Respiratory allergy caused by house dust mites: What do we really know?

Moisés A. Calderón, MD, PhD,[a] Allan Linneberg, MD, PhD,[b] Jörg Kleine-Tebbe, MD,[c] Frédéric De Blay, MD, PhD,[d] Dolores Hernandez Fernandez de Rojas, MD, PhD,[e] Johann Christian Virchow, MD, FRCP, FCCP,[f] and Pascal Demoly, MD, PhD[g] *London, United Kingdom, Copenhagen and Glostrup, Denmark, Berlin and Rostock, Germany, Strasbourg, Montpellier, and Paris, France, and Valencia, Spain*

The house dust mite (HDM) is a major perennial allergen source and a significant cause of allergic rhinitis and allergic asthma. However, awareness of the condition remains generally low. This review assesses the links between exposure to HDM, development of the allergic response, and pathologic consequences in patients with respiratory allergic diseases. We investigate the epidemiology of HDM allergy to explore the interaction between mites and human subjects at the population, individual, and molecular levels. Core and recent publications were identified by using "house dust mite" as a key search term to evaluate the current knowledge of HDM epidemiology and pathophysiology. Prevalence data for HDM allergen sensitization vary from 65 to 130 million persons in the general population worldwide to as many as 50% among asthmatic patients. Heterogeneity of populations, terminology, and end points in the literature confound estimates, indicating the need for greater standardization in epidemiologic research. Exposure to allergens depends on multiple ecological strata, including climate and mite microhabitats within the domestic environment, with the latter providing opportunity for intervention measures to reduce allergen load. Inhaled mite aeroallergens are unusually virulent: they are able to activate both the adaptive and innate immune responses, potentially offering new avenues for intervention. The role of HDM allergens is crucial in the development of allergic rhinitis and asthma, but the translation of silent sensitization into symptomatic disease is still incompletely understood. Improved understanding of HDMs, their allergens, and their microhabitats will enable development of more effective outcomes for patients with HDM allergy. (J Allergy Clin Immunol 2015;136:38-48.)

Key words: *Allergen, house dust mite, allergy, allergic asthma, allergic rhinitis, respiratory allergic disease, inflammation*

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The house dust mite (HDM) is globally ubiquitous in human habitats and a significant factor underlying allergic rhinitis and allergic asthma. These features make it one of the most important sources of indoor allergens.[1,2] Sensitization to mite allergens in the first years of life has a significant clinical effect on lung function in pediatric populations with wheeze and associates in the long term with poorer clinical outcomes in respiratory health.[3] This might explain why the approach advocated by current guidelines for allergic rhinitis (Allergic Rhinitis and its Impact on Asthma)[4] and allergic asthma (Global Initiative for Asthma)[5] classifies disease based on the severity of symptoms, often leaving the underlying allergic cause unaddressed. Although comprehensive reviews of HDM allergy exist, consideration of the link between exposure, allergenicity, and the pathologic consequences for the entire airway has yet to be thoroughly explored. This review seeks to provide a complete picture of the epidemiology of HDM allergy and the effect of HDM allergens on the human immune system.

From [a]the Section of Allergy and Clinical Immunology, Imperial College London–NHLI, Royal Brompton Hospital, London; [b]the Research Centre for Prevention and Health, Capital Region of Denmark, the Department of Clinical Experimental Research, Glostrup University Hospital, and the Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen; [c]the Allergy and Asthma Center Westend Outpatient Clinic Hanf, Ackermann & Kleine-Tebbe, Berlin; [d]the Chest Diseases Department, Hôpitaux Universitaires de Strasbourg, Fédération de médecine translationnelle, Université de Strasbourg; [e]the Department of Allergy, IIS Hospital La Fe, Valencia; [f]the Department of Pneumology and Intensive Care Medicine, Zentrum für Innere Medizin, Klinik I, Universitätsklinikum Rostock; and [g]the Department of Pulmonology, Division of Allergy, University Hospital of Montpellier, and Sorbonne Universités, Paris.

An educational grant for the development of this article was provided by ALK-Abelló.

Disclosure of potential conflict of interest: This study was funded by ALK-Abelló, Hørsholm, Denmark. M. A. Calderón has received compensation for board membership from ALK-Abelló and Stallergenes; has received consultancy fees from ALK-Abelló, Merck, Stallergenes, HAL Allergy, and Allergopharma, as well as payment for delivering lectures from ALK-Abelló, Merck, Stallergenes, and Allergopharma; and has received compensation for travel and other meeting-related expenses from ALK-Abelló, Merck, Stallergenes, and Allergopharma. A. Linneberg has received payment for delivering lectures from ALK-Abelló. J. Kleine-Tebbe has received or has grants pending from Circassia and has received compensation for board membership from ALK-Abelló, Novartis, and LETI, as well as consultancy fees from Merck, and has received payment for delivering lectures from Allergopharma, ALK-Abelló, Bencard, HAL Allergy, LETI Lofarma, Novartis, and Stallergenes. F. De Blay has received funding from Stallergenes and Chiesi; consultancy fees from Stallergenes, ALK-Abelló, Mundipharma, and Novartis; fees for participation in review activities from ALK-Abelló and Stallergenes; and compensation for board membership from Stallergenes, ALK-Abelló, Mundipharma, Novartis, and Same. J. C. Virchow has received consultancy fees from ALK-Abelló, as well as payment for delivering lectures. P. Demoly has received consultancy fees from ALK-Abelló, Circassia, Stallergenes, Allergopharma, Chiesi, Pierre Fabre Médicaments, and Ménarini and has received payment for delivering lectures from Ménarini, MSD, AstraZeneca, and GlaxoSmithKline. D. Hernandez Fernandez de Rojas declares no other relevant conflict of interest.

Received for publication May 2, 2014; revised September 18, 2014; accepted for publication October 2, 2014.

Available online November 22, 2014.

Corresponding author: Moisés A. Calderón, MD, PhD, Section of Allergy and Clinical Immunology, Imperial College London–NHLI, Royal Brompton Hospital, London SW3 6LY, United Kingdom. E-mail: m.calderon@imperial.ac.uk.

0091-6749

http://dx.doi.org/10.1016/j.jaci.2014.10.012

Abbreviation used
HDM: House dust mite

EPIDEMIOLOGY: SCOPING THE PROBLEM

Throughout the published literature, studies frequently cite the high prevalence of HDM allergy,[6,7] yet an accurate global estimate has proved elusive. A comprehensive thesis of HDM allergy suggests that 1% to 2% of the world's population might be affected, which is equivalent to 65 to 130 million persons.[8] Geographic variation complicates the picture: although HDM allergy is consistently found in Western nations, variation between countries, regions, and even individual test centers is significant.[9] One fundamental issue is the diversity of terminology and end points used in the literature, which can obscure the relationship between silent sensitization to HDM allergens and clinical disease. When evaluating data, a clear distinction must be made between epidemiologic studies conducted across a population selected at random and studies targeting sensitized symptomatic subjects selected from a group with diagnosed allergy.[10]

Focusing specifically on the proportion of patients with HDM allergen sensitization and rhinitis, asthma, or both, interpopulation differences are high. Among patients from 15 developed countries in the European Community Respiratory Health Survey I, the mean prevalence of sensitization to HDM was 21.7%.[9] Among Latino women in the United States of various ages, the prevalence of sensitization to *Dermatophagoides pteronyssinus* was 37% and to *D farinae* was 34%,[11] whereas the prevalence was greater than 80% in a pediatric study in Taiwan.[12] Given that study groups can be sampled from across continents, countries, ethnic groups, sexes, and/or age ranges, the heterogeneity of populations might confound potential comparisons of observed differences.

Significant differences exist not only between surveys but also within them. The European Community Respiratory Health Survey provided an opportunity to explore data from 13,558 subjects from 16 countries, focusing on the relationship among sensitization, allergy, and asthma.[13] A meta-analysis from this study reported a high overall prevalence for asthma with HDM sensitization (21%, $r = 0.64$) but with significant interpopulation heterogeneity ($P < .001$). The proportion of asthma attributed to any allergen had a wide range (4% to 61%) and was highly dependent on the diagnostic technique used.[13] This suggests that discrepancies in the use of diagnostic tools can confound epidemiologic studies.[9] The Environmental Health Risks in European Birth Cohorts project cited a lack of common definitions of exposure, health variables, and monitoring as critically limiting factors for establishing the prevalence of HDM allergy.[14]

FACTORS INFLUENCING EXPOSURE, SENSITIZATION, AND ALLERGY TO HDM

Allergen exposure and sensitization

The prevalence of HDM allergy is intricately linked to exposure to the mite itself. The German Multicentre Allergy Study, which followed newborn children (n = 1314) through the first 3 years of life, found a cumulative increase in the development of allergy with increasing exposure to the major HDM allergens Der p 1 and Der f 1.[15] This reached a peak level of 5.5% with exposure to greater than 10 μg/g in carpet dust in children from families with a known history of allergy; the corresponding prevalence for those without a family history was 3%. At levels of less than 0.1 μg/g, the risk of allergy was low.[15] Although sensitization is linked to allergen exposure, the correlation does not follow a linear pattern. A study showed a lower prevalence of mite atopy and asthma in the highest and lowest quintiles of exposure in children aged 0 to 5 years and also in the first 18 months from birth, with the highest prevalence observed at 3.5 to 23.4 μ/g.[16] Other studies have also reported a bell-shaped dose-response curve for HDM exposure versus sensitization.[17-19] The mechanism of the apparent protective effect of high exposure levels remains unclear. It has been proposed that it might be similar to the "high dose tolerance" reported for cat allergen[20]; however, reports of high dose tolerance for aeroallergens are inconsistent between studies.[16] Parental history of allergy and asthma has been reported to influence the relationship between HDM exposure and atopy; exposure to greater than 10 μg/g was associated with a decreased risk of atopic asthma in children with a parental history but with an increased risk in those without.[21] At present, this threshold is not well defined in the literature and is likely to be compounded by the presence of other allergens and some predisposing factors, such as viral infections, exposure to chemicals (eg, formaldehyde), individual susceptibility, and use of medication.[22,23] Studies seeking to quantify a level of exposure that can be considered "safe" suggest that levels of less than 2 μg/g of HDM allergens are the maximum level for the primary prevention of sensitization in atopic children and young adults.[24,25]

A study of HDM sensitization during the first 3 years of life found that sensitization was low during infancy (0.5%), with an increase during the second (1.4%) and third (1.9%) years of life, and concluded that interventions aimed at primary prevention of sensitization should be introduced as early as possible, preferably during infancy.[15]

The quantitative relationship between exposure to HDM allergens and symptoms in asthmatic patients is complex and, similar to sensitization, influenced by environmental and genetic factors. Many asthmatic patients are sensitized to more than 1 allergen, which makes determination of the contribution of a specific allergen to airway inflammation difficult.[26] Although a clear threshold for provocation of asthma symptoms has not been clearly defined, symptoms are likely to be more severe with increasing allergen exposure.[26]

Assessing HDM exposure presents a challenge to the physician. In the clinical trial setting exposure has been expressed as the maximum level found in the home, the percentage of sites with greater than 2 μg/g, and the mean value at the site with the maximum level.[27] However, a recent practice parameter on the environmental assessment and exposure control of HDM recommends the use of a hygrometer to estimate the amount of moisture available for propagation of HDM in the home and contains questions on home characteristics to assess the probability of HDM exposure.[28] This complexity could explain the relatively low predictive value of questionnaires in diagnosing sensitized subjects in the general population compared with other allergens (ie, 22% vs 64%, HDM vs pollen).[29] Moreover, HDM populations can also fluctuate seasonally,[30,31] exhibiting corresponding patterns of symptomatic response in patients.[32]

Environmental factors

The key species of HDM involved in allergy are shown in Table I,[8] along with a corresponding median value of the climatic