

Introduction

House Dust Mite Allergy

The etiology of respiratory allergies, primarily asthma, has been recognized for many centuries, and as early as 1698 Floyer reported dust as being one of the major factors involved in this problem. However, it was not until the beginning of this century that Kern (1), Cooke (2), and various other workers used skin tests to confirm the presence of allergens in house dust and introduced the concept of a common allergenic determinant present worldwide. The specific characteristics and the uniformity of the allergens in house dust have been greatly disputed, particularly since Linblad and Farr (3) demonstrated that cutaneous reactions to dust extracts depend on the concentration of the extract, and also that dust extracts induce a positive response in more than 50% of clinically diagnosed nonatopic patients, and in an even higher proportion if only skin reactions to extracts applied subcutaneously are considered. The work of these pioneers stimulated considerable interest in dust allergens in the scientific community and, as a result, various laboratories embarked on research programs to investigate the allergenic components of house dust and to determine their origins (4).

It is now well established that dust contains a heterogenous mixture, which varies according to region and house, of various allergenic substances, consisting primarily of the somatic and metabolic allergens of mites, and also allergens derived from domestic animals, human skin scales, and domestic insects such as cockroaches. In addition, fungal spores or mycelium and other products of animal or vegetable origin, such as feathers, wool, and natural fibers, may be sources of dust allergens (5,6).

The primary role of mites in house dust allergy was first suggested by Dekker (7), who recorded large numbers of unidentified mites in house dust, particularly in mattresses. He also found, in patients suffering from allergies, that their symptoms were greatly relieved when they lived and worked in a mite-free environment. Carter, Wedd, and d'Abrera (8) described, under the name of "pulmonary acariasis," an

asthmatic-type symptom that they attributed to the presence of mites in the lungs. However, it was another 20 years before Voorhorst et al. (9) established the major role played in house dust allergy by a domestic mite of the genus *Dermatophagoides*, namely *Dermatophagoides pteronyssinus*. These authors discovered that in Europe this mite was present, often in large numbers, in the majority of houses examined and, since extracts of this mite produced similar skin test reactions in atopic patients as does house dust, they concluded that *D. pteronyssinus* was the principal source of house dust allergens.

The hypothesis of Dekker that, although well founded, initially had been underestimated in the United States, was first verified in Europe (9), and then confirmed worldwide by studies in Japan (10) and also in North America (11,12). This knowledge gave rise to the hope of controlling, by the use of acaricides, the principal source of perennial allergies, and also formed the basis for much research into various aspects of the ecology and biology of house dust mites and into the nature and composition of the allergens produced by them.

During the last 20 years our knowledge of the geographical distribution of the Pyroglyphidae has progressed considerably, but the map of their distribution remains incomplete. Nevertheless, numerous investigations to date have confirmed that *D. pteronyssinus* predominates over all other species in most countries, and that *Dermatophagoides farinae* and *Euroglyphus maynei* may be present in numbers that vary according to climate (13). Some species that are abundant in certain countries are completely absent in other geographical regions with apparently similar climates. This is the case notably for *Dermatophagoides siboney*, which is very frequent in Cuba, but is rarely found in France (14). Conversely, similarities exist between the mite fauna of certain countries that are very different climatically and geographically; for example, *Dermatophagoides neotropicalis* frequently is found in Surinam and Brazil, but is also represented in India (15,16). The distribution of *E. maynei* is even more enigmatic; this species has been identified in every continent except Central Africa and Central and North America (13). More research into the biology and ecology of these mites is required before the reasons for their geographical preferences can be fully understood.

Zoogeographical studies have also revealed that the number of species of pyroglyphid mites is considerably larger than preliminary studies suggested and, therefore, the number of potentially allergenic mite species may be greater than initially supposed. The family Pyroglyphidae contains to date 18 genera and 46 species, of which 13 have been found in house dust (carpets, mattresses, cushions, clothes, etc.), 28 exclusively on birds or in their nests, and 5 in stored products

or on mammals. The existence of many nidicolous or nest-inhabiting species in this family suggests that the domestic species of Pyroglyphidae may have originated from nidicolous mites.

Despite the large number of species of Pyroglyphidae found in house dust, only four species (*D. pteronyssinus*, *D. farinae*, *Dermatophagoides microceras*, and *E. maynei*) have been the subject of immunological investigations to determine their potential allergenicity (17,18). Clearly, an important area for future research is to ascertain the precise role played by different species of the family in the pathology of house dust allergy.

Pyroglyphid mites are not the only mites to provoke respiratory and also contact allergies. Certain mites infesting stored products such as foods and belonging to the genera *Acarus*, *Tyrophagus* (Acaridae), *Glycyphagus*, and *Lepidoglyphus* (Glycyphagidae) have also been implicated in similar types of allergies (19–24). The people most exposed to these mites are primarily farmers and their families who, owing to their work, are in regular contact with the dust in barns containing hay, straw, or grain. The existence of common allergenic determinants in these various mites, seriously complicates the interpretation of skin or blood responses, as measured by various provocation tests.

It is also interesting to note that storage mites (Aracidae and Glycyphagidae) have been recognized for a considerable time as the agents responsible for contact allergies associated with various professions, such as that of grocers produced by *Glycyphagus domesticus*, that of bakers and of cheese produced by *Acarus siro*, dermatitis of copra ("copra itch") for which the usual causative agent is *Tyrophagus*, and the dermatitis associated with dried fruits that is produced by *Carpoglyphus lactis* (19). This suggests that storage mites may possess certain specific allergenic determinants associated with these various dermal allergies.

It has been suggested by Fain (25) that two different mites, *D. pteronyssinus* and *Sarcoptes scabiei*, both of which share the same nutritional requirement for human skin, may possess common antigens, so that it may therefore be possible to use extracts of *D. pteronyssinus* in the diagnosis and management of the problem. Recent studies of scabies mite antigens by Falk et al. (26) and Arlian et al. (27) support this hypothesis.

Since the association of mites with allergies, much research has been undertaken into the ecology and biology of these mites. As previously mentioned, the species and prevalence of mites differ in different geographical areas, but they also vary within regions according to habitat and season. For example, in house dust in Europe, the Pyroglyphidae are most abundant in mattress dust collected in late summer

(28,29), whereas the Acaridae and Glycyphagidae are seldom found in house dust, and if present are usually found in floor dust (30, personal observations).

The influence of predatory mites and fungal flora on the ecology of dust mites has also been investigated. The predatory mite *Cheyletus eruditus* is often abundant in house dust and stored products, and has therefore been suggested as a means of controlling allergenic mite populations; however, this predator has not yet proven effective in controlling mite populations in the home or in stored products (31,32). Fungi of the genus *Aspergillus* have been suggested to be an important dietary component of the Acaridia (32–34). The development of *D. pteronyssinus* reared without fungi in their diet is retarded (35,36) and consequently the use of fungicides to control mite populations has been investigated (37).

Laboratory studies have elucidated the life cycle and temperature, humidity, and nutritional requirements of several species, the details of which will be discussed in the article by Hart. In addition to clarifying the ecology of these mites in vivo, this information has been invaluable in enabling the cultivation of these mites under laboratory conditions for use in immunological (e.g., extraction of allergens) and other studies such as acaricide trials.

The application of mite extracts to modern laboratory techniques using starch, amidon, cellulose acetate, and polyacrylamide gel electrophoresis has utilized carboxylesterase isoenzymes to differentiate between various species of Pyroglyphidae, Acaridae, and Glycyphagidae (38–40). This approach is particularly useful when species are extremely difficult to separate using morphological criteria, for example, in *D. farinae* and *D. microceras*, where the characters presumed to be discriminating have been found to vary from one population to another or in various species of the genus *Tyrophagus*, which are almost undistinguishable morphologically. It is also now possible to use various immunochemical techniques to identify and quantify the species of mites present in dust samples by means of their specific allergens (41,42). Another recent method of quantifying mites and their allergens present in house dust involves a rapid chemical color detection of the amount of the guanine excretory product of mites. This Acarex test does not, however, provide any information on the species present (43).

Most important, the latest technologies have been applied to investigate the allergens associated with these mites that are responsible for perennial allergies and extrinsic asthma. Considerable progress in this field has been made, particularly in the past 10 years, with the development of new molecular biology techniques. A total of five allergens from three species of dust mites have been identified and

monoclonal antibodies against these have been produced (41,44,45). Our knowledge as to how the allergens are produced by the mites is as yet incomplete although recent studies by Thompson and Carswell (46) and Chua et al. (47) suggest that the major allergen of *D. pteronyssinus* (Der pI) is a soluble glycoprotein synthesized and excreted by the mite. The major mite allergens, this term being used in context of their ability to sensitize, have been found both in the feces and in the mite bodies themselves (48,49), however, the relative importance of the somatic and metabolic allergens is strongly disputed.

The presence of two opposing schools in this regard has also influenced the definition of two reference mite allergen extracts. One extract, proposed by the subcommittee of allergen standardization of the International Union of Immunology Societies and recognized by the World Health Organization, is based on primary material obtained from mature whole mite culture, which contains both somatic and metabolic antigens. The other extract, proposed by the Food and Drug Administration of the United States, contains only mite bodies, separated by sieving or differential flotation, from the rest of the culture, including secreted or excreted metabolites.

To date, control measures to eradicate dust mites from houses have involved the use of various acaricides (50), fungicides (34,51), plastic mattress covers, and rigorous cleaning procedures primarily directed at the bedding and carpeting (52). If certain studies have demonstrated a significant reduction in the number of mites in dust collected after treatment with these products (53,54), none of the studies of clinical symptoms of patients in whose homes these treatments have been applied have provided results that would justify their regular use. In this context, the treatment of allergies caused by mites remains dependent on various desensitization programs notably the "accelerated" technique (55) that is achieved using standardized aqueous allergen extracts. The success of this technique has been demonstrated, but its management is extremely difficult in patients with asthma that is unpredictable.

In conclusion, rather than a decrease in the incidence of dust allergy, we are now seeing a progressive increase in the incidence of asthma, which in some countries has practically doubled in the past 10 years (56). This phenomenon is not only seen in developed urbanized countries, but also in countries in the course of developing toward a more modern lifestyle (57). Clearly, further research on all factors influencing the incidence of asthma and the associated mites is urgently required to halt this alarming trend. Such research should involve, for example, techniques for identification of mite species and studies of their cross-allegenicity, which may influence specific desensitization

treatment, as well as a search for better measures for the reduction or elimination of mites in the human environment, and especially that of atopic patients.

We hope that this review, by assembling all the relevant information to date, will provide an invaluable tool to those working on this major clinical problem. It should be of interest equally to clinicians and biologists who are confronted daily with patients suffering from allergies or asthma caused by mites.

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