



Frequency of sensitizations and allergies to house dust mites

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Summary Domestic mites is the term used to describe dust mites and storage mites that prefer to live in houses and to which many people develop sensitization through the formation of specific IgE antibodies due to the high allergenic potency of mite allergens. As a result, mites can trigger allergic diseases of the upper and lower respiratory tract as well as cross-reactions to other allergens. Sensitization to house mites is widespread in the German population. About 11 million adults are sensitized in Germany (15.9%). Men are more frequently affected than women, and sensitizations occur more frequently in large cities and with higher socioeconomic status. Sensitizations are less frequent in old age. They can lead to diagnostic problems as clinically silent sensitizations, which is the case in about 40% of sensitizations.

Keywords Mite allergens · IgE antibody · Frequency · Mite allergy

Frequency of sensitization by house dust mites in the general German population

The best data on the frequency of sensitization in the adult German population come from the “Study on the Health of Adults in Germany” (DEGS1) published almost 10 years ago as part of the health monitoring of the Robert Koch Institute (RKI) [1]. The study includes interviews, examinations and tests between 2008 and

2011 on 8152 persons aged 18–79 years living in Germany (Fig. 1).

Using IMMUNOCAP (Thermo Fisher Scientific, Waltham, Massachusetts, USA), IgE-specific antibodies were determined against 50 allergens in 7025 sera, including *Dermatophagoides pteronyssinus* (D. pt., d1). Values of ≥ 0.35 kU/l were considered positive.

Across all age groups and both sexes, the frequency of sensitization to D. pt. (d1) was 15.9% (95% confidence interval [CI] 14.8–17.1) of the population. This puts the frequency of sensitization to house dust mites in seventh place behind tree and grass pollen and wasp venom in adults (hazel with 16.2% is not shown in Fig. 1). Approximately 11 million adults in Germany are sensitized to house dust mites.

Information on the strength or concentration of IgE antibodies (kU/L) was not provided in the study publication. However, it is clear that men in all age groups have a significantly higher prevalence of sensitization than women and that the prevalence decreases significantly with age (Fig. 2).

The prevalence of sensitization varies only slightly in the different regions of Germany. In the east, it is significantly lower than in the west and also the south, at 13.1%, while the state North Rhine–Westphalia has the highest prevalence at 19.6% (Fig. 3). Haftenberger and colleagues [1] discuss that this might be related to climatic differences (wetter climate in the northwest vs. drier climate in the east and south).

More important is the difference in prevalence by community type (Fig. 4). In rural areas or small towns, it is significantly lower than in large cities. There is a general tendency towards higher prevalence figures in large cities, so also for sensitizations to birch and grass pollens and to cat allergens.

The cause of more sensitization in large cities is not clear. It is possible that poor air quality in large cities is caused by, for example, the increased concentration

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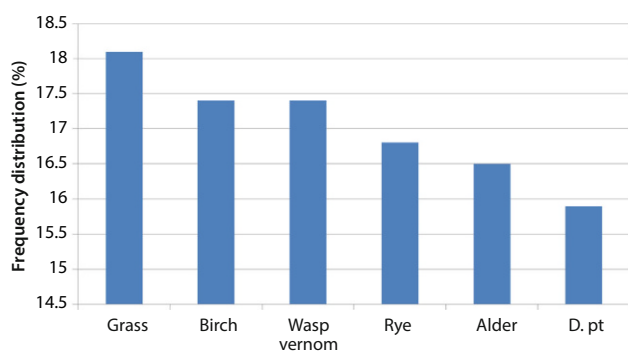


Fig. 1 Ranking frequency distribution (expressed in %) of sensitizations among adults in the general population in Germany. (After [1]. *D. pt* *Dermatophagoides pteronyssinus*)

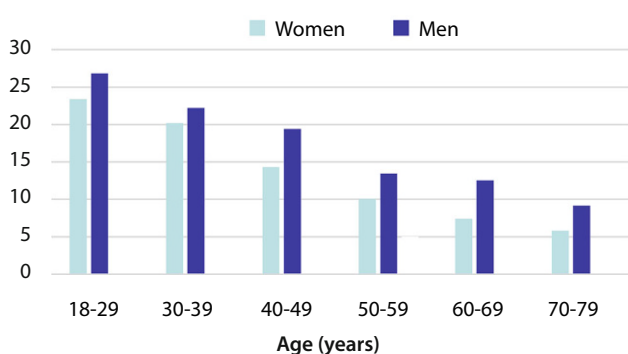


Fig. 2 Prevalence of sensitizations (%; $n = 7025$ Sera) to *Dermatophagoides pteronyssinus* (*D. pt.*, d1) in the German population by age group (years). (After [1])

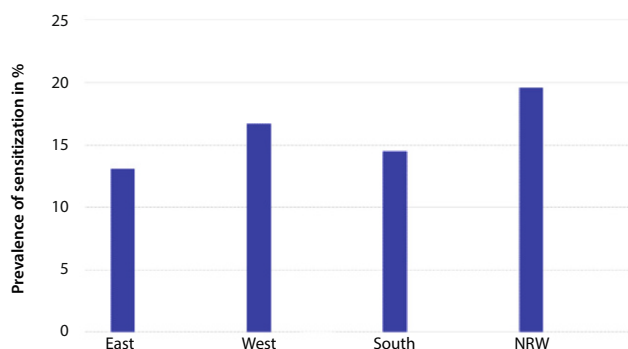


Fig. 3 Prevalence of sensitization (%) to dust mite *Dermatophagoides pteronyssinus* stratified by selected regions. (According to [1]; NRW North Rhine–Westphalia)

of nitrogen dioxide (NO₂) in cities. Elevated NO₂ concentrations have been seen in Sweden in association with an increased prevalence of sensitization [2].

In experimental studies, simultaneous exposure to nitrogen dioxide (0.1 or 1 ppm) and Der p 1 resulted in significant release of IL-6 and IL-8 in human nasal epithelial cells [3], which may support the induction of IgE-specific antibodies.

Another factor influencing sensitization is socioeconomic status. This has been known about pollen allergy for decades and also affects mite allergy. The

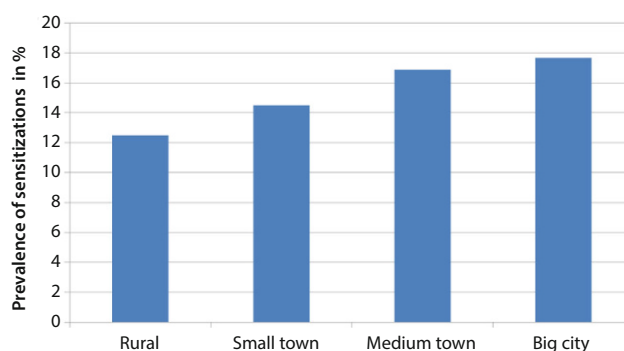


Fig. 4 Prevalence of sensitization (%) to *Dermatophagoides pteronyssinus* stratified by community type. (According to [1]). Classification according to the number of inhabitants in the classes: *rural* < 5,000 inhabitants, *small town* 5,000 to < 20,000 inhabitants, *medium town* 20,000 to < 100,000 inhabitants and *big city* > 100,000 inhabitants

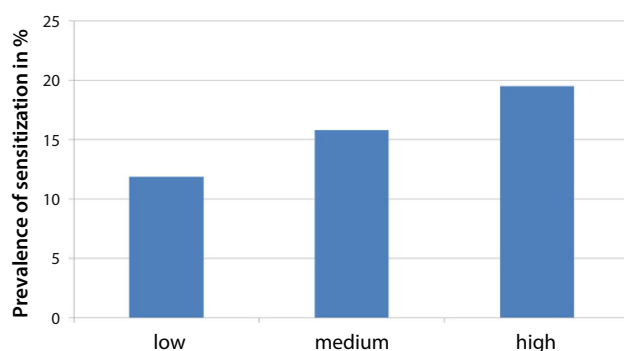


Fig. 5 Prevalence of sensitization to *dermatophagoides pteronyssinus* stratified by socioeconomic status. (After [1])

more highly educated and people with higher incomes are significantly more likely to have sensitizations by house dust mites (Fig. 5). Since they will not have more mites in their homes, offices or cars, other explanations like the “hygiene theory”, eating behavior or similar have to be used [4].

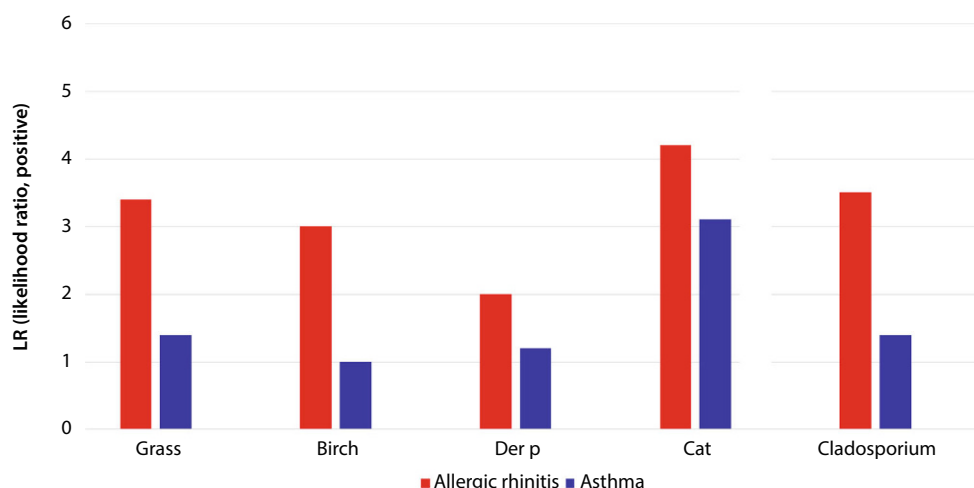
There are substantial differences in the prevalence of sensitization within Europe, as shown by an early study of 20- to 44-year-olds from 35 centers in 15 countries. Reactions to *D. pt.* in the prick test were very common in Europe at 21.7% (median) [5].

Medical risk of sensitization to dust mites

Any detectable presence of IgE-specific antibodies to an inhalant allergen in the blood or skin is a risk and is associated with an increased risk of developing allergic rhinitis and asthma, especially in school-aged children [6].

The risk of sensitization already in childhood became clear in the German Multicenter Allergy Study from 1990, in which 722 children were included after birth. In these children, the occurrence of allergic rhinitis and/or asthma was followed and documented by annual interviews until the age of 13 and again at

Fig. 6 Predictive diagnostic value for the development of allergic rhinitis or asthma in documented sensitization in schoolchildren (5–14 years) over a 9-year period. (After [7])



the age of 20. IgE antibodies to *D. pt.* were detectable in 26.5% of the participants. At 20 years of age, these were most frequently (>40%) antibodies to Der p 1, Der p 2, and Der p 23. Antibodies to Der p 5, Der p 7, Der p 4, and Der p 21 followed at 15–30%. Initially Der p 1, 2 and 23 were detectable, the others followed with increasing age. Children who had antibodies to Der p 1 or Der p 23 at age 5 years or younger had an increased risk of developing asthma at school age. Children with sensitization to multiple mite allergens were more likely to develop mite rhinitis as well as asthma [7].

Sensitization to Der p 23 seems to be of particular importance. In a 3-year observation, Jiménez-Feijoo et al. [8] found among 276 children with sensitizations to Der p 1, Der p 2, and Der p 23 that especially children with antibodies to all three allergens developed moderate to severe asthma. They recommend that special attention be paid to sensitization to Der p 23.

What is the significance of sensitization in childhood? For this purpose, Schäfer et al. [6] summarized the data of children (mean age 11.3 years, 52% boys) from 3 follow-up studies over (mean) 9 years (4–12 years) in eastern Germany, in which specific IgE against pollen of birch and grasses, house dust mite, cat and *Cladosporium* were measured.

In 1011 children with sensitization without disease, the 9-year incidence of asthma and hay fever was determined and regression analyses controlled for relevant confounders. Of these, 176 children developed allergic rhinitis (1.93%/year) and 78 developed asthma (0.86%/year). The strongest risk of developing allergic disease (rhinitis and/or asthma) was associated with sensitization to cat allergen, whereas house dust mites were least likely to cause rhinitis, but more likely to cause asthma (Fig. 6).

A study in Germany examined the predictive value of IgE antibodies in adults without known allergic diseases for the following 10 years. For this purpose, interviews and questionnaires of 2656 adults (25–74 years) were evaluated in 2004/2005, who had

already been examined in 1994/1995. Sensitizations (RAST) were an important predictor for the development of hay fever (OR 7.95, 95% CI 4.64–13.62) and asthma (odds ratio [OR] 1.82, 95% CI 1.29–2.57). Sensitization to outdoor airborne allergens, most common at baseline in 1994/1995 to pollen from birch and grasses, resulted in hay fever over the subsequent 10 years. Sensitization to dust mites and cat was a risk for developing asthma but not atopic dermatitis [9].

Sensitization rarely comes alone

In principle, sensitization to multiple allergens carries a higher risk of developing allergic rhinitis or asthma. What is the significance in this context of cosensitizations by house mites, e.g., in grass pollen allergy sufferers?

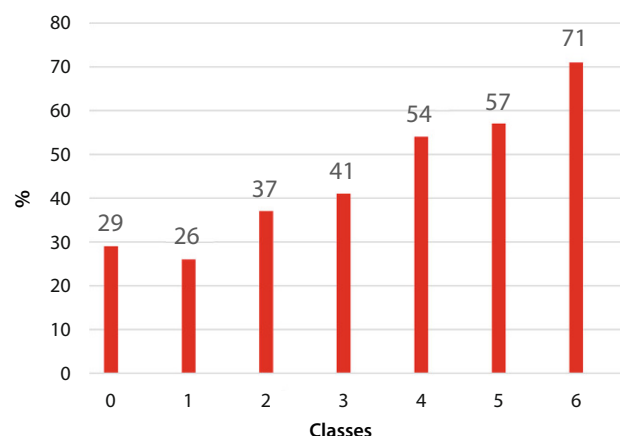


Fig. 7 Influence of cosensitization with IgE antibodies against *Dermatophagoides pteronyssinus* in grass pollen allergy sufferers on the frequency of asthma (%)—depending on the content of specific IgE against *Dermatophagoides pteronyssine* (classes 0–6). Classes: 0 = no sIgE, i.e., <0.35 kUA/l; 1 = 0.36–0.70 kUA/l; 2 = 0.71–3.50 kUA/l; 3 = 3.51–17.5 kUA/l; 4 = 17.51–50 kUA/l; 5 = 50–100 kUA/l; 6 ≥ 100 kUA/l. (According to [8])

In a study in Spain, it became clear that grass pollen allergic patients (positive for Phl p 1 and 5) also had sensitization to house mites in over 60%. Patients with this cosensitization had the highest risk of developing asthma depending on the degree of sensitization to *D. pt.* (d1; Fig. 7) and also of antibodies to *Lepidoglyphus destructor* [10]. In practice, this means that grass pollen allergic patients with additional mite sensitization are at particular risk of developing asthma—thus, allergen-specific immunotherapy should definitely be considered.

Sensitizations are not constant (detectable)

When stating the frequency of sensitization in a patient group or the total population, it must be taken into account that sensitization does not have to be constantly detectable. For example, results of the KiGGS cohort show that changes in sensitizations in children and adolescents occur over the course of 10 years. The determination of antibodies against an allergen mixture of eight common inhalation allergens (SX1 testing: timothy grass, rye, birch, mugwort, cat, house dust mite, *Cladosporium*; determinations with UNICAP 1000 [Phadia] test, positive from ≥ 0.35 kUA/l) showed significant changes: In girls, antibodies were no longer detectable in 11% with initially positive detection (KiGGS baseline survey; KiGGS=Study on the Health of Children and Adolescents in Germany) after 10 years in KiGGS wave 2, and in boys in 6%. On the other hand, 21% of initially nonsensitized girls became positive over 10 years; in boys, 29%. This clearly shows the dynamics of sensitization in childhood (Fig. 8).

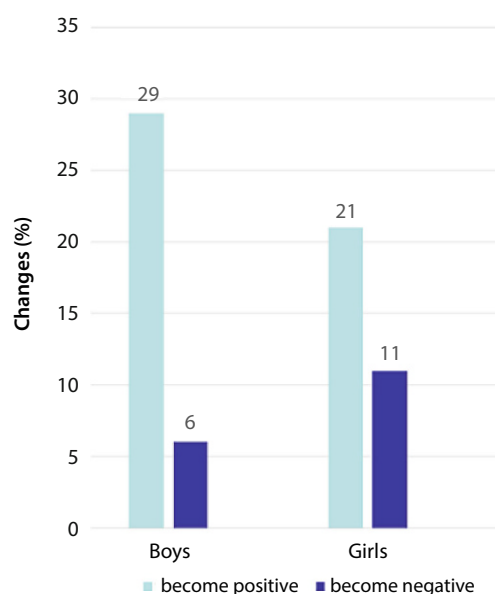


Fig. 8 Transition probabilities of sensitization to the allergen mixture (SX1) in the individual 10-year course (KiGGS basis to KiGGS wave 2) in girls ($n=2041$) and boys ($n=2143$). (After [11])

Overall, the progression of sensitizations for children and adolescents in Germany between 2003–2006 (KiGGS baseline survey) and 2014–2017 (KiGGS wave 2) did not reveal a statistically significant increase in sensitizations [11].

Problem and frequency of clinically silent sensitization

Every clinically active allergist has experienced it: A patient describes symptoms that point to rhinitis triggered by mites. The prick test is positive with mite allergens and/or IgE-specific antibodies are detectable in the blood. However, on nasal provocation, the patient experiences no symptoms and nasal flow does not decrease—the test is negative. A “clinically silent sensitization” was detected. This is not uncommon in cases of sensitization by mite allergens and may well lead to problems in the management of the present disease. In quite a few cases, a nasal hyperreactivity (rhinitis vasomotorica) is present in addition to the clinically silent sensitization.

In a 25-year observation, approximately 45% of individuals with a positive prick test and/or detection of IgE antibodies to *D. pt.* were without allergic rhinitis caused by *D. pt.* [12].

In a very recent and very systematic retrospective study from Munich with nasal provocations in 471 persons with clear anamnestic rhinoconjunctival complaints and a positive skin test with house dust mite allergen, 248 patients were positive in the nasal test (53%), but 223 persons (47%) were negative. Those patients who were positive in the nasal test were significantly more likely to also have atopic dermatitis (14% vs. 7%, $p=0.046$), but not asthma (20% vs. 19%, $p=0.851$). When comparing symptomatology, no differences were seen between the two groups in nasal obstruction, sleep quality, and ocular symptoms [13].

Thus, clinical data alone are usually insufficient to reliably identify allergic rhinitis due to mites, even when sensitization has been demonstrated.

A retrospective analysis was performed to determine whether the level of allergen-specific IgE antibodies to Der p 1 in 223 patients with positive or negative nasal tests could help distinguish clinically silent from clinically current sensitization [14]. This was also not the case.

Therefore, nasal provocation remains the gold standard to ensure the clinical relevance of sensitization against house dust mites—provided, however, that it is performed correctly, an optimal allergen extract containing all allergen components, and other parameters that are prerequisites for a correct result of provocation.

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Conflict of interest K.-C. Bergmann declares no conflicts of interest with the topic of house dust mites.

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