it is not known whether multiple hits to the respiratory system (ie, many small particles with allergens and/or irritants) or merely a few large allergen-laden particles are the main drivers in allergy (sensitization or exacerbation) or asthma (development or exacerbation). Long-term air sampling in homes that might lead to successful detection of dust mite allergens (and chitin fragments) in the smaller fractions is not feasible with conventional air sampling methods, which are cumbersome and loud, thus being unacceptable to residents. Passive collection using electrostatic cloths (ie, electret) has shown some promise in this area of long-term air sampling, but it is not selective for size. However, if the main issue is to determine whether dust mite allergen is present in the home and to plan a course of practical allergen avoidance strategies, then dust sampling is sufficient and relatively easy to obtain.

#### Mitigation

Mitigation involves the removal of dust mite allergens and other potentially proinflammatory and irritating dust mite emanations from reservoirs. The goal is to decrease exposure to these contaminants to levels that are low enough to avoid adverse health effects. Because mite allergens are highly stable over time, active removal is necessary to achieve the benefits of environmental control in a reasonable amount of time.

#### Vacuuming

**16. Recommend regular vacuuming using cleaners that have HEPA filtration or using a central vacuum with adequate filtration or that vents to the outside to decrease exposure to dust mite allergen-containing particles. (Strength of recommendation: strong, B evidence)**

Regular, thorough vacuuming can help remove dust mite allergens, although it is not capable of removing live mites. Vacuum cleaners should be equipped with a HEPA filtration system to retain dust mite fecal pellets within the vacuum bag. Emphasis should be placed on bedrooms, mattresses, and other locations where dust mites are likely to live. Ideally, allergic individuals should not do the

vacuuming because mite allergen exposure is increased during vacuuming and when the dust compartments are emptied.<sup>247</sup>

In 1 study, daily vacuum cleaning of mattresses over time significantly decreased house dust mite allergens from a median of 4 to 0.4  $\mu\text{g}$  after 8 weeks. In addition, endotoxin decreased from 13.6 to 3.4 EU and  $\beta$ -glucan decreased from 94.4 to 19.7  $\mu\text{g}$ . These decreases correlated with a decrease in total dust retrieved from those same mattresses.<sup>248</sup>

Der p 1 levels can vary substantially in different areas within a room. In 1 study, the coefficient of variation of samples obtained in different locations of the same room was as high as 80%. This means that the entire room needs to be cleaned as opposed to only areas near the bed or in high traffic areas.<sup>249</sup>

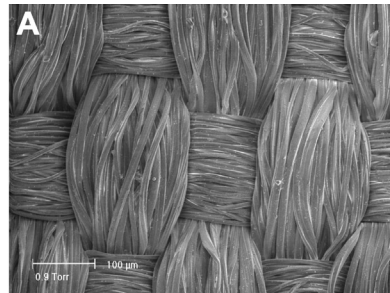
Carpet type needs to be considered for allergen avoidance. In 1 study, 26 types of carpet that differed in fiber density, cross-sectional shape, presence of fluorocarbon treatment, carpet style, pile height, and pile density were doped with an allergen-containing reference dust. Fluorocarbon treatment of fibers, square-hollow fiber shape, high-density fiber, low-pile height in cut-pile carpets, and low-pile density in loop carpets were associated with increased release and recovery of allergen.<sup>250</sup>

### Beds

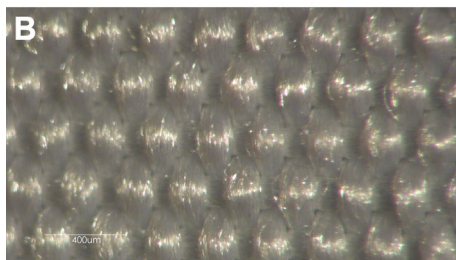
#### 17. Recommend that patients should use mite allergen–proof mattress, box spring, and pillow encasings to decrease exposure to mite allergens. (Strength of recommendation: strong, B evidence)

Mattresses and bedding are a major source of dust mites and mite allergens. This is particularly problematic because most people spend substantial amounts of time in proximity to these allergens. Box springs (mattress bases) generally contain even more mite allergen<sup>68,69</sup> than mattresses, although the relative contribution of these substrates to actual inhalational exposure is unclear. When new, mattresses generally are not contaminated by mites, although they can become contaminated and a significant source of mite exposure in as few as 4 months.<sup>251</sup> For that reason, mattress encasings have been used to prevent or contain dust mites. Theoretically, when a new mattress is encased, contamination can be prevented.

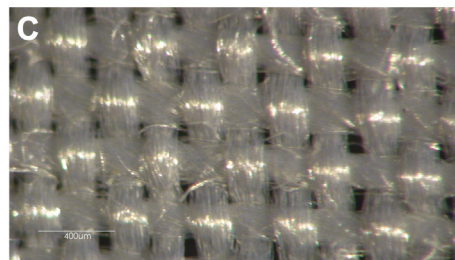
There are 4 basic types of allergen-barrier encasings: vinyl, laminates, woven microfiber fabric, and nonwoven microfiber fabric (Fig 7). The first 2 block all allergens, including Fel d 1, but are not permeable to air or water vapor and therefore are uncomfortable. They are used infrequently, having been supplanted largely by “breathable” microfiber encasings.



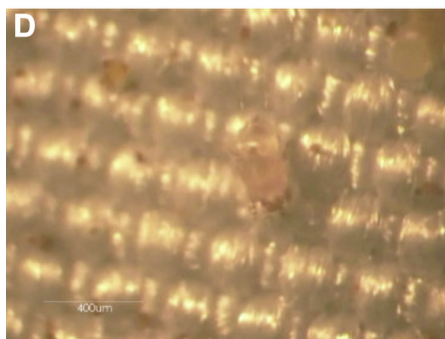
Electron micrograph of tightly woven microfiber encasing, showing numerous filaments in each yarn



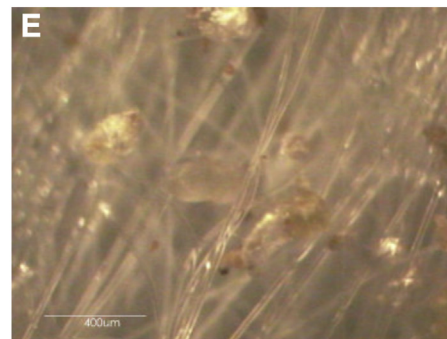
Light micrograph of tightly woven microfiber encasing



Light micrograph of loosely woven microfiber encasing



Dust mites and feces are unable to traverse tightly woven barrier fabric



Dust mite penetrating non-woven barrier fabric



Microfiber encasings are of 2 types: woven and nonwoven. Woven microfiber encasings are made from fabrics in which (as with all woven fabrics) the long warp and weft yarns have been alternately woven above and below each other on a loom. A microfiber woven fabric can be distinguished from other woven fabrics by the fact that each yarn used comprises 100 to 200 ultrathin microfilaments. The tightly woven microfiber fabric acts as a filter that prevents allergen escape yet allows air and water vapor to pass freely through the fabric.

Commercially available woven barrier fabrics vary considerably in the tightness of the weave, based on the number of yarns per inch, the number of filaments per yarn, and the diameter of each of those filaments. In general, woven microfiber fabrics with a mean pore size smaller than  $10\ \mu$  block Der p 1, but only those with a mean pore size smaller than  $6\ \mu$  block Fel d 1. The mean pore size is only a surrogate measurement of allergen impermeability, because the mean does not indicate the total number of pores, the distribution of pore sizes around that mean, or the “tortuosity” of the pores. Although pore size can be a useful rule of thumb, in the final analysis the issue is simply whether a particular allergen, measurable with an ELISA, can be suctioned through a given fabric. Many commercially available woven microfiber encasings block Der p 1 but not Fel d 1.<sup>252</sup>

In contrast to woven barrier fabrics, nonwoven fabrics are manufactured by fusing a mass of overlain short filaments to each other with heat, glue, and pressure. (Although not a microfiber, felt is an example of a nonwoven fabric.) Nonwoven microfiber fabrics are somewhat similar in appearance to a paper towel and can be recognized by an embossed pattern on their surface. Although pore size measurements apply only to woven and not to nonwoven fabrics, nonwoven microfiber fabrics do block allergen passage. However, recent information has indicated that the depth of the interstices between the randomly crisscrossing fibers of nonwoven encasings is deep enough to accumulate allergens—including Der p 1, Der f 1, and Fel d 1—over time, so that the patient is eventually sleeping on a layer of allergen on the surface of the non-woven encasing. This is not the case with the smooth surface of woven encasings. Ironically, in contrast to woven encasings, (which although washable do not need to be routinely washed because they do not accumulate surface allergen), non-woven encasings, which do collect surface allergen, are not washable. These findings suggest that nonwoven microfibers do not succeed in decreasing allergen exposure and should not be used for allergen avoidance.<sup>253</sup>

Mite-proof bedding covers, as part of a structured allergen-control program, decrease the level of exposure to mite allergens. Even so, this single avoidance measure does not lead to a significant alleviation of clinical symptoms in patients with allergic rhinitis.<sup>254</sup> A combination of education and mattress encasement to decrease mite allergen exposure can be used to decrease sensitization to mite allergens.<sup>255</sup> Nonallergenic pillows are not a substitute for covering them with allergy-proof encasements. Foam pillows are not less prone to dust mite allergens than are feather pillows.

Double-blinded, randomized, placebo-controlled studies of allergen-impermeable bed covers have demonstrated an ability to decrease exposure to Der p 1 and Der f 1 in mattress dust; however, there have been inconsistencies in demonstrating that mite-sensitive individuals show improvement as a result for asthma or for allergic rhinitis. In a prospective trial of 60 children with dust mite allergy and asthma, pillow and mattress encasings or sham encasings were used for 1 year. There was a significant decrease in the amount of dust mite allergen and in inhaled steroid use in the treatment group. Dust mite allergens (Der f 1 and Der p 1) were decreased to below detectable limits by fabrics with a pore size smaller than  $10\ \mu$ .<sup>256</sup> Other studies have shown that dust mite covers alone, without a comprehensive avoidance plan, may not achieve a clinical benefit in patients with asthma.<sup>257,258</sup>

In another 1-year study, significant decreases in dust mite allergen concentrations were associated with a decrease in the dose of inhaled

steroids for patients in the active treatment group.<sup>256</sup> Another controlled study of dust mite avoidance involved using zippered vinyl pillows, mattresses, and box spring covers. After 1 month, asthma signs and symptoms decreased in the treatment group.<sup>259</sup>

The use of a feather quilt and pillow and a mattress encasing alone was not effective in decreasing asthma symptoms in mite-allergic children after 1 year compared with nonallergic controls. This study did not actually measure the exposure, so it is hard to tell why the intervention failed to be effective.<sup>260</sup>

**18. Discourage members of families with an atopic background from sleeping in bunk beds. If bunk sleeping is necessary, the sensitized person ideally should sleep in the top bed and the top and bottom mattresses (and any fabric-covered “bunk-boards”) should be enclosed in allergen-impermeable encasings. (Strength of recommendation: moderate, B evidence)**

In a study of bunk beds, sleeping in bunks was found to increase the risk of developing asthma primarily for subjects sleeping in the bottom bed.<sup>261</sup> Concerns about sleeping in bunk beds arose because the top mattress on a bunk bed generally was supported by a wire-like mesh or sometimes by a few slats. As a result, a person sleeping supine on the lower mattress could look up and see much of the lower surface of the upper mattress. This created a situation in which the lower occupant was “sandwiched” between 2 mattresses and could thus, be exposed to mite allergen both falling from above and rising from the mattress below.

Most current bunk-beds have a “bunk-board” beneath the upper mattress. This is basically a bed board that is covered in fabric. However, the fabric above can be a source of mite allergen to the sleeper below, so if such a board is present, it too should be encased (in special encasings made for that purpose). If top and bottom mattresses are encased (in addition to any fabric-covered bunk-board, if present), then an allergic person sleeping on the bottom bunk most likely would not experience more mite exposure than the person sleeping on the top bunk. If the allergic person sleeps on the top bunk, it is still recommended that all mattresses (and pillows for that matter) in the patient’s bedroom be encased. This is because anyone moving on a nonencased mattress or pillow can create a plume of allergen that could potentially affect others in the room.

#### Denaturants

**19. Do not recommend tannic acid for decreasing mite allergens in carpet dust because it is only marginally effective. (Strength of recommendation: moderate, C evidence)**

Tannic acid is a protein-denaturing agent. It has been reported to decrease allergen levels in dust and is available commercially as 1% and 3% solutions. Initial studies suggested that tannic acid was effective at decreasing mite allergen levels in carpet dust. On further evaluation, tannic acid was found to elute from the dust along with the dust mite allergens. When mite allergen levels were assayed using ELISA, concentrations of tannic acid as low as 0.1% were found to inhibit the assays. As a result, although the apparent decreases in Der p 1 and Der f 1 levels were 89% and 96% with tannic acid initially, the product was less effective when the assays were rerun taking this inhibition into account. In an extreme case in which a carpet had been repeatedly treated with tannic acid, the apparent concentration of Der p 1 was lower than  $0.05\ \mu\text{g/g}$ , whereas the actual concentration was  $8.4\ \mu\text{g/g}$ .<sup>262</sup> This finding was confirmed in another study that found that tannic acid can decrease mite allergen levels in carpet dust but that the effects were not maintained for very long.<sup>199</sup>

#### Pathways to occupants

##### Air filtration

**20. HEPA filtration alone is of uncertain benefit for patients with mite allergy, although it can decrease local exposure to airborne**

**mite allergens and to some irritants. If used, recommend that HEPA cleaners should be placed in areas of mite contamination where air disturbance is likely to suspend particles so that they are available for removal. (Strength of recommendation: weak, C evidence).**

The effectiveness of air filtration as a means to decrease exposure to mite allergens depends on the extent to which mite allergens are contained on particulate material that is amenable to filtration and the efficiency of particle removal by the filtration device. Exposure to allergen-containing particles and the ability to filter them from air depends on the aerodynamic diameter and settling rate of the airborne particles and their concentrations. Analysis of the aerodynamic size of vacuumed dust samples showed that mite allergens were associated with relatively large particles, with a mean aerodynamic diameter of 28  $\mu$ , although smaller fragments also were present.<sup>263</sup> Particles of this size usually reside in settled dust and become airborne to varying degrees only when disturbed.

The efficiency of an air filter is usually described as a filter's MERV rating. MERV is an acronym for "minimum efficiency reporting value" and is assigned to filters based on the ASHRAE standard testing method (52.2, 2007).<sup>264</sup> Filter ratings typically range from MERV1 to MERV12, with higher ratings indicating better efficiency. Filters with a MERV12 rating are at least 80% efficient at removing particles in the 1- to 3- $\mu$  range and at least 90% in the 3- to 10- $\mu$  range. However, the efficiency of the filter is only 1 factor in determining overall effectiveness of an air filtration device, the other being the amount of air moved through the filter material per unit of time. These 2 factors determine the Clean Air Delivery Rate. Clean Air Delivery Rates of portable room air cleaners and devices are rated in accordance with the Association of Home Appliance Manufacturers Standard Test Method for the Performance of Portable Household Electric Room Air Cleaners.<sup>265</sup>

Air-cleaning devices for residential buildings include whole-house filters that are installed on the central HVAC system and free-standing portable room air cleaners. With whole-house filtration, indoor air is transported to the equipment HVAC, where it is cleaned before being sent back into the occupied space. Disposable filters range from inexpensive fiberglass filters to pleated materials with a large filtration area. Inexpensive coarse filters provide very little small-particle filtration and might even worsen the problem by capturing and then dumping particles downstream. They generally have no or a very low MERV rating, MERV1 to MERV2. Their low cost makes them popular in apartments or low-income housing. Multiple-extended surface filters are the most common type of panel furnace with higher efficiency and can reach a rating of MERV11 or MERV12. The pleating decreases the pressure necessary to push air through the filter. Filter change intervals are recommended every 3 months for normal residential use. Contamination of air ducts has been shown to decrease with improved whole-house air filtration. A recent standard published by ASHRAE established that "mechanical systems that supply air to occupied space through ductwork exceeding 10 ft (3 m) in length should have a filter with a designated minimum efficiency of MERV6, or better, when tested in accordance with standard ASHRAE Standard 52.2."<sup>266</sup>

Portable room air cleaners include ionizer cleaners, HEPA cleaners, and non-HEPA cleaners. The ionizer cleaners are not recommended because of their tendency to produce ozone, which can trigger asthma symptoms, and the non-HEPA cleaners do not remove enough particles to provide clinical benefit. For that reason, HEPA devices have been the subject of clinical trials. In a systematic review of HEPA devices,<sup>267</sup> 2 studies failed to show decreased symptoms in subjects with dust mite allergy; the other studies were small, had inadequate blinding, lack of measured airborne allergen concentrations, and varied in air-velocity rates relative to

room size, location, and occupants. Another review of 10 randomized trials found HEPA filtration to be associated with symptom decreases.<sup>268</sup> A 2-year controlled study of inner-city children with atopy and asthma showed decreases in asthma symptoms and bedroom dust mite and cockroach allergen levels in the environmental intervention group, which included bedroom HEPA filters.

An alternative to cleaning the air of an entire room is to clean a smaller area of air surrounding the patient, particularly during sleep. This requires a low, nonturbulent (ie, laminar) airflow out of the device. Three studies of this laminar flow HEPA filtration of the "breathing zone" showed clinical benefit.<sup>269</sup>

Two other pediatric asthma studies using room cleaning reported decreased medication requirements.<sup>270,271</sup> In another study, the use of active air cleaners in living rooms and bedrooms with or even without allergen-impermeable mattress covers decreased allergen exposure and alleviated airway hyper-responsiveness in patients with asthma.<sup>272</sup>

Although there is evidence that air filtration decreases levels of particles associated with dust mite allergens, filtration alone is unlikely to provide sufficiently decreased exposure to improve health. Air filtration therefore contributes to clinical improvement when used as a component in a more comprehensive program of decreasing exposure. Portable room air cleaners with HEPA filters, particularly if they filter the breathing zone during sleep, appear to be the most beneficial type of filtration.

#### Overall benefit

##### Effectiveness of interventions

**21. Recommend a multifaceted approach for dust mite avoidance using a combination of techniques that includes repetitive and sequential interventions shown to decrease mite exposure, as described earlier, for patients with dust mite allergy who are at risk of mite exposure. (Strength of recommendation: moderate, A evidence)**

Although many studies of dust mite avoidance have reported decreases in exposure, the challenge has been to show that the observed decreased exposure leads to health benefits in a cost-effective way. To maximize the likelihood of decreasing mite exposure sufficiently for there to be measurable health benefits, most studies have used a combination of interventions that address facilitative factors, sources, and reservoirs. For that reason, it is difficult to determine which single intervention or combination of interventions causes whatever health benefit is observed and which interventions are ineffective and therefore unnecessary. The latter should be avoided to decrease the overall cost of dust mite avoidance because, at least in the United States, most health plans do not cover the cost of environmental interventions.

To identify the most effective way to decrease mite exposure, some systematic reviews of dust mite avoidance studies have been performed to better understand the effect of these interventions. Unfortunately, a great deal of controversy surrounding several of the reviews and meta-analyses occurred from criteria used to include or exclude studies. A published series of 4 meta-analyses on this subject from the Cochrane Library suggested that decisions about which trials to include can have a major effect on the outcome.<sup>273</sup>

Some of this controversy has been the result of the Cochrane meta-analysis of 2008,<sup>274</sup> which included 54 studies on the clinical effect of mite-decreasing measures in mite-sensitive patients with asthma. Not only did the investigators conclude that "there were no statistically significant differences either in number of patients improved, asthma symptom scores, or in medication usage" and that "chemical and physical methods aimed at reducing exposure to house dust mite allergens cannot be recommended," but they went so far as to state that "it is doubtful whether further studies,



similar to the ones in our review, are worthwhile.” These conclusions have not gone unchallenged, however,<sup>25,273</sup> it having been noted that two thirds of the studies included in the Cochrane meta-analysis used measures that actually failed to lower allergen levels, and that measures that fail to lower allergens can hardly be expected to improve clinical outcomes. A reanalysis of those studies, separating the studies that used measures that lowered mite allergen from those that failed to do so, showed that there was indeed an improvement in clinical parameters in the former group.<sup>25</sup>

Similar caution must be applied to the interpretation of another well-publicized study of 1,122 adult patients with asthma, which concluded “the use of allergen-impermeable bed covers as a single intervention for the avoidance of mite allergen seems clinically ineffective for the routine management of asthma in primary care.”<sup>257</sup> A reading of the study, however, shows that 23% of patients were active smokers and an additional 22% were former smokers; patients were excluded if they did not require daily albuterol (most required an average of 3 puffs per day and 1–2 puffs per night, in addition to inhaled steroids); and 55% of patients owned a cat or dog.

The obvious message is that clinicians must deduce, from the medical and environmental histories and physical examination, what the patient’s relevant environmental exposures are and then take steps that have been shown to decrease exposure to those relevant allergens. When this was done in a multicenter study of children with asthma, allergen avoidance had an “effect similar to that described in placebo controlled studies of inhaled corticosteroids.”<sup>275</sup>

A demonstration of the value of complete dust mite avoidance was shown in 9 dust mite–allergic patients with asthma who lived in hospital rooms for at least 2 months. All their symptoms and peak expiratory flow rates improved. In addition, 7 were able to decrease their medications and had decreased bronchial hyper-responsiveness.<sup>179</sup> Unfortunately, such a profound and prolonged decrease of exposure is rarely achieved in regions where mites are prevalent.

Under more realistic circumstances, decreasing mite exposure is unlikely to be clinically useful unless the decrease is sufficient and persistent. This was demonstrated in a double-blinded, randomized trial comparing asthma progression over 1 year in children whose homes received standard environmental control intervention with those whose homes received aggressive intervention for dust mite elimination. Symptom scores and quality-of-life scores were similar in the 2 groups, but exposure and bronchial hyper-responsiveness improved in the aggressive group.<sup>276</sup>

A meta-analysis of 23 randomized trials that investigated the effects of chemical and/or physical measures to control mites vs untreated control groups concluded that current chemical and physical methods aimed at decreasing exposure to mite allergens were ineffective.<sup>277</sup>

One systematic review of 9 randomized controlled trials of dust mite control measures in patients with rhinitis triggered by dust mite exposure evaluated mattress encasings, acaricides, HEPA filters, and acaricide and mattress encasing in isolation and in combination. Seven of the 9 trials resulted in significant decreases in dust mite exposure.<sup>278,279</sup> Another Cochrane review looked at 54 trials involving patients with asthma using mattress encasings, chemical methods, and a combination of chemical and physical methods to decrease mite exposure. This review found no benefit for any of these interventions.<sup>280</sup>

A review of 2 studies of children with asthma using mattress encasings alone found improved peak expiratory flow rates, but no other improvements over 12 months. Another study found improved peak expiratory flow rates after 9 weeks and decreased use of medications after 6 months.<sup>281</sup>

In 1 study, 23 children with asthma living in Atlanta were randomly assigned to active or placebo groups. Active treatment included encasing mattresses, box springs, and pillows in allergen-impermeable covers; weekly hot water wash of bed linens; replacement of bedroom carpet with polished flooring; and 3% tannic acid spray to living room carpets. Placebo treatment included permeable encasing for bedding, cold water wash, and water spray for carpet. Allergen levels decreased in the active and placebo homes. Increases in peak expiratory flow rate were recorded in children in the active treatment group and in sensitized patients whose dust mite allergens decreased regardless of treatment group. The results were complicated by exacerbations triggered by respiratory tract infections.<sup>282</sup>

In another Atlanta study, 104 children with asthma were randomized to an active or placebo avoidance group. Avoidance included bed and pillow covers and hot washing of bedding. There was a difference between the active and placebo homes for asthma visits and dust mite concentrations.<sup>283</sup>

Thus, although there is little evidence for the clinical benefits of single avoidance, multifaceted interventions in carefully selected patients appear to be helpful. Such interventions should be tailored to the patient’s sensitization and allergen exposure; the interventions should be multifaceted, addressing facilitative factors, sources, and reservoirs; and to be of most benefit, especially for children, the interventions should be implemented as early as possible.<sup>284</sup>

Allergen avoidance is an evolving science. Future goals include the determination of the contribution of the various sources of mite allergen to inhalational exposure at different times of the day; a search for markers that might predict which patients are most likely to benefit from allergen avoidance measures; and a better understanding of the effect of allergen avoidance on other exposures, eg, endotoxin, which, depending on the stage of the patient’s atopy, might decrease or increase sensitization and/or symptoms.<sup>60</sup>

#### Cost–effectiveness

Home-based, multitriggger, multicomponent interventions with an environmental focus have been shown to be effective in improving overall quality of life and productivity in children and adolescents with asthma. What is not clear is the extent to which the various interventions contribute to this improvement. One systematic review of 20 studies in which environmental interventions were performed in homes of children and adolescents found that asthma symptoms were decreased by 21 symptom-days per year; schooldays missed were decreased by 12.3 days per year and the number of asthma acute care visits were decreased by 0.57 visits per year.<sup>285</sup>

Although environmental interventions appear to result in clinical benefit, the cost–effectiveness of these interventions needs to be considered. In a systematic review of 13 studies, intervention costs were evaluated with respect to the intensity of the interventions (minor, moderate, or major). Benefit/cost ratios ranged from 5.3 to 14.0, which means that for every dollar spent on the intervention, medical and productivity savings ranged from \$5.30 to \$14.00. In addition, the net cost ranged from \$12 to \$57 for each additional symptom-free day.<sup>286</sup> Because these studies decreased exposure to multiple allergens, it is impossible to determine the contribution of dust mite avoidance to these results.

Combinations of dust-mite-specific interventions, including dust-mite-impermeable mattress and pillow encasings, improved cleaning practices, HEPA vacuum cleaners, mechanical ventilation, and parental education, also are associated with decreased exposure and improved health outcomes for children with asthma. These combinations of interventions have proved to be cost–effective in the studies that have used them.<sup>287</sup> Ideally, a patient

should implement interventions and consider their cost when prioritizing them. To be effective, facilitative factors, sources, reservoirs, and pathways to occupants need to be addressed.

Table 4 presents the range of costs for various interventions that have been shown to be effective. Interventions for facilitative factors consist primarily of obtaining a hygrometer, and keeping the RH below 50% using a dehumidifier and/or central air conditioner. The cost of operating the latter depends on many factors, making it difficult to estimate the cost. The only recommended intervention for elimination of dust mites is regular washing of bedding and clothing; a cost estimate is difficult to make. Other interventions are more expensive and there is no evidence to support them or they are not recommended.

Reservoirs can be managed with HEPA vacuuming of carpets, installation of mattress, box spring, and pillow encasings, and probably with the use of dust-decreasing methods, although the latter have no evidence to support them. Tests for mite allergens are considered optional. Pathways to occupants can be blocked with portable air filters or central filters. The use of an N95 mask during dust-producing activities seems reasonable but there is no evidence to make a recommendation.

Thus, the overall cost of these interventions can range anywhere from \$100 to \$2,300, depending on which items are used. Because health plans generally do not pay for these interventions, it is up to the homeowner to determine how many interventions to implement. The most important interventions include control of humidity, regular washing, regular vacuuming, and installation of mattress, box spring, and pillow encasings.

### Immunotherapy for dust mite allergy

Extensive research has been conducted in past decades to determine whether immunotherapy (subcutaneous and sublingual) with dust mite extract is effective and safe for the treatment of rhinitis, asthma, and atopic dermatitis.

#### Subcutaneous immunotherapy

**22. Offer subcutaneous immunotherapy to dust mite–allergic patients with rhinitis or mild to moderate asthma if they meet the general criteria for receiving allergen immunotherapy. (Strength of recommendation: strong, A evidence for asthma; strength of recommendation: moderate, B evidence for rhinitis)**

There exist very few data on SCIT with dust mites in patients with allergic rhinitis, because most trials have been performed in patients with asthma. No randomized trials have been conducted with US extracts, but 1 English trial and several trials in Asia have shown efficacy of dust mite SCIT in patients with perennial allergic rhinitis.<sup>288</sup> A recent review of SCIT in pediatric patients concluded there was low-quality evidence for alleviation of rhinitis symptoms and decrease in medication scores.<sup>289</sup> The allergen specificity of SCIT was confirmed in an elegantly designed, randomized, blinded trial of dual dust mite and grass pollen in patients with perennial rhinitis receiving dust mite or grass pollen SCIT for 3 years.<sup>290</sup>

Most SCIT studies of dust mite have been carried out in patients with asthma. For ethical reasons, all trials allow for maintenance and rescue asthma treatment in addition to immunotherapy, which makes symptom improvement hard to demonstrate.<sup>291</sup> Thus, the prime efficacy outcome shown by most trials is a decrease in medication while asthma symptom control is maintained. Also, specific challenge testing generally shows a more pronounced improvement than nonspecific methacholine bronchial challenge tests.<sup>292</sup> In a controlled study of standardized dust mite SCIT given for 3 years, the active group had a 1.6-fold increase in the amount of mite allergen required to provoke a 20% drop in FEV1, a 60-fold increase in skin test histamine-equivalent dust mite allergen concentrations, and decreased immediate- and decreased or abolished late-phase skin reactions. In those patients with moderate persistent asthma, there was a decrease in the use of inhaled corticosteroids in the 2 groups, but the decrease was statistically significantly larger for those treated with SCIT compared with placebo after year 2 and year 3. Also, there was an initial increase in dust mite–specific IgE followed by a decrease to baseline.<sup>293</sup>

A review by the Cochrane Airways Group of randomized controlled trials using various forms of injection allergen immunotherapy for asthma found 42 trials of immunotherapy for house dust mite allergy, 39 of which used a house dust mite extract. Overall, it would have been necessary to treat 3 patients with immunotherapy to avoid 1 deterioration in asthma symptoms (number needed to treat = 3) and 4 patients to avoid 1 requiring increased medication (number needed to treat = 4). The number needed to harm for a local adverse reaction was 16, and for a systemic reaction the number needed to harm was 9, probably indicating the subreporting of local adverse reactions. In the house dust mite (HDM) SCIT subgroup analysis of double-blinded, placebo-controlled trials, there was a medium effect size for

**Table 4**  
Typical cost of interventions to decrease exposure to dust mite allergens

	Item	Cost range (US\$) <sup>a</sup>	Recommendation
Facilitative factors	Temperature/hygrometer	7.50–33.00	Strong
	Dehumidifier	204–414	Strong
	Central air conditioner	Varies	None
Sources	Washing	Varies	Strong
	Acaricides	N/A	Not recommended
	Freezing	Varies	None
Reservoirs	HEPA vacuum cleaner	100–750	Strong
	Mattress encasings	62–220	strong
	Pillow encasings	13–20	Strong
	Mite allergen home test kit	30	Weak
	8-allergen laboratory test kit	200	Weak
	Box spring encasings	19–90	Weak
	Denaturants	7–21	Not recommended
	Barrier-fabric comforter	140–220	None
	Decreasing dust (mops, dust cloth, etc)	5–22	None
	Pathways to occupants	Air filter portable (18 × 20 ft)	182–849
Central air filters		13–21	Moderate
N95 mask		10–12	None

Abbreviations: HEPA, high-efficiency particulate air; N/A, not applicable; none, no recommendation was made in this practice parameter regarding the intervention.

<sup>a</sup>Prices are based on quotes found on the Internet by various companies that sell dust mite–control products.

a decrease in asthma symptom score and a large effect size for a decrease in medication score. The effect size for improvement in specific bronchial hyper-reactivity after immunotherapy with dust mite was large.<sup>292</sup> In pediatric patients with asthma, there exists high-quality evidence for improvement in symptom and medication scores with European and Asian extracts.<sup>289</sup> Immunotherapy has been attempted with a recombinant Der p 1 and Der p 2 combination vaccine. In a preclinical study, immunization of rabbits induced production of specific IgG that was capable of blocking binding of IgE from dust mite-sensitized humans.<sup>294</sup>

**23. Consider subcutaneous immunotherapy for dust mite–allergic patients with atopic dermatitis if they meet the general criteria for receiving allergen immunotherapy; however, possible exacerbation of the disease during the initial phase of immunotherapy should be discussed with the patient (Strength of recommendation: moderate, A evidence)**

The first controlled trials with dust mite SCIT for atopic dermatitis reported a statistically significant dose-related decrease in Scoring Atopic Dermatitis (SCORAD). However, many patients experienced a flare of their symptoms and only 51 of 89 completed the trial.<sup>295</sup> Similar findings were published with accelerated immunotherapy schedules in dust mite-sensitized patients with atopic dermatitis using a 3-day or 1-day protocol. The 1-day protocol was associated with a 29% rate of systemic reactions, whereas 22% of patients using the 3-day protocol had a systemic reaction. Reactions occurred within 4 hours after the maximum dose was administered.<sup>296</sup> Hypoallergenic extracts might produce better results, as was found in a controlled trial of 168 patients with atopic dermatitis using SCIT with a depigmented hypoallergenic polymerized mite extract. A statistically significant decrease of the median total SCORAD by 18% was shown in the subgroup of patients with severe atopic dermatitis (SCORAD >50), without a difference in adverse events between the active and placebo groups.<sup>297</sup>

**24. Patients receiving immunotherapy for dust mite ideally should receive a dose that delivers approximately 7 µg of Der p 1 per injection or 500 to 2,000 AU per injection to obtain an optimal balance between efficacy and safety. (Strength of recommendation: strong, A evidence)**

A 24-month dose–response study was conducted in 1993 with a European dust mite extract adsorbed to alum for immunotherapy, with doses of 0.7, 7, and 21 µg of Der p 1 to 74 patients with asthma who were allergic to dust mite. A direct dose–response relation was demonstrated for systemic reactions and a dose-dependent increase in efficacy. An optimal dose providing the greatest improvement with the lowest rate of systemic reactions was identified as 7 µg of Der p 1.<sup>298</sup> However, the manufacturing process of US dust mite extracts is dissimilar. House dust mite extracts from US manufacturers are derived from 99% pure mite bodies, whereas in Europe extracts are derived mainly from spent cultures. As a result, not only the concentration but also the composition is different from the European extracts.<sup>163</sup> US dust mite extracts have a Der p 1-to-Der p 2 content close to 1:1, as opposed to the European extracts in which the relation is closer to 10:1.<sup>235</sup> Because these major allergens, Der p 1 and Der p 2, are important for the total potency of the extract, a US extract with the same content of Der p 1 can be expected to have greater total potency. Moreover, US extracts lack the depot effect of the European extracts, because no alum is added. In consequence, their application frequency is higher than with European extracts.<sup>299</sup> Thus, the exact significance of these findings for treatment with glycerinated US extracts is not clear.

The dosing interval of a probably effective dose as recommended by the Practice Parameters on Immunotherapy, Third Update, on HDMs is 500 to 2,000 AU weekly until a maintenance dose is reached and then monthly. There is no evidence to support administering lower doses more frequently or higher doses less frequently to obtain similar efficacy. US allergists tend to dose

usually near the lower limit, as was shown independently by 2 investigators. To determine how much mite is administered in a typical course of immunotherapy, a study was performed to determine the doses of standardized allergen extracts commonly used by 500 randomly selected board-certified allergists in the United States. Median doses of house dust mites were only slightly lower than those that have proved effective, suggesting that for the most part allergists are delivering an effective dose of dust mite allergen to their patients who receive SCIT.<sup>300</sup> A recent survey among AAAAI members confirmed this finding.<sup>289</sup>

In another study, 200 mite-sensitized patients with rhinitis or asthma were given SCIT using a cluster schedule in which an optimal dose was reached after 4 visits. In total 6 systemic reactions were observed in 6 patients (0.3% of administered doses), which is comparable to or lower than with traditional weekly SCIT.<sup>301</sup> Immunotherapy with different modified extracts of *D pteronyssinus* and *D farinae* have been studied and have shown efficacy, including polymerized extracts in asthma<sup>302</sup> and glutaraldehyde-modified extracts for rhinitis and asthma,<sup>303</sup> although neither of these extracts is currently available in the United States.

**25. US dust mite extracts can be mixed with pollen extracts, including grass and animal dander extracts. Also, at maintenance immunotherapy concentration US dust mite extracts can be mixed with fungal or cockroach extracts when glycerin content is kept at 10%. (Strength of recommendation: moderate, LB evidence)**

As stated earlier, HDM extracts from US manufacturers are almost exclusively derived from pure mite bodies and thus have a relatively low concentration of proteases. No detectable loss of allergen reactivity was observed after mixing timothy grass pollen with the various US manufacturers' mite extracts at concentrations equivalent to practice parameter recommendations for immunotherapy maintenance treatment concentrations.<sup>304</sup> The same holds true for tested cat hair and short ragweed pollen. When diluting mixes 1:100 and 1:1,000, some stabilizer (eg, human serum albumin, glycerin 10%) is needed to avoid potency loss.

The stability of extracts when mixed with dust mite extract has been studied extensively. In 1 study, mixtures were prepared using individual products from multiple sources at varied glycerin concentrations and were analyzed after storage for up to 1 year at 2°C to 8°C. Grass allergens were found compatible with dust mite extracts; however, recoveries of the grass allergens varied considerably when mixed with mold extracts, whereas cockroach extracts decreased dust mite allergen potencies. In all cases, glycerin improved the stability of mixed extracts, and in glycerin at 10% or higher, the protease activity was almost annulled.<sup>305</sup>

**26. Recommend 3 to 5 years of immunotherapy to obtain maximum benefit from immunotherapy for dust mite–induced asthma and rhinitis. (Strength of recommendation: moderate, A evidence)**

To determine how long SCIT for dust mite allergy should be given, SCIT was administered to mite-allergic asthmatic children for 3 or 5 years. Following SCIT discontinuation, annual follow-up visits were performed for 3 more years. Various measurements of effectiveness were used, including the need for inhaled corticosteroids, forced expiration in 1 second, and asthma symptoms. The 2 active groups did better than the control group. No differences were found between the 3- and 5-year groups, suggesting that 3 years of SCIT is an adequate duration for the treatment of childhood asthma for dust mite allergy and that 2 additional years add no clinical benefit.<sup>306</sup>

Another 5-year prospective, controlled clinical trial of SCIT with *D pteronyssinus* found decreases in rhinitis and asthma symptoms and quality of life by 3 years, although there was continued improvement in symptoms of rhinitis up to 5 years.<sup>307</sup>

It is important to note that these 2 trials were conducted in Europe using depot extracts. There are no prospective trial data on

duration of immunotherapy with US extracts. There are retrospective data from a survey among the AAAAI membership showing immunotherapy in the United States is generally continued for 5 years (median), clearly longer than the median duration in Europe, which is 3 years.<sup>289</sup>

### Sublingual immunotherapy

**27. Certain protocols and dosages of sublingual immunotherapy have been shown to be safe and effective for dust mite–allergic patients with rhinitis, mild to moderate asthma, and/or atopic dermatitis; however, because currently there is no Food and Drug Administration–approved product available in the United States, its use should not be recommended until such a product becomes available. (Strength of recommendation: moderate, A evidence)**

A 2013 review of evidence for SLIT in pediatric patients showed moderate-quality evidence for improvement of allergic rhinitis symptoms and medication scores and high-quality evidence for a decrease in specific nasal provocation testing. For asthma, the quality of evidence for a decrease in medication score (inhaled corticosteroids and/or rescue medication) was high, but—as explained earlier—the quality of evidence for symptom decrease was very low and there was no improvement in methacholine bronchial challenge testing.<sup>308</sup>

Early studies of dust mite–containing sublingual tablets have shown decreased inhaled corticosteroid requirements in adult patients with asthma compared with control groups, with minimal adverse effects consisting primarily of oral pruritis.<sup>309</sup>

In the United States, SLIT phase 1 trials were conducted with glycerinated US extracts, including HDM, showing acceptable tolerance profiles.<sup>310</sup> In a small double-blinded, placebo-controlled dose-finding study with a US allergen extract, high-dose (4,200 AU, containing approximately 70 µg of Der f 1; Greer Laboratories, Inc, Lenoir, North Carolina) vs low-dose (60 AU, 1 µg of Der f 1) *D farinæ* SLIT daily for 12 to 18 months, after a 1-month up-dosing phase, showed no severe systemic reactions and no differences in allergic rhinitis symptom medication scores between the active and placebo groups. High-dose SLIT did increase the bronchial threshold to allergen challenge and increased *D farinæ*–specific IgG4, whereas low-dose SLIT and placebo had no effect.<sup>311</sup>

A question is whether monoallergen HDM SLIT for dust mite–allergic patients would work as well for monosensitized individuals as for polysensitized individuals. In a 1-year observational trial conducted in Korea, dust mite SLIT was administered to monosensitized and polysensitized individuals. The 2 groups showed improvement in nasal symptom scores and medication requirements, although the polysensitized group received only SLIT to dust mite.<sup>312</sup>

Another question is whether dual allergen SLIT with a combined HDM–grass pollen extract would work. One study assessed 12 months of treatment with a US glycerinated solution of dual-SLIT in children with allergic rhinitis in a controlled trial. The investigators reported a statistically significant improvement in the rhinoconjunctivitis symptom score, medication score, and combined score at 12 and 24 months (12 months after treatment discontinuation).<sup>313</sup>

The efficacy and safety of SLIT for allergic rhinitis in adults and children was evaluated by the Cochrane ENT Group. A meta-analysis of 49 randomized, double-blinded, placebo-controlled trials of SLIT in adults or children found a significant decrease in symptoms and medication requirements in participants receiving SLIT compared with placebo. None of the included trials reported a severe systemic reaction or anaphylaxis. The conclusion was that SLIT is effective for allergic rhinitis and has been proved a safe route of administration. No subgroup analysis for dust mite SLIT was conducted.<sup>314</sup>

For the dosing of dust mite SLIT, maintenance solutions of *D pteronyssinus* from European manufacturers were compared with

the concentrated glycerinated extracts from US manufacturers. The quantity of dust mite allergen, as currently recommended for SLIT, varied more than 10-fold among European manufacturers. Compared with US concentrates, the relative potency was 10 times higher for US extracts than for European SLIT maintenance solutions of *D pteronyssinus*. In addition, European mite extracts contained a very low quantity of Der p 2 compared with US mite extracts.<sup>235</sup>

A study of SLIT in children with atopic dermatitis showed a significant difference from baseline in SCORAD between the active and placebo groups starting from month 9. There was a significant decrease in the use of medications in the active group.<sup>315</sup>

### Appendix A: moisture and humidity

Many difficulties with exposure to allergens in homes are caused, or made worse, by moisture. Floods from rain, broken pipes, or other leaks are usually visible. However, sources of moisture that are often overlooked are those generated by the occupants. These include activities such as cooking, showers, drying clothes, and cleaning and the number of house plants. Most homes are ventilated by a mixture of air leakage and exhaust fans typically in bathrooms and over the kitchen stove. If the amount of moisture exceeds the amount removed by ventilation, then the absolute humidity inside the house increases.

Humidity can be measured with a hygrometer, a simple and inexpensive instrument available in many hardware and discount stores. The dial or digital readout will range from near 0% to 100% in a unit called *relative humidity*. It is “relative” because it changes with temperature. If air is warmed, then the RH reading will decrease. Likewise, as air is cooled, the RH reading will increase. If the RH approaches 100%, then the airborne moisture condenses into water droplets on cold surfaces. This can often be seen on single-pane windows or on the outside of a glass of ice water where water condenses. Dust and lint that gather in carpets, mattresses, and pillows are hydroscopic, tending to absorb moisture in damp environments. If the RH increases above 65%, then these materials gain enough moisture to support the growth of some fungi and mites. A simple and effective action to mitigate this problem is to decrease the dust burdens in carpets and soft furniture by thorough cleaning with a vacuum cleaner equipped with a HEPA filter. A relatively recent study conducted in Canadian homes has shown 4 to 6 methodical cleanings might be necessary to decrease the fine dust in carpeting, but this has many benefits other than just decreasing potential exposure to dust mite allergens.<sup>316</sup>

Monitoring RH is not as simple as placing a hygrometer in the middle of a room. RH in one part of the room can differ from RH in another part, in different locations in a house, over time, and with different seasons or climates. Moisture in the air will migrate from wet areas to dry areas and warmer areas of a home toward cooler areas. A key to understanding where moisture can accumulate is to understand where the colder spots are in a house. For example, the air near a window in winter can sometimes be cold enough to be below the dew point, resulting in condensation on the cold window surface. Other cold surfaces, such as exterior walls on the north side of the house, also can condense water (Fig 8).

The most dramatic short-term changes in RH occur when cooking meals for a family gathering, showering, or washing the floors. Indoor humidity can build up in areas where there is not enough air movement, such as behind furniture and cabinets and inside closets. Surfaces can remain cooler than surrounding areas, which can lead to condensation. Furniture should be moved slightly away from walls so that air can freely pass behind them. Air should be allowed to circulate between rooms and, depending on the region of the country, the house should be regularly ventilated to remove humid air.

To lower indoor humidity during warm, humid weather, air conditioners and/or dehumidifiers should be used. In chronically



damp areas, such as basements or crawlspaces, it is often recommended that dehumidifiers be used to maintain humidity levels below 60%.

For example, the image on the right in Figure 8 shows how the RH can vary from 30% to 50%, in the same house, at the same time. Similar differences can occur at different heights. RH near the cooler floor is typically higher than RH near the warmer ceilings.

When the RH is in the “red range” of at least approximately 80%, measures need to be taken to decrease it. Warming the air can help, but in humid climates a dehumidifier may be necessary. RH in the “yellow range” of about 60% to near 80% should be monitored to prevent an increase lasting longer than a few hours. RH in the “green range,” approximately 60% to 40%, is considered comfortable by most people.

The relation among temperature, RH, and surfaces can be quite complex and not always easily understood. For example, the air in a room can be quite comfortable and not conducive to moisture condensation or accumulation. Conversely, the air near the ceiling surface next to the air conditioning vent can be so cold that it chills the surface temperature of the ceiling below the dew point, making the ceiling tile damp enough for long enough that mold has germinated and begun spreading (Fig 9).

Despite the difficulty in understanding these technical parameters of the multiple relations among moisture, temperature, humidity, and dew point in a house, there are some simple situations that can guide anyone toward what to look for as a starting point. Houses are designed to be dry, but not all locations remain that way. As mentioned earlier, there are activities such as showers in bathrooms and cooking in kitchens where there will be extra moisture; however, there are more remote parts of houses that can have dampness. Basements and crawlspaces can easily have increased dampness because the structures are below the surface of the ground and susceptible to water leaks. Open soil in crawlspaces is inherently damp, with slight amounts of moisture slowing evaporation through the surface but being trapped beneath items stored on the surface. Attics, especially in humid climates, can accumulate moisture as the humidity outside moves inside.

Another key to understanding where moisture can accumulate is to understand where the colder spots are in a house. As the image described earlier demonstrated, the air near a window in winter can sometimes be cold enough to be below the dew point, resulting in condensation on the cold window surface. However, other cold

surfaces, such as exterior walls on the north side of the house, also can condense water.

High humidity indoors also can occur seasonally, not only with high outside humidity in the summer migrating through the building envelope, but also with snowmelt and spring rains flooding into basements, crawlspaces, and foundations. Not all moisture events automatically and instantaneously indicate a problem. Elevated moisture, including in humid climates, takes time to increase the levels of dust mites or mold or to damage the structure and contents. A few days of dampness is necessary before problems arise, and several weeks of constantly high humidity are required before materials can absorb sufficient moisture for dust mites or mold to begin reproducing rapidly enough to cause contamination.

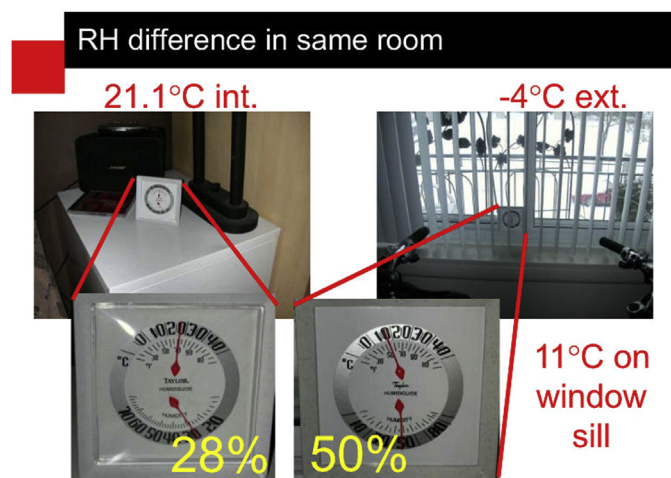
**Appendix B: dust mite exposure assessment and questionnaire**

This is an evidence-based set of questions that clinicians can use to determine whether exposure to dust mites in a patient’s house or apartment has an accumulation of house dust mites.

Dust mite allergens have become ubiquitous across most of the continental United States and Canada. However, in most regions, there are building-related factors that can be modified to decrease dust mite exposure. If *all* regional and building-related factors point to an inhospitable climate for dust mites, then an optional series of questions usually are not necessary. However, if *any* regional and building-related factors point to a favorable climate for dust mites, then a final series of questions are asked to determine potentially modifiable risk factors within the home. Then, the patient would be led to information about how to modify those risk factors to decrease exposure to dust mite allergens.

*Step 1: Determine the region of the country and if housing type is conducive to dampness*

1. *Region of the country:* The map presented in Figure 10 shows several different climates that are overlaid onto the map of the United States and Canada. Depending on this climate map, colors represent different levels of temperature and humidity. For example, a home could be warm and dry (eg, Tucson) or warm and humid (eg, Tampa). For more detailed delineation of the climate zones, please refer to the Köppen climate classification



**Figure 8.** Relative humidity (RH) differences in the same room. (Right) Image shows how the RH can vary from 30% to 50%, in the same house, at the same time. Similar differences can occur at different heights. RH near the cooler floor is typically higher than RH near the warmer ceilings.



**Figure 9.** Temperature and humidity are not uniformly distributed throughout a house. The ceiling near the air conditioning supply vent has been chilled by the cold air to a temperature low enough to condense moisture and support dust mite and mold growth. Other locations inside a typical house may have similar micro-environments with excess or accumulated moisture.

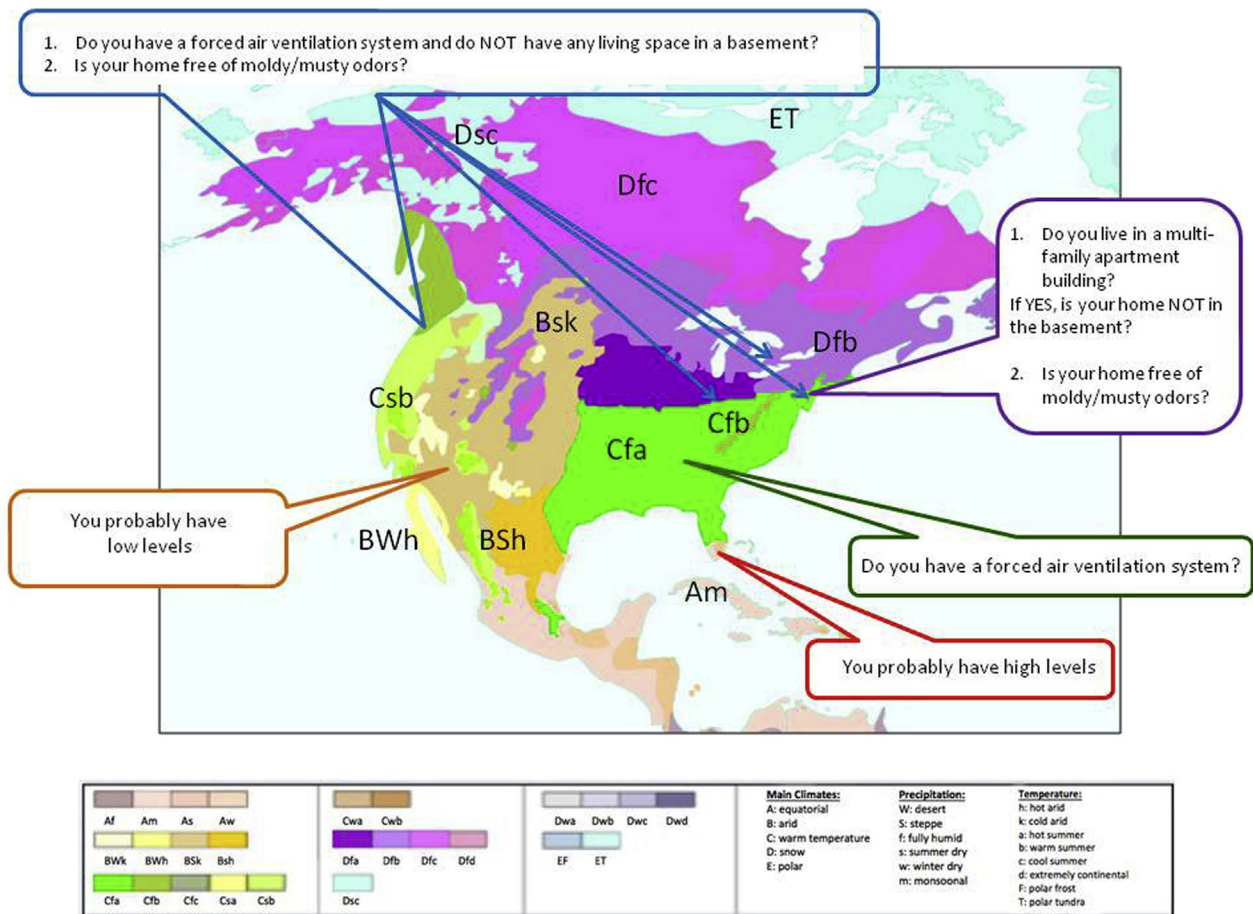


Figure 10. Map to determine whether housing type is conducive to dampness given the region of the country.

([http://webmap.ornl.gov/wcsdown/wcsdown.jsp?dg\\_id=10012\\_1](http://webmap.ornl.gov/wcsdown/wcsdown.jsp?dg_id=10012_1), accessed 8-14-2013).

- a. If patient lives in a consistently dry arid area (eg, Tucson), then one can assume, based on climate, that levels should be low. Then, the patient would be directed to step 2 to confirm that the building factors are still inhospitable to dust mites.
  - b. If patient lives in a consistently humid area (eg, Tampa), then one can assume, based on climate, that levels should be high. Then, the patient would be directed to step 3 to identify potentially modifiable risk factors within the home. The patient would be led to information about how to modify those risk factors to decrease exposure to dust mite allergens.
2. **Building type:** The age of a building has been used as a proxy for heating and ventilation in homes in the northern United States and Canada. The authors believe that they most likely capture forced air ventilation. In addition, underground living spaces are a risk factor for dampness and thus dust mites.
  3. **Dampness:** Although studies in the northern United States and Canada have used mold odor as a proxy for dampness, this has not been tested in the southern United States. Moldy odor might be a proxy for dampness, but the conservative assumption has been made in step 1 that all homes in humid southern states have dust mites.

#### Region of the country and housing type (Fig 10)

#### Step 2: Determine major dust reservoir and more factors related to dampness

1. **Carpeting:** For most regions, carpeting is a major risk factor for dust mites. Carpeting not only serves as a reservoir for dust, but

also provides a protective microclimate to the dust mites. Hardwood floors can easily be swept, but dust mites can burrow deep into the carpet and often are protected from effective removal by traditional vacuum cleaners. Even if HEPA vacuum cleaners remove allergens, the dust mites can remain.

2. **Hygrometer measurements:** One recommendation is to give a patient a hygrometer and place it over time throughout the home to monitor humidity. This should occur in several different seasons.

#### Major dust reservoirs and more factors related to dampness (Fig 11)

If the hygrometer level consistently shows an RH below 50% and if responses to all questions in steps 1 and 2 are yes, then the patient's home probably has low levels of live dust mites.

Nonetheless, it would be useful to proceed to step 3 to inquire about possible risk factors that might still contribute to dust mite allergen exposure.

*Step 3: If it has been established that levels in the home are probably not low, then inquire about some of these levels to see if patient can decrease levels as low as possible.*

The questions were selected as follows. Several studies have measured dust mite allergens, but not many have focused on assessing the relations between housing characteristics and dust mite allergen concentrations. The authors chose a 2-step approach to determine if conditions were conducive to dust mites: (1) Was there a study in the region of the country that showed associations between housing characteristics and elevated dust mite allergen concentration? (2) Would the questions found to be associated with



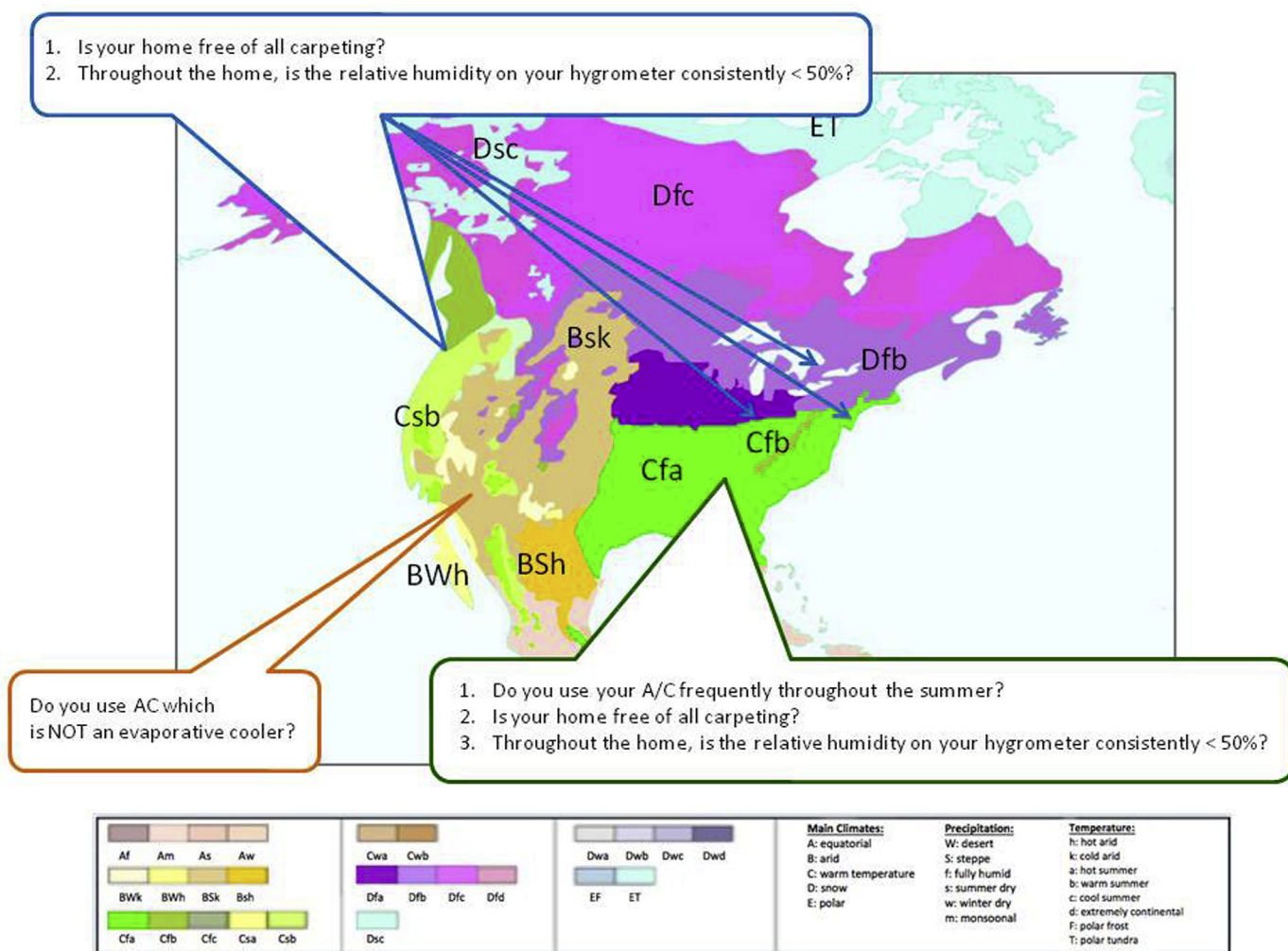


Figure 11. Major dust reservoirs and more factors related to dampness.

elevated dust mite allergen concentration be generalizable to that region?

Several studies often examined housing stock that was unique to their city or metropolitan area,<sup>55,236,317–320</sup> so questions such as “Do you live in a home built after 1951?” might be relevant for that city but not for others. To illustrate, “pre-war” apartment buildings in New York City represented by this pre-1951 question are brick-and-mortar, high-rise, multifamily buildings compared with “pre-war” single-family detached homes built of wood in the early 1900s in Richmond, Virginia. In this case, the pre-1951 variable is most likely a proxy for a combination of factors related to heating and ventilation of the home. One could debate whether asking “When was your building built?” would be a good question in those cities that had the studies with dust mite allergen and housing characteristics. However, many residents do not know when their building was built and a building date does not take into account potential retrofits and modifications that would affect the HVAC system.

The questions in this section have been found in studies not only in the United States and Canada but also in other locations around the world.

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## Home assessment for dust mite allergens (supplemental questions)

<b>Housing characteristics</b>			
<b>Building</b>			
Are all your windows sealed shut or don't open?	<input type="checkbox"/> yes	<input type="checkbox"/> no	
How long have you lived in this home?	___ years		
If <1 year, did you move from a region of the country that might have high levels of dust mites? (see climate maps)	<input type="checkbox"/> yes	<input type="checkbox"/> no	
If YES, did you bring furniture from your previous home?	<input type="checkbox"/> yes	<input type="checkbox"/> no	
Is any part of your living area below ground level?	<input type="checkbox"/> yes	<input type="checkbox"/> no	
If YES, does this area ever get wet or stay wet for long periods (>1 week)?	<input type="checkbox"/> yes	<input type="checkbox"/> no	
<b>Heating, ventilation, and cooling</b>			
Do you use a dehumidifier in your home?	<input type="checkbox"/> yes	<input type="checkbox"/> no	<input type="checkbox"/> N/A
During winter, are some outside walls cold?	<input type="checkbox"/> yes	<input type="checkbox"/> no	<input type="checkbox"/> don't know
Does your home sometimes smell "stuffy," "stale," or "musty"?	<input type="checkbox"/> yes	<input type="checkbox"/> no	
Does your air conditioner ever leak water onto walls or carpeting?	<input type="checkbox"/> yes	<input type="checkbox"/> no	<input type="checkbox"/> N/A (no A/C)
<b>Bedroom characteristics</b>			
Do you have upholstered furniture in your child's bedroom?	<input type="checkbox"/> yes	<input type="checkbox"/> no	
Do you allow your child to have stuffed animals/toys in the room?	<input type="checkbox"/> yes	<input type="checkbox"/> no	
<b>Dust reservoirs (overall home)</b>			
Do you have cloth sofa or chairs?	<input type="checkbox"/> yes	<input type="checkbox"/> no	
Do you have cloth curtains?	<input type="checkbox"/> yes	<input type="checkbox"/> no	
Can you see dust or dirt on your furniture, walls, ceiling, and curtains?	<input type="checkbox"/> yes	<input type="checkbox"/> no	
Do you have wall-to-wall carpeting in more than half the rooms in your home?	<input type="checkbox"/> yes	<input type="checkbox"/> no	
Do you have wall-to-wall carpeting in your kitchen or bathrooms?	<input type="checkbox"/> yes	<input type="checkbox"/> no	
Do you not own a vacuum cleaner?	<input type="checkbox"/> yes	<input type="checkbox"/> no	
Do you vacuum less than once a week?	<input type="checkbox"/> yes	<input type="checkbox"/> no	
<b>Dampness</b>			
In the past 12 months, have you noticed condensation on windows in your home?	<input type="checkbox"/> yes	<input type="checkbox"/> no	<input type="checkbox"/> don't know
If YES, does moisture regularly build up on your windows/walls?	<input type="checkbox"/> yes	<input type="checkbox"/> no	
In the past 12 months, have you had any water leaks?	<input type="checkbox"/> yes	<input type="checkbox"/> no	<input type="checkbox"/> don't know

Abbreviations: A/C, air conditioning; N/A, not applicable.

This questionnaire can be given to the patient. Affirmative (ie, YES) answers indicate potential dust mite allergen exposure.

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## Appendix C: mite allergens

### *Dermatophagoides pteronyssinus*

#### *Der p 1 (Cysteine protease)*

*Der p 1* belongs to group 1 mite allergens and is a protein of 25 to 27 kDa. *Der p 1* is a cysteine protease.<sup>321–323</sup> *Der p 1* has protease activity that can induce a significant IgE response. A proposed mechanism for its high allergenicity is that it cleaves the low-affinity IgE receptor (CD23) from the surface of human B lymphocytes, enhancing IgE immune responses by ablating the feedback inhibitory mechanism that normally limits IgE synthesis.<sup>29</sup> *Der p 1* also can activate eosinophils to release proinflammatory mediators<sup>324</sup> and it can prolong their survival.<sup>325</sup> It has 80% homology with *Der f 1*. The crystal structures of natural *Der p 1* and *Der f 1* in complex with a monoclonal antibody, 4C1, was shown to bind to a unique cross-reactive epitope on the 2 allergens that is associated

with IgE recognition. This epitope is formed by almost identical amino acid sequences and contact residues. Mutations of these common residues decrease IgE antibody binding.<sup>326</sup> More than 50% of allergic patients and up to 80% of children with asthma are sensitized to *Der p 1*. *Der p 1* appears to be sufficient to diagnose more than 97% of dust mite–allergic patients.<sup>30</sup>

#### *Der p 2 (lipid-binding molecule)*

A recombinant *Der p 2* has been developed that reacts with IgE from most patients who are sensitized to native *Der p 2*.<sup>327,328</sup> Removal of either or both disulfide links decreases IgE binding up to 10-fold, suggesting that these bonds play a critical role in stabilizing the antigenic structure of this mite allergen.<sup>329</sup> *Der p 2* is a homolog of MD-2, a protein involved in the binding of lipopolysaccharide and activation of toll-like receptor 4, which promotes T<sub>H</sub>2-mediated inflammation.<sup>330,331</sup> *Der p 2* peptides were found to induce multiple responses that were restricted through HLA-DPB1\*0401 and HLA-DRB1\*01.<sup>332</sup>

#### *Der p 3 (trypsin-like serine protease)*

*Der p 3* is encoded by a single gene. Most cDNA clones of this allergen show only minor sequence variation similar to that observed for group 1 and 2 house dust mite allergens.<sup>333</sup> This allergen contains a trypsin-like enzyme that has been shown to bind to human IgE. The protein is a 31-kDa protein that is enzymatically similar to invertebrate and vertebrate trypsins and shows homology with crayfish trypsin. All sera from a panel of mite-allergic individuals showed IgE reactivity to trypsin, suggesting that mite trypsin is a major allergen.<sup>322</sup>

#### *Der p 4 (α-amylase)*

*Der p 4* is a 57- to 60-kDa protein with amylase activity. It can be found in extracts of whole mite and spent growth medium but not in unused growth medium. It has been detected in extracts of dust obtained from mattresses and lounge room carpets. The enzyme activity correlates with counts of live mites and with concentrations of *Der p 1*. In 1 study, sera from 25% of mite-allergic children and 46% of mite-allergic adults contained specific IgE to this allergen and directly correlated with concentrations of total mite-specific IgE.<sup>334,335</sup> Complement DNA clones of *Der p 4* and *Eur m 4* were sequenced and were found to code for 496 amino acid mature proteins with highly conserved residues that are important for the function of α-amylase. *Der p 4* and *Eur m 4* were 90% identical and were 50% identical to insect and mammalian α-amylases.<sup>32</sup>

#### *Der p 5 (function is unknown)*

*Der p 5* is a 14-kDa protein that has been isolated and its DNA sequence determined. The deduced amino acid sequence was not homologous to any known protein sequences and it contains no cysteine or tryptophan. Sera from 21 of 38 mite-allergic subjects recognized recombinant *Der p 5*, which correlates with IgE binding to the native molecule. This protein has homology to *Der p 25*; however, the function is not known for either allergen.<sup>336</sup>

#### *Der p 6 (chymotrypsin, a serine protease)*

An ELISA has been developed for the measurement of *Der p 6*.<sup>337</sup>

#### *Der p 7 (lipid-binding molecule)*

*Der p 7* has 198 residues and a predicted molecular weight of 22 kDa. Sera from 14 of 38 dust mite–allergic children reacted strongly with this clone. Skin tests showed reactivity in 16 of 30 allergic patients (53%) and none of the controls.<sup>338</sup>

#### *Der p 8 (glutathione S-transferase)*

*Der p 8* is a 26-kDa polypeptide. Nucleotide sequencing showed a 219-amino acid protein. The molecule has a strong homology with glutathione S-transferases, containing all but 1 of the 19 conserved amino acid residues found in glutathione transferase.<sup>339</sup>



*Der p 9 (collagenase, a serine protease)*

Der p 9 is a 23.7-kDa protein that is enzymatically similar to chymotrypsin and cathepsin G-like enzymes and it has been shown to cleave collagen. It has homology with Der p 3 and with Der p 6, although inhibition studies have shown cross-reactivity between Der p 9 and Der p 3 but not Der p 6. Up to 92% of dust mite-allergic patients have specific IgE to Der p 9.<sup>340</sup>

*Der p 10 (tropomyosin)*

Der p 10 is a tropomyosin that shares more than 65% of residues with other invertebrate tropomyosins. The recombinant allergen cross-reacts with shrimp tropomyosin. In 1 study, 5.6% of sera from mite-allergic patients had IgE reactivity to Der p 10.<sup>33</sup> Another study found that up to 15.2% of dust mite-allergic patients had IgE to Der p 10.<sup>34</sup> In that same study, Der p 10-negative patients were sensitized primarily to Der p 1 and/or Der p 2.

Tropomyosin is believed to be responsible for clinical cross-reactivity between dust mites and seafood. In a study of dust mite-allergic patients from southern Bavaria, IgE antibodies to Der p 10 were found in 4 of 93 sera (4.3%). Two of these patients had oral symptoms accompanied by bronchospasm after consumption of shrimp. Thus, although there is some cross-reactivity, the low frequency of IgE to Der p 10 in dust mite-allergic patients and the low frequency of clinical reactions in these patients suggest that most shrimp reactions are due to other allergens.<sup>341</sup>

*Other dust mite allergens*

There is a large number of additional dust mite allergens (listed in Table 1). These include Der p 11 (paramyosin), Der p 13 (lipid-binding protein), Der p 14 (apolipoprotein), Der p 15 (chitinase), Der p 16 (gelsolin/villin), Der p 17 (Ca<sup>2+</sup>-binding protein), Der p 18 (chitinase), Der p 19 (antimicrobial protein), Der p 20 (arginine kinase), Der p 21 (similar to Der p 5), and Der p 24 (troponin C). The clinical relevance of sensitization to these allergens is not well understood.

*Dermatophagoides farinae (very similar to D pteronyssinus)**Der f 1 (cysteine protease)*

Der f 1, a major allergen from the house dust mite, is a 223-residue protein with a derived molecular weight of 25,191 kDa. It has significant homology to other cysteine proteases. Sequence alignment of Der f 1 and Der p 1 has shown a high degree of homology (81%).<sup>342</sup>

*Der f 2 (lipid-binding molecule)*

Der f 2 encodes a 129-residue protein with a calculated molecular weight of 14 kDa and an expected homology with Der p 2 of 88%. The 2 molecules also display a high degree of antibody cross-reactivity.<sup>343</sup>

*Der f 5*

Der f 5 has a molecular weight of 13.6 kDa and amino acid homologies with Der p 5, Blo t 5, Sui m 5, and Lep d 5. Der f 5 and Der p 5 are more similar to each other than to Blo t 5 and Ale o 5, most likely because they belong to different mite families (Echimyopodidae vs Acaridae).<sup>344</sup>

*Der f 6 (chymotrypsin-like serine protease)*

Der f 6 cDNA is 840 nucleotides long. In 20 patients with asthma, 45% had specific IgE to rDer f 6. Substantial homology has been shown between Der f 6 and Blo t 6, Sui m 6, Der f 3, and Der f 9.<sup>345</sup>

*Der f 7 (lipid-binding protein)*

Der f 7 is a 25-kDa protein with 31- and 30-kDa components that are glycosylation products of the 25-kDa form and an 18-kDa band consistent with a degradation product.<sup>346</sup> Immediate

hypersensitivity skin test reactions to Der f 7 have been found in 52% of mite-sensitive allergic patients.<sup>347</sup>

*Der f 10 (tropomyosin)*

Native Der f 10 reacted with specific IgE in the 31 sera tested at a high frequency (80.6%), comparable to that of Der f 1 (90.3%) and Der f 2 (74.2%).<sup>348</sup>

*Der f 11 (paramyosin)*

Der f 11 is a 98-kDa mite allergen. The sequence identity of Der f 11 with other known paramyosins is 34% to 60%.<sup>349</sup> Der f 11 cDNA has 2,625 base pairs encoding a 103-kDa protein with 875 amino acids with significant homology with the paramyosin of other invertebrates. It has greater than 89% identity with Blo t 1. IgE binding was found in 78% of mite-allergic patients. IgE cross-inhibition between rDer p 11 and rDer f 11 was up to 73% to 80%.<sup>350</sup>

*Der f 18 (chitinase)*

Der f 18 is a 60-kDa protein. In 1 study, the purified protein bound IgE in 54% of the sera from mite-allergic patients. Its cDNA encodes a protein with 462 amino acids with homology to multiple chitinases. Chitinase is found abundantly in the mite digestive system, but fecal pellets did not stain positively for this allergen.<sup>351</sup>

*Blo t 21*

In *B tropicalis*, the most prevalent and allergenic allergens are, in descending order, Blo t 21, Blo t 5, and Blo t 7. Blo t 21 has 40% sequence identity to and small to moderate immunologic cross-reactivity with Blo t 5.<sup>352</sup>

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