Exposure to indoor allergens and association with allergy symptoms of employees in a work environment

Barbara Brunetto(a), Sonia Brescianini(b), Bianca Barletta(a), Cinzia Butteroni(a), Daniela Rotondi(a), Rosalba Masciulli(d), Malaguti Aliberti(c), Carlo Pini(a), Gabriella Di Felice(a) and Patrizia Iacovacci(a)

(a) Centro Nazionale per la Ricerca e la Valutazione dei Prodotti Immunobiologici; (b) Centro Nazionale di Epidemiologia, Sorveglianza e Promozione della Salute; (c) Dipartimento di Malattie Infettive, Parassitarie ed Immunomediate; (d) Servizio Prevenzione e Protezione, Istituto Superiore di Sanità, Rome, Italy

Summary. Exposure to indoor allergens is an important risk factor for sensitisation and respiratory allergy. The aim of this paper was to evaluate the levels of mite, cat and latex allergens in dust collected from an indoor workplace and to assess whether the exposure to these allergens was associated with the allergy symptoms reported by employees. Sixty dust samples were collected. Allergen concentrations were measured with antibody based ELISAs. All 144 participants compiled a questionnaire exploring possible symptoms of allergy. No association between latex allergen exposure and symptoms was found in spite of the high frequency of latex allergens. Mite allergens were detected in a minority of rooms. Cat allergen was the most important indoor allergen in the sampled workplace and exposure to this allergen could represent a risk for employees.

Key words: asthma, cat allergen, indoor allergens, latex allergen, workplace.

Riassunto. (Esposizione agli allergeni indoor ed associazione con i sintomi di allergia dei dipendenti in un ambiente lavorativo). L’esposizione agli allergeni indoor costituisce un importante fattore di rischio per lo sviluppo di allergie. L’obiettivo di questo articolo è valutare i livelli degli allergeni degli acari, del gatto e del lattice in campioni di polvere raccolti in un ambiente lavorativo, al fine di stabilire una eventuale relazione tra l’esposizione a questi allergeni ed i sintomi di allergia manifestati dai dipendenti. La concentrazione degli allergeni è stata analizzata in sessanta campioni e 144 dipendenti hanno compilato un questionario avente lo scopo di valutare eventuali sintomi di allergia. Nonostante l’elevata frequenza degli allergeni del lattice, non esiste associazione tra sintomi ed esposizione a questi allergeni. La presenza di allergeni degli acari è stata riscontrata in una minoranza di ambienti. L’allergene del gatto è l’allergene indoor più diffuso nell’ambiente lavorativo esaminato e l’esposizione a tale allergene può costituire un rischio per i dipendenti.

Parole chiave: asma, allergene del gatto, allergeni indoor, allergeni del lattice, ambiente lavorativo.

INTRODUCTION

In industrialised countries people spend a large part of the day in indoor environments (offices, schools, hotels, public transports, domestic dwellings etc.). It is generally accepted that some allergic respiratory diseases such as asthma are the result of the interaction between genetic susceptibility and environmental exposures [1-8]. Furthermore, there is evidence of a dose response relationship between exposure and sensitisation to some indoor allergens, i.e. mite and cat allergens, or between allergen exposure and development of symptoms in allergic individuals. Cut-off concentrations for sensitisation (2 μg of allergen per gram dust) and for the development of symptoms (10 μg of allergen per gram dust) which were initially proposed for Der p I [9] were later also used for Der f 1. Similar cut-off values (sensitisation: 1-2 μg/g and development of symptom: 8-10 μg/g) have been proposed [10] for the cat allergen Fel d 1, another important allergen present in dust.

Address for correspondence: Barbara Brunetto, Centro per la Ricerca e la Valutazione dei Prodotti Immunobiologici, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy. E-mail: barbara.brunetto@iss.it.
However, the use of cut-off concentrations as threshold limits seems too restrictive, since it was shown that sensitisation can occur at lower mite allergen concentration [11]. This suggested that sensitisation towards such allergens should be studied without the use of cut-off concentrations [11].

On the other hand, nothing is known about the presence of latex allergens in dust collected from floors and other surfaces although the content of three representative allergens Hev b 1, Hev b 5 and Hev b 6.02 has been investigated in devices commonly used in hospitals [12]. Collecting information on indoor allergen exposure could be useful for at least two reasons: to assess risk factors for sensitisation and/or elicitation of symptoms in sensitised subjects and to address correctly the problem of reducing exposure levels, as strongly recommended in the most recent guidelines on asthma [13].

In the present paper we analysed dust samples collected from a research institute with laboratories and offices, taken as a paradigm of work environment. The peculiar characteristics of this environment gave us the opportunity to investigate the levels of common indoor allergens (i.e. mite and cat allergens), and to assess the presence of latex allergens, since latex gloves are routinely used in laboratories. To this aim, we analysed the level of the following allergens: Hev b 5, Hev b 6.02, Der p 1, Der f 1, Mite group 2, Fel d 1. Furthermore, we attempted to evaluate the association between exposure to these allergens and the allergy symptoms reported by people working in this workplace.

**METHODS**

**Sampling sites**

Sixty dust samples were collected between May and June 2004 in a research institute in Rome (Istituto Superiore di Sanità). Twenty four samples out of 60 were from laboratories, 36 from offices.

Environmental characteristics were also recorded. Temperature and relative humidity were collected by using a Q-TRAK (TSI instruments, Montreal, Québec).

No major structural differences were recorded in the two types of work environment considered (i.e. laboratories and offices). In both cases floor and other surfaces are cleaned with detergents and disinfectants about twice a week. Generally, offices are smaller than laboratories and furniture is quite different in the two categories of environment. People density is generally higher in offices than in laboratories. Another relevant difference between the two kinds of environments is that the usage and storage of gloves is restricted to laboratories.

**Dust collection and analysis**

Collection was performed as described by Dreborg et al. [14] with some modifications. Briefly, trained technicians collected the samples in a standardised manner by using the mitest Dust Collector by Indoor Biotechnologies (Cardiff, UK). We used a vacuum cleaner Miele Electronic 1600 W (Gütersloh Westfalia Germany). Dust samples were collected from floors, chairs (usually not upholstered), floor under the desks and desk surfaces in offices, and essentially from floors in laboratories.

Each room was vacuumed for a total time of 15 minutes. Routine cleaning was stopped in the selected rooms one week before dust sampling. Procedures for preparation and analysis of dust samples were essentially those suggested by quantitative ELISA kits (Indoor Biotechnologies). Allergen content of the supernatant was measured for Der p 1, Der f 1, Mite group 2, Fel d 1.

The kits used for latex allergens, Hev b 5 and Hev b 6.02 (FITkit, Indoor Biotechnologies) have been validated to test such allergens in glove extracts. In absence of other kits specifically designed for the evaluation of latex allergens in environmental dust samples, we adapted these kits to analyse Hev b 5 and Hev b 6.02 in dust extracts. Hev b 5 and Hev b 6.02 were also tested in glove extract as a positive control. Furthermore, we spiked pre-determined concentrations of both the allergens in dust extracts to evaluate possible interference with kit performance of other substances present in dust.

The results were obtained in ng of allergen/ml of sample (mite and cat allergens) or μg of allergen/l of sample (Hev b 5 and Hev b 6.02), and then converted in μg of allergen/g of dust. In this way, we were able to compare (essentially for mite and cat allergens) such data with the risk threshold for sensitisation and elicitation of symptoms.

Each value higher than the quantitative limit of the assay (LOQ) was regarded as “positive” (LOQ: Hev b 5 = 0.01 μg/g; Hev b 6.02 = 0.002 μg/g; Der f 1 = 0.07 μg/g; Der p 1 = 0.2 μg/g; Mite group 2 = 0.06 μg/g; Fel d 1 = 0.5 μg/g).

**Population**

People who had been working in the analysed workplace for at least 6 years (220 subjects in laboratories and/or offices) were asked to participate in the present study. One hundred and forty four subjects gave their informed consent (response rate: 65%), serum samples were collected and stored at -20 °C until use.

**Questionnaire**

All participants (144) were asked to complete a questionnaire exploring personal and family history of allergic diseases. The questionnaire was a simplified version of those previously reported [15, 16]. The questionnaire collected demographic data (age, sex, job, title), smoking habits, data on the work environment (ventilation, local air-conditioning, centralized air-conditioning, relative humidity and temperature), information about allergy symptoms of participants (asthma, rhinoconjunctivitis, urticaria) and family atopy. “Asthma” was defined as wheezing or whistling in the chest, or dry cough
at night (apart from cough associated with cold or chest infection), “Rhinoconjunctivitis” as sneezing, runny or blocked nose without having cold or flu. “Urticaria” was broadly defined in a more general meaning of the word including itching and/or cutaneous eruption.

It is important to underline that the questionnaire was self-reported and answers were “yes” or “no” to specific questions. For example, the question on history of allergy symptoms was asked as follows: “Have you ever suffered from the following symptoms?”. For each symptom (asthma symptoms, rhinoconjunctivitis and urticaria), the answer was “yes” or “no”. At the end of the questionnaire it was asked whether people had previously taken a skin prick test for allergy diagnosis. When the answer was “yes”, positive results were reported.

**Specific IgE**

Specific IgE in vitro detection was performed by CAP System (Pharmacia & Upjohn, Uppsala, Sweden). The allergen panel used for testing included mite (Dermatophagoides farinae), latex (Hevea brasiliensis), cat epithelium and dander.

The lower limit of the assay for specific IgE in vitro detection is 0.35 kU/L. Each value higher than this limit was regarded as “positive”.

**Statistical analysis**

Concentrations of different allergens were not normally distributed and were transformed using the logarithm base 10 scale in order to allow the use of parametric tests. Frequencies of detectable samples were compared using the chi² test or Fisher exact test when appropriate. The mean values of the transformed variables were then compared using the t-test for two groups. Comparisons were considered to be significant if p<0.05.

For each allergen under study the geometric mean and the 95% confidence intervals (95% CI) of the values higher than zero were calculated. In order to estimate the relative risk of reporting some kind of allergy symptoms for people working in rooms with detectable allergen concentrations, univariate and multiple logistic regression models were applied. Each subject working in a room with a detectable level of allergen was considered to be exposed to this allergen.

Four different models were estimated having the following outcomes: any symptom of allergy, rhinoconjunctivitis, asthma and urticaria (itching and/or cutaneous eruption). Only symptoms declared to occur during working hours were included in the analysis.

Independent variables included in the models were: age, gender, current smoking status, specific IgE values (present or absent), family history of allergy, latex allergens (present or absent), cat allergen (present or absent), room temperature, relative humidity, previous diagnosis of allergy (allergy test taken “yes or no”). In particular, we have included in the multivariate analysis all the covariates reported above that resulted with a significant OR (p-value <0.2) for at least one of the considered outcomes in the univariate analysis. Mites exposure was not included in the models because of the small number of exposed subjects.

**RESULTS**

**Environmental characteristics of work-places**

Relative humidity range was 39.2%-61.3% (mean 49.1% ± 5 SD ), temperature 19.7 °C -27.1 °C (mean 23.1 °C ± 1.9 SD). Most of rooms (70.1%) were ventilated by windows, in some cases a local air-conditioner (59.0%) or a centralised air-conditioner (23.6%) was also present. No significant differences in these parameters were recorded between laboratories and offices.

**Distribution and level of indoor allergens**

The frequency of rooms in which allergens were found and the allergen concentrations are shown in Table 1.

<table>
<thead>
<tr>
<th>Allergen</th>
<th>Samples from laboratories with detectable allergen (N=24)</th>
<th>Geometric mean of values in laboratories (95% CI) (n)</th>
<th>Samples from offices with detectable allergen (N=36)</th>
<th>Geometric mean of values in offices (95% CI) (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Der f 1</td>
<td>4.2%</td>
<td>7.90 μg/g (1)</td>
<td>2.8%</td>
<td>1.43 μg/g (1)</td>
</tr>
<tr>
<td>Der p 1</td>
<td>4.2%</td>
<td>1.53 μg/g (1)</td>
<td>2.8%</td>
<td>1.78 μg/g (1)</td>
</tr>
<tr>
<td>Mite Group 2</td>
<td>8.3%</td>
<td>1.08 μg/g (2) (0.008-135.83)</td>
<td>5.5%</td>
<td>4.28 μg/g (2) (2.25-8.17)</td>
</tr>
<tr>
<td>Fel d 1</td>
<td>58.3%</td>
<td>7.74 μg/g (14) (2.97-20.2)</td>
<td>77.8%</td>
<td>4.84 μg/g (28) (3.12-7.49)</td>
</tr>
<tr>
<td>Hev b 5</td>
<td>50%</td>
<td>0.34 μg/g (12) (0.19-0.61)</td>
<td>22.2%</td>
<td>0.21 μg/g (8) (0.14-0.31)</td>
</tr>
<tr>
<td>Hev b 6.02</td>
<td>87%</td>
<td>0.36 μg/g (21) (0.24-0.54)</td>
<td>38.9%</td>
<td>0.26 μg/g (14) (0.18-0.43)</td>
</tr>
</tbody>
</table>

N= number of samples analysed; (n)= number of positive samples.
Table 1. Mite allergens were detected in a minority of rooms (13%, Table 1) whereas cat allergen Fel d 1 was detected at high frequency in laboratories and in offices (58.3% and 77.8%, respectively, \( \chi^2 \) p-value = 0.107). Regarding the latex allergens, both the components Hev b 5 and Hev b 6.02 were found at higher frequency in laboratories (50.0% and 87.0%, respectively) than in offices (22.2% and 38.9%). Frequency comparison using \( \chi^2 \) test showed significant differences (p-value = 0.025 and p-value < 0.001 for Hev b 5 and Hev b 6.02, respectively).

The highest allergen levels were detected for Fel d 1 in samples from both laboratories and offices (geometric mean of values 7.74 μg allergen/g dust and 4.84 μg/g, respectively, Table 1 and Figure 1). In particular, in 12 out of 60 (20%) of rooms, levels of Fel d 1 were above the symptoms developing threshold. Although mite allergens (Der f 1, Der p 1, Mite group 2) were not common, concentration values were in three cases higher than the proposed sensitisation threshold (2 μg/g), and in one case over the threshold for symptom development (10 μg/g). Latex allergens were detected in the concentration range 0.13 μg/g -0.40 μg/g. Means of log transformed values of Fel d 1, and latex allergens were compared using a t-test. No statistically significant difference was detected. Furthermore, results from spiking experiments demonstrated no interference with the test performance by other substances present in dust (data not shown).

Characteristics of population

One hundred and forty four subjects were analysed (Table 2). Unfortunately, the response rate was only 65% and we have no information to compare respondents with non respondents apart from age and sex distributions that did not differ among the two groups. The mean age was 43.2 (± 8.23 SD) years. All the employees included in the study spent at least 8 hours/day in their work environment (5 days/week).

Of the 144 subjects who answered to the questionnaire, 51 reported at least one allergy symptom, 78 no symptom, and 15 subjects did not answer.

Forty four out of 144 subjects responded having previously taken a test for allergy diagnosis. Among these, 12 were positive to mite, 3 to latex and 8 to cat epithelia.

Other common allergies resulting from diagnostic tests were not related to indoor environment and included pollens, drugs, insect venom as well as foods. Thirty five out of 144 subjects had a cat at home (16 from laboratories and 19 from offices).

Specific IgE

Serum samples were collected from the 144 subjects and specific IgE for mite, cat and latex allergens were determined (Table 2). Twenty per cent of subjects were positive to mite, 11.81% to cat epithelium and dander, and 2.08% to latex.

Regression analysis

The univariate analysis (data not shown) was performed to evaluate whether the reporting of symptoms (asthma, rhinoconjunctivitis, urticaria) was associated with the following factors one at a time: gender, age, current smoking status, environmental characteristics (room temperature and relative humidity), family history of allergy, previous diagnosis by means of an allergy test (yes or no), exposition to Hev b 5, Hev b 6 and Fel d 1 allergen, specific IgE to mite allergens, specific IgE to cat epithelia and dander. Family atopy and previous test for allergy were significantly positively associated with two groups.

Table 2 | Summary of population characteristics (mean age: 43.2 ± 8.23 SD). Total number of subjects =144

<table>
<thead>
<tr>
<th>Characteristics of population</th>
<th>Subjects n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>36 (28.00)</td>
</tr>
<tr>
<td>Female</td>
<td>114 (79.17)</td>
</tr>
<tr>
<td>Family atopy</td>
<td>32 (25.00)</td>
</tr>
<tr>
<td>Previously diagnosis (allergy test)</td>
<td>44 (35.77)</td>
</tr>
<tr>
<td>Subjects exposed to Hev b 5</td>
<td>45 (37.82)</td>
</tr>
<tr>
<td>Subjects exposed to Hev b 6</td>
<td>76 (61.29)</td>
</tr>
<tr>
<td>Subjects exposed to Fel d 1</td>
<td>95 (76.00)</td>
</tr>
<tr>
<td>Specific IgE for mite</td>
<td>29 (20.14)</td>
</tr>
<tr>
<td>Specific IgE for cat epithelium and dander</td>
<td>17 (11.81)</td>
</tr>
<tr>
<td>Specific IgE for latex</td>
<td>3 (2.08)</td>
</tr>
<tr>
<td>Outcome (symptoms)</td>
<td></td>
</tr>
<tr>
<td>Any symptom</td>
<td>51 (39.53)</td>
</tr>
<tr>
<td>Rhinoconjunctivitis</td>
<td>39 (30.23)</td>
</tr>
<tr>
<td>Urticaria</td>
<td>17 (13.28)</td>
</tr>
<tr>
<td>Asthma</td>
<td>14 (10.94)</td>
</tr>
</tbody>
</table>

n = number of subjects.
symptoms (all together and separately). Similarly, IgE antibodies to cat epithelium and dander were significantly positively associated with all symptoms except rhinoconjunctivitis. Urticaria symptoms were also significantly associated with current smoking (negatively) and age (positively).

Four multivariate logistic regression models, one for each outcome (rhinoconjunctivitis, urticaria, asthma and at least one among those) were performed. The regression models that included, among the covariates, all the factors reported above, were estimated on 95 subjects due to the presence of missing values on some of the covariates. We could not include specific IgE to latex because of estimation problems.

No significant associations of latex or cat allergen exposure with higher risk for considered outcomes were found, except for Fel d 1 exposure and asthma symptoms. In details, when the symptoms were examined altogether (at least one among asthma, rhinoconjunctivitis, urticaria), statistically significant associations were found for room temperature (OR = 2.52, 95% CI: 1.29-4.94, p = 0.01), specific IgE for cat epithelium and dander (OR = 69.39, 95% CI: 1.89-2542.50, p = 0.02). In the last model, subjects exposed to Fel d 1 were 7 times more likely to report itching and/or cutaneous eruption but the association did not reach statistical significance. As regards asthma symptoms, the results demonstrated that it is associated with age (OR = 1.23 per year of age, 95% CI: 1.04-1.45, p = 0.01), family atopy (OR = 10.61, 95% CI: 1.45-77.65, p = 0.02) and exposure to cat allergen (OR = 40.05, 95% CI: 1.38-1159.89, p = 0.03). It is noteworthy that the univariate OR for IgE antibodies to cat epithelium and dander is positively associated with asthma symptoms (OR = 4.0, 95% CI: 1.3-12.8, p = 0.011) in the univariate analysis while they are negatively, even if not significantly, associated in the multivariate analysis.

In all models the variable “previously taken test for allergy” was a significant predictor of the outcome (Table 3).

![Table 3](image)

**DISCUSSION**

Allergen avoidance or separation of the allergic patient from the allergen source, when possible, is the most effective and least expensive way of treating human allergic disease [17-20]. Due to availability of reproducible and validated immunoenzymetric assays for the quantification of indoor allergen levels, it is possible to maintain such levels under the cut-off concentration for sensitisation and for the development of symptoms (asthma and allergy exacerbation) allowing the allergic patient to monitor the
effectiveness of environmental remediation actions [19]. Due to the fact that most people spend a large part of daily time at work, we thought it would have been important to analyse a model situation taking as an example a research institute, which encompasses a mixture of administrative as well as research and laboratory activities. A large number of subjects working in the institute reported having problems with allergic symptoms (asthma, rhinoconjunctivitis, urticaria etc.) during a routine annual check-up carried out by the internal Occupational Safety and Health Service. In order to monitor a possible association between symptoms and the presence of allergens in such an environment, we first decided to quantify the indoor allergen exposure. We measured the most common allergens such as Der p 1, Der f 1, Mite group 2 from dust mites, Fel d 1 from cat and, finally, Hev b 5 and Hev b 6.02 from latex, since latex gloves are commonly used by researchers during their laboratory work.

Dust samples were collected and analysed from both offices and laboratories and data on relative humidity and temperature were taken in the same environments. It has to be underlined that, although in this research institute offices and laboratories are located in different rooms, often only a door can separate them and researchers spend their time in both places.

Although relative humidity and temperature were in the range defined optimal for mite growth [21-23] in about 50% of rooms examined, mite allergens were found in a minority of rooms and in one case only concentration value was over the cut-off threshold for the elicitation of symptoms [2]. Results obtained by our group were quite different than those obtained by others [24-27], perhaps because samples were collected from surfaces that were not upholstered (i.e. usually leather chairs are present in offices and wooden stools in laboratories). In fact, when in a parallel study we analysed samples from homes (i.e. collected from some upholstered surfaces), we found a high frequency of rooms with a high concentration of mite allergens. Since twenty per cent of examined subjects had specific IgE for mite, we can conclude that the almost total absence of mite allergens is an interesting result, suggesting that exposure in the work environment, at least in our model, does not appear to be determinant for sensitisation and/or elicitation of symptoms.

On the contrary, very high concentrations of Fel d 1 were detected in many samples. These data were comparable to those from other studies [28, 29] reporting the ubiquity of cat allergen Fel d 1. Furthermore, the results suggest that, since about 12% of subjects had specific IgE for cat epithelia, adequate cleaning measures may be necessary in order to avoid challenging situation occurring during working hours.

An important and original aspect of the present study was our attempt to analyse the level of latex allergens (Hev b 5 and Hev b 6.02) directly in dust. These allergens have already been found in extracts from gloves and other medical devices [12] and in airborne particles [30], but we thought interesting to analyse them in dust because they could precipitate when associated to other particles and, after air disturbance, they could be resuspended and inhaled to cause conjunctivitis, rhinitis and asthma. Our hypothesis was strengthened by results, in fact both the components Hev b 5 and Hev b 6.02 were found in laboratories as well as in offices. The higher frequency in laboratories is not surprising due to a prevalent use of gloves in such environments but, since laboratories and offices are often next to each other, frequency of latex allergens in the latter was equally high. Furthermore, the higher frequency of Hev b 6.02 than Hev b 5 is in agreement with data reported by Crippa et al. [12]. In fact, the presence of the first was demonstrated in all glove extracts examined, whereas it was necessary to concentrate the extracts to detect Hev b 5. Probably, since Hev b 6.02 is present at higher concentrations in gloves, it is more dispersed in dust and therefore detectable at higher frequency.

Finally, we evaluated by means of a multivariate logistic regression whether any relation between symptoms self-reported by people and exposure to the evaluated allergens would exist, as well as with the other factors reported in Table 3.

As concerns rhinoconjunctivitis, we found an association only with family atopy, whereas environmental factors, including exposure to the studied allergens, do not seem to be significantly associated to such symptom. More interesting results were obtained when we examined asthma. Our data showed that asthma symptoms are associated with age, family atopy and exposure to Fel d 1. Exposure to cat allergen could therefore represent a risk for people working in these environments even if these results have to be interpreted with caution because of the small sample size. Similar data were obtained when itching and cutaneous eruption were examined. In fact, people who declared to suffer from these symptoms had higher level of cat allergens specific IgE in their sera. Moreover, people exposed to Fel d 1 were 7-times more likely to report such episodes although the association did not reach statistical significance.

We have found current smoking associated with the outcome “any symptom” and with urticaria. We think that this is a reverse causality result. Probably, allergic subjects tend to smoke less than non allergic ones after they developed the symptom/disease.

Despite the high frequency of latex allergens observed, we did not find any association between symptoms and exposure to these allergens. Since a cut-off level for the sensitisation and the elicitation of symptoms by latex allergens has not been defined, we can only argue that the concentration levels are not high enough to represent a risk. As for other indoor allergens it could be interesting to evaluate these cut-off levels in ad hoc studies.
In summary, although family history of atopy is a major predictor for symptom development, the factors above described remain significant.

Some limitations of the present study are the response rate (65%) and the difficulty to establish the association between exposure and sensitisation due to the lack of information about exposure in other environments (public transport, home etc.). The low response rate decreased the already not too high initial sample size, making the estimates less precise. Despite these difficulties, our data clearly show that Fel d 1 rather than mite allergens [20, 21, 31] is the most represented allergen, suggesting the former as a real problem in work environments. The analysis of the distribution of the various allergens in the institute indicates a marked discrepancy in the presence of indoor allergens in the same environment. This finding might be linked to the cleaning measures adopted, that are quite efficacious for mite, but are only to minor extent able to remove cat allergen.

It has been demonstrated that cat allergen can be transported into environments where cats have never been present through the clothes of cat owners, and their stickiness leads to widespread distribution in public building, which would explain the concentration and distribution of Fel d 1. At present, the most important remediation measure to reduce exposure to cat allergen particles is the introduction of more specific and vigorous environmental control measures [17].

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