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Rare indoor allergens

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Summary
Rare allergens in indoor environment are insufficiently recognized. The sources are diverse: they include animal, namely acaride, insect and mammalian allergens or vegetable allergens. The prevalence of sensitization to rare allergens depends on geographical and climatological characteristics, on people's habits and overall on dwelling specificities. Sensitizations to new rare allergens should be confirmed by documented clinical history, by immunological tests, and by the beneficial effects of avoidance. A review of rare and/or new allergens likely to be present in indoor environment is presented.

Introduction

Individuals are exposed to a wide range of foreign proteins or glycoproteins both in indoor and outdoor environments. Their sources are diverse and include frequent allergens such as house dust mites of the Dermatophagoïdes or Blomia genus, animals and fungal spores. However, a susceptible individual can produce specific IgE antibodies against rare allergens present at home.Such sensitizations depend on the genetic capability as well as on the airborne concentrations of the offending allergens. In this article, we focus on unusual indoor allergens. The arbitrary division between frequent and rare allergens does not necessarily indicate that rare allergens will be clinically insignificant in certain individuals, since their full avoidance may reduce allergy symptoms considerably.

We have excluded occupational allergens, but some of the rare allergens were first described as occupational allergens before they were recognized as major allergens when they were present in dwellings. With the use of monoclonal antibodies, some indoor allergens, first unsuspected, were recognized to be present in homes in significant levels.

Prevalence of sensitization to rare rare allergens depends on geographical and climatological characteristics, house and apartment specificities and persons' habits. Some proteins can act as indoor allergens because of either specific sensitization or special individuals with high allergen reactivity. Ideally, each new rare allergen source should be confirmed by documented clinical presentation, immunological tests, provocation tests and assessment of the beneficial effect of avoidance. Moreover, the proteins corresponding to the allergens in the complex source should be identified

Rare allergens in indoor environment

Acarids

1. Uncommon mites: Houses occasionally have a large

number of storage mites (i.e. Lepidoglyphus destructor, Tyrophagus putrescentiae and longior, Aleuroglyphus ovatus, Gohieria fusca (1-3). The sensitization rate to storage mites has been found high in city dwellers (4, 5). According to Arlian (6), 9.3% of the general population in Ohio (urban, suburban and rural) are sensitized to allergenic products of storage mites (Lepidoglyphus destructor and Tyrophagus putrescentiae). According to this author, surveys in homes should ideally determine the prevalence of allergens and mites of multiple species.

2. Spiders: Only occupational IgE mediated allergy has been reported with spiders; however, as these acarids are frequently brought up in homes as pets, a potential allergy risk may exist. Spiders can provoke rapid vibrations in their bodies, thereby scattering the hairs in the environment (7).
3. Silver fish: It has been demonstrated that house dust contains significant silver fish (Lepisma saccharina) levels. rLep s 1 is the first allergen cloned and characterized from silver fish extract. It is a tropomyosin and has been used to study the importance of the indoor sources of tropomyosin in sensitization (8). However a pathogenic role of silver fish remains to be proved (9).

Insects

1. Cockroaches: Cockroaches are not rare allergens in many countries especially in the warm parts of North America and Asia, but are found infrequently as causes of allergic diseases in Europe (10). The prevalence of cockroach allergy in France, determined by RAST, was less than 5% (11). Moreover, prevalence determined by cutaneous tests or in-vitro methods can be influenced by co-sensitization with other house dust allergens such as mites, which have cross reacting allergens with cockroaches (gluthation transferase and tropomyosin) (12).
2. Among insect allergens, the order of coleopters causes many occupational sensitization in mill workers. In indoor environment, cough and rhino-conjunctivitis exclusively present during house keeping were related to larvae of dermestidae (Attagenus pelio) and the diagnosis was confirmed by cutaneous tests, RAST and IgE determinations to larvae proteins (13). Another clinical case of asthma was reported by Cuesta-Herranz et al (14), induced by dermestidae larvae present in wooden floors, in a dwelling with stuffed animals on the wall. The diagnosis was confirmed by cutaneous tests and specific IgE; moreover a bronchial challenge test induced an immediate response. Environmental control measures were sufficient to control the patient's symptoms (scraping and deinfesting the wooden floor and covering it with a varnish, removing the stuffed animals). Another example is allergic asthma to psocus spp (Pscoptera); these insects have been shown to proliferate in hemp fibers which are used instead of glass-wool fibers for house insulation (15). These reports indicate that it is necessary to be aware of the fact that etiological agents such as, insects present in dwellings, may be important particularly when patients have negative skin test responses to the common indoor allergens.

Other inhalant allergens of insects have been described as outdoor allergens for epidemic asthma, possibly induced by crickets, locusts and moths (Caddis-fly). Some allergies to moths are related to hobbies: for instance, fishing may be a source of exposure to moths and their larvae (16). Fishing hobbyists who are in contact with larvae of chironomids or with their extracts when they feed fishes kept in aquariums reported immediate type hypersensitivity reactions (17, 18). Mairesse (19) reported 7 sensitized subjects (prick-test and specific IgE), among 38 aquarium hobbyists. Four of them suffered from rhinitis and/or asthma and one of them never even fed the fishes. The responsible allergens for sensitizations are haemoglobins of low molecular weight. The main allergens are Chi t 1 and the monomeric component Chi t 1III (20). A cross reactivity with numerous species has been demonstrated especially with IgE binding proteins from Anisakis, German cockroach, Chironomids with several IgE binding components located at 30 to 43 kDa region (21). Other food products such as crustacae or different worms and larvae can also lead to sensitization in fish hobbyists (22). In Japan, higher frequency of IgE antibody responses to insects (moth, butterfly, caddis fly and chironomids) was found in patients with bronchial asthma. Air samplings performed revealed the presence of insect-related particles less than 10 μ in diameter (23). Several cases have been reported recently in the literature describing patients suffering from allergic respiratory symptoms including rhinitis, conjunctivitis and asthma related to Harmonia axyridis exposure (Asian lady beetle, Japanese lady beetle or lady bug) (24, 25).

Any insect growing in large numbers within a house can become a significant source of allergens, this also shows that indoor environments are changing.

Several studies have found IgE antibodies to a wide range of insect species, due to cross reactivities between Der-

matophagoides pteronyssinus, silver fish, coachroach or chironomid, but this does not mean that IgEs antibodies to these insects can be taken as evidence of exposure. The first step towards the suspicion of a potential indoor allergen is to demonstrate its presence at home.

Mammalian allergens

In the indoor environment, household animals are significant sources of allergens. Almost every important mammalian respiratory allergen belongs to the lipocalin family of proteins (12). Outside of cats and dogs, human contact with unusual popular household pets can induce allergic respiratory diseases. Among them, rodents (especially rats and mice) are well known as inducers of occupational respiratory symptoms occurring in laboratory workers (the prevalence of sensitization varying from 14 to 15% (26). However, for other species, the number of exposed persons is unknown and the risk of sensitization is difficult to appreciate. Recently, a large size population survey was performed in Japan using a questionnaire dealing with household conditions including pet keeping and inquiring about respiratory symptoms. In a multivariate logistic regression analysis it appears that there was no association between either dog or cat ownership and respiratory symptoms, in contrast hamster ownership increased the odd ratio for respiratory symptoms (27). Among rodents, hamsters as pets have increased markedly. A clinical report of 30 cases suggests that hamster ownership is associated with mild to severe asthma, sometimes requiring hospital admission and occurring about 15 months after the onset of hamster exposure (28). The search for specific IgE was negative in 8 out of 30 cases. The main allergens differ among different species such as golden hamsters, European hamsters, dwarf Djungarian hamsters (29). Recently, several cases of anaphylaxis after hamster bites have been described (30, 31); a specific allergen from the hamster saliva has been identified. Similar cases have been described after bites by a Mongolian gerbil and prairie dogs (32). Severe asthma symptoms have been described in a patient washing a pet male ferret, specific IgEs were detected especially against urine proteins (33). In an other study of ferret allergy, Immunoblot revealed serum specific IgE binding strongly to a 66 kDa protein of the urine extract suggesting albumin as the relevant épitopes (34). Allergy to mink, a mammal from the same family as ferret has been described in occupational settings (35). Keeping minks as pets can be not unusual in certain countries. The contact to chinchilla in households may lead to sensitization; allergic rhinitis and/or asthma in children and adults have been confirmed by nasal provocation tests in 6 patients (36). Guinea pigs for which the prevalence of symptoms is about 30% in occupational settings can also be kept as pets and induce indoor asthma (37). Guinea pig dusts contain several allergens. These allergens are present mainly in fur, but also in dander, urine and saliva (38). The main allergen isolated from the hair extract is named Cav p 1 (20 kDa) and sensitizes about 70% of patients. IgEs against Cav p 2 (17 kDa) are found in about 55% of sensitized patients. 8% of guinea pig allergic patients exhibit IgE reactivity to serum albumin (39). 40% of guinea pig allergens are carried on small particles (<to 0.8 μ) (40). Rabbits, especially dwarf rabbits are also kept as pets. Among 1602 atopic patients, Liccardi et al. (41) in an Italian multicenter study, found 2.43% rabbit sensitization. Only half of these patients were in permanent or episodic contact with these animals. Only 10% of the sensitized subjects were mono sensitized, they were pet owners and had asthma symptoms. Ory c 1, a 17-18 kDa glycoprotein is found in saliva and in fur (42), Ory c 2 found in several source material and albumin are also rabbit allergens, but of minor importance.

Measuring allergens in settled house dust and in air samplings has shown that the levels of mouse allergens in indoor environments may be similar to those found in animal facilities; mouse allergens were detectable in respectively 80% of dust samples collected in schools (43) and in 100% of bed rooms in inner city homes (44). These recent studies should be completed by the search for sensitization in atopic patients having no occupational exposure in order to evaluate the clinical relevance of mouse allergens as indoor allergens.

Other furry animals, newly introduced as pets, are potential indoor allergens, such as dwarf horses, Vietnam pigs, unusual feline animals, monkeys, or squirrels. Recently a case of domestic allergy to cheetah has been described, confirmed by positive specific IgE to saliva and fur. Inhibition studies and immunoblots showed that besides an homologous allergen to Fel d 1, specific allergens to cheetah are involved (45); this may be explained by the fact that among the Felidae, cheetah and cat belong to different sub-families.

Other animal allergens

Scaly animals such as lizards were assumed not to be allergenic. However, allergy to iguana has been reported and confirmed by skin tests and in vitro studies to iguana scales (46, 47).

Respiratory sensitization to avian allergens has also been described (48). The responsible allergens, especially Gal d

5, an alphalivetin is implicated in the bird egg syndrome (49). More recently, a bird-egg syndrome caused by Agapornis sp. (Lovebirds) has been reported (50). In addition to alpha-livetin the patient developed allergy to sunflower seeds. Severe allergic reactions to sunflower seed and millet have been previously described among bird fanciers (51, 52).

Green algae

Green algae (chlorella) grow under similar conditions to molds and can be found as indoor allergens. Sensitizations to chlorella have been described in children (6% of outpatients in a study from Tiberg (53)) and are mainly found among mold- sensitized patients. The clinical relevance however has not been clearly demonstrated.

Plant derived allergens

The occurrence of allergy due to plant-derived allergens has increased over the past 15 years. These inhalant allergens are found in occupational environments mainly, but they may also be present in the home environment, the prevalence of sensitization to these indoor allergens depending on the number of plants at home. Among ornamental plants, Ficus, especially Ficus benjamina, was found to sensitize 6% of 395 outpatients in Sweden (54) and among them 3% were symptomatic (perennial asthma, rhinitis or conjunctivitis). A lower prevalence of sensitization has been found by Hemmer et al. (55): 2.5% among 2662 atopic patients. Specific ficus allergens were found in house dust samples (56, 57). Allergens are present in latex from ficus, which belongs to the Hevea Brasiliensis family. Other latex plants, such as Euphorbia pulcherina (58) and Araujia sericifera can induce immediate allergies in atopic patients (59). Patients sensitized to ficus have a potential risk of fruit allergy, especially to figs (60, 61). The presence of ficus in hospitals as well as in indoor public places should thus be avoided. In a recent study concerning ornamental plants sensitivity in patients with rhinitis, the most frequent positive prick tests were found with Ficus benjamina followed by yucca, ivy and palm tree (62). Most patients were sensitized to other inhalant allergens and only 13% were sensitized to plants only. Other clinical cases of allergy to ornamental plants have been described as indoor allergens, such as allergy to the coffee plant (63) and papyrus (Cyperus alternifolius) (64). Wütrich and Johansson (61) have reported an allergy case to the ornamental indoor green plant Tradescantia (Albifloxia) (65). Cut and dried flowers are potential allergenic sources, however their incidence as inducers of indoor allergy is a rare occurrence, whereas it is more frequent in gardeners and florists (66-68).

Other vegetable allergens, introduced by human beings, can be present in domestic environment. For instance, powders from Lycopodium clavatum used as dry shampoo (69, 70),or powders such as Fenugrec used as pharmaceutical products in certain ethnic groups (71). This emphasizes the importance of allergens from vegetable origins likely to be present at home and used increasingly for ecological reasons. For instance, pillow padding uses new material such as moth plant (59) and buckwheat, which have been involved in nocturnal asthma (72, 73, 74).

Allergens introduced by stinging and biting

Allergens introduced by stinging can induce allergic manifestations in indoor environment. An example is given by fleas and especially cat fleas as well as by ground bugs (75, 76). European pigeons soft tick Argas reflexus live inside houses and are more and more widespread because of the growing populations of pigeon colonies in urban areas. Bites by ticks usually occur at night and severe allergic reactions are reported (8 out of 12 requiring intensive care) (77). The dominant allergen is Arg r 1, which belongs to the lipocalin family (78); there is no evidence for an increased risk for atopic individuals of developing allergic reactions after an Argas bite (79).

Airborne food allergens

Exposure to airborne food allergens (including handling and cooking) can be induced by odors, fumes, vapors or sprays, which have a potential role in provoking clinical manifestations such as asthma, rhinitis and conjunctivitis in sensitized patients. Reactions induced by peeling vegetables such as raw potatoes, carrots, fresh asparagus are well known (80, 81); but the elicitation of asthma by the steam of cooking vegetables such as chick peas and lentils (82, 83) is also possible. The inhalation of steam when boiling fish or shrimps or other crustacean can also be an inadvertent exposure to allergens in the kitchen. Crespo et al (84) reported 21 children with symptoms of food allergy to fish: 12 among them had rhinitis or asthma after 3 patterns of exposure: fumes generated by frying fish, water vapor released during boiling and mere exposure to fish.

Exposure to airborne allergens, even in low amounts, can induce moderate to severe symptoms in highly sensitized patients. Classical examples are patients with latex allergy who get symptoms in sport settings, patients with mammalian allergy such as allergy to cat or horse, who get symptoms in contact with contaminated clothes brought

inside, or with allergens found in furniture. Patients with peanut allergy may present respiratory symptoms in closed environment such as an airplane cabin where peanut packages are opened. Sicherer et al. (85) reported 62 allergic symptoms occurring during a trip on commercial airliners, with 5 patients needing epinephrine injections. The demonstration of hidden inhaled food allergens (in particular eggs and milk) in indoor environment has been demonstrated by allergen measurements (86, 87).

Conclusion

A wide range of foreign proteins or glycoproteins may be responsible for sensitization in indoor environment. The allergenic content of environment depends on many factors including climatic and geographic variables. It also depends on people's new habits; for instance increasing using of certain plant species in gardening, which can lead to new sources of aeroallergens. One of the most striking points is the emergence of unusual indoor pet allergens related especially to newly-introduced furry animals. Owing to the enthusiasm for ecology, it may be assumed that in the future new unknown indoor allergens may appear. Allergists must know that new sensitizations are to be expected. In order to assess new etiologies, it is essential to document clinical cases by immunological tests; this implies that laboratory support should be available. In any case, the recommendation is to publish the documented clinical cases in order to increase the number of accessible and useful references in the literature, knowing that avoidance of the etiological factors of respiratory symptoms may lead to complete and definitive recovery.

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