Atopic Dermatitis due to House Dust Mite: A Review

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Abstract

Atopic dermatitis (AD), a chronic skin condition brought on by malfunction of the skin barrier, frequently manifests as eczema and itchy lesions in the flexural folds and other recognizable distributions. Environmental factors and immune system changes may also contribute to the development of these lesions. The chance of getting AD can be impacted by exposure to house dust mites. Atopic sensitization and allergy illness are primarily brought on by house dust mites (HDMs) globally. The primary source of allergens in HDM is mite feces, notably those from the species Dermatophagoides pteronyssinus, Dermatophagoides farinae, Euroglyphus maynei, and Blomia tropicalis. When a patient has AD brought on by HDM, atopy patch testing and prick testing can help with the diagnosis. Immunotherapy with allergens should be taken into consideration as the sole etiological therapy currently available when avoiding triggering variables is insufficient to minimize symptoms and IgE sensitization as demonstrated by skin prick testing and/or IgE testing. Physical and pharmacological therapies are used to lessen or prevent exposure to HDM (living, dead mites, and feces). Physical barriers, like mattress covers, are one type of physical intervention. Others include changing the floor coverings, getting rid of soft furnishings, vacuuming, air filtration, removing dolls and other delicate toys, heating, freezing, and washing (55°C or higher). Due to the apparent symbiotic interaction between mites and fungi, chemical interventions such as acaricide sprays and antifungal medications seem to diminish the amount of HDMs.

Keywords: Atopic Dermatitis; House Dust Mites; Immunotherapy; Human and Health

1. Introduction

Atopic dermatitis (AD), a chronic skin condition brought on by malfunction of the skin barrier, is characterized by eczematous and itchy lesions in the flexural folds and other distinctive distributions. These lesions are also influenced by changes in the immune system and the environment [1]. The primary symptom of this illness is itching. In extreme situations, the itching is hard to control, disrupting sleep, and the skin is vulnerable to infection. The quality of life is frequently impacted by atopic comorbidities in AD patients, such as allergic rhinitis and asthma [2].

According to estimates, AD affects 1-3% of adults and 15-20% of youngsters. Over the past ten years, developed nations have seen a twofold increase in its prevalence [3]. The number of pediatric AD patients in Dermatology and Venereology Outpatient Clinic Dr.Soetomo General Academic Hospital Surabaya tended to increase since 2007-2011 with the number of male patients (53.4%) being more than female (46.6%) and the

most prevalent age group was 5-14 years [4]. Groups with a strong family history of atopic disease and those with filaggrin gene mutations, particularly Caucasians in Eastern Europe and Asian populations, are at higher risk for AD. There is mounting data that suggests populations of black or African origin may have a higher prevalence of AD than Caucasians. Other elements that can influence the chance of developing AD include day care exposure, parental educational attainment, socioeconomic position, site of residence (rural vs. urban), smoking, vaginal vs. caesarean delivery, birth weight, extra weight, exposure to harsh water, and exposure to dust mites [5].

Atopic sensitization and allergy illness are primarily brought on by house dust mites (HDM) globally. Mite feces, especially those from the eight-legged arachnid species Dermatophagoides pteronyssinus, Dermatophagoides farinae, Euroglyphus maynei, and Blomia tropicalis, are the main source of allergen in HDM [6,7]. Furthermore, Tyrophagus putrescentiae was found to be the most prevalent cause of HDM sensitization in AD patients based on IgE examination according to a study [8]. When dust mite allergen-containing particles come into contact with the epithelium of the eyes, nose, lower respiratory tract, skin, and intestines, they can cause sensitization and atopic symptoms in a number of organs. In contrast to 42% of asthmatics and 17% of controls, patients with atopic dermatitis typically acquire a sensitivity to mites; 95% of these patients exhibit IgE allergens to mites. By activating the protease-activated receptor-2 (PAR-2) on epidermal keratinocytes and dermal nerves, house dust mite proteases undermine the skin's protective barrier, causing non-histamine-mediated itching, inducing inflammation through the production of cytokines, and slowing the healing process. and improvement of skin's impaired permeability functions [7].

It was found in a retrospective study that 41 out of 60 AD patients had sensitization to HDM [9]. The connection between the prevalence of AD and house dust mites, as well as how house dust mites contribute to AD pathogenesis, has received very little attention in the literature up to this point. Knowing the causes of AD allows us to adopt the proper preventative measures and therapeutic measures to lower the chance of AD recurrence, particularly in AD brought on by HDM.

2. Overview of Atopic Dermatitis

2.1 Etiopathogenesis

The complicated etiology of AD includes genetic, immunological, and environmental variables that result in abnormalities of the skin barrier and immune dysfunction. urban or rural settings, smoking, air pollution, air quality, breastfeeding, obesity, and food. The microbiome of the skin and digestive system, as well as the microbiome in living things like cattle and pets (such as dogs), all contribute to the prevalence of AD [10].

The stratum corneum functions as a barrier that prevents bodily fluid leakage, internal water retention in the cell layer, and biological defense. When the horny cell layer's ability to act as a barrier is compromised, the skin is more sensitive to non-specific stimuli and is more likely to become inflamed and have allergic reactions. Ceramides, cholesterol, and free fatty acids make up the majority of the stratum corneum's intercellular lipids. Because of an aberrant drop in ceramide level, the stratum corneum's intercellular lipid function is degrading, and AD patients have poor moisture retention abilities. Keratin and filaggrin make up the horn's cell layer, both of which have strong structural qualities. Patients with AD have mutations that cause a loss of filaggrin function and a filaggrin deficiency linked to inflammation.

Allergens can more easily infiltrate the skin due to their weakened protective function. Immunization and

allergic reactions help to eradicate allergens, which are foreign molecules. Protease activity is the mechanism by which allergens including protein and dust mite allergens trigger type 2 immune reactions. T helper 1 (Th1) and T helper 2 (Th2) cells are subtypes of helper T cells. Th1 cells have been shown to be involved in cell-mediated immunity, whereas Th2 cells are mostly associated with allergic reactions. The cytokines interleukin (IL)-33, IL-25, and thymic stromal lymphopoietin (TSLP), which are connected to Th2 cell migration in the lesion, are produced by epidermal keratinocytes. A type 2 immune response to allergen results in the production of IgE antibodies. Langerhans cells and mast cells, which have high-affinity IgE receptors (Fc3RI), produce cytokines and chemical messengers (such as histamine) to exacerbate inflammation by binding to allergen-specific IgE. When T helper 22 (Th22) cells migrate to the skin, they most likely are controlled by skin dendritic cells that are stimulated to create IL-22, which causes epidermal acanthosis. Epidermal injury can create the S100 protein, which can further activate lymphocytes [11].

2.2 Clinical Symptoms

Depending on the patient's age, AD can present a wide range of clinical manifestations. The phases of AD are called the infancy, childhood, adolescence, or adult phases. Patients may experience extremely painful and frequently excoriated acute, subacute, and chronic eczematous lesions.

After the second month of birth, the infantile or infantile phase of AD typically appears, frequently starting as edematous papules and papulovesicular on the cheeks with a slight center of the face. The lesions could grow into big plaques with fluid that is leaking and crusting. In addition to the body, the scalp, neck, and extensor portions of the extremities may also be affected, though typically with a smaller diaper area. More than 90% of AD individuals experience facial symptoms during the first six months of life.

Lesions in children with AD (ages 2 to 12 years) are typically less exudative and frequently lichen. The antecubital and popliteal fossa are the traditional areas of preference (**Figure 1**). Although any place can be afflicted, other common locations include the neck, eyes, ankles, and feet. Xerosis typically manifests itself and spreads widely.

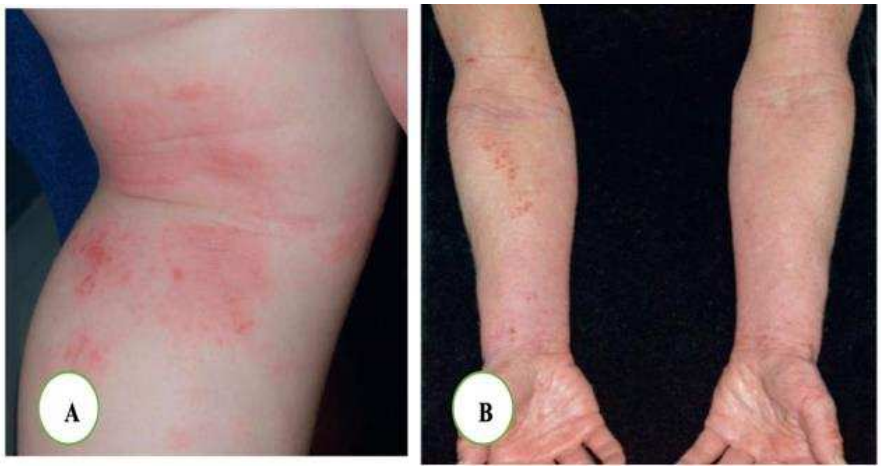

Figure 1. Childhood atopic dermatitis: (A) Excoriation; (B) Excoriation and lichenification of the cubital fossa to the wrist. Reprinted from McAleer, et al., 2018 [12]. Copyright 2018 by Elsevier.

Subacute to chronic lesions, lichenification, and typically ongoing fold involvement is also evident in adolescent or adult AD (>12 years of age). The clinical picture can, however, also alter. Adults with AD frequently appear with chronic hand dermatitis, whereas others have primary facial dermatitis, frequently involving the eyelids severely. A patient is more likely to acquire severe, treatment-resistant AD if they have had chronic AD since childhood. Because they have a habit of scratching and rubbing their skin, these people may also have severe excoriations and persistent papular skin lesions [12].

3. House Dust Mites

House dust mite (HDM) and warehouse mites are two basic categories of mites that are present in humans all around the world. Mites can be found on pillows, mattresses, textiles, carpets, and upholstery [6]. HDM is an eight-legged member of the arachnid class. Spiders, scorpions, and acarii—an order that also includes parasitic mites, ticks, chiggers, ground mites, and Bastigmata—are considered arachnids. Mite taxonomy is shown in **Figure 2.**

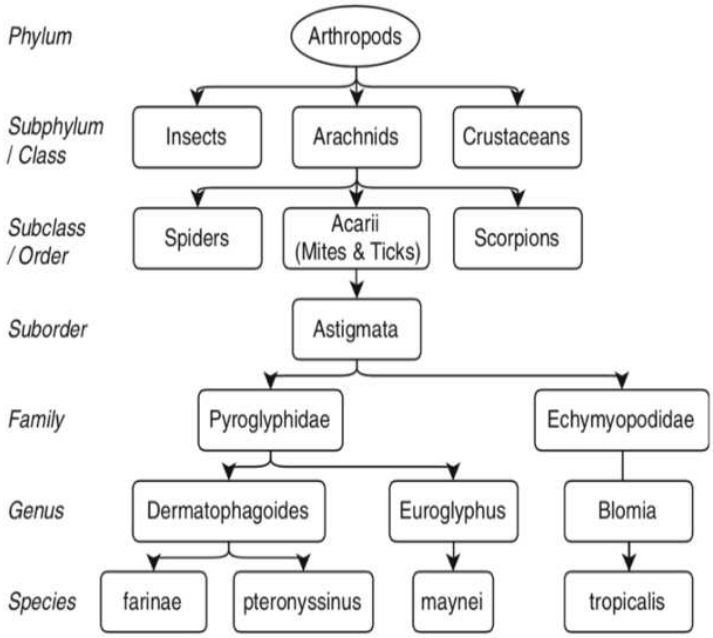

Figure 2. Mite Taxonomy. Reprinted from Miller, 2019 [7]. Copyright 2018 by Springer Science+Business Media, LLC, part of Springer Nature.

A mature mite's body is between 250 and 350 m long, or between a quarter and a third of a millimeter. They may be quite small for multicellular organisms, but they are big enough for bacteria that are just visible. HDM is visible under a microscope with ease [7,13]. Electron microscopy is only required to observe small details like the outer cuticle's rim. HDMs are not visible on surfaces in the daytime due to their photophobic reaction to light. HDM has a high moisture content and is influenced by humidity. It appears solid gray under an electron microscope but is pale yellow and translucent with a light microscope. Although HDMs lack eyes and it is unknown what kind of light receptors they have, they are photophobic and prefer to remain indoors due to their propensity for moving around in shadowy locations. HDMs walk on four pairs of legs, have

touchers on their feet and bodies that mimic hairy structures called "setae," and have legs that resemble suction cups that allow them to cling to fibers and surfaces.

The sexual reproduction process of HDM might take up to 48 hours. Each stage of life develops more swiftly at higher temperatures and more constant humidity levels than HDM, which normally lives 65 to 100 days [7,13]. Females typically lay 50 to 80 eggs in their lifetimes at room temperature. The eight-day six-legged larval stage starts after that. The larvae grow into protonymphs in the first stage, tritonymphs in the second stage, and adults in the third stage. Each developmental stage (eggs, larva, protonymph, and tritonymph) lasts roughly the same amount of time, dividing the overall lifespan evenly between development (fresh egg to adult) and adulthood. The mite must shed its exoskeleton in order to advance to the next immature stage. Because it can produce a Th2 response, its exoskeleton provides an additional source of chitin and mite allergens [7,14].

Mites rely heavily on the surrounding vaporized water for their water demands. At a relative humidity of 75%, dust mite reproduction is at its peak. The mites can maintain moisture in the water when the relative humidity exceeds 75% but competing fungus can flourish in such conditions. Dust mite feeding, reproduction, and allergen generation gradually decrease when humidity levels fall below the ideal 75% (but remain above the essential 50% level). Because the supracoccal glands are unable to maintain water balance at that level, the adult HDM will begin to dry and eventually die if the relative humidity is regularly lower than 50%. The quiescent, immobile, dehydrated nymph stage of the mite survives the dry winter months in temperate climates [7]. Temperature also affects metabolism, reproduction rate, and allergen generation. 20–28° C is the ideal temperature range for HDM. Dermatophagoides farinae takes 35 days to go from egg to adult at 23°C; at 30°C, it takes just about half as long. Extreme temperatures render mite eggs and mites dead outside of this ideal range. At 40°C, 80% Dermatophagoides pteronyssinus eggs will hatch, however dry heat at 50°C will quickly kill all eggs and dust mites within 20 minutes. Mites and eggs are both promptly killed by moist heat at 60°C. While eggs must be killed at a deep freezer temperature of -70°C, HDM shuts off at a home freezer temperature of -17°C [7,15].

The digestive system of the HDM consists of a mouth with movable chelicera that allows food to be gripped and transferred, an anal canal, salivary glands, an esophagus, small and large intestines, etc. The diet of HDM consists of scales shed from warm-blooded animals as well as fungi, bacteria, and yeasts. In addition to living in modern homes close to people and their pets, HDMs also nest in dog and bird nests in the wild. It was discovered that there were more HDMs in close proximity to people with flaky skin who had skin conditions. Similar to barn mites, HDMs can consume wheat [7]. Each solid fecal waste particle produced by mites during their life cycle has a diameter of 25 m and is enclosed in a peritrophic membrane that contains digestive enzymes. These digestive enzymes enable HDM to take advantage of coprophagia, which ingests fecal particles on its own, at least while food is available. Enzymes in the peritrophic membrane allow further nutrient digestion to occur extracorporeally when fecal particles are digested many days after deposition. These nutrients are then available for absorption by the HDM.

Humidity and temperature are the primary factors that determine where the HDM is located in the world. Dust mites often do not thrive at high elevations. HDM sensitivity and growth are significantly less than at sea level in the Alps. Except in homes with high indoor humidity, little to no HDM was observed in a study of residences in the Rocky Mountains. D. pteronyssinus and D. farinae are present throughout most of the United States, with B. tropicalis and E. maynei restricted to the southern states.

Private residences had the largest mite counts, and there was a correlation between socioeconomic status and HDM exposure, with more HDM allergen exposure being connected with greater family income, greater population density, and higher levels of education. low in private residences where there are fewer roommates. Residences without air conditioning (AC) had greater levels of mite allergens than did older homes and homes

with AC. Rat and cockroach allergens are the main factors contributing to the low HDM of apartments in the city center [7,13].

There are multiple degrees of HDM outside the house. The fact that hospitals in the United States have no mites in the winter and very few in the summer is probably due to the use of air conditioning, carpet-free flooring, plastic-covered mattresses, little upholstered furniture, and hygienic cleaning. Mite allergies are less common than they are in homes in public places like schools, trains, buses, and bars, with the exception of daycare centers and the upholstered seats in movie theaters. While there are fewer mites in university dorm rooms than in houses, there are still a lot of them, especially if the rooms are carpeted. The majority of businesses, with the exception of those that recycle textiles, offer fur bedding, and clean carpets and upholstery, contain significantly fewer dust mite allergens than do residences.

HDM and its allergens are present in items that fit the mites' needs for high humidity and little light. The most common carpets in living rooms and bedrooms were also where the most mites and allergens were located indoors. Sofas and beds had the greatest HDM counts and allergen levels. Mattresses with high allergen counts and total HDM, particularly innerspring and wool mattresses, accumulate clinically significant levels of mite allergens in just four months after purchase. The most allergenic mite levels are found in old mattresses. Particularly because of their proximity to the airway during sleeping, pillows are thought to be a significant site for dust mite proliferation and allergen exposure. The HDM remains on the blanket while avoiding the electric blanket's heat. Typically, the mattress's underside contains more allergens and dust mites than the mattress itself [7,13].

When it's dark outside at night, some dust mites may relocate briefly to carpet surfaces, but the majority of dust mites live deep within carpets, where there are the highest concentrations of mite allergens. The largest allergen in unwashed wool clothing is present in clothes, which is a significant site of HDM proliferation and allergen buildup. HDM living in the home is spread through clothing as well. According to one study, there are three times as many mite allergens in children's toys as there are in mattresses. HDMs consume peeled human skin and infest human bedding, but they also consume peeled animal skin and infest pet bedding [7,16].

3.1 House Dust Mite Allergen

When an allergen comes into touch with the conjunctiva, skin, upper or lower respiratory tract, or intestines, atopic sensitization results. The fecal excrement is the main source of allergens in HDM. These 20–25 particles resemble pollen grains in terms of size. Due to their size and weight, HDM fecal particles might become airborne when doing certain activities, such as walking on carpets, hugging dolls, or wearing sweaters. Smaller particles, potentially flaking exoskeleton fragments or dead HDM bodies, make up some HDM allergens. The respiratory system may become reactive as a result of cutaneous sensitization.

According to the World Health Organization (WHO), there are currently 31 allergens for D. farinae, 20 for D. pteronyssinus, 14 for B. tropicalis, and 5 for E. maynei. The main allergens associated with D. pteronyssinus are listed in **Table 1**. Der p1 and Der p2 are the primary allergens that have been studied the most. One of the 20 HDM allergens with proteolytic activity is Der p1, a cysteine protease, along with Der p3, p6, and p9, serine proteases. The effects of these proteolytic characteristics on allergy sensitization are profound. Der p2 is interesting because of its sequence homology to MD-2, which when linked to lipopolysaccharide binds to TLR-4, the pattern-recognition receptor for endotoxins (LPS). Der p2 can therefore act as an auto-adjuvant. Shrimp and dust mites react differently to one another because they both contain the muscle protein tropomyosin, which is also present in other invertebrates. A prominent dust mite allergen in atopic dermatitis is der p11, a distinct muscle allergen that is found in dust mite bodies as opposed to feces. It is discovered in dust mite bodies rather than feces and has an extremely large molecular weight of

100 kDa, similar to the protein paramyosin found in invertebrates. Der p23, a recently identified dust mite allergen, is peritropin from the mite stomach, which is located in the mite's outer membrane. The most recent dust mite allergen to be identified is der f 24, a substantial allergy and functional homolog of ubiquinol cytochrome c reductase binding protein (UQCRB) [7,17].

Table 1. Allergens found in Dermatophagoides pteronyssinus

Der p allergen	Biological function	Significance
p1	Cysteine protease	Major allergen. PAR activator
p2	Lipid binding	Major allergen. Homologous to MD-2, the LPS-binding link to TLR4; "auto-adjuvant"
p3	Serine protease (trypsin)	PAR activator
p4	Amylase	
p5	Lipid binding	
p6	Serine protease (chymotrypsin)	PAR activator
p7	Lipid binding	
p8	Glutathione transferase	
p9	Serine protease (collagenase)	PAR activator
p10	Muscle tropomyosin	Responsible for shrimp cross-reactivity
p11	High molecular weight muscle paramyosin	Major allergen in atopic dermatitis
p15,18	Chitinase; chitin-binding protein	Major allergens in allergic dogs
p23	Peritrophin, chitin binding	

Abbreviations: Der p, Dermatophagoides pteronyssinus; PAR, protease-activated receptor; LPS, lipopolysaccharide; TLR4, toll-like receptor 4. Adapted from Miller, 2019 [7]. Copyright 2018 by Springer Science+Business Media, LLC, part of Springer Nature.

HDM particles contain two different types of active components: proteolytic enzymes and pathogen-associated molecular patterns (PAMPS), which function on protease-activated receptors (PAR) and pattern recognition receptors, respectively (PRR). These PRRs include the lectin-type, TLR-2, TLR-4, TLR-9, and formyl peptide receptors.

3.2 House Dust Mite Sensitization Route

Respiratory Tract

HDM allergen sensitization primarily occurs through the airway mucosa because it is an inhalant allergen. The highest levels of sensitivity, according to one study, ranged between 3.5 and 23.4 g/g of dust. As a result, the primary prevention of sensitization study has suggested that a safe threshold for preventing dust mites is a maximum of 2 g of allergen per g of dust. HDM sensitization may occur when the allergen is in the air. Despite their limitations, measurements of dust mite allergens in household dust are used as an approximate predictor of exposure to these allergens. Dust mite allergens tend to be big (>20 M) and settle quickly, as opposed to cat or pollen allergies.

The size of the dust mite allergen particles that enter the respiratory tract to cause sensitization and allergic reactions are still unknown. However, research has revealed that when the dust mite reservoir is disturbed, little amounts of dust mite allergen particles inhaled by humans (1.1 to 4.7 M) become airborne (e.g., by unfiltered vacuum cleaning). Since the amounts of airborne allergens are so low, an ELISA technique is required to measure them. This is how dust mite allergens are thought to enter the lower respiratory tract.

HDM allergens can be found in the body parts and excretions of mites. These allergens are strong inducers of the T-helper 2 (TH2) response, which leads to the development of IgE antibodies when combined with non-

allergenic components. These particles' ability to stimulate the immune system comes from the allergen itself. The primary Group 1 allergens, such as Der p 1 and Der f 1, are cysteine proteases that increase the respiratory epithelium's permeability by enzymatically breaking down tight connections. Comparable results were seen in skin, where a cysteine protease papain that is similar to Der p 1 promotes immediate innate inflammation but particular sensitization is unrelated to enzymatic activity. Recent research has revealed that Group 2 allergens like Der p 2 and Der f 2 have homologs of the adaptor protein MD-2, a co-receptor of the toll-like receptor/TLR, which can facilitate lipopolysaccharide-mediated activation via TLR-4. These HDM particles also include pathogen-associated molecular patterns (PAMPS), such as mite DNA, bacterial DNA, and endotoxins, which act as adjuvants for allergic reactions by activating the innate immune system. The effect of this HDM allergen on epithelial cells resulted in the production of many epithelial-derived Th-2-promoting cytokines, including thymic stromal lymphopoietin (TSLP), IL-25, and IL-33. **Figure 3** outlines the pathophysiology of HDM allergen sensitivity.

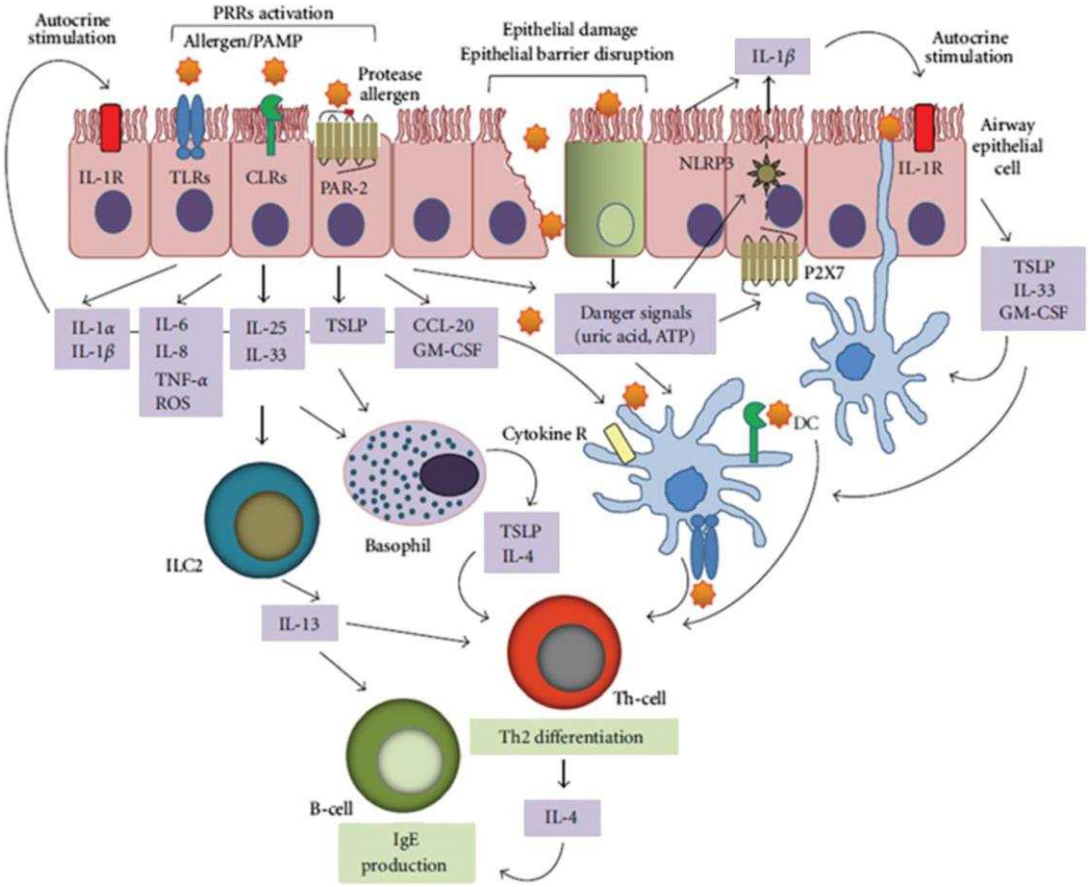

Figure 3. The pathogenesis of house dust mite allergen sensitization. Abbreviations: PRR; pattern recognition receptors; PAMP, pathogen-associated molecular patterns; IL, interleukin; TLR, toll-like receptor; CLR, C-type lectin receptor; PAR, protease-activated receptors; NLRP3, NLR family pyrin domain containing 3; P2X7, P2X purinoceptor 7; TNF-α, tumor necrosis factor-α; ROS, reactive oxygen species; TSLP, thymic stromal lymphopoietin; CCL-20, Chemokine ligand 20; GM-CSF, granulocyte-macrophage colony-stimulating factor; ATP, adenosine triphosphate; ILC2, innate lymphoid type-2; Th, T helper. Reprinted from Sánchez-Borges, et al., 2017.[6]

Skin

In recent years, it has been abundantly obvious that the skin can also develop an allergy sensitivity, particularly when dermatitis compromises the skin's protective layer. This hypothesis is consistent with the association between the degree of aeroallergen sensitivity and transepidermal water loss (TEWL) in infants with dermatitis. It has been demonstrated that even filaggrin mutations, which increase the chance of developing dermatitis, can lead to allergen sensitivity. According to research conducted on animals, dermatitis-affected skin produces too many TSLP cytokines, which makes the air more sensitive to HDM and leads to the development of allergic asthma.

HDM allergens likely trigger Th2 activity through the skin epithelium using a similar immunological mechanism to the respiratory tract. HDM allergens typically penetrate through the epidermal barrier as a result of their direct proteolytic activity (such as Der p 1) and capacity to bind lipids (eg Der p 2). The ability of allergens and other substances in HDM particles to act as adjuvants is a function of the innate immune system, particularly dendritic cells. This causes Th2 skewing and IgE synthesis.

4. House Dust Mite Allergy in Atopic Dermatitis

4.1 Diagnosis

Atopy Patch Test

The use of aeroallergen extracts for skin patch testing was first described in 1937. When Mitchell and colleagues conducted the first patch test employing pure mite antigens in atopic dermatitis patients in 1982, they found that acute dermatitis lesions may be brought on by the administration of inhalant allergens to the skin. The atopy patch test (APT), which was created in 1989 by Ring et al., can be applied to AD patients.

Skin prick tests or specific IgE antibodies to food or airborne allergens are frequently positive in AD patients. After coming into contact with animal dander or being in dusty conditions, many individuals experience recurrence. The APT is an epicutan patch test that uses protein allergens to cause IgE-mediated reactions (and maybe delayed eczematous skin lesions). Skin assessment is done 24 to 72 hours after the test. The primary purpose of this test was to diagnose AD, a chronic inflammatory skin disease brought on by aeroallergens.[18] APT (SCORAD) scoring >40, absence of known allergic contact dermatitis trigger, ineffective topical therapy (including immunomodulators) and phototherapy (in adults), suspicion that symptoms are exacerbated by food or airborne allergens, negative specific IgE and/or negative prick test, multiple IgE sensitization without clinically relevant trials, and in children with moderate AD (SCORAD between 0 and 4) are all indicators of atopic dermatitis and persistent or severe AD.

Skin that is lesion-free, non-abrasive, and has not been treated in remission is used for APT. Results from the vehicle and the applied allergen dosage were compared. APT was performed with a strong connection to clinical parameters like allergen-specific IgE or recent patient history, and it was done in a manner that is very comparable to conventional patch testing for the diagnosis of classic (hapten-induced) contact allergy. It is important to consider the possibility of contact urticaria as well as the exclusion criteria (use of antihistamines, systemic and local steroids for one week; calcineurin antagonists for one week; UV radiation for three weeks; and relapsing acute eczema). In epicutaneous tests, lyophilized allergens from sources such cat dander, pollen, and house dust mites (Dermatophagoides pteronyssinus) were utilized as a carrier (including control vehicles). The patient's eczema must be completely under control. APT treats non-exfoliated, non-eczematous skin on the back for 48 hours in a large Finn chamber (12 mm in diameter). Skin stripping and other practices that could irritate the skin barrier should never be used [18].

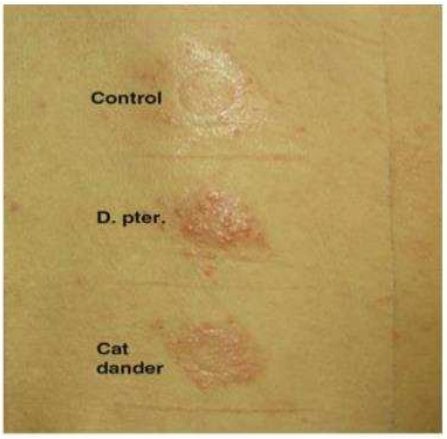

Figure 4. Atopy patch test responded to several allergens following the removal of Finn Chambers 48 hours later. Dermatitis appears clearly with distinct infiltration, papules dispersed throughout, some in a follicular pattern. Control: petrolatum. Reprinted from Darsow and Ring, 2006 [19]. Copyright 2006 by Springer Nature Switzerland AG.

If the test is conducted on the back, the various APT methods have great repeatability. More than twice as many APT reactions are brought on by petrolatum allergens as by those in hydrochemical vehicles. Although a suitable positive skin prick test was seen in 62% of individuals with positive APTs for D. pteronyssinus and in 77% of them, significant allergen-specific IgE levels were also seen. The importance is significantly more important for other allergies. Comparatively, petrolatum was used to expose 57 people to allergen concentrations of 500, 3,000, 5,000, and 10,000 Protein Nitrogen Units (PNU)/g [19]. Information from a randomized double-blind multicenter investigation involving 253 adult patients and 30 children with AD was used to identify the ideal dose of APT allergen. Between 5,000 and 7,000 PNU/g is the optimal allergen dosage. Children seem to have lower allergen concentrations. The most significant aeroallergens in Europe at dosages of 7,000 PNU/g and 200 IR/g (biological units; reactive index) in a subsequent study including 50 AD patients shown comparable concordance with a patient history indicating clinical importance. In a 2-week placebo-controlled trial, results from pre-loco research with 1% pimecrolimus showed that this calcineurin antagonist reduced the severity of the APT reaction. An example of a positive APT reaction to a physiologically standardized allergen formulation is shown in **Figure 4.**

Table 2 Interpretation of patch test results based on The European Task Force on Atopic Dermatitis (ETFAD)

Result	Skin Reaction
-	Negative
?	Questionable, only erythema
+	Erythema, infiltration
++	Erythema, few papules
+++	Erythema, many or spreading papules
++++	Erythema, vesicles

Adapted from Darsow and Ring, 2006 [19]. Copyright 2006 by Springer Nature Switzerland AG.

The European Task Force on Atopic Dermatitis (ETFAD) amended the international standards for reading patch tests, and only palpable and infiltrating reactions were categorized as positive in **Table 2**. Only papular

or infiltrating reactions have clinical relevance, thus it's critical to properly identify these from negative or dubious ones. Babies and children often have more severe reactions than adults do because of their weaker skin.

Skin Prick Test

The prick test is the simplest way to determine whether someone has an allergy to immunoglobulin E (IgE), such as someone who has asthma, urticaria, anaphylaxis, or rhinoconjunctivitis [20,21]. There are several available commercial and local allergens. The locally produced HDM allergen was also analyzed for its accuracy compared to standard allergen and showed a good sensitivity (84.6%) and specificity (83.3%) [22]. Three days before prick testing, or for 15 days if taking ketotifen, antihistamines such as cetirizine, loratadine, fexofenadine ebastine, myzolastin, desloratadine, and levocetirizine should be stopped.

To do a prick test, the volar portion of the forearm or the top of the back is rubbed with the allergen solution. Avoid wearing clothing with elbow creases since they might cause difficult-to-read reactions, both positive and negative. The skin will be punctured with a specific lancet after being dripped with the allergy solution. Since the puncture is made with light pressure, bleeding shouldn't occur. To prevent reading reactions from overlapping, the optimal stitch spacing is between 3-5 cm. 50–100 M histamine chlorhydrate in 0.9% NaCl was used as a positive control, while 0.9% NaCl was utilized as a negative control. Allergens and controls are removed with a tissue after 15 to 20 minutes. If the urticaria measured more than 3 mm, the results were considered positive. On positive test results connected to history and clinical symptoms, a relevance assessment was done [20].

To identify HDM-induced AD, Liu and associates in 2017 performed a meta-analysis contrasting APT and prick tests. The study's findings support the use of APT in conjunction with prick testing to detect HDM sensitivity in AD patients. However, because the likelihood of a positive reaction varies depending on the allergen type, the selection of the allergen extract is still a significant and deciding element in determining AD [23].

4.2 Management

Desensitization or immunotherapy with allergens is one of the treatments that has been utilized to help manage and reduce allergic symptoms in a variety of individuals [24]. Patients with asthma and allergic rhinitis have been treated with allergen-specific immunotherapy utilizing HDM extracts. While there have been few double-blind placebo-controlled trials, there has been considerable dispute on the effectiveness of particular immunotherapy in AD. But numerous blinded, placebo-controlled studies of immunotherapy in AD patients showed a considerable reduction in clinical symptoms [25].

The purpose of immunotherapy is to reduce IgE-mediated illness by administering specific allergens in gradually increasing dosages. Inhibiting IL-4-secreting T cells and mast cell degranulation can be used to treat allergy illness in addition to biological therapies that target TH2 inflammation. Immunotherapy causes regulatory T cells to produce more IL-10 and TGF-, which compete with IgE for binding to allergens, lowering allergen capture and presentation and, eventually, lessening the allergic reaction [24].

When avoiding precipitating factors is not sufficient to reduce symptoms and IgE sensitization as evidenced by skin prick test and/or IgE test, immunotherapy with allergens should be considered, as they are the only etiological therapy available so far [26]. Immunotherapy can be administered via two different routes, subcutaneous (SC) and sublingual (SL), and both treatment modalities have been tried in patients with AD.

A 2019 study by Liu and colleagues in China examined the effectiveness and security of SL immunotherapy using D. farinae extract in AD patients who had HDM. A multicenter, randomized, double-blind, placebo-controlled clinical trial with 239 HDM-induced AD patients served as the control. Patients

were placed into two groups for the duration of the 36-week study: those who got sublingual drops of D. farinae and those who received a placebo (high, medium, and low doses). Prior to the study's conclusion, 48 patients withdrew. According to the study's findings, the medium and high dose D. farinae groups significantly reduced their AD scores as well as their overall therapy scores. The area of skin lesions revealed a significant difference between the high-dose and moderate-dose SL D. farinae group and the placebo group at the sixth patient visit. Most side effects are mild, and no life-threatening drug reactions occur. The study demonstrated a beneficial effect with moderate and high doses of D. farinae immunotherapy SL in HDM-induced AD patients, and the treatment was well tolerated [27].

A study on the efficiency and security of SL immunotherapy in Korean AD patients was carried out by you and your colleagues. SL (mixed extract of DP and DF, 200 units of treatment/standard dose, SLIT one®; ALK-abello, Hrsholm, Denmark) was administered to AD patients for a minimum of 12 months. The dosage per day is 0.2 ml. The droplets are held for two minutes under the tongue before being ingested. After inhaling the drops, the patient must wait five minutes before drinking or eating anything. According to the study's findings, SL immunotherapy using HDM extract was efficient and well-tolerated in Korean patients with AD, as evidenced by a notable reduction in Eczema Area and Severity Index (EASI) scores [28].

Slavyanakaya and colleagues conducted a study with SC immunotherapy in children aged 5-18 years with moderate and severe AD and sensitivity to HDM allergens showing positive results. The group of children with AD who had used SC immunotherapy for 3 years showed a significant decrease in the SCORAD index and a decrease in exacerbations and hospitalizations. Patients showed improved quality of life and long-term treatment effects (observation period of about 5 years). In addition, SC immunotherapy has pharmaco-economic efficiency [29].

When using immunotherapy, problems might happen both locally and systemically. Based on an assessment of systemic adverse effects in SC immunotherapy over a three-year period (2008–2011), there were no fatal consequences and just 0.1% of the 18.9 million SC immunotherapy procedures resulted in systemic side effects. Most systemic side effects appear within 30 minutes of injection, while some may take longer due to mild flu-like symptoms. Urticaria or pruritus are frequent local side effects that may occur, but the majority of these reactions last under 24 hours and are infrequently regarded as complications [25].

4.3 Prevention

To lessen or prevent exposure to HDMs—alive, dead, or in their feces—many therapies are performed. Chemical and physical therapies made up the interventions. Physical measures include barriers (such as mattress covers), lowering relative humidity in the space (such as ventilation), switching out the floor coverings, removing soft furnishings, vacuuming, air filtration, removing sensitive toys like dolls, heating, freezing, and washing (55 Celsius or higher). Due to the apparent symbiotic interaction between mites and fungi, chemical interventions such as acaricide sprays and antifungal medications seem to decrease the quantity of HDMs [30].

The majority of HDM exposure reduction or avoidance strategies are carried out at home. As most HDM exposures are bed-related, these efforts are typically concentrated in the rooms of patients who are allergic to HDM. For growth and reproduction, HDMs rely on the humidity of their environment. Since HDM can persist for a long period in a low-humidity setting, bedrooms should ideally be situated next to the part of the home that receives the most sunlight [31,32]. Bedrooms ought to be ventilated. Low relative humidity should be maintained, preferably with the help of an air conditioner. The dust has the capacity to absorb moisture from its surroundings, and in various layers of dust, conditions may be ideal for mite development. The best flooring options are tile, wood, linoleum, or vinyl because they are less dusty and easy to maintain. Dry dust should be avoided, and the floor should be wiped with a moist cloth.

Because mattresses are typically not dirty, they are not cleaned frequently, which leads to the buildup of an unseen layer of dust. Mattresses are therefore a key environment for HDM. At least once a month, the mattress should be vacuumed, and if feasible, both sides should be exposed to direct sunshine. Every two to three weeks, sheets, blankets, pillowcases, and bedcovers should be cleaned at 60 degrees or higher. Heat destroys HDM and eliminates the majority of allergies [32].

It is not recommended to use thick carpets in bedrooms, particularly those made of wool. Long-fibered carpets are a significant HDM biotope where dust gathers at lower fiber levels. If a carpet is being used, it must be cleaned frequently and exposed to sunshine. Large volumes of dust can be removed by strong vacuum cleaners like those with high-efficiency particle air filters (HEPA).

On items that are not frequently used, such as table decorations, books, magazines, dolls, toys, clothes, and bedding, dust can gather. Allergen-proof plastic bags should be used to store these things or they should be frequently washed. Clothes should be stored in locked drawers and cabinets, while books should be kept in closed cabinets. Lightweight, washable drapes should take the place of heavy ones [32].

5. Conclusion

Itching is a prominent feature of AD, a chronic inflammatory skin condition that goes through phases of exacerbation and remission. Dust mite exposure may influence the chance of developing AD. In order to avoid the development of chronic AD and improve the patient's quality of life, appropriate therapy and prevention are required.

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