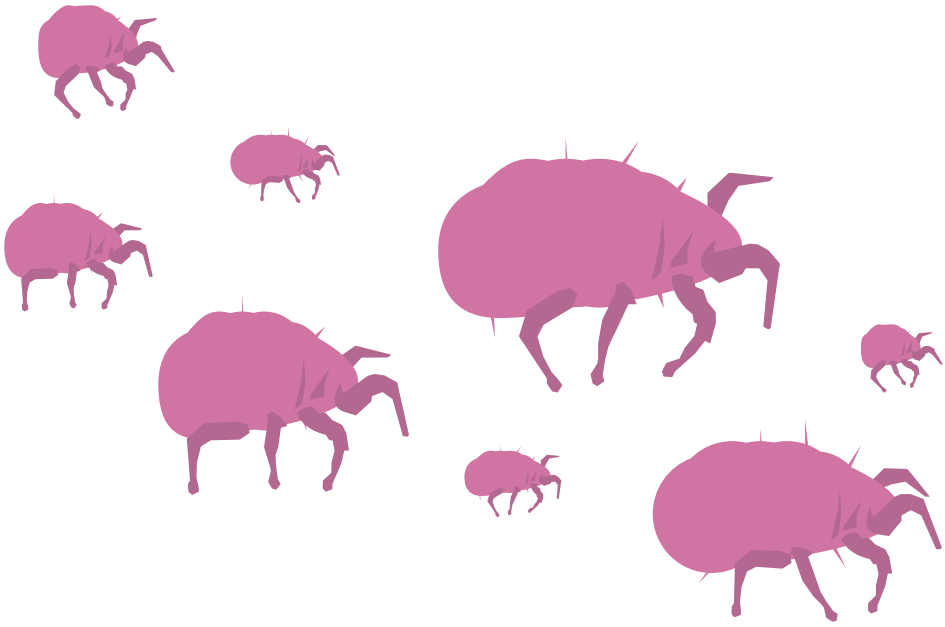
ImmunoCAP®

Mites

Allergy – Which allergens?



Thermo SCIENTIFIC

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Contents

Mite Allergens

Mites comprise a huge and various group of tiny arthropods in the class *Arachnida*, which they share with scorpions and spiders, and in the subphylum *Chelicerata*, which they share with ticks. But while some mites are visible to the naked eye, like ticks, others are microscopic; and while some mites are parasitic like ticks, most are not. Mites have 8 legs instead of 6 (except in the nymph stage), differentiating them from insects. Their bodies are plump, sparsely haired, oval and not in themselves articulated. The mandibles and feelers resemble tongs.

As a very ancient organism, the mite is enormously diversified and adapted to a wide variety of environments, including plants, animals, humans, soil, fresh and salt water, organic rubbles, houses, mattresses, and old books. There are free-living, saprophitic, parasitic and predator mites.

Mites are important in soil and forest ecology and agriculture. Depending on the species and the circumstances, they can be either economically destructive pests (especially in food stores) or essential to the balance of biological systems; and either harmless to health, or direct or indirect causes of diseases in humans and animals. Among the disease-causing mites that usually act non-allergenically are the Itch or Scabies mite *Sarcoptes scabiei hominis* and the Straw itch mite *Pyemotes tritici* (1). Some mites whose environment is stored food may affect foodstuff workers, causing characteristic dermatitis: they can act either directly, by stings and bites, or indirectly, provoking an allergic hypersensitivity (2).

Certain species of microscopic mites occupy an insidious place among allergens. Not only, like pollens, are they invisible and from very common environmental sources, forming ambient mediators of allergic disease, but their sources are not even as distinct as certain widespread species of trees. These mites are instead basically part of the atmosphere of human civilisation. They prevail in domestic settings, agriculture and certain industries—especially domestic settings, where most people spend most of their time.

But a great number of factors play a role in exposure to these mites. The prevalence of different categories of mites may vary considerably among geographical locations (3). Different socioeconomic conditions influence the prevalence of domestic mites. For example, in Salvador, a Brazilian city, the mite *Dermatophagoides pteronyssinus* was found more frequently in the beds of the wealthy than of the poor (4) Mite allergens may spread where mites do not. Public transport vehicles and schools can be sources of mite allergens (5-7). The allergens accumulate on the skin and hair of dogs (8).

Humans themselves can be carriers as well as victims of allergenic mites. Among 1,994 individuals with different occupations, 8.07% were shown to carry mites in their urine and/or stool. The species of mites in the samples were consistent with those found in the individuals' working environments. A significant association was found between mite infection and occupation, in particular among those working in medicinal herb storehouses and rice storehouses and mills; and in miners, railway workers, pupils and teachers (9).

There are 3 basic kinds of well recognised allergenic mites: House dust mites, Storage mites, and Plant mites—among these latter are the Red spider mite and Citrus mites. (It should be kept in mind, however, that these 3 major types are not the only causes of mite allergy; *Hemisarcoptes cooremani*, for example, which preys on scale insects, can cause allergic reactions (10)

The most important allergy-causing mites worldwide are the House dust mites *Dermatophagoides farinae*, *D. pteronyssinus*, *Euroglyphus maynei*, and the Storage mite *Blomia tropicalis,* which because of its common presence in house dust is now recognised as a domestic mite. Most mite infestations involve multiple species, but proportions differ among geographical regions (11), among buildings and even among areas within a building. Mites' preference for high relative humidity keeps them abundant in moist climates and in homes, and scarce in desert climates, public buildings and transportation facilities (12).

House dust mites, belonging to the *Pyroglyphidae* family, live mainly in households, where they eat the human skin cells which are the chief component of house dust. Their numbers have apparently grown enormously because of the now much better enclosed and heated houses of the Northern Hemisphere, and because of the trend worldwide toward Western furnishings: window curtains, upholstery, mattresses, pillows, and carpeting, all of which tend to be thick and layered, providing superb havens for House dust mites (13), and which are difficult to clean, adding to the challenges that the physical properties of House dust mites themselves create for cleaning (see below).

The main species of Storage mites are *Glycophagus domesticus*, *Lepidoglyphus destructor*, *Blomia kulagini* and *Blomia tropicalis*. *Blomia tropicalis* predominates in subtropical and tropical areas. Since the primary habitat of Storage mites is the grains and cereals they eat, they are most common on farms, in granaries and in factories. "The walking dust" consists of millions of mites moving on barn or stable surfaces. Such dust is naturally a potent trigger of occupational allergy. (Interestingly, though, Storage mite is not homogenously present in grains and cereals. In a flat storage facility for wheat, most mites were found in the upper 0.5 m of the bulk (14).

Exposure to these mites has been increasingly recognised as a cause of asthma and rhinitis. And according to recent evidence, some Storage mites have penetrated into the habitats of House dust mites. Studies from several countries have shown that IgE-mediated allergy to Storage mites is of considerable importance in both rural and urban populations; sensitisation is not restricted to those with occupational exposure (15) Populations in damp urban housing would be at special risk (16). Moreover, these mites have been found even in dry regions, as reported after examination of house dust in Cairo, Egypt, for example (17).

Some of the same allergens are produced by both House dust and Storage mites; therefore, the allergic diseases they cause should be very similar (18-19). The allergens from different types and species of mites can, however, be quite different, and clinicians should consider *non*-cross-reactive allergens also as possible causes of reactions. The full range of possible environmental factors should always be kept in mind.

Exposure to Storage mite allergens can be by ingestion (20), which can cause devastating allergic reactions. Recently, anaphylaxis was reported. A 13-year-old boy experienced a sore throat and tight chest approximately a minute after eating home-made wheat flour hotcakes; this reaction was followed by a stuffy throat and paleness of the face. A 7-year-old girl experienced coughing, wheezing, streaming eyes and skin flushing an hour after eating homemade "tako-yaki". Fifteen months later, sneezing, coughing, wheezing, generalised pruritus, and streaming eyes occurred after she ate homemade buns. Both children had high levels of IgE antibodies to *Dermatophagoides farinae*. Mites were found in the boy's hotcake. Three of 176 packages of wheat flour from local retail outlets and 7 of the 127 from homes were found to be infested with mites (21). Storage mites also endanger public health also because they produce transmit mycotoxin-producing fungi (22).

The third category, broadly known as Plant mites, is found on living plants in fields and orchards. One example is the Red spider mite, common on Tomatoes. Since the mites persist on the product after harvest and frequently survive until reaching the consumer, they can produce commonly misdiagnosed reactions. Even more common and more commonly confusing reactions are occupational. For example, a person having allergic reactions from work exposure to fresh Tomato naturally suspects only a Tomato allergy, and a clinician needs to confirm or refute this suspicion through testing and not simply rely on the report (23).

This is particularly true because Plant-feeding mites are among the most important arthropods in greenhouses. The stable environmental conditions maintained in

these buildings for optimal growth of plants, especially in the case of monoculture, also nurture mites. Sometimes mites are pests, causing economic damage to greenhouse crops, but they can also be useful and may be deliberately employed in the biological control of insects. Typical pest mites in greenhouses are the Spider mites (*Tetranychus* species) and Bulb mites (*Rhizoglyphus* species). Predatory mites used in biological control in greenhouses include Phytoseiid and Laelapid mites. A range of mite species can cause allergic reactions in greenhouse workers.

Mites are complex organisms, which produce thousands of different proteins and other macromolecules. Mite extracts for testing are made from an aqueous extraction of a variable mixture of whole mites, nymphs, faecal pellets, eggs and spent culture media. The extracts contain over 30 different proteins that can induce IgE antibody production in patients allergic to mite. Out of the 19 denominated groups of allergens, major IgE binding has been reported for the Group 1, 2, 3, 9, 11, 14 and 15 allergens. The high-molecular-weight Group 11, 14 and 15 allergens have recently been described. The Group 1 and 2 allergens represent dominant specificities, which can account for much of the allergenicity of extracts (24). Data on Storage mites could be extrapolated from House dust mites, which have been the main focus of research.

Mite extracts contain a variety of biochemically active enzymes, including trypsin, chymotrypsin, carboxypeptidase A and B, glucoamylase and lysozyme. Marked differences in the relative concentrations of some of these enzymes, particularly trypsin and carboxypeptidase A, occur in different mite extracts (25-26). (A number of these enzymes are physicochemically similar to corresponding enzymes from vertebrate and invertebrate sources.) The age of the faeces could be important, or there could be a threshold where proteolytic activity becomes dominant. Low concentrations of allergens may occur for a variety of other reasons: allergens could be secreted proteins, and some of these (e.g., Der p 14) are unstable in aqueous extracts. Allergens in the mite are compartmentalised, so destruction by hydrolytic enzymes may occur; for example, haemolymph proteins, previously not mixed with a mite's digestive enzymes, may be destroyed upon mixing.

Even when allergens are well preserved, mite extracts used for commercial testing may not mimic the native mite allergen environment in general at all accurately. All that can broadly be said about the concentrations of most allergens in the environment is that these are unknown but are probably sparse. For an accurate diagnosis and effective treatment of mite allergy, specimens should be collected and identified by trained specialists.

But once a diagnosis is made, it can be very difficult to remove House dust mites from a home or workplace. Allergenic mites are extremely well adapted for infecting households. Adults are about 300 µm in size. Some species have a stage, termed hypopial, that conveys resistance to adverse environmental influences. In any case, it is apparently not mainly mite bodies or body parts causing allergic reactions but the faeces and other excreted substances. These are especially potent allergens because of the various digestive enzymes they contain (27).

Cleaning is difficult first of all because the faeces are extremely tenacious. Special vacuum machines for breaking up the faeces may spew the material back into the home and make the problem worse: the tiny size of mite wastes, once they are broken up, makes them easily airborne. Ordinary cleaning and vacuuming may achieve little or nothing, or may merely bring mite material to the surface of soft furnishings. Some commercial aracides may be effective in killing mites, but could presumably produce substantive drops in allergen levels only in conjunction with stringent measures to remove the mite material that is the operative source of allergens. A study of various measures for removing mites had gloomy results, with only 4 out of 23 trials achieving a reduction in mite allergen levels (28).

However, since high indoor aeroallergen levels are an important risk factor for the development and exacerbation of allergic disease and asthma, efforts at environmental control are widely recommended (27). The obvious steps may be most effective. For many years, doctors have advised the parents of asthmatic children to rip up carpeting and use special mattress covers. Frequent washing of textiles in very hot water is also recommended. An old-fashioned remedy for respiratory disease is probably very sound: send the patient to the mountains. Some of the great spas of Europe are in the Alps, where the air is in fact more pure, and not just of industrial pollution: mite populations are far lower. (Installing dehumidifiers or air cleaners or filters in a home may produce some of the same benefits.) Damp, lowland areas, in contrast, harbour far more mites.

Storage and Citrus mites appear to cause only respiratory allergies in the majority of cases. House dust mites commonly worsen eczema and other skin conditions as well. In a study comparing sensitisation to House dust mite with sensitisation to Storage mite, the mean age for the onset of sensitisation was 6.7 years for House Dust mites and 18.7 years for Storage mites. Conjunctivitis was more frequent in patients allergic to Storage mites, whereas perioral syndrome (itching of the tongue and swelling of the lips) was seen only in patients sensitised to *Tyrophagus putrescentiae*. This study concluded that damp climatic and indoor conditions and human activity, but not urban or rural living environments, influenced the differential sensitisation to House Dust mites and Storage mites (29).

Particularly interesting is the question of mites as a primary allergic trigger and their role in the spread of allergy into populations where it was unknown a generation before. Competing with the hygiene hypothesis (which holds that overly sanitary conditions can compromise the immune system early in life) is a theory that mites entering third-world households along with mattresses and carpets lead to dramatic increases in allergic sensitisation. In many such communities, in fact, Western furnishings long precede modern sanitation, creating an ideal environment for mites (13)

Potential cross-reactivity

The pyroglyphid mites are commonly referred to as House dust mites. Among the Storage mites, the *Glycyphagidae* and *Acaridae* families predominate, and the *Tetranycidae* family contains the Plant mites.

Potential cross-reactivity between mites varies from very low to very high the more closely the species are related. Common and species-specific allergens exist.

For example, a higher degree of cross-reactivity occurs among the House dust mites, in particular among the *Dermatophagoides* species, and a moderate degree of cross-reactivity among these species and other House dust mites such as *Euroglyphus maynei* (30-32). Amino acid sequences of Eur m 1 and Eur m 2 were reported to have a 84 to 86% sequence identity with the corresponding allergens from *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* mites. This was reported to be the same as the degree of sequence identity found between *D. pteronyssinus* and *D. farinae,* despite *Euroglyphus* being a member of the *Pyroglyphinae* subfamily rather than the *Dermatophagoidinae* subfamily (33).

Co-sensitisation to Storage mites is a frequent finding in patients sensitised to *Dermatophagoides pteronyssinus*. However, there is only low immunological cross-reactivity between *Pyroglyphidae* (House dust mites) and non-*Pyroglyphidae* mites (Storage mites) (34). This is in spite of antigenic and allergenic determinants being shared by *Dermatophagoides* species and *Tyrophagus putrescentiae*, and in spite of the fact that the 16 kDa group 2 allergen of *Dermatophagoides* is one of the most prevalent allergens of *T. putrescentiae* (35-37).

Storage mites and *D. pteronyssinus* possess their own unique allergen or allergens. Cross-reactivity among the Storage mites is more common. *Lepidoglyphus destructor*, *Glycyphagus domesticus* and *Tyrophagus putrescentiae* are allergenically more closely related to each other than to *Acarus siro* (38). Similarly, results of other studies have suggested that the major allergens of *T.*

Main types of allergenic Mites

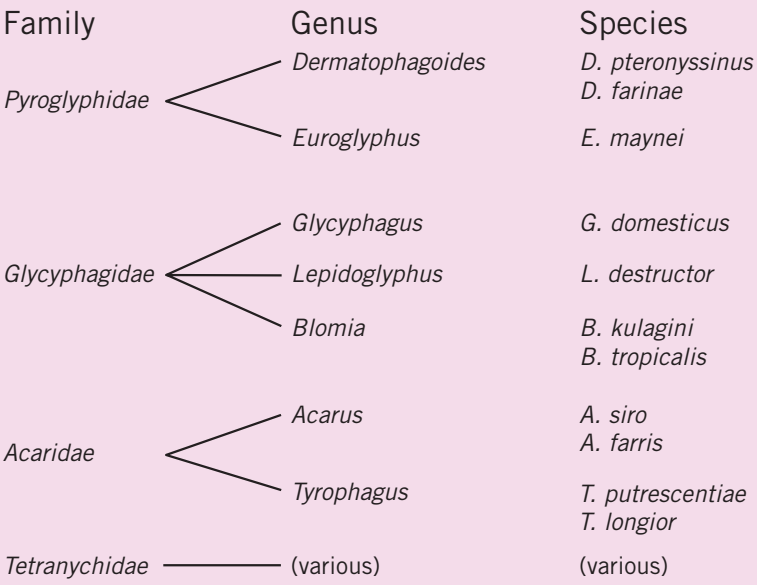

Figure 1. Adapted from: RD. Allergy to storage mites. Clin Exp Allergy 1994;24(7):636-40

putrescentiae have a strong cross-reactivity with *D. pteronyssinus* extracts, but that *D. pteronyssinus* allergens have only partial cross-reactivity with *T. putrescentiae* extracts (37,39). Similarly, extensive cross-reactivity was demonstrated among Gly d 2, Lep d 2, and Tyr p 2, but little cross-reactivity was found between these allergens and Der p 2 (40).

Spider mite extracts contain species-specific allergens as well as allergens commonly shared with House dust mite and Citrus red mite (41-42).

Although allergic reactions are not commonly reported to the human pathogenic mite *Sarcoptes scabiei* (Scabies), a degree of cross-reactivity with *Dermatophagoides pteronyssinus* may exist (43-44).

The reader is referred to individual mite allergen overviews for more details.

ImmunoCAP® mite allergens available for IgE antibody testing

d70	*Acarus siro* (Storage mite)
d201	*Blomia tropicalis* (Storage mite)
d2	*Dermatophagoides farinae* (House dust mite)
d3	*Dermatophagoides microceras* (House dust mite)
d1	*Dermatophagoides pteronysssinus* (House dust mite)
d74	*Euroglyphus maynei* (House dust mite)
d73	*Glycyphagus domesticus* (Storage mite)
d71	*Lepidoglyphus destructor* (Storage mite)
d72	*Tyrophagus putrescentiae* (Storage mite)

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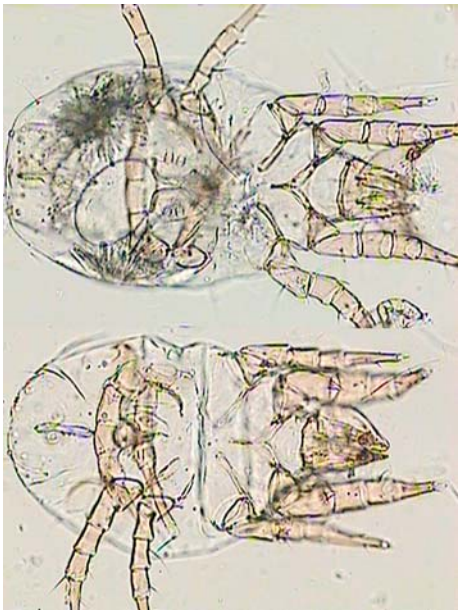
Acarus siro	
Family:	*Acaridae*
Common names:	Storage mite, Flour mite, Grain mite
Source material:	Whole body culture



Allergen Exposure

Geographical distribution

See common geographical background to mites in the Introduction.

Acarus siro is an important agricultural pest and environmental allergen. This Storage mite is 0.2- 0.5 mm in length, with a shiny, soft, cream-white body. The mandibles and the legs are coloured yellow to brown, depending on what the mite eats. The mite's predominant food source is flour, other cereal products, cheese, hay, and dried fruit. Some authors report that fungi growing in the feed are also consumed by these mites. Development from egg to adult occurs in 10 days at normal room temperature. Adults live for 30-50 days.

Though morphologically similar to other mites, *A. Siro* does have some distinct characteristics: on the back of the body is an incision between the 2nd and 3rd pair of legs. The males possess tarsal and anal suckers as well as a clearly expressed hook-like extension at the thighs of the first leg pair. The females possess a claw at the end of each foot. Both sexes possess 4 long, dragging hairs on the back end. This set of features is important in that, whereas many mites, collected from both outdoor and stored product habitats, are described in the literature as *A. siro*, many may in fact belong to a sibling species, *A. farris* or *A. immobilis*. The 3 species are difficult to separate morphologically, gene exchange between some of them is possible, and although each species displays environmental preferences, they occur together in some environments (1).

Environment

See common environmental background to mites in the Introduction.

A. siro and other Storage mites should be considered as possible causes of allergic disorders among farming populations even in northern climates such as Finland, where they have been found in byres and hay and grain storage facilities on farms (2). Storage mites can also cause allergies in individuals in urban homes, even in more-arid environments such as Brunei (in southeast Asia), where this mite was present in house dust, resulting in positive skin reactions in 35% of asthmatics. This demonstrated persuasively that Storage mites are significant allergens in such climates (3).

Unexpected exposure

Storage mites may contaminate processed food. Seven categories of cereal-based food products purchased at food retail outlets in the UK were examined for the presence of mites. Mites were found in 21% of 571 samples examined soon after purchase, and in 38% of 421 samples examined after 6 weeks of storage. Although most of the samples where mites were detected had

fewer than 5 mites, a few samples contained more than 20 mites. A single sample contained 428 mites. The most common species recovered were *Acarus siro*, *Tyrophagus putrescentiae*, *Lepidoglyphus destructor* and *Glycyphagus domesticus* (4). Although the clinical significance of these findings was not evaluated, *A. siro* and *Blomia kulagini* present on cheese rind have been reported to result in occupational allergy (5).

See also under Other reactions for intestinal and urinary acariasis.

Allergens

This mite's extracts contain a number of allergens, which range in size from 10 kDa to 95 kDa. The 15 and 17 kDa allergens are important, but of these only the 15 kDa allergen has been characterised (6-7).

Two allergens have been characterised to date:

Aca s 2, a 15 kDa protein, a Group 2 mite allergen (8).

Aca s 13, a 14.2 kDa protein, a fatty acid binding protein (FABP) (7,9).

rAca s 13, a recombinant allergen (7).

rAca s 13, a 14.2 kDa recombinant allergen, corresponds to the similar native 15 kDa protein. rAca s 13 was shown to have 64% sequence identity with Blo t 13 from *Blomia tropicalis*, as well as homology with several other fatty acid binding proteins from different organisms. rAca s 13 was recognised decisively by 3 of 13 (23%) subjects investigated (7).

Potential cross-reactivity

Stronger cross-reactivity has been reported among *L. destructor*, *G. domesticus*, and *T. putrescentiae* than between these storage mites and *A. siro* (10-11). Other studies have reported a high degree of cross-reactivity between *T. putrescentiae* and *Acarus siro* (12).

Although cross-reactivity of *A. siro* with other storage and with House dust mites has been shown (10-13), the cross-reactivity between Storage and House dust mites appears to be limited. Even though molecular cloning has demonstrated that the Group 2 allergens from Storage mites (Lep d 2 and Tyr p 2) have more than 40% sequence identity with the Group 2 allergens from *Dermatophagoides* species,14 studies have concluded that there is no or poor cross-reactivity between *D. peteronyssinus* and nonpyroglyphid mites (11,13,15).

Aca s 13 has a 64% sequence identity with Blo t 13 from *Blomia tropicalis*, as well as homology with several other fatty acid-binding proteins (FABPs) from other organisms (7).

Nevertheless, co-sensitisation to Storage mites is a frequent finding in patients sensitised to *D. pteronyssinus*, and the immunologic responses to the different mite species may be complex (12,16).

A study has reported cross-reactivity among several allergens in *Anisakis simplex*, *A. siro*, *L. destructor*, *T. putrescentiae*, and *D. pteronyssinus* (17).

Clinical Experience

IgE-mediated reactions

Acarus siro may commonly induce symptoms of occupational allergy in farmers and bakers (2,13,18-23), but sensitisation has also been found in non-farming populations, as described below (7). Furthermore, a study in Denmark concluded that in humid and temperate regions of Europe, allergy to Storage mites in farmers is not caused exclusively by occupational exposure; damp housing conditions and indoor domestic exposure to Storage mites may also be important (20).

In a study of the prevalence of Storage mite allergy in 440 farmers with respiratory symptoms on Gotland, an island in the Baltic Sea, allergy to at least 1 of 4 storage mites was found in 52 of the subjects (12%). The corresponding prevalence among farmers with hypersensitivity symptoms was 15.4%, and among those with possibly IgE-mediated symptoms, it was as high as 37.8% (18).

A study of Wisconsin dairy farmers found that the most prevalent allergies were to House dust mites (21.6%), Storage mites (11.2%), grain smuts (11.2%), *Cladosporium* (7.5%), *Aspergillus* (6.0%), and Cattle (5.2%). Among Storage mites, the most prevalent sensitisation was to *L. destructor* (7 of 8), followed by *T. putrescentiae* (6 of 8), *G. domesticus* (5 of 8), *Chortoglyphus arcuatus* (5 of 8), and *A. siro* (2 of 8) (21). Serum samples from 600 people, randomly selected from a 1-day submission of approximately 3,000 samples from a southwestern Ohio population to a clinical diagnostic laboratory, were screened for IgE to allergens of *L. destructor* and *A. siro*. Thirty-two (5.3%) of the 600 serum samples screened had IgE to allergens from at least 1 of the 2 mite species; 14 (2.3%) and 20 (3.3%) had serum IgE to proteins of the mites *A siro* and *L destructor*, respectively (24).

Among 136 eastern Polish farming students, skin reactivity to *L. destructor* was found in 18.4%, to *T. putrescentiae* in 15.4%, to *D. pteronyssinus* in 14.0%, and to *A. siro* in 13.2% (25). In a study of 14 Polish farmers, of whom 19.2% complained of work-related skin symptoms, mostly related to working with Hops (11%), grain (5.6%), hay (5.5%) and straw (4.1%), sensitisation to *A. siro* was found in 9.6%, to *L. destructor* in 17.8%, and to *T. putrescentiae* in 13.7% (26).

The prevalence of mite sensitisation among 4,379 patients residing in a cereal industrial region of Spain was found to be 18.96%. Sensitisation to Storage mites among mite-sensitive patients was 11.88%. In 50 selected patients, the most frequent sensitisation was to *D. pteronyssinus* (58%), followed by *D. farinae* (48%), *L. destructor* and *T. putrescentiae* (38%), *B. kulagini* (34%), and *A. siro* and *C. arcuatus* (24%). Importantly, 22% of the patients not sensitised to *Dermatophagoides* species were found to be sensitised to Storage mites (27).

Forty-four percent of 139 workers in 4 grain elevator stores in Aalborg, Denmark, reported pulmonary symptoms; 31% complained of work-related respiratory symptoms. Although only 6.4% were diagnosed with respiratory Storage mite allergy, 15.9% were sensitised to Storage mites. Examination of samples of grain and dust revealed Storage mites (in particular *A. siro*, *L. destructor* and *T. putrescentiae*) in 73% of grain samples, while all dust samples contained mites (18).

In a study of bakery workers and salt packing workers in the United Kingdom, 42% of both groups were found to be atopic, and 33% had skin-specific IgE sensitisation to at least 1 of 4 storage mites (*L. destructor*, *G. domesticus*, *T. putrescentiae* and *A. siro*) (28).

In an investigation of the prevalence of various domestic mite species in Kutahya, Turkey, an 18.05% prevalence of domestic mites was found. The following species were identified: *Tyrophagus putrescentiae* (43.96%), *Dermatophagoides pteronyssinus* (31.03%), *Acarus siro* (13.79%), *Lepidoglyphus destructor* (1.72%), and *Glycyphagus domesticus* (2.58%). A very high rate of *A. siro* was found in July (29).

In a study of bakers, IgE antibodies to flour was related to IgE antibodies to *A. siro* and *L. destructor*, but not to *T. putrescentiae*. Almost all bakers sensitised to flour were also sensitised to Storage mites (6 of 7). The authors suggested that if a baker became sensitised to flour, he would be more prone to develop IgE antibodies to Storage mites too (18).

Occupational allergy as a result of *A. siro* and *Blomia kulagini* present on cheese rind has been described (5).

Sensitisation to Storage mites may also occur among urban populations (3,12, 30-37).

In an early study in France, of 248 allergic urban children, 44 (21%) were moderately or strongly positive on skin-specific IgE tests to *A. siro*.38 In Brunei (in southeastern Asia), *A. siro* was found to be present in house dust and resulted in positive skin-specific IgE reactions in 35% of asthmatics, demonstrating that Storage mites are significant allergens in this climate also (3).

Similarly, in 512 patients with rhinitis and/or asthma, living in urban or rural areas of central Germany, 103 (20.1%; 77 urban dwellers and 26 farmers) were found to be sensitised to at least 1 of the Storage mites. The study concluded that sensitisation to Storage mites in Germany was frequently connected with sensitivity to *D. pteronyssinus*, and that sensitisation to Storage mites was more prevalent in rural than in city dwellers (39).

In the warm, humid climate of Cuba, 148 Cuban asthmatic patients with a clinical history of asthma and possible mite allergy were evaluated for sensitisation. Skin reactivity was found to *D. siboney* in 88%, to *D. pteronyssinus* in 87%, to *A. siro* in 85%, to *B. tropicalis* in 85%, and to *D. farinae* in 83% (33).

In a study of 100 children living in Mexico City, who had a history of mild and moderate asthma, 7% were found to be sensitised to *A. siro* (34).

In Barcelona, Spain, 39 of 356 (11%) children were sensitised to Storage mites (*Acarus siro*, *Lepidoglyphus destructor* and *Tyrophagus putrescentiae*). However, only 3 children were sensitised exclusively to Storage mites, the rest being sensitised to House dust mites as well. The most prevalent Storage mite sensitisation was to *L. destructor* (35). In a second Spanish study, of 50 children with rhinitis and asthma, no skin sensitisation to Storage mite was found without concomitant sensitisation to House dust mites. *A. siro* sensitisation was found in 4% (40).

In Russia, in a group of patients with allergic disease and sensitisation to *D. pteronyssinus*, 80% were sensitised to *D. farinae*, 55% to *E. maynei*, 45% to *A. siro*, and 35% to *L. destructor* (41).

In a study of 196 individuals from an urban environment who were not occupationally exposed to Storage mites, IgE antibodies to *D. pteronyssinus* was found in 24%, and in 14% to at least 1 of 3 Storage mites: *A. siro*, *L. destructor*, and *T. putrescentiae* (37).

In a Bavarian study using sera of patients with known House dust mite allergy, a sensitisation prevalence of 7% was shown for *A. siro*, 17% for *L. destructor*, 3% for *T. putrescentiae,* and 13% for *G. domesticus*. The authors concluded that Storage mites are important allergens in allergic rhinitis and that routine testing of patients with perennial rhinitis should be undertaken (36).

In Valdivia, Chile, of 100 consecutive asthmatic paediatric patients evaluated, 80 were confirmed to have skin-specific IgE to at least 1 mite species. All patients with skin-specific IgE for mites were positive to *D. pteronyssinus*, 99% to *D. farinae*, 92% to *Euroglyphus maynei*, 80% to *Lepidoglyphus destructor*, 73% to *Tyrophagus putrescientae*, 72% to *Blomia tropicalis*, 70% to *A. siro* and 68% to *Chortoglyphus arcuatus*. All of the patients with severe persistent asthma, 85% of those in the moderate group, and 73% of those in the mild group had skin-specific IgE to mites. Ninety-five percent of patients with asthma and allergic rhinitis were shown to have skin-specific IgE to mites, along with 92% of patients with asthma and eczema, and 100% of patients with asthma, allergic rhinitis and eczema (42).

Other reactions

Intestinal and urinary acariasis has been described. In a study of 1,994 individuals, skin-specific IgE tests were positive in over 9%. Mite was positive in 4.61% of stool samples, 1.86% of urine samples, and 1.60 % of both. The mites from stool and urine samples comprised a number of species, including *A. siro*. The species of mites in stool and urine samples were consistent with those separated from the working environment. The frequency of mite infection in individuals correlated with occupation among medicinal herb storehouse workers (15.9%), rice storehouse and mill workers (13%), miners (3.3%), railway workers (2.5%), pupils (5%), and teachers (2.6%) (43).

Systemic anaphylaxis can occur after the ingestion of heated or unheated mite-contaminated foods. This problem may be more prevalent in tropical and subtropical countries than previously recognised. The most common symptoms following the ingestion of mite-contaminated flour were breathlessness, angioedema, wheezing, and rhinorrhoea, and these started between 10 and 240 minutes after eating (44).

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d201 *Blomia tropicalis*

Blomia tropicalis	
Family:	*Glycyphagidae*
Class:	*Arachnida*
Subclass:	*Acari*
Common names:	Storage mite, Flour mite, Grain mite
Source material:	Whole body culture

Allergen Exposure

Geographical distribution

See common geographical background to mites in the Introduction.

Blomia tropicalis, a Storage mite, was earlier found predominantly in agricultural environments but is now being recognised as an important contributor to the allergen content in house dust in indoor urban dwellings (1).

B. tropicalis is a notable mite species in many parts of the world, and the most common and most important mite species in tropical countries. *B. tropicalis* and *Dermatophagoides pteronyssinus* occur in a significant percentage of homes in tropical and subtropical regions of the United States and Europe, and in Central and South America and Asia, along with the House dust mites *Euroglyphus maynei* and *Dermatophagoides farinae*. *Blomia tropicalis* is the 4th most common mite in the United States (2).

Environment

See common environmental background to mites in the Introduction.

Unexpected exposure

Mites were found in 21% of 571 samples of cereal-based food products purchased at food retail outlets in the UK, and in 38% of 421 samples, derived from the 571 samples, which were examined after 6 weeks of storage in volunteers' homes. The most common species were *A. siro*, *T. putrescentiae*, *L. destructor* and *G. domesticus* (3).

Allergens

In a study of 60 Taiwanese patients, *B. tropicalis* extract was shown to contain at least 30 protein components. The most frequently detected allergens were proteins with molecular weights of 14.3, 106.5, 94.0, 72.0, 91.9, 63.7, 100.3, 43.6, 27.3, 62.0, 34.7, 18.3, 41.1 and 21.9 kDa. The frequencies of IgE binding of 60 patient sera to those proteins were, respectively, 87.0, 65.2, 56.5, 43.4, 39.1, 39.1, 34.8, 30.4, 30.4, 17.4, 17.4, 17.4, 13.0 and 8.7% (4).

In a study investigating the IgE reactivity of allergens present in extracts of *B. tropicalis* and comparing the IgE responses to these allergens in asthmatics and patients with atopic dermatitis and allergic rhinitis, as well as in 199 nonatopic volunteer controls, 18 out of 29 protein bands present in *Blomia* extracts were recognised by the allergic and control sera. Of these allergens, 4 showed a high IgE binding frequency; these had molecular weights of 104, 80, 68 and 14 kDa. The 14 kDa allergen demonstrated the highest IgE binding frequency. The authors concluded that extracts from pure bodies of *B. tropicalis* contain 1 immunodominant and 3 important allergens (5).

d201 *Blomia tropicalis*

At least 23 IgE-binding components have been demonstrated for *B. tropicalis* (13).

The following allergens have been characterised (6-8):

Blo t 1, a Group 1 mite allergen, a cysteine protease, a major allergen, and a homologue of Der p 1 (9-11).

Blo t 2, a 14.5 kDa protein, a Group 2 mite allergen (12-13).

Blo t 3, a Group 3 mite allergen, a trypsin-like protease (8,12,14-16).

Blo t 4, a Group 4 mite allergen, an alpha-amylase (12).

Blo t 5, a 14 kDA Group 5 mite allergen, a homologue of Der p 5. (6,8,12,17-25).

Blo t 6, chymotrypsin, a protease (12).

Blo t 7 (26).

Blo t 8, a glutathione-S-transferase (26).

Blo t 9, a collagenolytic serine protease (26).

Blo t 10, a tropomyosin (12,27).

Blo t 11, a Group 11 mite allergen, a paramyosin (12,28-30).

Blo t 12, a 14.2 kDa protein (8,31).

Blo t 13, a Group 13 allergen, a fatty acid binding protein (8,17,32-34).

Blo t 14 (35).

Blo t 15, a chitinase (26).

Blo t 18, a 60 kDa protein, a chitinase (26).

Blo t 19 (8,17).

Blo t 20, an arginine kinase (26).

Blo t 21 (36).

The following recombinant allergens have been produced to date:

rBlo t 3 (14-15).

rBlo t 5 (19-21,23-25).

rBlo t 12 (31).

rBlo t 13 (32-34).

Recombinant Blo t 1 has been shown to have a 90% frequency of reactivity with IgE in sera from asthmatic children and a 65% frequency in sera from asthmatic adults, indicating that it represents a major allergen. Cross-reactivity between the Group 1 mite allergens of *B. tropicalis* (Blo t 1) and *D. pteronyssinus* (Der p 1) was demonstrated to be low (9-10).

Of 80 *B. tropicalis*-sensitive Taiwanese patients, 7% were allergic to Blo t 2 (12). However, among sera from Brazilian and Swedish patients, more than 80% revealed sensitisation to this allergen (13).

Of 80 *B. tropicalis*-sensitive Taiwanese patients, 4.7% were allergic to Blo t 3 (12). However, in a study of mite-allergic subjects in Singapore, the frequency of IgE reactivity to the recombinant Blot t 3 was 50%; but the IgE titer was generally low (15). A study in this population, using native Blo t 3 in 44 mite-allergic sera, reported an IgE reactivity frequency of 57% (16).

Among 80 *B. tropicalis*-sensitive Taiwanese patients, 7.5% were shown to be allergic to Blo t 4 (12).

Frequencies of sensitisation to Blo t 5 in Taiwanese and Malaysian patients' sera were shown to be 91.8% and 73.5%, respectively (24). Other studies have reported Blo t 5 to be a major allergen, with sensitisation rates of up to 70% in populations prone to *B. tropicalis* allergy (22). Most patients appear to be concurrently sensitised to *D. pteronyssinus*, and around 18% of patients may be found to be sensitised to *B. tropicalis* as a result of cross-reactivity of *D. pteronyssinus* (12). In a Colombian study, 24% of mite-allergic patients were shown to have IgE binding to *B. tropicalis* extract (20). A study compared the importance of 2 types of sensitisation: to *B. tropicalis* and *D. pteronyssinus* among asthma patients from Florida, Puerto Rico, and Brazil; and to *D. pteronyssinus* among patients from the United States and the United Kingdom. IgE antibodies to recombinant Blo t 5 was found in 45% of sera from *B. tropicalis*-allergic asthmatics in the group from Florida, Puerto Rico, and Brazil, compared to 69% of similar patients in the United States and United Kingdom group. *In vivo* and *in vitro* comparisons of IgE responses to *B. tropicalis*, *D. pteronyssinus*, rBlo t 5, and rDer p 5 showed that *B. tropicalis* has unique

allergens that cause allergen-specific IgE responses, suggesting that *B. tropicalis* is an independent cause of sensitisation (21).

Blo t 5 is a major allergen of *B. tropicalis*, with up to 92% of allergic patients sensitised to it. Native Blo t 5 has been purified and shown to consist of multiple isoforms (37). In a study in Barbados, Blo t 5 sensitivity was present in 46% of 261 subjects and was associated with younger age, higher total serum IgE level, and asthma – the prevalence of asthma in the Blo t 5-sensitive subjects was more than 3-fold greater (42 vs. 13%). Der p 1 sensitivity was less common (27%) but showed similar associations with age, IgE, and asthma. Of the 261 subjects sensitised to Blo t 5, 116 were also sensitised to Der p 1; they were younger, had higher total and Blo t 5-specific IgE levels, and had more than twice the asthma prevalence as those sensitised to Blo t 5 alone (59 vs. 29%). As in other studies, Der p 1 sensitivity without Blo t 5 sensitivity was uncommon; 90% of those sensitised to Der p 1 were also sensitised to Blo t 5 (38).

A study of asthmatics' homes in Hong Kong concluded that Der p 1 and Blo t 5 were the major allergens found in this region, and that Blo t 5 was a more potent allergen in Hong Kong, probably reflecting the high level of exposure to *B. tropicalis* (39).

Sensitisation to Blo t 6 has been reported in 11.1% of 80 *B. tropicalis*-sensitive Taiwanese patients (12).

A study using rBlo t 10 demonstrated that up to 96% amino acid identity was shared with tropomyosin of other mites, and skin-specific IgE and ELISA IgE immunoassay tests found rBlo t 10 sensitisation rates of between 20% and 29% in atopic subjects. As in the case of other specific *Blomia* allergens, some allergic individuals had unique IgE epitopes for Blo t 10 (27).

Sensitisation to Blo t 11 has been reported in 10% of 80 *B. tropicalis*-sensitive Taiwanese patients (12). A study using rBlo t 11 found sensitisation in 52% of 63 sera from asthmatic patients (30).

Of 80 *B. tropicalis*-sensitive Taiwanese patients, 16.3% were allergic to Blo t 12 (12).

In a study with Bt6 (Blo t 13), the frequency of IgE binding of allergic sera was generally low (11%) and weak, with the exception of 1 serum which did show strong specific IgE reactivity (33).

Blo t 21 shares 39% identity with Blo t 5. It is present in the midgut and hindgut contents as well as in faecal particles of *B. tropicalis*. IgE antibodies to Blo t 21 was detected in 93% (40/43) of *B. tropicalis*-sensitised individuals by means of ELISA and 95% (41/43) by means of skin reactivity in an evaluation of 43 adult patients with ongoing persistent allergic rhinitis. However, sera of 494 consecutive individuals attending outpatient allergy clinics over 18 months showed that 57.9% (286/494) were sensitised to Blo t 21. Although the majority (>75%) of sensitised individuals were co-sensitised to both Blo t 5 and Blo t 21, these 2 allergens had a low to moderate degree of cross-reactivity (36).

A study evaluated the presence of IgE, IgG1, and IgG4 to concanavalin A-binding antigens (Bt-Con-A) isolated from *B. tropicalis* (Bt)-total extract in sera of 121 patients with allergic rhinitis. Skin reactivity for *B. tropicalis* was found in 58% of the patients. Proteins of 14-152 kDa were isolated from Bt-total, and components >27 kDa from the Bt-Con-A extract. The authors concluded that Con-A-binding components isolated from *B. tropicalis* constitute major allergens and are involved in both allergen sensitisation (IgE response) and homeostasis maintenance (IgG1 and IgG4 responses) (40).

Potential cross-reactivity

B. tropicalis contains multiple allergens, of which most are species-specific, although there are common allergens present (41-42). A high degree of cross-reactivity exists between the 2 main species of *Blomia* (*B. kulagini* and *B. tropicalis*). IgE-binding components belonging to both species are very similar from the immunological point of view (43). A high degree of cross-reactivity has been demonstrated between *B. tjibodas* and *B. tropicalis* (44).

Although the extent of cross-reactivity between *B. tropicalis* and *D. pteronyssinus*

was estimated at 30% to 43% (12), only minor cross-reactivity has been observed in RAST inhibition and immunoblotting inhibition studies among *B. tropicalis*, *D. pteronyssimus,* and *D. farinae* (6,9,25,41-42,20,45), and among *B. tropicalis*, *Tyrophagus putrescentiae* (42) and *Lepidoglyphus destructor* (13). They exhibit not only low IgE cross-reactivity but also different immunobiology (46). In a Taiwanese study of 60 patients, inhibition studies showed that there was IgE cross-reactivity between *B. tropicalis* and *D. pteronyssinus*; however, there were 2 major allergenic components of *B. tropicalis*, of about 14.3 and 27.3 kDa, not inhibited by *D. pteronyssinus* (4).

A greater degree of cross-reactivity was demonstrated between *B. tropicalis* and *L. destructor* than between *B. tropicalis* and *Dermatophagoides* species (47).

rBlo t 1 was demonstrated to exhibit no IgE cross-reactivity with *D. pteronyssinus* allergens (11). As *B. tropicalis* allergens are distinct and have relatively low to moderate cross-reactivity with *Dermatophagoides* allergens, it has been suggested that *B. tropicalis* should be included in the diagnostic panel for the evaluation of allergic disorders in the tropics (25). This may well be applicable to temperate areas of the world also.

Although most *B. tropicalis*-sensitised individuals are concurrently sensitised to *D. pteronyssinus* and *B. tropicalis,* approximately 18% may have *B. tropicalis* sensitisation caused by cross-reactivity (12).

Cross-reactivity among several proteins from *L. destructor* and *B. tropicalis* has been demonstrated. Evidence suggests that the allergen responsible is Blo t 2, which is antigenically cross-reactive with recombinant *L. destructor* Lep d 2 (13).

Blot t 3 has a high homology, of between 48 and 54%, with serine proteases (Group 3 allergens) from House dust mites and may play a role in cross-reactivity between *Blomia* and other mites (14).

Blo t 5, a homologue of Der p 5, has been reported to be cross-reactive to it; it is thought that this would explain almost all the cross-reactivity between the 2 mite extracts (20). However, in most Group 5 mite studies, only low to moderate cross-reactivity was demonstrated at the molecular level (6,24). A report suggested that the Group 5 mite allergens of *D. pteronyssinus* and *B. tropicalis* are species-specific (23). This suggests that highly specific clinical reagents are necessary for precise diagnosis and immunotherapeutic treatment of sensitisation to Group 5 mite allergens (24).

Cloned Blo t 10 was shown to have up to 96% amino acid identity with tropomyosin of other mites. Nonetheless, although Blo t 10 and Der p 10 share 95% amino acid identity and are significantly cross-reactive, unique IgE epitopes do exist (27).

An 89% sequence identity exists between Der f 11 and Blo t 11 (48).

Recombinant paramyosin from the Sheep scab mite *Psoroptes ovis* has a predicted homology of 97%, 95% and 89% with the paramyosins of *D. pteronyssinus* (Der p 11), *Sarcoptes scabiei* and *B. tropicalis* (Blo t 11), respectively (49).

Blo t 13 has homology with several other fatty acid-binding proteins (FABPs) from different organisms. A 64% sequence identity exists between Blo t 13 and Aca s 13 from *Acarus siro*, an allergen strongly recognised by 23% of 13 allergic subjects investigated (50).

Blo t 21 has 39% identity with Blo t 5. Although more than 75% of sensitised individuals appear to be co-sensitised to Blo t 5 and Blo t 21, these 2 allergens have a low to moderate degree of cross-reactivity (36).

B. tropicalis extract has been shown to inhibit IgE binding to 9 of 14 allergens identified in *Suidasia medanensis* (Scaly grain mite). Four *B. tropicalis* allergens were inhibited by *S. medanensis* extract. RAST inhibition studies demonstrated a higher degree of inhibition by *B. tropicalis* (87.2%) and *D. farinae* (90.9%) than by *S. medanensis* (32%) (51).

Clinical Experience

IgE-mediated reactions

Several investigations have demonstrated that allergens from *B. tropicalis* may play an important role in sensitisation and allergic symptoms (41,52-55). Sensitisation to *B. tropicalis* has been associated with acute asthma that requires emergency room treatment both among children (52) and adults (53).

B. tropicalis occurs in a significant percentage of homes in tropical and subtropical regions of South America and Asia, as well as in the United States and Europe (4,56-65). In these areas, *B. tropicalis* has been shown to be a clinically important allergenic component of house dust, inducing IgE antibody response in patients with allergic diseases such as asthma and rhinitis. In a Brazilian study, patients with atopic dermatitis showed a high degree of sensitisation to *B. tropicalis*, and the authors suggested that exposure to it can thus be considered a risk factor for the development of AD exacerbations (66).

In a study in Tampa, Florida, subjects with allergic rhinitis were challenged with *B. tropicalis* extracts. Ten out of 12 (83%) subjects had positive nasal challenge responses to *B. tropicalis*, as measured by rhinometry. The authors concluded that *B. tropicalis* should be considered a risk factor for allergic rhinitis when a patient is evaluated who lives in an area where it is endemic (67).

In studies in Lima, Peru (56), Cartagena, Colombia (57), Singapore (58) and Malaysia (59), *B. tropicalis* was the mite most frequently detected. A study in Tampa, Florida, identified *B. tropicalis* in 30% of the dust samples from homes in the area (60).

In the Canary Islands, in a study of patients who were sensitised to 2 mite species, *D. pteronyssinus* and *B. tropicalis*, it was confirmed that individuals may react only to 1 of these, supporting the evidence that, although there is some *in vitro* and *in vivo* allergenic cross-reactivity between *B. tropicalis* and *D. pteronyssinus*, clinical symptoms induced by the inhalation of *B. tropicalis* and *D. pteronyssinus* seem to be species-specific; however, some patients may react to common allergens (6,68).

Among Thai patients, skin reactivity to *D. pteronyssinus* was found in 62.5% of 40 adults and 51.1% of 45 children; and to *B. tropicalis* in 37.5% and 40%, respectively (69). In a study in Taiwan and Singapore, although Der p 1, Der p 2 and Blo t5 were found to be major sensitising allergens in both countries, Blo t 5 was found to be a more potent one in Singapore than in Taiwan, probably reflecting the high level of exposure to *Blomia* in that country (70). Similarly, in a Taiwanese study of 498 atopic children aged 2 to 16, a high prevalence of sensitisation – 90.2% to *D. pteronyssinus,* 88.2% to *D. farinae*, 79.5% to *D. microceras*, and 76.7% to *Blomia tropicalis* – was documented (71).

In a study of 124 individuals with allergic rhinitis in Malaysia and Singapore, it was found that sensitisation to Blo t extract was positive in 73% of 124 individuals, while sensitisation to Blo t 5 was positive in 50%. Among 105 patients without rhinitis, sensitisation to Blo t extract was found in 57%, and to Blo t 5 in 23%. Of Malaysian asthmatic adults, 37% were sensitised to Blo t 5, and of the asthmatic children, 90% were sensitised to Blo t 5. The study clearly demonstrated that dual sensitisation to *B. tropicalis* and *D. pteronyssinus* was common in the general populations of Singapore and Malaysia, and that sensitisation to Blo t 5 was more prevalent than to Der p 1 and Der p 2 (72). In a subsequent study of 175 patients with newly diagnosed allergic rhinitis, with a mean age of 7.9 years (range 2-16), 39% reported a concomitant diagnosis and/or clinical complaints of bronchial asthma, and 48% of atopic dermatitis. Skin prick test results were positive for familiar House dust mites (*D. pteronyssinus* and *D. farinae* mix) in 85% of patients, and for *B. tropicalis* in 62%. The authors concluded that in this population, *B. tropicalis* sensitisation is more prominent in children with pure respiratory allergy (73).

In Taiwan, 73.3% of asthmatic patients were reported to be sensitised to *Blomia*. Concurrent sensitisation to both *B. tropicalis*

and *D. pteronyssinus* occurred in 63.3% of these patients (4).

A number of studies from South America have demonstrated the importance of *Blomia* as a sensitising agent on that continent. *B. tropicalis* sensitisation was shown to occur, among allergic patients, in prevalences ranging from 47% in Mexico City to 93.7% in São Paulo. Even very young children may be sensitised to this allergen, the mean age in São Paulo being 2.9 years. In Caracas the prevalence of sensitisation was 77.8% (74). In a repeat study in Caracas ten years later, the prevalence had increased to 91.6% for *B. tropicalis*, and 97.2% for *D. pteronyssinus* (75).

A high prevalence of sensitisation to *B. tropicalis* has also been reported in patients with persistent allergic respiratory symptoms in Venezuela. Skin reactivity in 92.2% of 115 patients was shown to either *B. tropicalis* or *D. pteronyssinus* or both; 70.4% were positive to both, 10.4% only to *D. pteryonyssinus*, and 11.3% only to *B. tropicalis*. IgE antibodies to either or both was detected in 93%, in 69.6% to both, in 11.3% only to *D. pteronyssinus*, and in 12.2% only to *B. tropicalis* (45). In a second Venezuelan study, 204 allergic patients attending specialised clinics in Caracas were studied. Sensitisation to *B. tropicalis* was documented in 90.6%. Monosensitisation to *B. tropicalis* occurred in 2.4%, whereas none reacted exclusively to *B. kulagini* (76).

In a Brazilian study, the presence of skin-specific IgE to *B. tropicalis* was found in 61.8% of patients with atopic dermatitis and 83.33% of asthmatic patients, and in 12.5% of the control group. IgE antibodies was present in 44.1% of those with atopic dermatitis and in 61.9% of asthmatic patients, but in none of the control group (77). Among 110 Brazilian patients with allergic rhinitis with or without asthma, 56% had skin reactivity to *B. tropicalis*, 51% to both *B. tropicalis* and *D. pteronyssinus*, and 6% to *B. tropicalis* only. IgE antibodies for *B. tropicalis* was found in 43% of these patients (78).

In Brazil, nasal challenges with *B. tropicalis* in a group of sensitised patients were positive in 60% of cases (and 90% had positive challenges to *D. pteronyssinus*) (79). In Singapore, positive nasal challenges to *B. tropicalis* were demonstrated; it was also shown that *B. tropicalis* may provoke a concomitant asthmatic response during the late-phase reaction (80). A clinical study was recently made of patients with allergic respiratory disease who attended an allergy clinic in Brazil. Of 212 medical records evaluated, 61.7% were of patients sensitised to Der p, 59.9% to Der f and 54.7% to *B. tropicalis* (81). The high prevalence of sensitisation is not surprising, considering the high level of *B. tropicalis* infestation of dwellings. In an investigation of mites and the presence of Blo t 5 on beds used by individuals with different socioeconomic backgrounds in Salvador, a major Brazilian city, 89% of the beds analyzed were found to harbour at least 1 mite species. *B. tropicalis* was found in 71.8% and *D. pteronyssinus* in 39.9%. *B. tropicalis* was found with a similar frequency in beds of both socioeconomic groups, whereas *D. pteronyssinus* was found more frequently in the beds of the wealthy than of the poor group (82).

In Valdivia, Chile, among 100 consecutive asthmatic paediatric patients evaluated, 80 were confirmed to have skin-specific IgE to at least 1 mite species. Sixty patients had asthma and allergic rhinitis, 12 asthma and eczema, and 8 asthma, allergic rhinitis and eczema. All patients with skin reactivity for mites were positive to *D. pteronyssinus*, 99% to *D. farinae*, 92% to *Euroglyphus maynei*, 80% to *Lepidoglyphus destructor*, 73% to *Tyrophagus putrescientae*, 72% to *B. tropicalis*, 70% to *Acarus siro* and 68% to *Chortoglyphus arcuatus*. All of the patients with severe persistent asthma, 85% of those in the moderate group, and 73% of those in the mild group had skin reactivity to mites. Ninety-five percent of patients with asthma and allergic rhinitis were shown to have skin reactivity to mites, along with 92% of patients with asthma and eczema and 100% of patients with asthma, allergic rhinitis and eczema (83).

D. pteronyssinus, *D. siboney* and *B. tropicalis* have also been reported to be the most important allergenic mites in Cuba.

A total of 88.4% of patients were positive to *D. siboney*, 87.1% to *D. pteronyssinus*, and 68.1% to *B. tropicalis*. Sensitisation to *Dermatophagoides* species was predominant, as demonstrated by the fact that 31.9% of patients showed positive SPT to either *D. siboney* or *D. pteronyssinus* only, whereas only 5.6% was sensitised solely to *B. tropicalis*. Nevertheless, most patients (58.6%) were polysensitised to the 3 species (84).

Although a very high rate of sensitisation to *B. tropicalis* has been found in atopic individuals in tropical and subtropical environments, studies have reported high prevalences of sensitisation in countries with temperate climates; the species *Blomia tjibodas*, *B. kulagini*, and *B. thori* appear to partake of this phenomenon (6).

In Germany, a high rate of IgE antibodies to *B. tjibodas* and *B. tropicalis* in allergic city dwellers and farmers was reported (44). In a study of *B. tropicalis*-sensitive patients in Florida, 83% had a positive nasal challenge with *B. tropicalis* extract, suggesting that the presence of IgE antibodies to this mite is a good predictor of allergic symptoms due to inhalation of allergens from the mite (41).

Other reactions

Occupational allergy to *Blomia kulagini* present on cheese rind has been reported (85).

Systemic anaphylaxis can occur after the ingestion of heated or unheated mite-contaminated foods. This problem may be more prevalent in tropical and subtropical countries than previously recognised. The most common symptoms following the ingestion of mite-contaminated flour were breathlessness, angioedema, wheezing, and rhinorrhoea, and these started between 10 and 240 minutes after eating (86).

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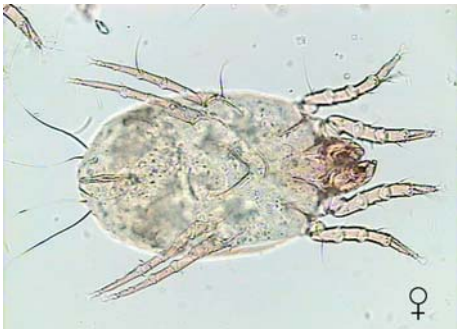
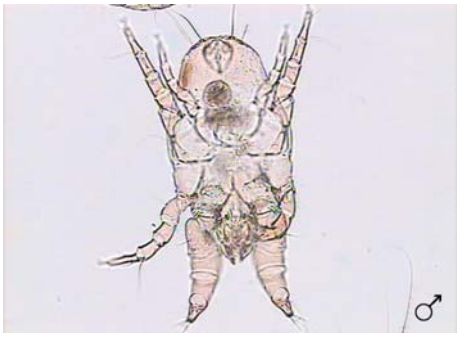
Dermatophagoides farinae

Family:	*Pyroglyphidae*
Order:	*Astigmata*
Common names:	House dust mite, Dust mite
Source material:	Whole body culture





Allergen Exposure

Geographical distribution

See common geographical background to mites in the Introduction.

The most important House dust mites are *Dermatophagoides farinae*, which is more common in drier areas, and *D. pteronyssinus*. *D. farinae* has many of the same characteristics as *D. pteronyssinus*, which co-exists with the Storage mite *Blomia tropicalis* in subtropical and tropical regions as a major source of allergens. Recent evidence shows that even these very general boundaries are blurring and that in many instances all 3 mite species may be highly relevant, causing frequent sensitisation.

The prevalence of allergic reactions to the mite species *D. farinae* is shown to be extremely high in North America and Japan. However, large numbers of this species have also been found in parts of Italy and Turkey, and in the Far East outside Japan.

The *Dermatophagoides* species are very similar but have differences in some physical characteristics: for example, in the male ventral posterior idiosoma and the aedeagus, and in the female genital opening and bursa copulatrix. The morphologically most conspicuous difference in the 3 *Dermatophagoides* species is that there are no 4 long train hairs on the abdomen end.

D. farinae is found worldwide but it is more abundant in North America than in Europe. It seems to prefer more continental and barren climates than *D. pteronyssinus* does. The duration of the life cycle from egg to adult is 35 days, and the female longevity is approx 70 days, but these periods depend on the temperature and humidity of the environment. *D. farinae* lays eggs over a 30-day period, producing about an egg a day, while *D. pteronyssinus* lays about 80 -120 eggs over a 45-day period.

Environment

See common environmental background to mites in the Introduction.

Allergens

The most important allergenic proteins in *D. farinae* are Der f 1 and Der f 2. It has been shown that approximately 80% of tested sera from mite-sensitive patients have IgE antibodies to Der p 1 and Der p 2, and the situation is very likely similar for Der f 1 and Der f 2, as the Group 1 and 2 allergens are highly homologous between *D. farinae* and *D. pteronyssinus* (1). About 20% of patients, however, do not have IgE antibodies to the Group 1 and 2 allergens, and even though this is a minority, it constitutes a large population. There are many other House dust mite allergens which have high IgE binding activity, but these are present in low and variable concentrations in mite extracts, usually at less than 1% of

the levels of the Group 1 and 2 allergens. But importantly, mite extracts are preparations that do not accurately represent the relative concentrations of allergens in inhaled air. In fact, mite extracts used for commercial testing may not mimic the native mite allergen environment in general at all accurately. All that can broadly be said about the concentrations of most allergens is that these are unknown but are probably sparse (1).

The results of studies on allergen groups other than 1 and 2 may be extrapolated to *D. pteronyssinus* and *D. farinae*. Experiments measuring the trypsin enzymatic activity of Der p 3 and demonstrating a 200-fold higher concentration in spent mite media (2) will likely hold for Der f 3. The case would be similar for studies of further relevant allergens: Der p 5, 10, 11 and 14, which appear to be present in low quantities (3-5). There is evidence that Der p 3, 7 and 14 are unstable in the extracts (1); nonetheless, allergens present in low amounts in extracts can induce high titres of IgE. Also, non-allergenic polypeptides such as the ferritin heavy chain may be highly immunogenic and induce a balanced Th1/Th2 cytokine response (6)

The following allergens have been characterised:

Group	Name	MW (kDa)	Function	Location	Sequence identity to *D. pteronyssinus*	Refs
1	Der f 1	25	Cysteine proteinase	Intestinal tract, faeces	80% (Der p 1)	7-16
2	Der f 2	14	Epididymal protein?	The gut	88% (Der p 2)	11-13,17-22
3	Der f 3	25	Serine proteinase	Faeces	81% (Der p 3)	1,11,13, 23-27
4	Der f 4	56-60	Amylase			28,11
5	Der f 5	15	Unknown			1, 11
6	Der f 6	25-27	Chymotryptic serine proteinase			23,29-31
7	Der f 7	22-25	Unkown		86% (Der p 7)	1,32-33
8	Der f 8	26	Glutathione-S-Transferase			34
9	Der f 9	30	Collagenolytic serine protease			1
10	Der f 10	33-37	Tropomyosin		98.5% (Der p 10)	1,23,3,3
11	Der f 11	98-103	Paramyosin			1,4,23,35-38
13	Der f 13	15	Fatty acid binding protein			1
14	Der f 14	177	Vitellogenin, an apolipophorin-like protein			5,23,39,40
15	Der f 15	98	Unknown			1,23,41-42
16	Der f 16	55	Gelsolin, a gelosinase			43,44
17	Der f 17	30	Calcium-binding protein			43
18	Der f 18	60	Chitinase			1,23,42,45
20	Der f 20		Arginine kinase			34
	Der f 22					46
	Der f HSP70	67	A heat shock protein			47

The following recombinant allergens have been characterised:

rDer f 1 (8-10,12,15-16).

rDer f 2 (12,19).

rDer f 3 (26).

rDer f 6 (31).

rDer f 7 (33).

rDer f 11 (35-37,48-49).

rDer f 14 (40).

rDer f 16 (44).

The major House dust mite Group 1 allergens Der p 1 and Der f 1 are the most potent of indoor allergens (15). Both allergens are major allergens and result in sensitisation in approximately 80% or greater of *D. farinae*-sensitised patients (1,30). Although Der p 1 and Der f 1 were first isolated as cysteine proteases, some studies reported that natural Der f 1, similarly to Der p 1, exhibits mixed cysteine and serine protease activity (7).

Der f 1 and Der f 2 sensitise approximately 80% to 90% of *D. farinae*-sensitised individuals. Most patients (80%) appear to have IgE antibodies to more than 1 allergen. Similarly to Der p 1 and Der p 2, Der f 1 and Der f 2 exist as a number of isoforms. rDer f 1 and rDer f 2 are highly homologous to the native forms. The Group 2 allergens induce humoral and cellular responses in 80-90% of mite-allergic individuals (13).

Although Der p 3 was reported to sensitise approximately 50% of *D. pteronyssinus*-sensitised patients (1), and although the same may hold true for Der f 3, IgE to Der f 3 was detected in only 16% of the sera tested in one study (13).

In sera from 88 mite-allergic patients, IgE antibodies to Der p 6 and/or Der f 6 were detected in only 41% of the sera (30).

The Group 7 mite allergens react with IgE antibodies in 50% of sera from allergic patients (32).

Der f 10, a tropomyosin, is a major allergen and has been shown to react with IgE antibodies in over 80% of mite-sensitised patients (3).

Der f 11, a paramyosin, has been shown to be a major allergen (37). IgE reactivity to Der f 11 was reported for more than 80% of mite-sensitive asthmatic patients (4). Skin reactivity and IgE antibodies showed that 62% (13/21) and 50% (10/20) of mite-sensitive asthmatic patients reacted positively with the recombinant Der f 11, respectively (37). This is similar to findings about rDer p 11, which detected IgE antibodies in a range of 41.7% to 66.7% in different allergic patient groups (36). In a preliminary study of 18 asthmatic children, 72.2% reacted positively to rDer f 11, and 88.9% showed positive reactivity to *D. farinae* extracts. Further evaluation of rDer f 11 in 24 asthmatic children who were skin test-positive to mite found that, whereas 70.8% had positive skin tests to rDer f 11, 75% had positive serum IgE reactivity to rDer f 11. Serum IgE reactivity to rDer f 11 was further investigated in a large panel of 49 mite skin test-positive asthmatic children, and similarly to before, 77.6% had positive serum IgE reactivity to rDer f 11 (49).

Der f 14 has also been demonstrated to be a major allergen, detecting IgE antibodies in 65.8% of 38 sera samples from patients allergic to mites. Der f 14 is a protease-sensitive allergen. The breakdown products of this allergen provoked higher allergenic activity than did the intact allergen (5).

The House dust mites *D. pteronyssinus* and *D. farinae* cause allergic disease in dogs as well as humans. In geographical regions where the 2 mite species coexist, they both elicit specific IgE responses in humans, whereas dogs preferentially react to *D. farinae* extracts. In dogs the main IgE binding is directed to the *D. farinae* chitinase allergens Der f 15 and Der f 18, and not to the groups 1 and 2 allergens, as is found for humans (42). However, one study, aimed at characterising the chitinase allergens Der p 15 and Der p 18 of *D. pteronyssinus* and discovering whether they are important allergens for humans, as they are for dogs, reported that Der p 15-specific IgE was detected in 70% and Der p 18-specific IgE in 63% of a panel of 27 human allergic sera. The *D. pteronyssinus* chitinases Der p 15 and Der p 18 show a high frequency of binding to IgE in allergic human sera. They

are therefore potentially important allergens for humans as well as dogs (42).

rDer f 16 protein was shown to bind IgE from mite-allergic patients at a 47% (8/17) frequency (44).

rDer f 18 binds IgE in 54% of the sera from patients with *D farinae* allergy (45).

Potential cross-reactivity

Allergens from mites have both common and species-specific determinants. Allergenic determinants in *D. farinae* are shared with other mites belonging to the *Pyroglyphidae* family and are highly cross-reactive with other *Dermatophagoides* species (50-51). There seems to be a limited cross-reactivity with Storage (nonpyroglyphid) mites (51). Allergen cross-reactivity has been reported between House dust mites and other invertebrates (52).

In a study that investigated the individual allergens responsible for the cross-reactivity between *D. siboney* and other mite allergens in mite-allergic patients, IgE inhibition was shown to be higher with *D. farinae* (86%), *D. pteronyssinus* (54%) and *D. microceras* (49%) extracts than with *Lepidoglyphus destructor* (20%), *Tyrophagus putrescens* (11%), *Acarus siro* (18%) and *Blomia tropicalis* (6%) extracts. A diverse pattern for the individual allergens was demonstrated. The N-terminal sequences of Der s 1, 2 and 3 allergens showed higher homology to *D. farinae* and *D. microceras* than to *D. pteronyssinus*. The homology of the Group 2 allergens was higher than that of the Group 1 allergens. The individual allergens of *D. siboney* were more similar to those of *D. farinae* and *D. microceras* than to those of *D. pteronyssinus*. There was a limited and variable cross-reactivity with nonpyroglyphid mites. No single allergen was unique to *D. siboney* (53).

Although a high prevalence of sensitisation occurs to the Group 1 mite allergen Blo t 1 from *Blomia*, there was a low correlation of IgE reactivity between this allergen and the Group 1 mite allergen Der p 1 (54), and presumably Der f 1, an allergen highly homologous to Der p 1. Pso o 1 from the Sheep scab mite (*Psoroptes ovis*) displays strong homology to the Group 1 House dust mite allergens Der p 1, Der f 1 and Eur m 1 (55).

Der f 7 has a predicted 213 residue polypeptide with 86% homology to and serological cross-reactivity with Der p 7 (33).

D f 10 is a tropomyosin. The tropomyosin of the American cockroach *Periplaneta americana* has an 80%, 81%, and 82% sequence identity to the tropomyosins from *D. pteronyssinus*, *D. farinae*, and Shrimp, respectively, which have been previously shown to be important allergens (56). The IgE recognition by Shrimp-allergic individuals of similar amino acid sequences, homologous to Pen a 1 epitopes in mite, Cockroach and Lobster tropomyosins, indicates the basis of the *in vitro* cross-reactivity among invertebrate species. On the evidence of amino acid sequence similarity and epitope reactivity, Lobster tropomyosin has been shown to have the strongest and Cockroach the weakest cross-reactivity with Shrimp (57). In sera of 30 patients tested and found to harbour *P. fuliginosa*-specific IgE, the IgE binding reactivity of the *P. fuliginosa* extract was inhibited as much as 79.4% by a *B. germanica* extract and as much as 63.3% by a *D. farinae* extract. The deduced amino acid sequence of cloned cDNA was identical to that of *Periplaneta americana* tropomyosin (58).

rDer p 11 showed positive IgE binding reactivity in 78% of 50 *D. pteronyssinus*-sensitive asthmatic children. Der p 11, a paramyosin, has an 89% sequence identity with Der f 11 and Blo t 11 (35,38). A second study reported the sequence identity of Der f 11 with other known paramyosins to be 34-60% (48).

Clinical Experience

IgE-mediated reactions

In 1964, when *D. pteronyssinus* and *D. farinae* were identified in house dust samples from all over the world, it became clear that mites of the genus *Dermatophagoides* were the main cause of asthmatic reactions (50,59-61). A large body of evidence suggests that exposure to the House dust

mite allergens *D. pteronyssinus* and *D. farinae* is an important risk factor for allergic sensitisation, asthma development, and asthma symptom exacerbation (59,62-69).

Studies of house dust-allergic individuals around the world have shown that House dust mites cause symptoms such as perennial-type asthma, rhinitis and conjunctivitis, often with nocturnal or early morning episodes (70-73). A study of *D. pteronyssinus* allergens found that House dust mite extract constituents other than Der p 1 or Der p 2, with no significant influence on the IgE-mediated early asthmatic response, contribute significantly to the allergen-induced late asthmatic response and bronchial hyper-reactivity (74).

D. pteronyssinus has also been reported to play an important role as a trigger in patients with atopic dermatitis, including adult patients (75). However, in a cross-sectional study of 1669 school beginners 6 to 7 years old in Augsburg (Bavaria, Germany), it was concluded that current eczema in these children were related to Der f 1 exposure and not to Der p 1 exposure (76). Patients in whom the House dust mite-induced reaction continues for more than 48 hours and contributes to eczematous eruptions are characterised by considerably increased levels of IgE antibodies for House dust mite antigens, high activity of atopic dermatitis, and increased exposure to House dust mite (77).

It is possible that a number of features ascribed to *D. pteronyssinus* will be applicable to *D. farinae* but have not specifically been investigated for this mite. The reader is referred to the entry on *D. pteronyssinus* d1.

Various studies have reported that the rate of sensitisation is higher among atopic children, and that high mite infestation increases the rate of sensitisation (70). The European Community Respiratory Health Survey, an international study of asthma prevalence and risk factors for asthma, collected information on IgE antibodies to common allergens in over 13,000 adults living in 37 centres in 16 countries, and found a median prevalence of 20.3% (range 6.7 - 35.1%) for sensitisation to *D. pteronyssinus* (78). In a follow-up study, home visits with 3580 participants from 22 study centres in the European Community Respiratory Health Survey II were conducted; mattress dust was sampled and analysed for Der p 1, Der f 1, and Der 2 allergens. Der 1 and Der 2 allergens were detectable (>/=0.1 mug/g) in 68% and 53% of the samples, respectively. Large differences in allergen levels among study centres were observed, and geographic patterns for Der p 1 and Der f 1 were different. Low winter temperatures reduced Der p 1 but not Der f 1 (79).

D. pteronyssinus and *D. farinae* appear to be significant allergens in most geographic regions but may vary within these regions. In a study in the homes of 111 asthmatic children in 3 climatic regions in Sweden, the major allergen Der m 1, together with Der p 1 from *D. pteronyssinus* and Der f 1 from *D. farinae*, was analysed. Der f 1 was the predominant House dust mite allergen, Der p 1 was the least often found, and Der m 1 represented 31% of the allergen load. However, in the Linkoping area Der m 1 was the major House dust mite allergen (58%). Of the children with IgE antibodies against House dust mite, 67% reacted to all 3 mites. Mite sensitisation rates were marginally increased (7%) by the addition of IgE analysis of *D. microceras* to the routine analysis of IgE antibodies against *D. pteronyssinus* and *D. farinae*. The authors concluded that Der m 1 may in this instance be an important House dust mite allergen and should be considered when House dust mite exposure data are assessed in areas with a climate like that of Sweden (80).

However, in another Scandinavian population, in Denmark, a study found that both immunochemically and microscopically, *D. farinae* was dominant, *D. pteronyssinus* less frequent but important, and *D. microceras* insignificant (81).

In a study assessing specific allergen content in dust samples from the homes of 106 allergy clinic patients in Baltimore in the USA, House dust mite allergens were detected in 99% of homes. *D. farinae* was found in 95%, *D. pteronyssinus* in 88% and

D. microceras in 31%. Although sensitisation to these allergens was not evaluated, the study indicates that *D. microceras* may be an important allergen in this geographical region (82).

In tropical Singapore, a prospective evaluation was made of 175 newly diagnosed allergic rhinitis patients, of whom 39% reported a concomitant diagnosis and/or clinical complaints of bronchial asthma, and 48% of atopic dermatitis; skin reactivity for *D. pteronyssinus* and *D. farinae* mix was detected in 85% of patients (and 62% for *B. tropicalis*) (83).

In studies of house dust in Bursa, Turkey, approximately 34% of houses were found to be infested with House dust mites. The rate of infestation was 18.75% and 50% in the houses with and without central heating systems, respectively. The prevalence of *D. pteronyssinus* was found to be 58.34%, compared with 16.67% for *Glycophagus domesticus* and 4.16% for *D. farinae* (84).

In an evaluation of house dust collected from dwellings at 7 locations in Upper Silesia, Poland, mites were found in 56.1% of the samples. *D. farinae* was predominant (75.3%), followed by *D. pteronyssinus* (18.6%) and *Euroglyphus maynei* (1.5%) (85).

A number of studies in South America have documented the significance of *D. pteronyssinus* sensitisation. In Valdivia, Chile, out of 100 consecutive paediatric asthma patients evaluated, 80 were confirmed to have skin reactivity to at least 1 mite species. All patients with skin reactivity for mites were positive to *D. pteronyssinus*, and 99% to *D. farinae*. All of the patients with severe persistent asthma had skin reactivity to mites, as did 85% in the moderate group, and 73% in the mild group. Ninety-five percent of patients with asthma and allergic rhinitis were shown to have skin reactivity to mites, as were 92% of patients with asthma and eczema and 100% of patients with asthma, allergic rhinitis and eczema (86). In a study of patients with allergic respiratory disease attending an allergy clinic in Brazil, out of 212 medical records evaluated, 61.7% showed sensitisation to Der p, 59.9% to Der f and 54.7% to *Blomia tropicalis* (87).

In a study of 579 asthmatic patients in Taiwan, it was shown through measuring allergen-specific IgE antibodies that almost 59% were sensitised to *D. microceras*, compared to 59.8% to *D. pteronyssinus* and 56.8% to *D. farinae*. Sensitisation to Cockroach was found in 38.3%, to Dog dander in 26.3%, to *Candida albicans* in 13.3%, to Cat dander in 10%, and to *Cladosporium herbarum* in 6.6%. The study indicates the importance of considering *D. microceras* when evaluating allergic individuals (88).

Among 93 Taiwanese asthmatic children aged 3 to 15 years evaluated for sensitisation to 5 species of mites, 63 were found to have IgE antibodies to at least 1 of the following mites: *D. pteronyssinus*, *D. farinae*, *D. microceras*, *Euroglyphus maynei*, and *Blomia tropicalis*. Sensitisation to *D. pteronyssinus* was found in 87%, to *D. farinae* in 85%, to *D. microceras* in 84%, to *Euroglyphus maynei* in 77%, and to *Blomia tropicalis* in 65% (89). Similarly, in a Taiwanese study of 498 atopic children aged 2 to 16 years, high prevalences of sensitisation were documented: 90.2% to *D. pteronyssinus,* 88.2% to *D. farinae*, 79.5% to *D. microceras*, and 76.7% to *Blomia tropicalis* (90).

A group of 25 atopic children under 11 years of age in Oxford in the UK was studied for skin reactivity and IgE antibodies to 4 species of House dust mites: *D. pteronyssinus*, *D. farinae*, *D. microceras* and *Euroglyphus maynei*. All of the children were sensitised to *D. pteronyssinus*, and 80% of these children were also sensitised to *D. farinae* and *D. microceras*. Importantly, dust samples from various sites in the homes of the children revealed *D. pteronyssinus* in all the homes, but no *D. farinae* or *D. microceras*. A control group of 20 atopic children of similar ages who were not sensitised to House dust mite allergens had similar exposure to the 4 mite species. These results suggest that factors in addition to mite exposure are important in the development of specific IgE responses to House dust mites (91).

Interestingly, in habitats were conditions are not favourable for mites, mites have still managed to survive and may cause sensitisation. The presence of *D. farinae* and *D. pteronyssinus* have been reported in Egypt (92).

A large body of studies from around the world has demonstrated the relevance of this allergen (93-94). The reader is referred to references listed in the first paragraph of this section for more detailed clinical information.

Other reactions

Systemic anaphylaxis can occur after the ingestion of heated or unheated mite-contaminated foods. This problem may be more prevalent in tropical and subtropical countries than previously recognised. The most common symptoms following the ingestion of mite-contaminated flour were breathlessness, angioedema, wheezing, and rhinorrhea, and these started between 10 and 240 minutes after eating (95).

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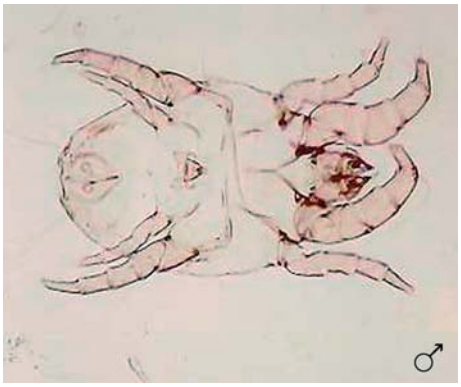
Dermatophagoides microceras

Family:	*Pyroglyphidae*
Order:	*Astigmata*
Common names:	House dust mite, Dust mite
Source material:	Whole body culture



Allergen Exposure

Geographical distribution

See common geographical background to mites in the Introduction.

The House dust mite species *Dermatophagoides microceras* was first found in 1966 and first described in 1971 (1). Its distribution in the Scandinavian countries has been studied extensively (2). The mite has been identified in house dust in Great Britain, Scandinavia, the Netherlands, Spain and the United States, but the distribution of *D. microceras* in the rest of the world has not been well explored.

The *Dermatophagoides* species are very similar but have differences in some physical characteristics: for example, in the male ventral posterior idiosoma and the aedeagus, and in the female genital opening and bursa copulatrix. The morphologically most conspicuous difference in the 3 *Dermatophagoides* species is that there are no 4 long train hairs on the abdomen end.

Environment

See common environmental background to mites in the Introduction.

Allergens

Mites are complex organisms, which produce thousands of different proteins and other macromolecules. Mite extracts are made from an aqueous extraction of a variable mixture of whole mites, nymphs, faecal pellets, eggs and spent culture media. Mite extracts contain over 30 different proteins, which can induce IgE antibody production in patients allergic to mite. Out of the 19 denominated allergens, major IgE binding has been reported for the Group 1, 2, 3, 9, 11, 14 and 15 allergens. The high-molecular-weight Group 11, 14 and 15 allergens have recently been described. The Group 1 and 2 allergens represent dominant specificities, which can account for much of the allergenicity of extracts (3). Data on storage mites could be extrapolated from House dust mites.

In a study using body and faecal extracts of *D. pteronyssinus*, *D. farinae*, *D. microceras*, *Euroglyphus maynei* and *Gymnoglyphus longior*, 21 of 29 protein bands, bound by sera from a mite-sensitive population and from the international reference pool of sera, were common to all 5 species of mite. All sera were unique with respect to proteins bound and species recognised. Mite proteins bound by more than 40% of sera included the Group 2 and 3 main allergens and 40.4 kDa and 27.8 kDa protein bands, all of which were found in every mite species studied. Similar response profiles among mite species suggest that human-specific IgE may bind predominantly to cross-reactive determinants on mite allergens (4).

Although approximately 20 allergens have been identified in the close family member *D. pteronyssinus*, to date only 1 allergen has been identified in *D. microceras*:

Der m 1, a Group 1 mite allergen, a major allergen (5-7).

Potential cross-reactivity

Allergens from mites have both common and species-specific determinants. In this case, allergenic determinants are shared with other mites belonging to the *Pyroglyphidae* family and are highly cross-reactive with other *Dermatophagoides spp*. (4,8). Some mite allergenic proteins such as tropomyosin are widely cross-reactive among invertebrates such as Shrimp, Snails, Cockroaches and chironomids (9-10).

In a study investigating the individual allergens responsible for the cross-reactivity between *D. siboney* and other mite allergens in mite-allergic patients, inhibition studies had more positive results with *D. farinae* (86%), *D. pteronyssinus* (54%) and *D. microceras* (49%) extracts than with *Lepidoglyphus destructor* (20%), *Tyrophagus putrescentiae* (11%), *Acarus siro* (18%) and *Blomia tropicalis* (6%). A diverse pattern for the individual allergens was demonstrated. The N-terminal sequences of Der s 1, 2 and 3 allergens showed higher homology to *D. farinae, D. pteronyssinus* and *D. microceras* allergens. The homology of the Group 2 allergens was higher than that of the Group 1 allergens. The individual allergens of *D. siboney* were more similar to *D. farinae* and *D. microceras* than to *D. pteronyssinus* (6).

Clinical Experience

IgE-mediated reactions

Unlike *D. pteronyssinus* and *D. farinae*, which appear in studies to be significant allergens in most geographic regions, the prevalence of *D. microceras* may vary widely. On one end of the spectrum, in a study of the homes of 111 asthmatic children in 3 climatic regions in Sweden, the major allergen Der m 1, together with Der p 1 from *D. pteronyssinus* and Der f 1 from *D. farinae*, was analysed. Der f 1 was the predominant House dust mite allergen, Der p 1 was the least often found, and Der m 1 represented 31% of the allergen load. However, in the Linkoping area, Der m 1 was the major House dust mite allergen (58%). Of the children with IgE antibodies against House dust mite, 67% reacted to all 3 mites. Mite sensitisation rates were marginally increased (7%) by the addition of IgE analysis of *D. microceras* to the routine analysis of IgE antibodies against *D. pteronyssinus* and *D. farinae*. The authors concluded that Der m 1 may be an important House dust mite allergen and should be considered when House dust mite exposure data are assessed in areas with a climate like that of Sweden (11).

However, in another Scandinavian population, in Denmark, a study found that both immunochemically and microscopically, *D. farinae* was dominant, *D. pteronyssinus* less frequent but important, and *D. microceras* insignificant (12).

In a study examining the specific allergen content of dust samples from the homes of 106 allergy clinic patients in Baltimore in the US, Dust mite allergen was detected in 99% of homes. *D. farinae* was found in 95%, *D. pteronyssinus* in 88% and *D. microceras* in 31%. Although sensitisation to these allergens was not evaluated, the study indicates that *D. microceras* may be an important allergen in this geographical region (13).

In a study of 579 asthmatic patients in Taiwan, it was shown through measuring IgE antibodies that almost 59% were sensitised to *D. microceras*, compared to 59.8% to *D. pteronyssinus* and 56.8% to *D. farinae*. Sensitisation to Cockroach was found in 38.3%, to Dog dander in 26.3%, to *Candida albicans* in 13.3%, to Cat dander in 10%, and to *Cladosporium herbarum* in 6.6%. The study indicates the importance of considering *D. microceras* when evaluating allergic individuals (14).

Among 93 Taiwanese asthmatic children aged from 3 to 15 years evaluated for sensitisation to 5 different species of mites, 63 were found to have IgE antibodies to at least 1 of the following mites: *D. pteronyssinus*, *D. farinae*, *D. microceras*, *Euroglyphus maynei*, and *Blomia tropicalis*. Sensitisation to *D. pteronyssinus* was found in 87%, to *D. farinae* in 85%, to *D. microceras* in 84%, to *Euroglyphus maynei* in 77%, and to *Blomia tropicalis* in 65% (15).

Similarly, in a Taiwanese study of 498 atopic children aged 2 to16 years, high prevalences of sensitisation were documented: 90.2%, to *D. pteronyssinus*, 88.2% to *D. farinae*, 79.5% to *D. microceras*, and 76.7% to *Blomia tropicalis* (16).

A group of 25 atopic children under 11 years of age in Oxford in the UK was studied for skin reactivity and IgE antibodies to 4 species of House dust mites: *D. pteronyssinus*, *D. farinae*, *D. microceras* and *Euroglyphus maynei*. All of the children were sensitised to *D. pteronyssinus*, and 80% of these children were also sensitised to *D. farinae* and *D. microceras*. Importantly, dust samples from various sites in the homes of the children revealed *D. pteronyssinus* in all the homes, but no *D. farinae* or *D. microceras*. A control group of 20 atopic children of similar ages who were not sensitised to House dust mite allergens had similar exposure to the 4 mite species. These results suggest that factors in addition to mite exposure are important in the development of allergen-specific IgE responses to House dust mites (17).

Other reactions

Systemic anaphylaxis can occur after the ingestion of heated or unheated mite-contaminated foods. This problem may be more prevalent in tropical and subtropical countries than previously recognised. The most common symptoms following the ingestion of mite-contaminated flour were breathlessness, angioedema, wheezing, and rhinorrhea, and these started between 10 and 240 minutes after eating (18).

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d1 *Dermatophagoides pteronyssinus*

Dermatophagoides pteronyssinus	
Family:	*Pyroglyphidae*
Order:	*Astigmata*
Common names:	House dust mite, Dust mite
Source material:	Whole body culture

Allergen Exposure

Geographical distribution

See common geographical background to mites in the Introduction.

The most important House dust mites are *Dermatophagoides pteronyssinus* and (in drier areas) *D. farinae*. In subtropical and tropical regions the Storage mite *Blomia tropicalis* is also a major source of allergens, co-existing with *D. pteronyssinus*. Recent evidence shows that even these very general boundaries are blurring, and in many instances all 3 mite species may be highly relevant, causing widespread sensitisation. But *D. pteronyssinus* is especially important because its distribution is for all practical purposes worldwide.

The *Dermatophagoides* species are very similar but have differences in some physical characteristics: for example, in the male ventral posterior idiosoma and the aedeagus, and in the female genital opening and bursa copulatrix. The morphologically most conspicuous difference in the 3 *Dermatophagoides* species is that there are no 4 long train hairs on the abdomen end.

D. pteronyssinus, though it has a worldwide distribution, seems to be more abundant in Europe than in America. It prefers more humid climates than *D. farinae* does. The duration of the life cycle from egg to adult is 31 days and the female longevity is approximately 70 days, but these periods depend on the temperature and humidity of the environment. *D. farinae* lays eggs over a 30-day period, producing about an egg a day, while *D. pteronyssinus* lays about 80 - 120 eggs over a 45-day period.

Environment

See common environmental background to mites in the Introduction.

Allergens

The most important allergenic proteins in *D. pteronyssinus* are Der p 1 and Der p 2. Extracts of *D. pteronyssinus* contain high concentrations of the Group 1 and 2 allergens, usually between 20 and 100 µg/ml (1). It has been shown that approximately 80% of tested sera from mite-sensitive patients have IgE antibodies to Der p 1 and Der p 2. About 20% of patients, however, do not have IgE antibody to the Group 1 and 2 allergens, and even though this is a minority, it constitutes a large population. In further allergen groups, there are many other House dust mite allergens which have high IgE binding activity, but these are present in low and variable concentrations in mite extracts, usually at less than 1% of the level the Group 1 and 2 allergens (2).

But importantly, mite extracts are preparations that do not accurately represent the relative concentrations of allergens in

d1 *Dermatophagoides pteronyssinus*

inhaled air. In fact, mite extracts used for commercial testing may not mimic the native mite allergen environment in general at all accurately. All that can broadly be said about the concentrations of most allergens is that these are unknown but are probably sparse. Der p 7 is present at under 1 µg/ml. Der p 3 is present at less than 1 µg/ml (3). Experiments measuring the trypsin enzymatic activity of Der p 3 demonstrated a 200-fold higher concentration in spent mite media (1). Der p 5, 10, 11 and 14 appear to be present in low quantities (2-6). There is evidence that Der p 3, 7 and 14 are unstable in the extracts (2). Nonetheless, allergens present in low amount in extracts can induce high titres of IgE antibodies. Also, non-allergenic polypeptides, such as the ferritin heavy chain, may be highly immunogenic, and can induce a balanced Th1/Th2 cytokine response (7).

A study concludes that Der p 1 levels in German mattress dust samples have been reduced by a factor of approximately 3 to 4 by the consecutive cold winters of 1995/1996 and 1996/1997 (8).

The following allergens have been characterised:

Group	Name	MW (kDa)	Function	Location	Sequence identity to *D. farinae*	Refs
1	Der p 1	25	Cysteine proteinase	Intestinal tract, faeces	80% (Der f 1)	2,9-16
2	Der p 2	14	Epididymal protein?	The gut	88% (Der f 2)	2,9,11,17-18
3	Der p 3	25	Serine proteinase	Faeces	81% (Der f 3)	2,9,17, 19-24
4	Der p 4	56-63	Amylase			17,19,20, 47,25-28
5	Der p 5	14	Unknown			2,3,10,11 17,19-21, 27,29
6	Der p 6	25	Chymotryptic serine proteinase			9,17,19-21,23,27, 30
7	Der p 7	22-31	Unkown		86% (Der f 7)	2,17,12, 19-21,27, 31-32
8	Der p 8	26	Glutathione-S-transferase			17,19-21, 27, 33-35
9	Der p 9	24-28	Collagenolytic serine proteinase			2,9,17, 19-21,27
10	Der p 10	33-37	Tropomyosin		98.5% (Der f 10)	2,17,19-21,27,36
11	Der p 11	103	Paramyosin			2,19,21, 37,38
14	Der p 14	177	Vitellogenin, an Apolipophorin			2,19,39,40
15	Der p 15	98	Chitinase	The gut		41-43
18	Der p 18	60	Chitinase			43-44
20	Der p 20		Arginine kinase			45

The following recombinant allergens have been characterised:

rDer p 1 (13,46).

rDer p 2 (47-48).

rDer p 4 (25).

rDer p 5 (29,47-50).

rDer p 7 (32,47-48,51-52).

rDer p 8 (47).

rDer p 10 (47,53).

rDer p 11 (37).

Der p 1 and Der p 2 are both products of single genes but are highly polymorphic and exist as a number of isoforms (2). Thirteen of the 20 sequences reported for Der p 1 have been unique (54). Although the major Group 1 mite allergens Der p 1 and Der f 1 were first isolated as cysteine proteases, some studies reported that natural Der p 1 exhibits mixed cysteine and serine protease activity (46). Der p 1 and Der p 2 have been shown to be potent inducers of nitric oxide release from alveolar macrophages (55). Both allergens are major allergens and result in sensitisation in approximately 80% or more of *D. pteronyssinus*-sensitised patients (2, 6,30). Some studies have, however, reported lower levels of sensitisation. In a Thai study, skin reactivity to Der p 1, Der p 2 and Der p 5 was positive in 35% and 30% of 40 atopic children, respectively, and in 26.7% and 28.9% of 45 atopic adults, respectively (11).

Through the use of the recombinant allergens rDer p 2, rDer p 5 and rDer p 7 in skin tests, immediate hypersensitivity was demonstrated in 70, 60 and 52% respectively of a group of mite-sensitive allergic patients who were strongly positive to whole mite extract. Comparable results were obtained for allergen-specific IgE tests (48).

Der p 3 is a major allergen, sensitising approximately 50% of *D. pteronyssinus*-sensitised patients, but usually at low titres (2,19).

IgE sensitisation to Der p 4 has been reported to occur frequently, but usually at low titres (28). Children may be less sensitised to this allergen: in a study, 25% of mite-allergic children and 46% of mite-allergic adults harboured serum-specific IgE to the mite amylase Der p 4 (26). Recombinant Der p 4 appears to have comparable activity to that of the native form, binding specific IgE in 3 of 10 House dust mite-allergic patients tested (25).

Der p 5 induces IgE antibodies in about 50% of subjects, but usually at low titres (19). Other studies have reported variability of sensitisation depending on the study group. Skin tests with rDer p 5 indicated sensitisation in about 60% of patients with asthma and 29% of those with allergic rhinitis alone (29). In a Thai study, sensitisation to Der p 5 was reported to range from 2.5% of atopic children to 11.1% of atopic adults (11). With recombinant rDer p5, sera of 21 of 38 mite-allergic subjects were shown to be sensitised to this allergen; these results strongly correlated with observed IgE-binding to the native allergen (50).

Der p 6 has been reported to be 37% identical to the trypsin allergen Der p 3 (23). Der p 6 induces IgE antibodies in 40-50% of subjects but usually at low titres (19,30).

Der p 9 manifested homology with the mite tryptic allergen Der p 3 and the chymotryptic allergen Der p 6. Allergen-specific IgE analyses showed that the frequencies of reactivity to Der p 9, Der p 1, Der p 2, Der p 3, and Der p 6 were 92%, 97%, 100%, 97%, and 65%, respectively (n = 35) (9).

The Group 7 mite allergen Der p 7 results in IgE sensitisation in 50% of allergic patients but usually at low titres (19,31). Sensitisation may occur at a lower prevalence in children (52). rDer p 7 reacted with about 50% of sera from mite-allergic patients (51). Although Der p 7 reacts with only 50% of allergic sera, it has been reported to often have a high level of IgE binding activity and may be more important than the major Der p 2 allergen in a high percentage of subjects. A competitive binding assay showed that rDer p 7 inhibited 91% of IgE binding to natural Der p 7 in sera from 2 patients and 73% in a further 2. The IgE binding of rDer p 2 and Der p 7

from 41 sera was then compared. Of the sera, 88% and 46% respectively showed positive binding. All of the 19 sera which bound Der p 7 also bound Der p 2, but 11 (58%) had bound IgE to Der p 7 at a high level or at least a higher one than that of the binding to Der p 2 (32). Further, the proliferative and cytokine response to the Group 1 and Group 7 allergens for *D. pteronyssinus* and *D. farinae* indicates that there is a high degree of T-cell cross-reactivity between the whole purified allergens from each species (12).

The allergen Der p 8 is reported to induce IgE in about 40 to 50% of subjects, usually at low titres (19). Recent work has found less IgE binding to Der p 8 than the original estimate (47,34). However, in a study of sera from Taiwanese asthmatics, IgE reactivity of 96% and 84% was demonstrated to native Der p 8 and recombinant Der p 8, respectively. Native Der p 8 showed 75% and 65% IgE reactivity with sera from similar subjects from Malaysia and Singapore, respectively. Although a high frequency of sensitisation to mite GST among allergic subjects was observed, the titres of IgE reactivity were low (35).

Der p 9 manifested homology with the mite tryptic allergen Der p 3, and with the chymotryptic allergen Der p 6. IgE antibody analyses showed that the frequencies of reactivity to Der p 9, Der p 1, Der p 2, Der p 3, and Der p 6 were 92%, 97%, 100%, 97%, and 65%, respectively (n = 35). A study reported that Der p 9 is a serine protease different to the trypsin and chymotrypsin Group 3 and 6 allergens. It was shown to have very high IgE binding activity, but the same study also showed unusually high titres against the Group 3 allergens (9).

The Group 10 tropomyosin allergens are conserved by evolution and cross-react among organisms such as shellfish and parasites (56). The frequency of sensitisation to the tropomyosin allergen Der p 10 has varied from extremely high, in Japan (80%) and Zimbabwe (55%) (4), to low, in Europe (57).

Paramyosin is a structural muscle protein of invertebrates (19). The Group 11 allergen Der p 11, a paramyosin allergen, binds IgE in 80% of allergic subjects (5), and the 98 and 60 kDa chitinase enzymes Der f 15 and 18 bind IgE from about 70% and 54% of allergic subjects (58-59). The recombinant allergen rDer p 11 showed positive IgE binding in 78% of mite-sensitised patients (37). A study reported that the prevalence of serum IgE reactivity to rDer p 11 on immunodot assays ranged from 41.7% to 66.7% in different allergic patient groups, whereas it was rare in non-atopic patients with urticaria (18.8%) and in normal individuals (8%) (38).

Group 14 mite allergens have sequence homology to a vitellogenin- or apo-lipophorin-like protein. These molecules are for lipid transport or lipid storage, which may explain their instability in aqueous extracts (19). Der p 14 binds IgE in 80% of subjects allergic to *D. farinae* (6,60) and *D. pteronyssinus* (2). The allergen degrades in extracts or is processed into smaller peptides (6).

The House dust mites *D. pteronyssinus* and *D. farinae* cause allergic disease in dogs as well as in humans. In geographical regions where the 2 mite species coexist, they both elicit IgE antibody responses in humans, whereas dogs preferentially react to *D. farinae* extracts. In dogs, the main IgE binding is directed to the *D. farinae* chitinase allergens Der f 15 and Der f 18 and not to the Group 1 and 2 allergens, as found for humans. One study, aimed at characterising the chitinase allergens Der p 15 and Der p 18 of *D. pteronyssinus* and discovering whether they are important allergens for humans, as they are for dogs, reported that Der p 15-specific IgE was detected in 70% and Der p 18-specific IgE in 63% of a panel of 27 human allergic sera. The *D. pteronyssinus* chitinases Der p 15 and Der p 18 show a high frequency of binding to IgE in allergic human sera. They are therefore potentially important allergens for humans as well as dogs (43).

Group 15 mite allergens are homologous to insect chitinases. In *D. farinae*, they have been shown to be located in the gut, suggesting they have a function in digestion rather than in moulting. The Group 15 allergens are therefore very significant because they are the major allergens recognised by dogs and cats, and because they are highly glycosylated, consisting of almost 50% carbohydrate (19).

Potential cross-reactivity

Allergens from mites have both common and species-specific determinants. In this case, allergenic determinants are shared with other mites belonging to the *Pyroglyphidae* family and are highly cross-reactive with other *Dermatophagoides* species (61-62). There seems to be a limited cross-reactivity with Storage (nonpyroglyphid) mites (62). Allergen cross-reactivity has been reported between House dust mites and other invertebrates (20).

In a study that investigated the individual allergens responsible for the cross-reactivity between *D. siboney* and other mite allergens, IgE inhibition was shown to be higher with *D. farinae* (86%), *D. pteronyssinus* (54%) and *D. microceras* (49%) extracts than with *Lepidoglyphus destructor* (20%), *Tyrophagus putrescens* (11%), *Acarus siro* (18%) and *Blomia tropicalis* (6%). A diverse pattern for the individual allergens was demonstrated. The N-terminal sequences of Der s 1, 2 and 3 allergens showed higher homology to *D. farinae* and *D. microceras* than to *D. pteronyssinus*. The homology of the Group 2 allergens was higher than that of the Group 1 allergens. The individual allergens of *D. siboney* were more similar to *D. farinae* and *D. microceras* than to those of *D. pteronyssinus*. There was a limited and variable cross-reactivity with nonpyroglyphid mites. No single allergen was unique for *D. siboney* (63).

Although a high prevalence of sensitisation occurs to the Group 1 mite allergen Blo t 1 from *Blomia*, there was a low correlation of IgE reactivity between this allergen and the Group 1 mite allergen Der p 1 (64). Pso o 1 from the Sheep scab mite (*Psoroptes ovis*) displays strong homology to the Group 1 House dust mite allergens Der p 1, Der f 1 and Eur m 1 (65-66). Recently, the Shrimp allergen rPen a 1 was shown to extensively and specifically compete for IgE binding to extracts of other crustacean species, House dust mite and German cockroach (67).

In general, as a number of specific allergens in *D. pteronyssinus* are homologous with other allergens, varying degrees of cross-reactivity can be expected.

For example, a high homology of between 48 and 54% occurs between Blo t 3 and the Group 3 allergens from House dust mites, and this results in cross-reactivity between *Blomia tropicalis* and *D. pteronyssinus* (68).

Der p 4 and Eur m 4 were calculated to be 90% identical, and were also calculated to be approximately 50% identical to insect and mammalian alpha-amylases (25).

A degree of cross-reactivity has been demonstrated between rBlo t 5 and rDer p 5 (49). Nonetheless, Group 5 allergens of *D. pteronyssinus* and *B. tropicalis* are species-specific (69). Through the use of a large panel of asthmatic sera and a combination of *in vitro* and *in vivo* assays, Blo t 5, the major allergen of *B tropicalis*, was shown to exhibit low levels of cross-reactivity with homologous Der p 5. These findings suggested that highly specific clinical reagents are necessary for precise diagnosis and immunotherapeutic treatment of sensitisation to Group 5 mite allergens (70).

D. pteronyssinus glutathione S-transferase (Der p 8) has been shown to be cross-reactive with the homologous GST allergen from *Sarcoptes scabiei* (Scabies), an allergen which may play a role in the pathophysiology associated with crusted scabies (71). Cross-reactivity has also been demonstrated between mite GST and Cockroach GST, suggesting that GST is a panallergen (35).

Der p 9 has a degree of homology with Der p 3 (trypsin) and Der p 6 (chymotrypsin). IgE antibody inhibition studies demonstrated some cross-reactivity between this allergen and Der p 3 but not Der p 6 (9).

Some mite allergenic proteins such as tropomyosin (Der p 10) are widely cross-reactive among invertebrates such as Shrimp, Snails, Cockroaches and chironomids (62,72-73). Mite tropomyosin has a high homology with tropomyosin from these other sources. *P. americana* (American cockroach) tropomyosin showed 80%, 81%, and 82% sequence identity to tropomyosins from *D. pteronyssinus*, *D. farinae*, and Shrimp, respectively, which are important allergens in their own right (74). rBlo t 10 has been reported to have a 96% amino acid identity to tropomyosin of other mites. Although Blo t 10 and Der p 10 are highly conserved and significantly cross-reactive, unique IgE epitopes do exist (75).

Tropomyosin from *Dermanyssus gallinae*, a protein with 89% and 88% identity to tropomyosins from the ticks *Boophilus microplus* and *Haemaphysalis longicornis*, respectively, has been shown to have an 85% identity to the House dust mite tropomyosin Der p 10 (76).

Recombinant tropomyosin from the Sheep scab mite *Psoroptes ovis* appears to have a 98% and 97% identity to the House dust mite allergens Der f 10 and Der p 10 respectively. Similarly, the recombinant paramyosin had a predicted 97%, 95% and 89% identity to the paramyosins of *D. pteronyssinus* (Der p 11), *Sarcoptes scabiei* and *Blomia tropicalis* (Blo t 11) respectively (77).

One third of the children allergic to House dust mite were sensitised to Snails without any previous ingestion of Snails: this observation suggests that House dust mite was the sensitising agent and that the cross-reaction could be clinically relevant in countries where eating Snails is common (78). Cross-reactivity has also been reported between IgE-binding proteins from Anisakis simplex and *D. pteronyssinus* (79). In 5 patients with asthma and allergic rhinoconjunctivitis to mites, and with IgE-mediated allergy to barnacle, the allergens isolated from this crustacean were shown to be cross-reactive with *D. pteronyssinus* in 2 patients(80).

There is a high prevalence of sensitisation to *C. arcuatus* in northern Spain. Minimal cross-reactivity between *C. arcuatus* and *D. pteronyssinus* was reported (81).

Clinical Experience

IgE-mediated reactions

In 1964, when *D. pteronyssinus* and *D. farinae* were identified in house dust samples from all over the world, it became clear that mites of the genus *Dermatophagoides* were the main cause of asthmatic reactions (61,82-84). A large body of evidence suggests that exposure to the House dust mite allergens *D. pteronyssinus* and *D. farinae* is an important risk factor for allergic sensitisation, asthma development, and asthma symptom exacerbation (82,85-94)-

Studies of House dust-allergic individuals around the world have shown that House dust mites cause symptoms such as perennial-type asthma, rhinitis and conjunctivitis, often with nocturnal or early morning episodes (95-98). House dust mite extract constituents other than Der p 1 or Der p 2, with no significant influence on the IgE-mediated early asthmatic response, contribute significantly to the allergen-induced late asthmatic response and bronchial hyper-reactivity (99). In a Croatian study, asthmatic children with greater asthma severity were reported to have a higher serum concentration of both total IgE (>288.0 kU/L) and allergen-specific IgE to *D. pteronyssinus* (>44.1 kU_A/L), respectively (100).

D. pteronyssinus has also been reported to play an important role as a trigger factor in patients with atopic dermatitis, including adult patients (101). Patients in whom the House dust mite-induced reaction continues for more than 48 hours and contributes to eczematous eruptions are characterised by considerably increased levels of IgE antibodies for House dust mite antigens, high activity of atopic dermatitis, and increased exposure to domestic House dust mite (102). *D. pteronyssinus* may also result in allergic conjunctivitis but appear to have seasonal expression: in a Japanese study evaluating the relationship between IgE

antibodies in the serum and allergic conjunctivitis in autumn, found that IgE antibody levels caused by house dust, *D. pteronyssinus*, and Orchard grass were higher in the autumn group than in the spring group (103).

House dust mite is also reported to have a prenatal influence on atopic expression. In a Korean study, House dust mite-positive asthmatics were more likely to have been born in August and September, times of high House dust mite exposure. This birth month pattern was evident in asthmatics who were sensitive only to House dust mites, but was not observed in those sensitive to House dust mites and other allergen(s) (104). The level of prenatal exposure to Der p 1 was also reported to influence the immune profile of cord blood T lymphocytes and the clinical outcome in early life, with the result that exposure to House dust mites during pregnancy tended to be higher in mothers of children with atopic dermatitis during the first year of life, when compared with those without atopic dermatitis ($p = 0.08$) (105).

Various studies have reported that the rate of sensitisation is higher among atopic children, and that high mite infestation increases the rate of sensitisation (95). The European Community Respiratory Health Survey, an international study of asthma prevalence and risk factors for asthma, collected information on IgE antibodies to common allergens in over 13,000 adults living in 37 centres in 16 countries, and found a median prevalence of 20.3% (range 6.7 - 35.1%) for sensitisation to *D. pteronyssinus* (106). In a follow-up study, home visits with 3580 participants in the European Community Respiratory Health Survey II, involving 22 study centres, were conducted; mattress dust was sampled and analysed for Der p 1, Der f 1, and Der 2 allergen. Der 1 and Der 2 allergens were detectable (≥ 0.1 µg/g) in 68% and 53% of the samples, respectively. Large differences in allergen levels among study centres were observed, and geographic patterns for Der p 1 and Der f 1 were different. Low winter temperatures reduced Der p 1 but not Der f 1 (107).

D. pteronyssinus and *D. farinae* appear in studies to be significant allergens in most geographic regions but may vary within these regions. In a study in the homes of 111 asthmatic children in 3 climatic regions in Sweden, the major allergen Der m 1, together with Der p 1 from *D. pteronyssinus* and Der f 1 from *D. farinae*, was analysed. Der f 1 was the predominant House dust mite allergen, Der p 1 was the least often found, and Der m 1 represented 31% of the allergen load. However, in the Linkoping area, Der m 1 was the major House dust mite allergen (58%). Of the children with IgE antibodies against House dust mite, 67% reacted to all 3 mites. Mite sensitisation rates were marginally increased (7%) by the addition of IgE analysis of *D. microceras* to the routine analysis of IgE antibodies against *D. pteronyssinus* and *D. farinae*. The authors concluded that Der m 1 may in this instance also be an important House dust mite allergen and should be considered when House dust mite exposure data are assessed in areas with a climate like that of Sweden (108).

However, in another Scandinavian population, in Denmark, a study found that both immunochemically and microscopically, *D. farinae* was dominant, *D. pteronyssinus* less frequent but important, and *D. microceras* insignificant (109).

In a study assessing the specific allergen content in dust samples from the homes of 106 allergy clinic patients in Baltimore in the USA, Dust mite allergen was detected in 99% of homes. *D. farinae* was found in 95%, *D. pteronyssinus* in 88% and *D. microceras* in 31%. Although sensitisation to these allergens was not evaluated, the study indicates that *D. microceras* may be an important allergen in this geographical region (110).

In tropical Singapore, a prospective evaluation of 175 newly diagnosed allergic rhinitis patients, of whom 39% reported a concomitant diagnosis and/or clinical complaints of bronchial asthma and 48% of atopic dermatitis, skin-specific IgE for *D. pteronyssinus* and *D. farinae* mix was detected in 85% (and 62% for *B. tropicalis*) (111). In Huelva, Spain, in the 136 dust samples studied, *D. pteronyssinus* was the

most frequently identified mite species (94.8%). *Tyrophagus putrescentiae* was found in third position (41.1%), after Glycyphagus domesticus (54.4%) (112-113). In studies of house dust in Bursa, Turkey, approximately 34% of houses were found to be infested with House dust mites. The rate of infestation was 18.75% and 50% in the houses with and without central heating systems, respectively. The prevalence of *D. pteronyssinus* was found to be 58.34%, compared with 16.67% for *Glycophagus domesticus* and 4.16% for *D. farinae* (114). Similar results emanated from another study in the same area, which reported a very high rate of *D. pteronyssinus* being found in August (115).

In an evaluation of house dust collected from dwellings at 7 locations in Upper Silesia, Poland, mites were found in 56.1% of the samples. *D. farinae* was predominant (75.3%), followed by *D. pteronyssinus* (18.6%) and *Euroglyphus maynei* (1.5%) (116).

A number of studies in South America have documented the significance of *D. pteronyssinus* sensitisation. In Valdivia, Chile, of 100 consecutive paediatric asthma patients evaluated, 80 were confirmed to have skin reactivity to at least 1 mite species. All patients with skin reactivity IgE for mites were positive to *D. pteronyssinus* and 99% to *D. farinae*. All of the patients with severe persistent asthma had skin reactivity to mites, as did 85% in the moderate group, and 73% in the mild group. Ninety-five percent of patients with asthma and allergic rhinitis were shown to have skin reactivity to mites, as were 92% of patients with asthma and eczema and 100% of patients with asthma, allergic rhinitis and eczema (117). In a study of patients with allergic respiratory disease who attended an allergy clinic in Brazil, out of 212 medical records evaluated, 61.7% showed sensitisation to Der p, 59.9% to Der f and 54.7% to *Blomia tropicalis* (118).

D. pteronyssinus, *D. siboney* and *Blomia tropicalis* are the most important allergenic mites in Cuba. A total of 88.4% of patients were found to be positive to *D. siboney*, 87.1% *to D. pteronyssinus*, and 68.1% to *B. tropicalis*. Sensitisation to *Dermatophagoides* species was pre-dominant, demonstrated by the fact that 31.9% of patients had skin reactivity to either *D. siboney* or *D. pteronyssinus* only, whereas only 5.6% were sensitised solely to *B. tropicalis*. Most patients (58.6%) were polysensitised to the 3 species (119).

In a study of 579 asthmatic patients in Taiwan, it was shown through measuring IgE antibodies that almost 59% were sensitised to *D. microceras*, compared to 59.8% to *D. pteronyssinus* and 56.8% to *D. farinae*. Sensitisation to Cockroach was found in 38.3%, to Dog dander in 26.3%, to *Candida albicans* in 13.3%, to Cat dander in 10%, and to *Cladosporium herbarum* in 6.6%. The study indicates the importance of considering *D. microceras* when evaluating allergic individuals (120).

In 93 Taiwanese asthmatic children aged from 3 to 15 years who were evaluated for sensitisation to 5 different species of mites, 63 were found to have IgE antibodies to at least 1 of the following mites: *D. pteronyssinus*, *D. farinae*, *D. microceras*, *Euroglyphus maynei*, and *Blomia tropicalis*. Sensitisation to *D. pteronyssinus* was found in 87%, to *D. farinae* in 85%, to *D. microceras* in 84%, to *Euroglyphus maynei* in 77%, and to *Blomia tropicalis* in 65% (121). Similarly, in a Taiwanese study of 498 atopic children aged 2 to 16 years, high prevalences of sensitisation were documented: 90.2% to *D. pteronyssinus,* 88.2% to *D. farinae*, 79.5% to *D. microceras*, and 76.7% to *Blomia tropicalis* (122).

In Xuzhou, China, 15.3% of a population of 222 students were shown to be sensitised to mites; and of 515 young patients with allergic symptoms, 82.3% were shown to be sensitised to mites. The prevalence of sensitisation declined with the age group evaluated (123).

A group of 25 atopic children under 11 years of age in Oxford in the UK was studied for skin reactivity and IgE antibodies to 4 species of House dust mites: *D. pteronyssinus*, *D. farinae*, *D. microceras* and *Euroglyphus maynei*. All of the children were sensitised to *D. pteronyssinus*, and 80% of these children were also sensitised

to *D. farinae* and *D. microceras*. Importantly, dust samples from various sites in the homes of the children revealed *D. pteronyssinus* in all the homes, but no *D. farinae* or *D. microceras*. A control group of 20 atopic children of similar ages who were not sensitised to House dust mite allergens had similar exposure to the 4 mite species. These results suggest that factors in addition to mite exposure are important in the development of allergen-specific IgE responses to House dust mites (124).

Interestingly, in habitats where conditions are not favourable for mites, mites have still managed to survive and may cause sensitisation. The presence of *D. farinae* and *D. pteronyssinus* have been reported in Egypt (125). In Reykjavik, Iceland, studies have reported that 6 to 9% of young adults are sensitised to *D. pteronyssinus*; however, only negligible amounts of House dust mite and House dust mite allergens were detected in their homes. These patients are often men who spent time on farms in childhood and now have a high prevalence of IgE antibodies cross-reactive to *D. pteronyssinus* (126).

Although most studies have focussed on immediate-type hypersensitivity, House dust mite may play a role in delayed reactions. Patch testing (APT) may help in evaluating these patients. It has been reported that APT with House dust mite assists in identifying mite-sensitive children with respiratory allergy. Positive APT results may imply that delayed hypersensitivity reactions affect children with asthma and rhinitis who are allergic to House dust mite (127).

A large body of studies from around the world has demonstrated the relevance of this allergen (128-129). The reader is referred to references listed in the first paragraph of this section for more-detailed clinical information.

Other reactions

Systemic anaphylaxis can occur after the ingestion of heated or unheated mite-contaminated foods. This problem may be more prevalent in tropical and subtropical countries than previously recognised. The most common symptoms following the ingestion of mite-contaminated flour were breathlessness, angioedema, wheezing, and rhinorrhoea, and these started between 10 and 240 minutes after eating (130).

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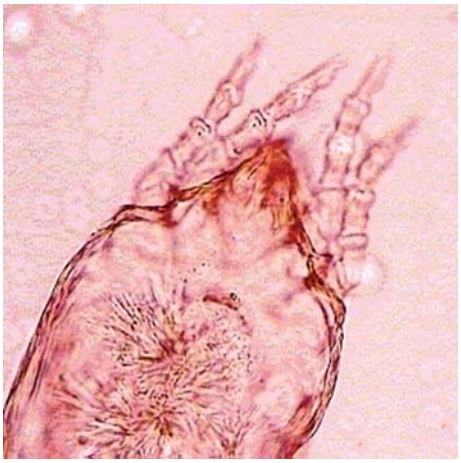
d74 *Euroglyphus maynei*

Euroglyphus maynei	
Family:	*Pyroglyphidae*
Common names:	House dust mite, Dust mite
Source material:	Whole body culture



Allergen Exposure

Geographical distribution

See common geographical background to mites in the Introduction.

Euroglyphus maynei is prevalent in humid geographical areas throughout the world (1). These mites thrive in humid human dwellings where there is no liquid water to drink. Their bodies contain 70 to 75% water by weight, which must be maintained in order for the mites to reproduce. Their primary source of water is water vapour, which is extracted from the air. At relative humidities above 65 to 70%, adequate amounts of water can be extracted from unsaturated air to compensate for that lost by all avenues (2). Study of the biology of *E. maynei* has been relatively uncommon because the mite is difficult to culture. *E. maynei* has been increasingly recognised as an important source of allergen exposure for patients with House dust mite allergy (3).

Environment

See common environmental background to mites in the Introduction.

Allergens

E. maynei is the source of at least 47 individual allergens. Twenty-two of the allergens were recognised by more than 50% of sera from 16 *E. maynei*-allergic individuals, and all but 1 of the subjects had IgE that bound to more than 10 allergens. One of the proteins was identified as the allergen Eur m 2 (3).

Although a number of allergens have been isolated from this mite, only a few have been characterised:

Eur m 1, a thiol cysteine protease (4-6).

Eur m 2 (1,4,6).

Eur m 3, a Group 3 mite allergen (7).

Eur m 4, a 57 to 60 kDa protein, an alpha-amylase (6,8-9).

Eur m 14, vitellogenin, an apolipophorin from haemolymph (6,10).

rEur m 14, a recombinant allergen (10).

Group 2 allergens (e.g., Der p 2, Eur m 2) have been reported to induce humoral and cellular responses in 80 to 90% of mite-allergic individuals (11).

Potential cross-reactivity

A moderate degree of cross-reactivity exists between the House dust mite *E. maynei* and the House dust mite *Dermatophagoides* species (12). Other studies have reported a higher degree of cross-reactivity between these 2 types of House dust mites, with a high level of primary structure similarity being demonstrated among Eur m 1, Der p 1 and Der f 1. Eur m 1 and Der p I showed 85% amino acid identity, and the 3 allergen amino acid sequences taken together showed a 78% identity (5,13-14).

Similarly, amino acid sequences of Eur m 1 and Eur m 2 were reported to have an 84 to 86% sequence identity with the corresponding allergens from *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*

mites. This was reported to be the same as the degree of sequence identity found between *D. pteronyssinus* and *D. farinae,* despite *Euroglyphus* being a member of the *Pyroglyphinae* subfamily rather than the *Dermatophagoidinae* subfamily (4,15). Pso o 1 from Sheep scab mite (*Psoroptes ovis*) has also been shown to be homologous to mite Group 1 allergens (16), and Pso o 2 to mite Group 2 allergens (17).

Other authors have also reported significant cross-reactivity among *Dermatophagoides* and *Euroglyphus* species. *Blomia kulagini* demonstrated a medium degree of cross-reactivity with *Euroglyphus maynei*. Immunological cross-reactivity between *Pyroglyphidae* and non-*Pyroglyphidae* mites was reported to be very low (18).

After an examination of cross-reactivity at the T-cell level, *E. maynei* Group 1 allergens were reported to be a significant source of primary T-cell sensitisation and to have little T-cell cross-reactivity with *D. pteronyssinus* or *D. farinae* (19).

Although *E. maynei* and *B. tropicalis* are the source of both species-specific and cross-reactive allergens, most allergens in each appear to be species-specific (20).

Eur m 3, a Group 3 mite serine protease allergen, has been shown to exhibit 42-57% homology with a cloned trypsin gene from the German cockroach (21). As Blo t 3 from *B. tropicalis* is highly homologous to Group 3 Dust mite allergens, cross reactivity is likely between *B. tropicalis* and *E. maynei*.7 (22).

Der p 4 and Eur m 4 were calculated to be 90% identical, and their amino acid sequences demonstrated an approximately 50%-identical match to insect and mammalian alpha-amylases, although the clinical relevance of this latter finding is unknown (8).

Of 2 recombinant allergens constructed from *Sarcoptes scabiei*, 1 was homologous to and cross-reactive with the *E. maynei* allergen Eur m 14, an apolipophorin from haemolymph (23). Amino acid sequence data has demonstrated similarity between Eur m 14 and other allergens in *D. pteronyssinus* and *D. farinae*; these allergens showed strong similarity to the insect apolipophorins that exist in the lipid transport particles in haemolymph (10).

Clinical Experience

IgE-mediated reactions

E. maynei may commonly induce symptoms of asthma and rhinoconjunctivitis and exacerbate atopic dermatitis in sensitised individuals (24-26).

House dust mites from the family *Pyroglyphidae – Dermatophagoides pteronyssinus*, *D. farinae* and *Euroglyphus maynei* – are recognised as the major source of allergens in house dust and the indoor environment, producing multiple potent allergens. They are common inhabitants of homes worldwide (27-29). In fact, the House dust mites to which humans are most frequently sensitised are these very 3 (4,30).

Sensitisation to *E. maynei* has been reported throughout many countries of the world.

In Germany, sensitisation to *E. maynei* was shown to be common (31). In 86 German farmers with rhinitis and/or asthma evaluated by skin-specific IgE determination, the most frequent sensitisations were found to be to the 3 *Blomia* species, *E. maynei* and *G. domesticus* (25).

In a survey of mites in 30 homes in Oxfordshire, UK, *D. pteronyssinus* and *E. maynei* were found to be the most abundant species, but *D. farinae* was absent (32). In Oxford, UK, 25 atopic children under 11 years of age were studied through skin test and IgE antibody response to *D. pteronyssinus*, *D. farinae*, *D. microceras* and *Euroglyphus maynei*. All of the children were sensitive to *D. pteronyssinus*, 20 (80%) were also sensitive to *D. farinae* and *D. microceras*, and of this latter group16 (64%) were also sensitive to *E. maynei* (33).

Similarly, a survey was done of the House dust mite population in the homes of 50 asthmatics residing in Liverpool, UK, who had strong skin reactivity to *D. pteronyssinus*.

It was demonstrated, as expected, that *D. pteronyssinus* was the commonest species. However, *E. maynei* made up 37% of the total adult mite count and was the predominant species in 48% of beds examined (34). Glasgow, with a mild, high-rainfall climate, combined with deteriorating housing and low standards of living in many parts of the city, is said to be a particularly suitable place for thriving populations of House dust mites. In a study, 31 species were detected, of which the most abundant were *D. pteronyssinus* (64.3%), *Glycyphagus domesticus* (16.7%), and *Euroglyphus maynei* (11.6%) (35-36).

In a Polish study, more than 30 mite species were found, of which the most common were those of the Pyroglyphid family, especially *D. pteronyssinus* and *D. farinae*. *E. maynei* occurred in very small numbers (37). These findings concurred with those of a study examining house dust samples from 335 dwellings at 27 different localities in Poland. This study identified 15 species, including 4 species from the family *Pyroglyphidae*. *D. farinae* predominated, followed by *D. pteronyssinus*, and only 1.6% of the homes contained *E. maynei* (38).

Among farmers working and living in rural regions of Austria (Styria, Lower Austria), and 26 citizens of Vienna, elevated levels of IgE antibodies specific for *E. maynei* were more frequently observed in the urban dwellers (39). In the Czech Republic, *E. maynei* was found more commonly in recreation houses and some hospitals (40).

In Russia, in a group of patients with allergic disease who were sensitised to *D. pteronyssinus*, 80% were also sensitised to *D. farinae*, 55% to *E. maynei*, 45% to *A. siro* and 35% to *L. destructor* (41).

Sensitisation to this mite has been reported in Scandinavian countries (42). In Sweden, *E. maynei* was shown to be a common cause of sensitisation among the whole farming population, with a prevalence of 4.5%, as shown by on the detection of serum-specific IgE (43). However, sensitisation to this mite in Swedish bakers was reported to be rare (44).

In Israel, the House dust mites *D. pteronyssinus*, *D. farinae* and *Euroglyphus maynei* constituted 94.8% of the mites. The most prevalent species of mites were shown to be *D. pteronyssinus* (85.6%) and *D. farinae* (71.3%) (45).

E. maynei has also been shown to be an important mite in the Americas. In a study involving 8 geographic areas of the United States, it was demonstrated that the most common Dust mites found in homes were *D. farinae*, *D. pteronyssinus*, *E. maynei*, and *B. tropicalis* (46). In Hawaii, dust was collected from 102 university student dormitory rooms. Thirty-three samples were selected for analysis and shown to contain *D. pteronyssinus* in 81.9% and *D. farinae* in 11.2%. The presence of the *Euroglyphus* species was reported to be very low (47).

In the city of Juiz de Fora, Brazil, *E. maynei* and *Tyrophagus putrescentiae* were some of the main species found (48). In 99 subjects with acute asthma and 100 controls in Cartagena, Colombia, sensitisation to *E. maynei* was demonstrated to be 68.7% vs. 22% (49). In a study involving 56 asthmatics in Santa Fe, Argentina, 46 were found to be positive on skin test to *D. pteronyssinus*, 43 to *D. farinae*, 27 to *Aleuroglyphus ovatus*, 38 to *B. tropicalis* and 27 to *Chortoglyphus arcuatus*; 38 of 54 individuals had IgE antibodies to *E. maynei*, and 22 of 54 to *L. destructor* (50). In 100 children with a history of mild or moderate asthma living in Mexico City, skin tests demonstrated that *D. pteronyssinus* was positive in 96, *D. farinae* in 80, and *E. maynei* in 41 (51).

In an allergen exposure study in Uberaba, Brazil, 240 dust samples were collected from 60 houses. *D. pteronyssinus* was reported to be the most frequent species found (15.6%), followed by *D. farinae* (12.3%) and *E. maynei* (7.9%) (52).

In Valdivia, Chile, among 100 consecutive paediatric asthma patients evaluated, 80 were confirmed to have skin reactivity to at least 1 mite species. All patients with skin reactivity for mites were positive to *D. pteronyssinus,* 99% to *D. farinae,* 92% to *E. maynei*, 80% to *L. destructor*, 73% to *T. putrescientae*, 72% to

B. tropicalis, 70% to *A. siro* and 68% to *C. arcuatus*. All of the patients with severe persistent asthma had skin reactivity to mites, as did 85% in the moderate group and 73% in the mild group. Ninety-five percent of patients with asthma and allergic rhinitis were shown to have skin reactivity to mites, as were 92% of patients with asthma and eczema and 100% of patients with asthma, allergic rhinitis and eczema (53).

Mites from mattresses in homes of 11 cities in Puerto Rico were assessed, and *E. maynei* was found in 5.3% of homes (54).

The predominant mite species in Perth and Bunbury in Australia were *D. pteronyssinus*, *E. maynei* and *Tarsonemus* species. Surprisingly, *D. farinae* was found to be absent from all dust samples examined. *E. maynei* was present in the 10 Bunbury homes and in 50% of the Perth homes, ranging up to 81% of mites identified (55).

E. maynei has been reported from China (56). In 93 Taiwanese asthmatic children aged from 3 to 15 years examined for IgE antibodies to 5 different species of mites, 63 were found to have IgE antibodies to at least 1 mite. Seventy-seven percent were shown to be sensitised to *E. maynei*. Some patients were shown to have IgE antibodies to *E. maynei* (3.2%) and *B. tropicalis* (3.2%), even though they had none to *D. pteronyssinus* and *D. farinae* (57).

In the manufacture of "chorizo" sausage, occupational allergy has been reported to *E. maynei* (58).

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d73 *Glycyphagus domesticus*

Glycyphagus domesticus	
Family:	*Acaridae*
Common names:	Storage mite, Furniture mite, Food mite
Source material:	Whole body culture

Allergen Exposure

Geographical distribution

See common geographical background to mites in the Introduction.

This Storage mite of the *Glycyphagidae* family, also known as Furniture mite, is found in foods and grains in warehouses and other storage areas. In homes, it thrives in infested foodstuffs and in damp areas, where it feeds on moulds.

A hairy mite, 0.3 – 0.7 mm in length, it has a soft, cream-white body with yellow-brown legs. For both sexes, the body bristles are very long and feathery. Microscopically, they are recognised by the long hairs at their tips. Development from egg to adult occurs in 22 days at room temperature. The adult lives for approximately 50 days. Its main food sources are flour, cereals, other cereal products and fungi.

Environment

See common environmental background to mites in the Introduction.

These mites are often found in old-fashioned upholstered furniture, in particular in damp items where the stuffing has rotted. They feed on the fungus and multiply in large numbers. Like all other mites, they quickly die if they become desiccated.

Unexpected exposure

Mites were found in 21% of 571 samples of cereal-based food products purchased at food retail outlets in the UK, and in 38% of 421 samples, derived from the 571 samples, which were examined after 6 weeks of storage in volunteers' homes. Most of the samples had fewer than 5 mites, but a few samples contained more than 20 mites, with a maximum of 428 mites detected in a single sample. The most common species were *Acarus siro*, *Tyrophagus putrescentiae*, *Lepidoglyphus destructor* and *Glycyphagus domesticus* (1).

Allergens

Gly d 2, a Group 2 mite allergen (2-4).

Gly d 3, a Group 3 mite allergen (5).

Gly d 5 (5).

Gly d 7 (5).

Gly d 8 (5).

Gly d 10, a tropomyosin (5).

Gly d 13, appears to be a lipocalin (5).

Potential cross-reactivity

There is little cross-reactivity between House dust mites and Storage mites (6). Storage mites and *D. pteronyssinus*, for example, each possess their own unique allergen or allergens. Cross-reactivity among the

Storage mites is more common. *L. destructor*, *G. domesticus* and *T. putrescentiae* are allergenically more closely related to each other than to *A. siro* (7). The protein sequence of Gly d 2 from *G. domesticus* was demonstrated to have a 79% identity to Lep d 2 of *L. destructor*, a 46% identity to Tyr p 2 of *T. putrescentiae*, and a 41% identity to Der p 2 of *D. pteronyssinus*. Extensive cross-reactivity was demonstrated among Gly d 2, Lep d 2, and Tyr p 2, but little cross-reactivity was found between these allergens and Der p 2 (2). Nevertheless, the immunologic responses to the different mite species are complex (8).

Varying degrees of cross-reactivity can be expected between *G. domesticus* and House dust and Storage mites as a result of the presence of Group 2 and Group 3 mite allergens. For example, recombinant Pso o 2, a Group 2 allergen from Sheep scab mite (*Psoroptes ovis*), was shown to be homologous to related Group 2 allergens Lep d 2 of *Lepidoglyphus destructor*, Der f 2 of *Dermatophagoides farinae*, Der p 2 of *Derrmatophagoides pteronyssinus*, Tyr p 2 of *Tyrophagus putrescentiae*, Eur m 2 of *Euroglyphus maynei* and Gly d II of *Glycophagus domesticus* (3). In a Spanish study, a low IgE cross-reactivity was observed between *D. pteronyssinus* and *G. domesticus*, but an important IgE cross-reactivity was detected among glycyphagid mites at the level of Group 2 allergens (9).

The ingestion of third-stage larvae of *Anisakis simplex* in uncooked or undercooked seafood may cause a human disease known as anisakiasis or anisakidosis. In a study of 400 Italian subjects evaluated to identify the factors associated with the risk of *A. simplex* sensitisation, this sensitisation was shown to be associated with the consumption of uncooked seafood (anchovies and Squid), increasing age, and sensitisation to *G. domesticus* (10).

Clinical Experience

IgE-mediated reactions

In line with other evidence that Storage mites have allergenic effects well beyond those in farmers and grain workers (11-12) (and in hay storage more than in grain storage workers (13), recent studies have reported that the Storage mite *G. domesticus* may commonly induce symptoms of asthma and rhinoconjunctivitis in sensitised individuals in both rural and urban settings (14-22).

G. domesticus has been demonstrated to be an important sensitising Storage mite in many parts of the world, including Europe. In the UK, Glasgow's mild, high-rainfall climate, combined with deteriorating housing and low standards of living in many parts of the city, creates a particularly suitable place for thriving populations of House dust and Storage mites. Thirty-one species were detected, of which the most abundant were *D. pteronyssinus* (64.3%), *G. domesticus* (16.7%) and *E. maynei* (11.6%) (23-24).

In 86 German farmers with rhinitis and/or asthma investigated by skin tests, the most frequent sensitisations were found for the 3 *Blomia* species, *E. maynei* and *G. domesticus* (23). In a mite survey conducted in the working environments of 121 farms in 5 regions of Germany, out of 859 samples, 743 (86.4%) contained mites. Ninety-three percent of all mites belonged to the order *Astigmata* (Storage and House dust mite species); 35 *Astigmata* and 14 *Prostigmata* mite species were identified. The prevalence of Storage mites was in the following order: *L. destructor* > *Glycyphagus domesticus* > *Acarus siro* > *Tyrophagus longior* > *Blomia tjibodas* > *Chortoglyphus arcuatus* > *Thyreophagus entomophagus* > *Tyrophagus putrescentiae* > *Euroglyphus longior* > *Tyrophagus palmarum* > *Acarus farris* > *Acarus immobilis* > *Gohieria fusca* (25).

In Spain, among 50 children with rhinitis and bronchial asthma, 10% were shown by means of skin test to be sensitised to *G. domesticus* (26). *G. domesticus* has also been demonstrated to be present in house dust in Scandinavian countries (27). The

presence of *G. domesticus* has also been reported from Turkey (28). Sensitisation to this Storage mite in Swedish bakers was reported to be rare (29).

In southwest Spain, a study was done of the prevalence of sensitisation to *G. domesticus* in patients naturally exposed to this mite; sensitisation to the more ubiquitous *D. pteronyssinus* was also investigated, along with the IgE cross-reactivity between the 2 mites. *D. pteronyssinus* was present in about 95% of house dust samples, and *G. domesticus* in about 50% of the samples. *Tyrophagus putrescentiae* and *Lepidoglyphus destructor* were detected in 3rd and 4th place, respectively. Approximately 50% of the patients with *G. domesticus* at home were sensitised to this mite. The authors suggest the inclusion of glycyphagid mite extracts in diagnostic tests in areas where this mite is prevalent (9).

The importance of *T. putrescentiae* in Huelva, in southeastern Spain, was studied in a group of patients sensitised to *D. pteronyssinus*. Among the 136 dust samples studied, *D. pteronyssinus* was identified in 94.8%. *T. putrescentiae* was found in 41.1% of samples, *G. domesticus* in 54.4%. Sensitisation to *G. domesticus* was not evaluated, but the high prevalence of this mite in house dust indicates the potential prevalence of sensitisation (30). Similarly, in a study of the prevalence of mite species in houses in Bursa, Turkey, 34.38% of houses were found to be infested with House dust mites. *G. domesticus* was found in 16.67% (31). A lower prevalence, of 2.58%, has been reported from Kutahya in Turkey (32).

In 100 children with a history of mild and moderate asthma who lived in Mexico City, skin tests demonstrated that *D. pteronyssinus* was positive in 96, *D. farinae* in 80, *E. maynei* in 41, *Chortoglyphus* in 22, *B. tropicalis* in 17, *T. putrescentiae* in 12, *Glycyphagus* in 12, *A. siro* in 7, *L. destructor* in 7 and *Gophieria* in 7 (33). Similarly, *G. domesticus* has been shown to be present in homes in Chile (34). In Punta Arenas, Chile, the species of Storage mites most representative in homes were: *Blomia tjibodas* (30.1%), *G. destructor* (22.5%) and *T. putrescentiae* (10.8%). The seasons that presented the higher proportions of mites were autumn (39.4%) and spring (37.1%) (35).

The presence of this mite has also been reported from the USA. Among Storage mite sensitisations in Wisconsin dairy farmers, sensitisation to *L. destructor* was the most frequently found, followed by *T. putrescentiae*, and *G. domesticus* (36).

In Brunei, examination of dust from sleeping areas showed that Storage mites, especially of Glycyphagid species, were predominant in house dust. On skin tests on 60 asthmatics with 1% extracts of 6 mite species, *D. pteronyssinus* was found to provoke the greatest number of positive skin reactions (66.7%), but positive reactions for *G. domesticus* were found in 40%. Skin reactivity to *L. destructor* was positive in 45%, demonstrating that Storage mites were significant allergens. The authors concluded that the role of Storage mites in the causation of asthma in the tropics may have been underestimated (37).

Allergy to *G. domesticus* may result in late respiratory reactions. Bronchial provocation tests performed on 2 separate occasions on a farmer with dust from his own grain led to immediate and late respiratory reactions, followed, without further exposure to grain dust, by severe respiratory reactions during subsequent nights (38).

d73 *Glycyphagus domesticus*

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d71 *Lepidoglyphus destructor*

Lepidoglyphus destructor	
Family:	*Acaridae*
Common names:	Storage mite
Source material:	Whole body culture

Allergen Exposure

Geographical distribution

See common geographical background to mites in the Introduction.

These food mites are tiny and barely visible, varying from 0.3 to 0.6 mm. Using strong magnification, one can notice that the body has no incision between the 2nd and the 3rd leg pairs. The males possess no suction pads; in the females, a short copulation pipe is visible. For both sexes, the body bristles are very long and feathery. Unlike *Gylcyphagus domesticus*, these mites have an inserted, elongated, and pointed scale on the end segment of the legs. Nevertheless, the scale is difficult to recognise if it is not spread out. Their eggs are quite large, compared with the size of the adult.

Environment

See common environmental background to mites in the Introduction.

This mite can often be found where plant or even animal foods are processed and stored at a humidity level that is too high. Fungi that grow in the foodstuffs, as well as the foodstuffs themselves, are consumed by the mites; this has been demonstrated in the case of *Alternaria* and *Penicillium species*. This species is rarely detected in house dust, do not carry any diseases and do not infest any form of life directly, but may result in allergic reactions. These mites develop at a relative air humidity of 65 - 100% and a temperature of approximately 20 - 30°C, and do not tend to avoid the light.

Unexpected exposure

Mites were found in 21% of 571 samples of cereal-based food products purchased at food retail outlets in the UK, and in 38% of 421 samples, derived from the 571 samples, which were examined after 6 weeks of storage in volunteers' homes. Most of the samples had fewer than 5 mites, but a few samples contained more than 20 mites, with a maximum of 428 mites detected in a single sample. The most common species were *Acarus siro*, *Tyrophagus putrescentiae*, *Lepidoglyphus destructor* and *Glycyphagus domesticus* (1).

Allergens

Many allergenic proteins have been isolated from *L. destructor* (2-3).

Early studies recognised that at least 2 of these were major allergen components, as they were recognised by more than 50% of the 43 sera used in the study. The 2 IgE-binding components had molecular weights of approximately 18 kDa and 16 kDa (4). Other important allergens detected were a 39 kDa (5-6), a 15 kDa and a high-molecular-weight allergen complex (of 79 and 93 kDa) (7-8). A 14 kDa protein was identified as a major allergen, binding with 95% of the patient sera (9).

A number of allergens have subsequently been characterised:

Lep d 1, renamed Lep d 2.

Lep d 2, a 13.2 kDa protein (10-23).

Lep d 3 (24).

Lep d 5 (17-18,25).

Lep d 7 (17-18,25).

Lep d 8 (26).

Lep d 10, a tropomyosin (17-18,27).

Lep d 12 (28).

Lep d 13 (17-18,25).

Lep d 39kD (5-6).

Lep d alpha-tubulin (17).

Recombinant allergens:

rLep d 2 (13,23).

rLep d 3 (24).

rLep d 5 (17).

rLep d 7 (17).

rLep d 8 (26).

rLep d 10 (17).

rLep d 12 (28).

rLep d 13 (25).

rLep d alpha-tubulin (17).

A protein belonging to the alpha-tubulin protein family has also been recognised (17).

Lep d 2 is recognised by about 90% of patients allergic to this mite (10). Two variants of Lep d 2 have been detected: Lep d 2.0101 and Lep d 2.0201. These differ at 13 amino acid positions. The Lep d 2 sequence diversity appears to have no significant impact on the allergen's IgE binding or its ability to induce T cell cytokine release (29).

In an evaluation of rLep d 2 and rTyr p 2 of *T. putrescentiae* through skin tests and serological analysis in sensitised and non-sensitised farmers chronically exposed to Dust mites, it was demonstrated that of the 44 subjects with skin reactivity to *L. destructor* and/or *T. putrescentiae* extract, 26 (59%) had skin reactivity to one or the other of the recombinant allergens, while 21 (48%) had it to both. The results suggested that the allergens have similar or shared IgE epitopes (14).

Lep d 5, Lep d 7 and Lep d 13 have been shown to bind to 4/45 (9%), 28/45 (62%) and 6/45 (13%) sera from *L. destructor*-sensitised subjects, respectively (25).

Recombinant Lep d 10 and alpha-tubulin were demonstrated to bind to 13% (18/136) and 12% (11/95) of patients with IgE reactivity to mites and/or crustaceans, respectively (17).

Lep d 39 kD has been shown to bind 46.5% (20/43) of sera from Swedish farmers who were serum-specific IgE-positive to *L. destructor*. There was a moderate degree of correlation between IgE antibody results to *L. destructor* and to the 39 kDa allergen. Of 14 sera from Stockholm residents with IgE antibodies to both *D. pteronyssinus* and *L. destructor*, 6 detected the 39 kDa allergen component. However, 3 sera from urban subjects lacking IgE antibodies against both mite species also had IgE antibodies against the 39 kDa allergen (5).

Potential cross-reactivity

Co-sensitisation to Storage mites is a frequent finding in patients sensitised to *Dermatophagoides pteronyssinus*. In a study, extracts of *Tyrophagus putrescentiae* almost completely inhibited IgE binding to *Acarus siro*, and vice versa. *D. pteronyssinus* inhibited IgE binding to all Storage mites up to 60%, whereas IgE binding to *D. pteronyssinus* was only minimally inhibited by extracts of Storage mites (30). Clinically, though, *L. destructor* does not have any major allergens in common with the *Dermatophagoides* species. Although Lep d 1 shows approximately 40% identity with the overlapping regions of Group 2 allergens from the genus *Dermatophagoides*, these do not share common allergenic epitopes with Lep d 1 (10).

Other studies have confirmed very low immunological cross-reactivity between *Pyroglyphidae* and non-*Pyroglyphidae* mites (31), in particular between *D. pteronyssinus* and *L. destructor* (32).

The protein sequence of Gly d 2 (*Glycyphagus domesticus*) has been shown to have a 79% identity with Lep d 2 (*L. destructor*) and 46% and 41% identity with Tyr p 2 (*Tyrophagus putrescentiae*) and Der p 2 (*Dermatophagoides pteronyssinus*), respectively. An evaluation of rLep d 2 and rTyr p 2 from *T. putrescentiae* suggested that the allergens have similar or shared IgE epitopes (14). Extensive cross-reactivity was demonstrated among Gly d 2, Lep d 2, and Tyr p 2, but little cross-reactivity was found between these allergens and Der p 2 (21). Similarly, other studies have reported strong cross-reactivity between *L. destructor* and the allergenic components of *A. siro* and *T. putrescentiae*, while the latter mite species only to a very low degree inhibited the allergenic components of *L. destructor* (33).

A recombinant clone of Pso o 2 from *Psoroptes ovis*, the Sheep scab mite, has been shown to be homologous to Group 2 mite allergens Lep d 2 of *L. destructor*, Der f 2 of *D. farinae*, Der p 2 of *D. pteronyssinus*, Tyr p 2 of *T putrescentiae*, Eur m II of *E. maynei* and Gly d 2 of *G. domesticus* (34).

A significant though not strong correlation have been reported between IgE antibody responses to *G. domesticus* and to *L. destructor*, and to *T. putrescentiae* and *L. destructor* ($p<0.05$). Homologous and heterologous IgE antibody inhibition studies showed there was low cross-reactivity between Storage mites and *D. pteronyssinus*. *L. destructor* showed the least inhibition by the other antigens, suggesting it possessed the fewest common allergens (35).

Considerable cross-reactivity has been reported to exist between *Blomia tropicalis* and *L. destructor*: *L. destructor* possesses unique as well as common allergens (36). A 14.5 kDa allergen from *B. tropicalis* was reported to be antigenically cross-reactive with the recombinant *L. destructor* allergen rLep d 2 (37).

A study demonstrated allergenic cross-reactivity between several allergens in *Anisakis simplex* and 4 Dust mite species (*A. siro*, *L. destructor*, *T. putrescentiae*, and *D. pteronyssinus*). The clinical significance of this cross-reactivity remains to be evaluated (38).

rTyr p 13 from *Tyrophagus putrescentiae* has a 61.1 to 85.3% identity with amino acid sequences of other mite Group 13 allergens (39).

Clinical Experience

IgE-mediated reactions

Storage mite allergy was initially reported to involve mainly farmers and grain workers (40-41) (and hay storage workers more than grain storage workers) (42), but more recent studies have reported that the Storage mite *G. domesticus,* among others, may commonly induce symptoms of asthma and rhinoconjunctivitis in sensitised individuals in both rural and urban settings (43-53). As these Storage mites are found in barns and grain stores, they are important causes of occupational respiratory diseases in farmers (54).

In Europe, *L. destructor* has been reported to be a major source of mite allergy in rural and urban environments. In the east of France, 43.1% and 44.95% of 105 young adults were shown by a combination of skin tests and IgE antibody measurements to be sensitised to *Tyrophagus putrescentiae* and *L. destructor* respectively (55).

In Barcelona, Spain, of 356 children studied, 39 showed cutaneous sensitisation to Storage mites (*Acarus siro*, *Lepidoglyphus destructor* and *Tyrophagus putrescentiae*), which represented 11% of the population studied, and 20% of the total sensitised to mites. However, only 3 of these children were sensitised only to Storage mites, the remaining 36 (92%) also showing sensitisation to House dust mites. Of the Storage mites studied, *L. destructor* was the most significant (56). A study conducted in household environments of Valencia, Spain, found that only 3 houses showed levels of *L. destructor* that were comparable to those found in bakeries (57). Higher levels of sensitisation have been reported from other areas in Spain. In 4379 patients residing in an area of cereal industries in Spain, the prevalence of mite sensitisation was 18.96%. The prevalence of sensitisation to Storage mites among mite-sensitive patients was 11.88%. Among 50 selected

patients, the most frequent sensitisation was to *Dermatophagoides pteronyssinus* (58%), followed by *Dermatophagoides farinae* (48%), *Lepidoglyphus destructor* and *Tyrophagus putrescentiae* (38%), *Blomia kulagini* (34%), and *Acarus siro* and *Chortoglyphus arcuatus* (24%) (58).

A study was done of the prevalence of sensitisation to *Glycyphagus domesticus* in patients naturally exposed to this mite together with *D. pteronyssinus* in southwest Spain; it was reported that after *D. pteronyssinus* and *G. domesticus, T. putrescentiae* and *L. destructor* were detected in 3rd and 4th place, respectively (59).

Among 512 consecutive patients with rhinitis and/or asthma, living in urban or rural areas of central Germany and tested for IgE antibodies or skin-tested with extracts of *D. pteronyssinus*, *A. siro*, *L. destructor*, *T. putrescentiae* and other Storage mites, 103 (20.1%; 77 urban dwellers and 26 farmers) were sensitised to at least 1 of the Storage mites (60). A mite survey conducted in the working environments of 121 farms in 5 regions of Germany reported that of 859 samples, 743 (86.4%) contained mites. Ninety-three percent of all mites belonged to the order *Astigmata* (Storage and House dust mite species); 35 *Astigmata* and 14 *Prostigmata* mite species were identified. The prevalence of the Storage mites was found to be in this order: *Lepidoglyphus destructor* > *Glycyphagus domesticus* > *Acarus siro* > *Tyrophagus longior* > *Blomia tjibodas* > *Chortoglyphus arcuatus* > *Thyreophagus entomophagus* > *Tyrophagus putrescentiae* > *Euroglyphus longior* > *Tyrophagus palmarum* > *Acarus farris* > *Acarus immobilis* > *Gohieria fusca* (61).

In 136 eastern Polish farming students, skin tests to Storage mites were positive in 30.9%: most frequently to *Lepidoglyphus destructor* (18.4% of all students), *Tyrophagus putrescentiae* (15.4%), *Dermatophagoides pteronyssinus* (14.0%), and *Acarus siro* (13.2%) (62). In Polish farmers, tests for Storage mites showed positive reactions to *Acarus siro* in 9.6%, *Lepidoglyphus destructor* in 17.8%, and *Tyrophagus putrescentiae* in 13.7% (63).

In 26 male paper mill workers and 36 postmen evaluated, the paper mill workers manifested a significantly higher frequency of positive skin tests and increased specific IgE to *L. destructor* and *T. putrescentiae*, compared to the postmen. Respiratory symptoms were found in 40% of paper mill workers with positive test results to *L. destructor*, and in 53.8% with positive test results to *T. putrescentiae*. All postmen with positive test results to *L. destructor* and 83.3% with positive test results to *T. putrescentiae* had respiratory symptoms (64).

Farmers working and living in rural regions of Austria (Styria, Lower Austria), as well as a group of 26 citizens of Vienna, demonstrated sensitisation to *Lepidoglyphus destructor* and *Tyrophagus putreus*. The sensitisation rate to Storage mites was markedly high in city dwellers, though not as high as in the farmers (65).

L. destructor has also been studied in Scandinavian countries and shown to be a relevant allergen there (66). In 2,578 Swedish farmers, 6.2% were found to have an allergy to Storage mites. The Storage mite *L. destructor* was identified by both allergen-specific IgE antibodies and bronchial challenges as a significant cause of occupational asthma in rural environments (67). On the island of Gotland, Sweden, 5 genera of Storage mites were detected on 16 farms, but the different mite species were not represented on all farms. *L. destructor* was the dominant species on 13 of 16 farms. The authors' earlier studies showed that *L. destructor* was the most important allergen causing both upper and lower airway symptoms among farmers (68-69). Surprisingly however, sensitisation to Storage mites in Swedish bakers was rare (70).

In Russia, Storage mites play a significant role in sensitisation of the population. In a group of patients with allergic disease and sensitisation to *Dermatophagoides pteronyssinus*, 80% were sensitised to *Dermatophagoides farinae*, 55% to *Euroglyphus maynei*, 45% to *Acarus siro* and 35% to *Lepidoglyphus destructor* (71).

In a randomly selected urban group in Reykjavik, Iceland, tested for skin reactivity, 6.3% showed IgE-mediated allergy to *L. destructor*. These were often polysensitised atopics with a high prevalence of clinical symptoms associated with exposure to hay (72).

Storage mite sensitisation has been reported to be relevant in Turkey (73) and among the urban population of Croatia, where the prevalence of subjects with positive skin tests was 35.8% for *T. putrescentiae*, 26.8% for *L. destructor* (26.8%), and 22. 4% for *D. pteronyssinus* and *D. farinae*. The prevalence of serum-specific IgE for for *T. putrescentiae* was 22.4%, and 14.9% for *L. destructor* (74). In a study of the prevalence of domestic mites in Kutahya (Turkey), *L. destructor* was found in 1.72% of homes (75).

L. destructor was reported to be a significant allergen in South America and surrounds, including Cuba (76). In a study, by means of skin tests, of the prevalence of sensitisation to *L. destructor* in 297 asthmatic adults and children living in 7 cities of 5 Latin American countries, sensitisation to *L. destructor* varied from 30% in Mexico City to 76.2% in Sao Paulo (77). A study of inhaled allergens in 80 Brazilian children aged 6 to 16 years reported on sensitisation with skin tests with *Alternaria alternata*, Cat, Dog, *Lolium perenne*, grasses and the following domestic mites: *Blomia tropicalis*, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Lepidoglyphus destructor*, *Chortoglyphus arcutus* and *Aleuroglyphus ovatus*. The results were positive tests in 15%, 11%, 11%, 6%, 7%, 95%, 92%, 88%, 76%, 75% and 71%, respectively (78).

In a study in the city of Juiz de Fora, Brazil, *Euroglyphus maynei* and *Tyrophagus putrescentiae* were some of the main species found, and to a lesser degree, *Lepidoglyphus destructor* (79). In 100 children with a history of mild and moderate asthma living in Mexico City, skin tests demonstrated that *Dermatophagoides pteronyssinus* was positive in 96, *Dermatophagoides farinae* in 80, *Euroglyphus maynei* in 41, *Chortoglyphus* in 22, *Blomia tropicalis* in 17, *Tyrophagus putrescentiae* in 12, *Glycyphagus* in 12, *Acarus siro* in 7, *Lepidoglyphus destructor* in 7 and *Gophieria* in 7 (80).

In 77 subjects in Caragena, Columbia, with clinical symptoms of asthma and/or allergic rhinitis and a positive skin prick test to *Dermatophagoides pteronyssinus* and/or *D. farinae*, skin tests were positive to *L. destructor* in 59.7% (81). Dust samples collected from the pillows and mattresses of 56 asthmatics in Santa Fe, Argentina, showed that 46 had positive skin test to *D. pteronyssinus*, 43 to *D. farinae*, 27 to *A. ovatus*, 38 to *B. tropicalis*, and 27 to *C. arcuatus*; 38 of 54 individuals had IgE antibodies to *E. maynei*, and 22 of 54 to *L. destructor* (82).

In Valdivia, Chile, of 100 consecutive paediatric asthmas patients evaluated, 80 were confirmed to have positive skin test to at least 1 mite species. All patients with skin reactivity for mites were positive to *D. pteronyssinus,* 99% to *D. farinae,* 92% to *E. maynei*, 80% to *L. destructor*, 73% to *T. putrescientae*, 72% to *B. tropicalis*, 70% to *A. siro* and 68% to *C. arcuatus*. All of the patients with severe persistent asthma had skin reactivity to mites, as did 85% in the moderate group, and 73% in the mild group. Ninety-five percent of patients with asthma and allergic rhinitis were shown to have positive skin test to mites, as were 92% of patients with asthma and eczema and 100% of patients with asthma, allergic rhinitis and eczema (83).

In sensitisation of Wisconsin dairy farmers in the US, *L. destructor* was the most frequently found Storage mite culprit, followed by *Tyrophagus putrescentiae* and *Glycyphagus domesticus* (84). Six hundred serum samples randomly selected from a 1-day submission of approximately 3,000 samples by a southwestern Ohio population to a clinical diagnostic laboratory were screened for IgE antibodies to allergens of *L. destructor* and *A. siro*. Thirty-two (5.3%) of the 600 serum samples screened had IgE antibodies to allergens from at least 1 of the 2 mite species; 14 (2.3%) and 20 (3.3%) had serum IgE antibodies to proteins of the mites *A. siro* and *L. destructor*, respectively (85).

d71 *Lepidoglyphus destructor*

L. destructor also occurs in the arid countries of the Middle East. House dust mites collected from 8 different areas in greater Cairo showed that 9 species of mites could be recovered from indoors, including *Tyrophagous putrescentiae*, *Acarus siro*, and *Lepidoglyphus destructor* (86).

In Brunei, examination of dust from sleeping areas showed that Storage mites, especially Glycyphagid species, were predominant in house dust. On skin tests of 60 asthmatics with 1% extracts of 6 mite species, *Dermatophagoides pteronyssinus* was found to provoke the greatest number of positive skin reactions (66.7%), but positive reactions for *Glycyphagus domesticus* (40%), and *Lepidoglyphus destructor* (45%) demonstrated that Storage mites are also significant allergens. The authors point out that the role of Storage mites in the causation of asthma in the tropics may have been underestimated (87).

Occupational allergy due to hypersensitivity to cereal flours is relatively common among bakers and grain store workers (88). Storage mites can contaminate Wheat flour and could be an important cause of allergic symptoms due to inhalation. Among 43 patients with sensitisation to Wheat flour, co-sensitisation to *L. destructor* was found in 30%. Of these, 23% did not have a relationship with any bakery or agricultural site (89). Other studies have reported similar or higher rates of sensitisation to Storage mites. For example, almost all of a group of bakers sensitised to flour were found to also be sensitised to the Storage mites *Acarus siro*, *Lepidoglyphus destructor* and *Tyrophagus putrescentiae* (6 of 7) (90). Grain workers may also be affected, developing immediate nasal and conjunctival symptoms and late-phase asthmatic reactions following the handling of stored grain (91). Occupational sensitisation may also occur in farmers not directly involved in the handling of grain. Specific bronchial provocation tests confirmed a diagnosis of occupational asthma in a poultry farmer sensitised to *L. destructor* (92).

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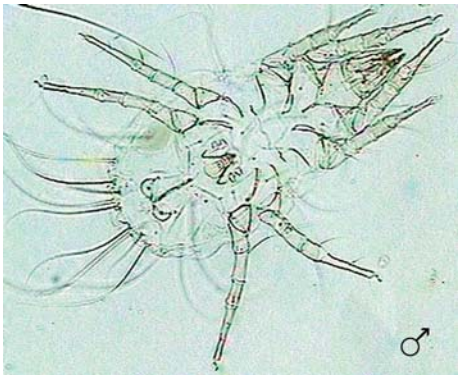
d72 *Tyrophagus putrescentiae*

Tyrophagus putrescentiae	
Family:	*Acaridae*
Common names:	Storage mite, Mould mite
Source material:	Whole body culture



Allergen Exposure

Geographical distribution

See common geographical background to mites in the Introduction.

These mites are 0.2 - 0.5 mm in length and have a small translucent body with almost colourless mouthparts and legs. They also have a scale on the end segment of the legs. Their somewhat slender bodies bear a train of hairs that are more numerous and longer than those on *Acarus siro*. On the underside of the males, on either side of the anus, there are two dome-shaped suckers.

Under optimum conditions, a generation can be completed in 8 to 21 days. As the temperature falls, the length of the life cycle increases greatly. This mite will tolerate high temperatures. Unlike *A. siro*, it does not produce a hypopus. This mite is a pest of many foods, in particular those having a high fat or protein content. It has been found, inter alia, in wheat flour, soy flour, wheat germ, cheese, rye bread, white bread, mixtures of oats, barley and wheat, cultivated mushrooms, various seeds and fruits (including dried bananas), straw stacks in the field, decaying animal and vegetable matter, dried milk, and ham.

Tyrophagus putrescentiae, a dominant species of Storage mite in Korea, is a particularly important cause of allergic disorders in this country (1).

Environment

See common environmental background to mites in the Introduction.

Unexpected exposure

Mites were found in 21% of 571 samples of cereal-based food products purchased at food retail outlets in the UK, and in 38% of 421 samples, derived from the 571 samples, which were examined after 6 weeks of storage in volunteers' homes. Most of the samples had fewer than 5 mites, but a few samples contained more than 20 mites, with a maximum of 428 mites detected in a single sample. The most common species were *Acarus siro*, *Tyrophagus putrescentiae*, *Lepidoglyphus destructor* and *Glycyphagus domesticus* (2).

Allergens

Earlier studies have shown that *T. putrescentiae* contains at least 20 allergenic components (1,3-4). A 16 kDa allergen was found to be the most important to *T. putrescentiae*-allergic patients, with the sera of 52% containing IgE antibodies to this allergen (5).

To date, the following allergens have been characterised:

Tyr p 2, a 16 kDa Group 2 mite protein (1,6-10).

Tyr p 13, a fatty acid binding protein.

Tyr p alpha-tubulin (11).

Recombinant allergens:

rTyr p 2 (7,10).

rTyr p 13 (1).

rTyr p alpha-tubulin (11).

In an evaluation of rTyr p 2 and rLep d 2 of *L. destructor* through skin tests and serological analysis in sensitised and non-sensitised farmers chronically exposed to Dust mites, it was demonstrated that of the 44 subjects with skin reactivity to *L. destructor* and/or *T. putrescentiae* extract, 26 (59%) had skin reactivity to one or the other of the recombinant allergens, while 21 (48%) had it to both. The results suggested that the allergens have similar or shared IgE epitopes (6).

rTyr p 13 was detected in 5 of 78 (6.4%) *T. putrescentiae*-positive sera tested (1).

The frequency of IgE reactivity of rTyr p alpha-tubulin was 29.3% in sera from Storage mite-allergic subjects (11).

Potential cross-reactivity

Co-sensitisation to Storage mites is a frequent finding in patients sensitised to *Dermatophagoides pteronyssinus*. However, there is only low immunological cross-reactivity between *Pyroglyphidae* (House dust) mites and non-*Pyroglyphidae* (Storage) mites (12). This is in spite of antigenic and allergenic determinants being shared by *Dermatophagoides* species and *Tyrophagus putrescentiae* and the fact that the 16 kDa Group 2 allergen of *Dermatophagoides* is one of the most prevalent allergens of *T. putrescentiae* (5,4).

Similarly, results of other studies have suggested that the major allergens of *T. putrescentiae* have a strong cross-reactivity with *D. pteronyssinus* extracts, but that *D. pteronyssinus* allergens have only partial cross-reactivity with *T. putrescentiae* extracts (13). Significant though not strong correlations were found between IgE antibody responses to *G. domesticus* and to *L. destructor,* and to *T. putrescentiae* and to *L. destructor*. Homologous and heterologous IgE antibody inhibition studies showed there was low cross-reactivity between Storage mites and *D. pteronyssinus* (14). As opposed to the other storage mites, *T. putrescentiae* shows some cross-reactivity with *D. farinae*. *T. putrescentiae* also shares some major allergens with *Acarus siro* and consequently might show cross-reaction with that Storage mite. Authors have suggested that it is an important allergen source and should be considered when *D. pteronyssinus* is thought to be a problem (15).

The protein sequence of Gly d 2 (*Glycyphagus domesticus*) showed 46% and 41% identity to Tyr p 2 (*T. putrescentiae*) and Der p 2 (*Dermatophagoides pteronyssinus*) respectively. Extensive cross-reactivity was demonstrated among Gly d 2, Lep d 2, and Tyr p 2, but little cross-reactivity was found between these allergens and Der p 2 (16). Considerable cross-reactivity has been demonstrated between *T. putrescentiae* and 2 *Dermatophagoides* species in urban areas where these species cohabit, and was shown to be due to a Group 2 mite allergen (5). A recombinant clone of Pso o 2 from *Psoroptes ovis*, the Sheep scab mite, has been shown to be homologous to the Group 2 mite allergens Lep d 2 of *L. destructor*, Der f 2 of *D. farinae*, Der p 2 of *D. pteronyssinus*, Tyr p 2 of *T putrescentiae*, Eur m 2 of *E. maynei* and Gly d 2 of *G. domesticus* (17). An evaluation of rTyr p 2 and rLep d 2 from *L. destructor* suggested that the allergens have similar or shared IgE epitopes (6). Similarly, studies have reported that *L. destructor*, *G. domesticus* and *T. putrescentiae* seem to be allergenically more closely related to each other than to *A. siro* (18).

In a study, *T. putrescentiae* almost completely inhibited IgE binding to *A. siro*, and vice versa. *D. pteronyssinus* inhibited IgE binding to all Storage mites up to 60%, whereas IgE binding to *D. pteronyssinus* was only minimally inhibited by extracts of Storage mites (19). Similar findings have been reported in other studies. Allergenic components in extracts of *A. siro* and *T. putrescentiae* were identified. Five and 4 allergenic components, respectively, were detected in sera from farmers sensitised to Storage mites. The highest frequencies of IgE-binding were to a 15 kDa component of *A. siro* (7/9 sera) and to a 16 kDa component of *T. putrescentiae* (23/29 sera). Cross-reactivity between *D. pteronyssinus* on the one hand and *A. siro* and *T. putrescentiae* on the other was shown, as the IgE reactivity to a 25 kDa component of

D. pteronyssinus was inhibited to the same degree by extracts of *A. siro*, *T. putrescentiae* and *D. pteronyssinus*. However, *D. pteronyssinus* was a poor inhibitor of the allergenic components of *A. siro* and *T. putrescentiae*. Strong cross-reactivity was also shown between *L. destructor* and the allergenic components of *A. siro* and *T. putrescentiae*, while the latter mite species only to a very low degree inhibited the allergenic components of *L. destructor* (20).

Blomia tropicalis has been shown to contain multiple allergens, of which most are species-specific. A limited amount of cross-reactivity was demonstrated between *B. tropicalis* and the 2 common House dust mite species *D. pteronyssinus* and *D. farinae*, and between *B. tropicalis* and the Storage mite *T. putrescentiae* (21).

A study demonstrated allergenic cross-reactivity among several allergens in *Anisakis simplex* and 4 Dust mite species (*A. siro*, *L. destructor*, *T. putrescentiae*, and *D. pteronyssinus*). The clinical significance of this cross-reactivity remains to be evaluated (22).

The deduced amino acid sequence of Tyr p 13 showed 61.1 to 85.3% identity with other mite Group 13 allergens. This may result in varying degrees of cross-reactivity among mites containing a Group 13 allergen (1).

Tyr p alpha-tubulin showed as much as 97.3% identity to the alpha-tubulin sequences from other organisms. The highly conserved amino acid sequences of alpha-tubulins across different species of mites may indicate cross-reactivity (11).

Clinical Experience

IgE-mediated reactions

In line with the realisation that Storage mite allergy has effects far beyond farmers and grain workers (23-24) (and hay storage workers more than grain storage workers (25)), recent studies have reported that the Storage mite *T. putrescentiae* may commonly induce symptoms of asthma and rhinoconjunctivitis in sensitised individuals in both rural and urbanised settings (26-39).

Conjunctivitis was more frequent in patients allergic to Storage mites, whereas perioral syndrome (itching of the tongue and swelling of the lips) was seen only in patients sensitised to *T. putrescentiae*. This study concluded that damp climatic and indoor conditions, and human activities, but not urban or rural living environments *per se*, influenced the differential sensitisation to House dust mites and Storage mites (40).

In a study of 105 young adults in the east of France, 43.10% of the subjects were shown, through a combination of skin tests and IgE antibody measurements, to be sensitised to *Tyrophagus putrescentiae* (41).

In Barcelona, Spain, of a total of 356 children studied, 11% (39) showed cutaneous sensitisation to Storage mites (*Acarus siro*, *Lepidoglyphus destructor* and *Tyrophagus putrescentiae*). Only 3 of these children were sensitised to Storage mites alone, the majority (92%; 36) being sensitised to Storage and House dust mites both. The majority of the study group were sensitised to *L. destructor* (42). Among 4379 patients residing in an area of cereal industries in Spain, the prevalence of mite sensitisation in was 18.96%. The prevalence of sensitisation to Storage mites among mite-sensitive patients was 11.88%. Among 50 selected patients, the most frequent sensitisation was to *D. pteronyssinus* (58%), followed by *D. farinae* (48%), *Lepidoglyphus destructor* and *Tyrophagus putrescentiae* (38%), *Blomia kulagini* (34%), and *Acarus siro* and *Chortoglyphus arcuatus* (24%) (43).

The importance of *T. putrescentiae* in Huelva, in southeastern Spain, was studied

in a group of patients sensitised to *D. pteronyssinus*. Among the 136 dust samples studied, *D. pteronyssinus* was identified in 94.8%. *T. putrescentiae* was found in 41.1% of samples, and *G. domesticus* in 54.4%. Sensitisation to *G. domesticus* was not evaluated, but the high prevalence of this mite in house dust indicates the potential prevalence of sensitisation. Among the 45 patients studied, 23 (51.1%) presented 2 positive tests, 18 (40%) were not sensitised to *T. putrescentiae*, and 4 (8.8%) showed contradictory results. Twenty-six patients (57.7%) inhabited urban areas and 19 (42.2%) rural regions. IgE antibody assessment for *T. putrescentiae* in 25 patients was positive in 12, with only 7 having values greater than 2 kU_A/L. The IgE antibody inhibition studies confirmed the low cross-reactivity between these mites, and only in 1 patient did *D. pteronyssinus* partially inhibit the IgE binding (44).

In a study of sensitisation to *T. putrescentiae* in the urban population of Upper Silesia, Poland, 56.7% (17/30) of patients who were positive to skin tests showed specific cross-reactivity with antigens isolated from extracts of T. *putrescentiae*. Forty percent reacted specifically with new allergens identified as protein fractions of extracts from excrement of *T. putrescentiae*. Approximately 13.3% of patients with positive skin tests showed specific cross-reactivity with antigens isolated from mite excrement rather than from mite whole extracts (45).

Through 64 samples of dust from houses in Bursa, Turkey, 22 (34.38%) houses were found to be infested with domestic mites. The prevalence of the mite species were: 58.34% for *D. pteronyssinus*, 16.67%, for *G. domesticus*, 4.16% for *D. farinae*, and 4.16% for *Tyrophagus* species (46). In a second study in Turkey, in Kutahya, the prevalence of domestic mites was found to be 18.05%. *T. putrescentiae* was found in 43.96%, *D. pteronyssinus* in 31.03%, *A. siro* in 13.79%, *L. destructor* in 1.72%, *G. domesticus* in 2.58% and *Cheyletus* species. in 1.72%. A very high rate of *D. pteronyssinus* was found in August and of *T. putrescentiae* and *Acarus siro* in July (47).

In 512 consecutive patients with rhinitis and/or asthma, living in urban or rural areas of central Germany and tested for Storage and House dust mite sensitivity using skin- and IgE antibody tests, 103 (20.1%; 77 urban dwellers and 26 farmers) were shown to be sensitised to at least 1 of the Storage mites (48). The working environments of 121 farms in 5 regions of Germany were examined for mites. Of 859 samples, 743 (86.4%) contained mites. The prevalence of Storage mite species were in the following order: *Lepidoglyphus destructor* > *Glycyphagus domesticus* > *Acarus siro* > *Tyrophagus longior* > *Blomia tjibodas* > *Chortoglyphus arcuatus* > *Thyreophagus entomophagus* > *Tyrophagus putrescentiae* > *Euroglyphus longior* > *Tyrophagus palmarum* > *Acarus farris* > *Acarus immobilis* > *Gohieria fusca* (49).

Farmers working and living in rural regions of Austria (Styria, Lower Austria), and a group of 26 citizens of Vienna, demonstrated sensitisation to *Lepidoglyphus destructor* and *Tyrophagus putreus*. The sensitisation rate to Storage mites was markedly high in city dwellers, though higher in farmers (39).

In the urban population of Croatia, the prevalence of subjects with detectable skin reactivity to *T. putrescentiae* was 35.8%; it was 26.8% for *L. destructor*, and 22. 4% for *D. pteronyssinus* and *D. farinae*. Serum-specific IgE for *D. pteronyssinus* and *D. farinae* was detected in 23.9%, followed by *T. putrescentiae* (22.4%), and *L. destructor* (14.9%) (50).

In a study of 136 eastern Polish farming students, skin reactivity for *T. putrescentiae* was detected in 15.4%, more than was found for *D. pteronyssinus* (14.0%) or *Acarus siro* (13.2%) (51). Similarly, in Polish farmers, sensitisation to *Acarus siro* was found in 9.6%, *L. destructor* in 17.8%, and to *T. putrescentiae* in 13.7% (52).

In 26 male paper mill workers and 36 postmen evaluated, the paper mill workers manifested a significantly higher frequency of positive skin tests and IgE antibody levels to *L. destructor* and *T. putrescentiae* than the postmen. Respiratory symptoms were

found in 40% of paper mill workers with positive test results to *L. destructor*, and in 53.8% with positive test results to *T. putrescentiae*. All postmen with positive test results to *L. destructor* and 83.3% with positive test results to *T. putrescentiae* had respiratory symptoms (53).

In a Finnish study of 106 farmers with allergic rhinitis, challenges with any one of *Acarus siro*, *Lepidoglyphus destructor*, and *Tyrophagus putrescentiae* were positive in 18%, and with Cow dander in 20% of farmers with allergic rhinitis. The results indicate that, among dairy farmers, Storage mites are as common as Cow dander as a cause of allergic occupational rhinitis (54).

Storage mites were reported to be the most important allergens for grain elevator workers (23), as confirmed by a Danish study (55). Surprisingly, Storage mite sensitisation was reported to be rare in Swedish bakers (56).

Storage mites have been reported to be common even in arid regions. In a study of mites collected from 8 different areas in greater Cairo, 9 species of mites were recovered from indoors, including *T. putrescentiae* (57).

In a skin test study in Singapore performed on 391 individuals – 289 patients with asthma and/or allergic rhinitis and 102 healthy controls – using extracts of 6 species of local dust mites, 71.3% of the former group was demonstrated to be sensitised to *T. putrescentiae* (58).

Korean studies have reported that *T. putrescentiae* is found in association with *D. pteronyssinus* and *D. farinae* in more than 25% of houses in urban areas of Korea, and that many atopic subjects are co-sensitised to both species (5). Storage mites appear to be ubiquitous. Skin tests in Korean apple farmers demonstrated that the most common sensitising allergen was European red mite (23.2%), followed by *T. putrescentiae* (21.2%), Two-spotted spider mite (16.6%), *Dermatophagoides farinae* (16.3%), *D pteronyssinus* (14.4%), Cockroach (13.1%), and Hop Japanese (*Humulus Japonicus*) pollen (12.0%) (59).

Studies from South America report that Storage mite sensitisation is as important there as elsewhere in the world. In 100 children with a history of mild or moderate asthma living in Mexico City, skin tests to *D. pteronyssinus* were positive in 96%, to *D. farinae* in 80%, to *Euroglyphus maynei* in 41%, to *Chortoglyphus* in 22%, to *Blomia tropicalis* in 17% and to *T. putrescentiae* in 12% (60). In Juiz de Fora, Brazil, a study demonstrated that *Euroglyphus maynei* and *T. putrescentiae* were some of the main species (61). Similarly, in Lima, Peru, *Blomia tropicalis* was the mite most frequently detected in house dust samples, followed by *D. pteronyssinus*, *Chortoglyphus arcuatus* and *T. putrescentiae*. Altogether, these 4 mites comprised 90% of the mites detected (62).

In Punta Arenas, Chile, the most common mite species in homes were: *Blomia tjibodas* (30.1%), *Glycyphagus destructor* (22.5%) and *Tyrophagus putrescentiae* (10.8%) (63). The prevalence of Storage mites was also reported in other parts of Chile (64).

In Valdivia, Chile, of 100 consecutive paediatric asthma patients evaluated, 80 were confirmed to have positive skin test to at least 1 mite species. All patients with skin reactivity for mites were positive to *D. pteronyssinus*, 99% to *D. farinae*, 92% to *E. maynei*, 80% to *L. destructor*, 73% to *T. putrescientae*, 72% to *B. tropicalis*, 70% to *A. siro* and 68% to *C. arcuatus*. All of the patients with severe persistent asthma had skin reactivity to mites, as did 85% in the moderate group, and 73% in the mild group. Ninety-five percent of patients with asthma and allergic rhinitis were shown to have skin reactivity to mites, as were 92% of patients with asthma and eczema and 100% of patients with asthma, allergic rhinitis and eczema (65).

In the US, the Storage mite sensitisation most frequently reported in Wisconsin dairy farmers was to *L. destructor*, followed by *T. putrescentiae* in 6 of 8 subjects studied (66). Serum samples from 600 people randomly selected from a 1-day submission of approximately 3,000 samples from a southwestern Ohio population to a clinical diagnostic laboratory were screened for IgE to allergens of *L. destructor* and *A. siro*.

d72 *Tyrophagus putrescentiae*

Thirty-two (5.3%) of the 600 serum samples screened had IgE antibodies to allergens from at least 1 of the 2 mite species; 14 (2.3%) and 20 (3.3%) had allergen-specific IgE to proteins of the mites *A. siro* and *L. destructor*, respectively. Thirty-nine (6.5%) and 55 (9.2%) had serum IgE antibodies to proteins of *T. putrescentiae* and *Dermatophagoides* species, respectively. Fifteen (21.4%) of the 70 mite-positive people were sensitised to only *T. putrescentiae*, and 24 (34.3%) were co-sensitised to both Storage and House dust mites (67).

Researchers have stated that persons exposed to stored product mites through occupational settings, or through consumption of food containing these mites, are at risk of sensitisation and allergic reaction (68). Therefore, not surprisingly, food-contaminating mites are reported to have caused IgE-mediated allergic reactions, including anaphylaxis, in persons who consumed mite-contaminated foods (69). Anaphylaxis has been described in 2 individuals shortly after they ate food contaminated by *T. putrescentiae* (70). Similarly, occupational allergy to *T. putrescentiae* has been reported in food manufacturers (71).

Airborne contact dermatitis to *T. putrescentiae* has been described (72), as well as occupational contact urticaria-dermatitis (73).

The 3 mm threshold in skin tests has been reported not to be reliable in evaluating sensitisation to *T. putrescentiae*, due to an insufficient specificity of the allergen extract (74).

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