

# Is there a need for special preventive medical check-ups in employees exposed to experimental animal dust?

Klaus Schmid · Barbara Jüngert ·  
Meta Hager · Hans Drexler

Received: 19 October 2007 / Accepted: 4 June 2008  
© Springer-Verlag 2008

## Abstract

**Objective** Due to new legal requirements in Germany, the employer must request preventive medical check-ups for activities involving exposure to dust from experimental animals in the rooms in which the animals are kept. The objective is to report our first experiences with these medical check-ups in the context of academic research.

**Methods** The check-ups were carried out since November 2005 and comprised a questionnaire and a medical examination, including a pulmonary function test with whole-body plethysmography. Respiratory, nasal and ocular symptoms related to occupational exposure to animals were documented. Participation in skin prick tests (ubiquitous inhalation allergens and laboratory animal allergens), a bronchial provocation test with methacholine, and serological examinations for total IgE and specific IgE antibodies was voluntary.

**Results** Data on 132 persons are presented. One hundred and six of these had already been exposed for at least 1 year. Main complaints at the workplace were sneezing and runny nose. Ocular symptoms and bronchial asthma were reported infrequently. The development of at least one of these symptoms occurred in 34% of employees with an exposure of at least 1 year. If the weekly exposure duration was at least 5 h, the proportion of employees with complaints rose to 44.9%. In employees occupationally exposed to mice and rats, work-related complaints occurred in 33.7 and 37.8%, respectively, and sensitisation rates were 12.7

and 16.3%, respectively. Employees with and without complaints differed in history of allergic symptoms, and workplace safety measures.

**Conclusions** In employees with occupational contact with laboratory animal dust, the frequency of complaints was high. The results confirm the necessity of regular medical check-ups for employees with contact with laboratory animal dust. Nevertheless, the medical check-ups must be part of a prevention strategy including education, engineering controls, administrative controls, use of personal protective equipment and vocational integration.

**Keywords** Occupational exposure · Laboratory animals · Sensitisation · Preventive medical check-ups · University research

## Introduction

Animal allergy (e.g. dog and cat) is an important health problem in the general population, and also in those who work in animal shelters (Krakowiak et al. 2007a) or veterinarians (Krakowiak et al. 2007b). In research laboratories, mainly rats and mice are used and allergy is a significant occupational hazard for workers in a number of research settings, including universities. Symptoms may progress from conjunctivitis and rhinitis to asthma. In recent years, most major laboratory animal allergens have been identified and characterized, and various epidemiological studies have been carried out concerning animal-related symptoms and specific sensitisation (Bush and Stave 2003). Epidemiological studies have shown that between 11 and 44% of the individuals working with laboratory animals report work-related allergic symptoms (Bush and Stave 2003). Prevention, safety at work, education, reduction of exposure

K. Schmid (✉) · B. Jüngert · M. Hager · H. Drexler  
Institute and Outpatient Clinic of Occupational,  
Social and Environmental Medicine of the University  
Erlangen-Nuremberg, Schillerstrasse 25+29,  
91054 Erlangen, Germany  
e-mail: klaus.schmid@rzmail.uni-erlangen.de

and early detection of allergies are important, because the illness can affect both health and career.

Meanwhile, awareness of the disease has increased. The New German Hazardous Substances Ordinance from December 2004 includes experimental animal dust as a hazardous substance (Ordinance on Hazardous Substances 2004). The employer must request preventive medical check-ups for activities involving exposure to animal dust in the rooms in which animals are kept. Preventive medical check-ups are now mandatory for working with experimental animals. In cases of clinically relevant allergies, occupational health physicians can object to further allergen contact. When confronting our scientists with the need for medical check-ups, acceptance was not very good, possibly from fear of negative consequences for their future scientific careers.

When starting our investigation, a brand-new central department for animal experiments with all necessary safety equipment went into service. Nevertheless, it should be taken into consideration that most employees included in our study had worked previously at different peripheral laboratories under suboptimal working conditions.

The data presented here were not collected in the context of a clinical survey, but rather during everyday life, i.e. regular medical check-ups according to legal requirements. The medical check-ups were carried out in accordance with German guidelines and included the completion of a standardised questionnaire and a medical examination, which included a pulmonary function test with whole-body plethysmography. In addition, allergy tests were offered. As early laboratory animal allergy seemed to be associated with increased bronchial responsiveness (Renström et al. 1995), a bronchial provocation test was also recommended.

When introducing new preventive medical check-ups, it is necessary to consider what benefit they bring and whether there is a real need for this medical surveillance. From a scientific viewpoint, the routine monitoring of persons exposed to experimental animal dust will shed light on the prevalence, incidence, risk factors, disease course, and intervention. Here, we report our first experiences with these medical check-ups in the context of academic research.

## Methods

### Study population

The medical check-ups were carried out at the University Erlangen–Nuremberg since November 2005. All employees coming in contact with experimental animal dust were included. Fifty-six executive investigators from 32 institutes and clinics with a licence to conduct animal experiments were informed about the new ordinance, and were

requested to send their employees for the medical check-ups. The completion of a standardised questionnaire and a medical examination, including a pulmonary function test with whole-body plethysmography, were mandatory. Participation in skin prick tests, a bronchial provocation test with methacholine, and serological examinations for total IgE and specific IgE antibodies was voluntary.

### Ethics

The occupational health medicals were performed as obligatory preventive medical check-ups in accordance to the German Hazardous Substances Ordinance. Therefore, consultation with an ethics committee was not necessary. The scope of examinations was carried out in accordance with German guidelines (Berufsgenossenschaftlicher Grundsatz für arbeitsmedizinische Vorsorgeuntersuchungen G23) (Hauptverband der gewerblichen Berufsgenossenschaften 2004). Nevertheless, participation in skin prick tests, a bronchial provocation test with methacholine, and the taking of blood samples was voluntary. Written informed consent was obtained before carrying out these tests. The data collected were anonymized in accordance with legal requirements regarding data protection and medical confidentiality.

### Questionnaire

The questionnaire inquired about general respiratory, nasal, ocular and skin symptoms, smoking habit, and personal and family history of allergic diseases. The questionnaire items also included job characteristics and a description of occupational exposure. In particular, symptoms related to occupational exposure to animals were documented.

### Skin prick tests

Skin prick tests were performed and interpreted according to the recommendations of the European Academy of Allergology and Clinical Immunology. A wheal diameter of at least 3 mm was considered positive in the absence of a reaction to NaCl, and in the presence of a positive reaction to histamine. Commercially available extracts were used (Allergopharma, Joachim Ganzer KG, Reinbek, Germany). The allergens included environmental allergens (one mixture of grass and cereals, two mixtures of tree pollens, two mould mixtures, *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*) and extracts from animal epithelium (mouse, rat, cat, dog, guinea pig, golden hamster and rabbit).

### Serological testing

We offered serological examinations for total IgE and specific IgE antibodies. For reasons of economy, serological

examination for specific IgE antibodies against rat and mouse epithelia and proteins (Pharmacia Upjohn Diagnostics, Uppsala, Sweden) was offered only in cases of positive skin prick test and/or work-related symptoms.

### Pulmonary function

A pulmonary function test was performed with whole-body plethysmography (MasterScreen Body; VIASYS Healthcare, Höchberg, Germany). Bronchial provocation test was performed in accordance with the recommendations of the “German Society for Occupational and Environmental Medicine” (DGAUM 2004). Methacholine was administered in five steps starting with a dose of 0.015 mg.

### Statistical analysis

Data were analysed using SPSS version 15.0 for windows. Descriptive statistics were used to identify the demographic and subject-related details. Univariate tests (e.g. Mann–Whitney *U* test or chi-square test) and logistic regression analysis were used to establish whether samples differed significantly.  $P < 0.05$  was considered statistically significant.

## Results

So far, data from 132 persons (48 men and 84 women) are presented. Mean age was  $33.2 \pm 9.1$  years. Sixty employees (45.5%) were working as scientists, 34 (25.8%) as assistant medical technicians, 21 (15.9%) as animal keepers and 17 (12.9%) as crafts persons or cleaning personnel. The persons had worked with laboratory animals for about 3 years (median) with a median weekly exposure of 4 h.

One hundred and six (80.3%) of these had already been exposed for at least 1 year, 49 of whom had at least 5 h

weekly exposure to experimental animal dust. Research with mice (87.9%) and rats (70.2%) was most common.

Participation in the voluntary tests was good. Skin prick tests were performed in 78.8%, bronchial provocation tests in 73.5%, and serological examinations for total IgE in 86.4%. In 32 (24.2%) cases, serological examinations for specific IgE antibodies were considered necessary due to positive skin prick tests and/or work-related symptoms.

Major complaints at the workplace were sneezing and runny nose. Ocular symptoms and bronchial asthma were reported infrequently. Complaints were generally more frequent in those persons with a weekly exposure to experimental animal dust for at least 5 h. The development of at least one of these symptoms occurred in 34% of employees with an exposure of at least 1 year. If the weekly exposure duration was at least 5 h, the proportion of employees with complaints rose to 44.9% (Fig. 1).

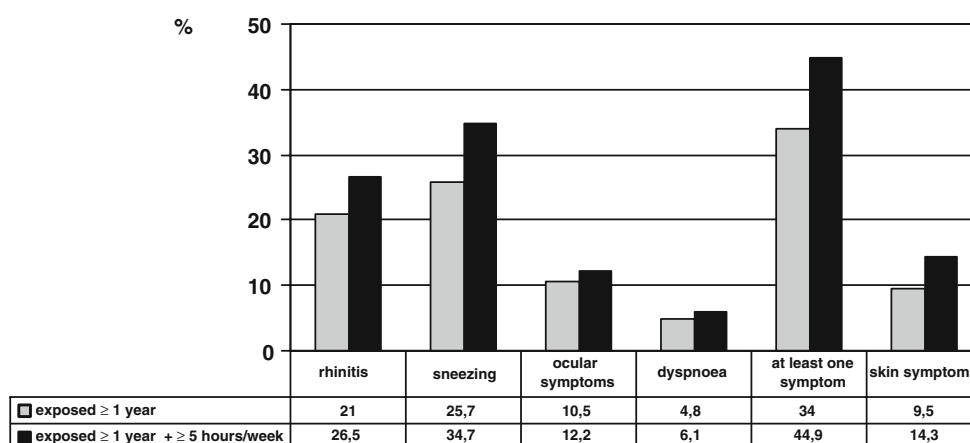
When testing ubiquitous inhalation allergens, positive reactions were mainly seen with grass pollen (30%). Positive test results against ubiquitous inhalation allergens were seen both in beginners and in those exposed for at least 1 year. Concerning laboratory animals, positive skin prick tests were common with allergens from mouse (8%) and rat (8%) only in those employees already occupationally exposed.

In those persons, with a positive test result concerning rat and/or mouse allergens 31.3% had an asymptomatic sensitization. Rhinitis and/or conjunctivitis occurred in 43.7%, whereas 25.0% reported about additional pulmonary symptoms. Thirty-three percent of the sensitized employees reported also about skin problems and in one case typical signs of contact urticaria occurred.

In persons exposed to experimental animal dust for less than 1 year, no positive test results against allergens from mouse or rat were observed. (Figure 2).

Considering the results of tests for specific IgE antibodies, the frequency of positive results in employees with at

**Fig. 1** Prevalence of work-related symptoms of a type I allergy (rhinitis, sneezing, ocular symptoms, dyspnoea) were given as well as the percentage for the occurrence of at least one of these symptoms in workers exposed to experimental animal dust for  $\geq 1$  year, and for  $\geq 1$  year and  $\geq 5$  h/week. Additionally, the prevalence of skin symptoms was shown



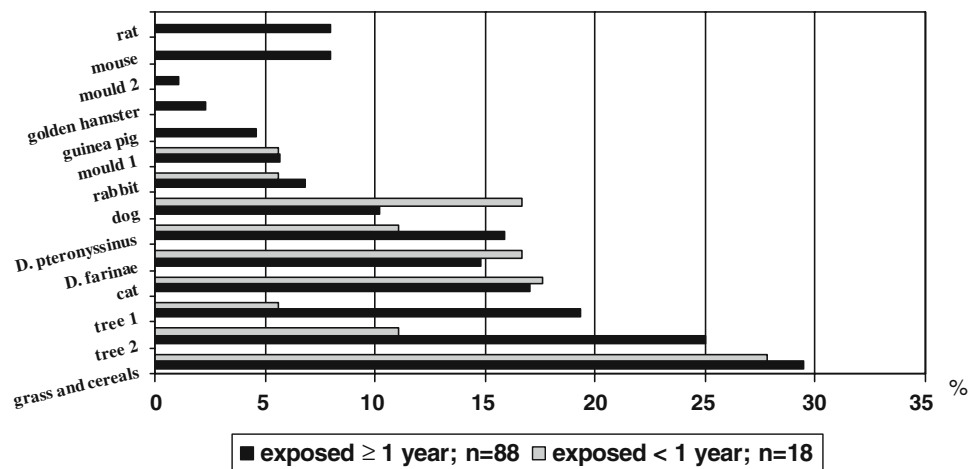


**Fig. 2** Frequency of positive skin prick test in 106 employees who agreed to participate, separately displayed for workers exposed for  $\geq 1$  year (black bars) and  $< 1$  year (grey bars). Allergen mixtures were: Mould 2: mixture of *Aspergillus fumigatus*, *Mucor mucedo*, *Penicillium notatum*, *Pullularia pullulans*, *Rhizopus nigricans*, *Serpula lacrymans*. Mould 1: mixture of *Alternaria tenuis*, *Botrytis cinerea*,

*Cladosporium herbarum*, *Curvularia lunata*, *Fusarium moniliforme*, *Helminthosporium halodes*. Tree 1: mixture of early-blooming trees (alder, hazel, poplar, elm, willow tree); Tree 2: mixture of mid-blooming trees (birch, beech, oak, plane tree); Grass and cereals: mixture of grasses, barley, oat, rye, wheat

least 1 year occupational exposure to mice was 12.7% (Fig. 3) and 16.3% for rats (Fig. 4). Clinically relevant sensitisation against allergens from mice and rats was seen in 9.5 and 12.2%, respectively (Figs. 3, 4). The frequency of work-related complaints in employees with at least 1 year of occupational exposure to mice or rats was 33.7 and 37.8%, respectively. However, in  $\sim 65\%$  of these employees with work-related complaints, negative test results were documented for the corresponding animal allergens when using our test procedure with regular skin-prick test and specific IgE antibodies only in certain cases. In employees with a complaint, but a negative test result, total IgE was significantly lower in comparison to that in persons in whom the complaint could be explained by positive test

results (median values 27.0 vs. 343.5 IU/mL;  $P < 0.01$ ; Mann–Whitney  $U$  test).

Altogether, 106 employees were exposed to experimental animal dust for at least 1 year. When comparing persons with work-related complaints and symptom-free employees, we found differences in exposure data, anamnestic data and test results (Table 1). Those with complaints were exposed to experimental animal dust for more hours per week; they used an FFP2 mask more often; and they frequently had a history of hay fever, rhinitis, allergic conjunctivitis to ubiquitous allergens and a positive skin prick test. In pulmonary function tests, the specific resistance was elevated. Employees with work-related complaints had a higher total serum IgE level and were more often sensitised

**Fig. 3** Prevalence of complaints and positive test results in workers exposed to mice for  $\geq 1$  year

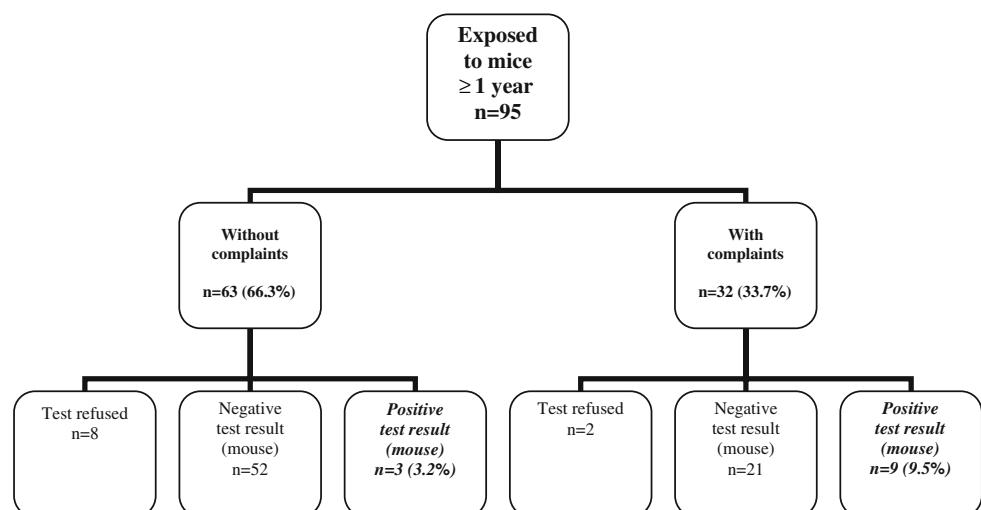
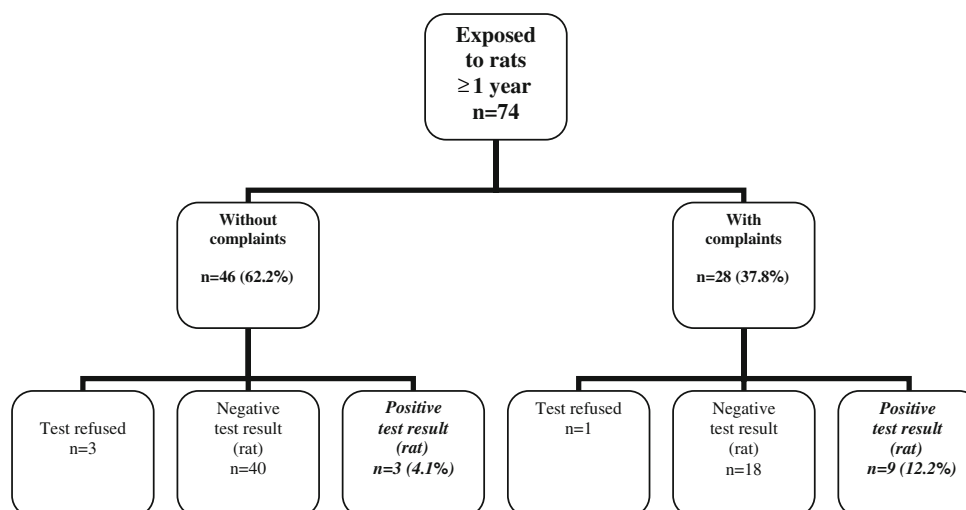


**Fig. 4** Prevalence of complaints and positive test results in workers exposed to rats for  $\geq 1$  year



against grass pollen. When performing a logistic regression analysis we found a history of rhinitis to ubiquitous allergens, a skin prick test in the past and the use of an FFP2 mask as relevant factors.

When comparing employees with positive test results to mouse and/or rat allergens and those with no corresponding sensitisation, we were able to confirm significant differences in the history of rhinitis and allergic conjunctivitis to ubiquitous allergens and total serum IgE levels. In a logistic regression analysis significant factors were total serum IgE levels and a skin prick test with positive result for laboratory animals in the past. Twenty-five percent of those found to be sensitised against mouse and/or rat allergens reported having a previous positive skin prick test for laboratory animals (Table 2).

## Discussion

According to the literature, the frequency of complaints and sensitisation against animal allergens is high in employees with occupational contact with laboratory animal dust. Nowadays in Germany, preventive medical check-ups for activities involving exposure to experimental animal dust in the rooms in which the animals are kept are required by law. The data presented here are therefore not collected in the context of a clinical survey, but rather during regular medical check-ups carried out according to legal requirements. With our study design, we were able to verify whether the data in the literature are relevant to the real life situation of university research laboratories. Nonetheless, the findings should be interpreted in the light of possible bias, including the potential for affected employees to have avoided the medical check-ups, or to have selected work away from animals on their own initiative (healthy-worker effect).

When starting our preventive medical check-ups, we found that our study group was very heterogeneous, and included employees that had just started work and long-serving workers, and those who only infrequently came in contact with experimental animal dust. As the median of the weekly exposure was 4 h in our study population and it was known from literature that symptoms of affected individuals usually begin within 6 months of exposure (Bush and Stave 2003) we decided to look especially upon those employees with an intensive and higher-than-average exposure. Therefore, we made the decision to stratify our data according to duration of exposure ( $<1$  year and  $\geq 1$  year) and to weekly exposure ( $<5$  h/week and  $\geq 5$  h/week).

Twenty-five percent of those employees found to be sensitised against mouse and/or rat allergens reported about a previous positive skin prick test for laboratory animals. On the other hand, in 75% of employees, the sensitisation was diagnosed for the first time at the occasion of the preventive medical check-up. In these workers, the new awareness that sensitisation against mouse and/or rat allergens was the cause of their complaints, enabled them to take adequate preventive measures (e.g. use of a FFP2 mask) supported by the assurance of compensation. It is beyond doubt that these workers did benefit from the preventive medical check-ups.

Our data concerning work-related complaints (33.7 and 37.8%) and sensitisation rates (12.7 and 16.3%) in persons occupationally exposed to mice and rats, respectively, are in good agreement with the data in the literature (Bush and Stave 2003). Surprisingly, only 32% of our workers with work-related symptoms were sensitised to rat allergens. In our study, the diagnosis of sensitisation was primarily based on skin prick tests against allergens from rats and mice, and was supplemented by measuring specific IgE in serum in ambiguous cases. It is to point out that for reasons of economy serological examinations for specific IgE antibodies against rat and mouse epithelia and proteins were

**Table 1** Characteristics of persons (exposed for  $\geq 1$  year), with and without complaints

|                                             |                                                             | No complaints $n = 70$ | With complaints $n = 36$ |                                 |
|---------------------------------------------|-------------------------------------------------------------|------------------------|--------------------------|---------------------------------|
| Exposure data                               | Time of working with laboratory animals (years)             | 4.5 (1.8; 9.3)         | 4.5 (1.5; 6.0)           | n.s.                            |
|                                             | Weekly contact with laboratory animals (hours)              | 3.0 (1.0; 10.0)        | 6.5 (2.0; 20.0)          | $P < 0.05$                      |
|                                             | Use of breathing protection                                 | 48.5%                  | 63.9%                    | n.s.                            |
|                                             | <b>Use of a FFP2 mask</b>                                   | <b>8.6%</b>            | <b>41.7%</b>             | <b><math>P &lt; 0.05</math></b> |
| Anamnestic data                             | Smoker                                                      | 28.6%                  | 22.2%                    | n.s.                            |
|                                             | History of hay fever                                        | 15.7%                  | 36.1%                    | $P < 0.05$                      |
|                                             | <b>History of rhinitis</b>                                  | <b>12.9%</b>           | <b>44.4%</b>             | <b><math>P &lt; 0.05</math></b> |
|                                             | History of asthma                                           | 7.1%                   | 19.4%                    | n.s.                            |
|                                             | History of allergic conjunctivitis                          | 10.0%                  | 27.8%                    | $P < 0.05$                      |
|                                             | History of bronchitis                                       | 4.3%                   | 2.8%                     | n.s.                            |
|                                             | History of other respiratory disease                        | 2.9%                   | 5.6%                     | n.s.                            |
|                                             | History of neurodermatitis                                  | 11.6%                  | 19.4%                    | n.s.                            |
|                                             | History of flexural eczema                                  | 4.3%                   | 11.1%                    | n.s.                            |
|                                             | History of hand eczema                                      | 5.7%                   | 8.3%                     | n.s.                            |
|                                             | History of food allergy                                     | 5.7%                   | 16.7%                    | n.s.                            |
|                                             | History of drug allergy                                     | 7.1%                   | 0%                       | n.s.                            |
|                                             | <b>SPT in the past</b>                                      | <b>31.4%</b>           | <b>75%</b>               | <b><math>P &lt; 0.05</math></b> |
|                                             | SPT in the past with positive result                        | 15.7%                  | 47.2%                    | $P < 0.05$                      |
|                                             | SPT in the past with positive result for laboratory animals | 1.4%                   | 13.9%                    | $P < 0.05$                      |
| Results                                     | $R_{\text{tot}}$ (percentage of threshold)                  | 53.6 (46.2; 70.0)      | 66.6 (43.2; 75.2)        | n.s.                            |
|                                             | SR (percentage of threshold)                                | 59.5 (49.3; 70.9)      | 69.5 (52.8; 85.8)        | $P < 0.05$                      |
|                                             | FEV <sub>1</sub> /VC                                        | 83.0 (78.9; 85.8)      | 83.7 (79.4; 88.4)        | n.s.                            |
|                                             | FVC (percentage of threshold)                               | 110.5 (101.8; 121.0)   | 104.6 (98.1; 115.3)      | n.s.                            |
|                                             | PEF (percentage of threshold)                               | 102.2 (92.8; 116.0)    | 98.5 (85.7; 112.7)       | n.s.                            |
|                                             | MEF75 (percentage of threshold)                             | 106.9 (91.1; 117.1)    | 102.8 (87.2; 116.1)      | n.s.                            |
|                                             | MEF50 (percentage of threshold)                             | 89.9 (80.1; 108.6)     | 87.5 (74.7; 106.2)       | n.s.                            |
|                                             | MEF25 (percentage of threshold)                             | 77.8 (66.4; 94.7)      | 74.6 (63.2; 96.4)        | n.s.                            |
|                                             | Airway hyper responsiveness                                 | 37.5%                  | 52.2%                    | n.s.                            |
| Results from SPT<br>(% of positive results) | Totale IgE (IU/mL)                                          | 19.0 (10.0; 53.5)      | 38.1 (15.9; 213.0)       | $P < 0.05$                      |
|                                             | Grass pollens                                               | 20.7%                  | 46.7%                    | $P < 0.05$                      |
|                                             | Tree 1                                                      | 13.8%                  | 30.0%                    | n.s.                            |
|                                             | Tree 2                                                      | 19.0%                  | 36.7%                    | n.s.                            |
|                                             | Mould 1                                                     | 5.2%                   | 6.7%                     | n.s.                            |
|                                             | Mould 2                                                     | 1.8%                   | 0%                       | n.s.                            |
|                                             | Dog                                                         | 8.6%                   | 13.3%                    | n.s.                            |
|                                             | Cat                                                         | 12.1%                  | 26.7%                    | n.s.                            |
|                                             | <i>D. pteronyssinus</i>                                     | 12.1%                  | 20.0%                    | n.s.                            |
|                                             | <i>D. farinae</i>                                           | 12.1%                  | 23.3%                    | n.s.                            |

Percentages and median values (25th and 75th percentile in parentheses). FEV<sub>1</sub>/VC, forced expiratory volume in one-second/vital capacity; FVC, forced vital capacity; MEF, maximum expiratory flow rate at 75, 50 and 25% of FVC (MEF 75, MEF 50, and MEF 25); PEF, peak expiratory flow;  $R_{\text{tot}}$ , total resistance; SPT, skin prick test; SR, specific resistance. Significant factors in the logistic regression analysis were marked in bold letters

offered only in certain cases. There might be persons with negative skin prick test and positive specific IgE who were missed by this approach. However, it has also been reported that only 63% of persons with symptoms are sensitised to rat allergens (Platts-Mills et al. 1987). Our results suggest that other agents present in animal facilities also play some

role. Sensitisation to feeding stuff or straw may occur, as well as milder non-specific nasal symptoms arising from organic dust. Also, exposure to endotoxin is high during cleaning and feeding tasks (Lieutier-Colas et al. 2001). Airborne endotoxin is associated with respiratory symptoms resulting from exposure to mice in non-mouse-sensitised

**Table 2** Characteristics of persons (exposed for  $\geq 1$  year), with negative and positive test results against mouse and/or rat allergens

|                                             |                                                                    | Negative test result<br>(mouse/rat allergens) $n = 90$ | Positive test results<br>(mouse/rat allergens) $n = 16$ |                                 |
|---------------------------------------------|--------------------------------------------------------------------|--------------------------------------------------------|---------------------------------------------------------|---------------------------------|
| Exposure data                               | Time of working with laboratory animals (years)                    | 4.0 (1.4; 8.0)                                         | 5.0 (2.0; 9.5)                                          | n.s.                            |
|                                             | Weekly contact with laboratory animals (hours)                     | 4.0 (1.8; 15.5)                                        | 4.5 (2.0; 8.0)                                          | n.s.                            |
|                                             | Use of breathing protection                                        | 48.9%                                                  | 75.0%                                                   | n.s.                            |
| Anamnestic data                             | Use of a FFP2 mask                                                 | 15.6%                                                  | 43.8%                                                   | n.s.                            |
|                                             | Smoker                                                             | 26.7%                                                  | 25.0%                                                   | n.s.                            |
|                                             | History of hay fever                                               | 21.1%                                                  | 31.1%                                                   | n.s.                            |
|                                             | History of rhinitis                                                | 18.9%                                                  | 50.0%                                                   | $P < 0.05$                      |
|                                             | History of asthma                                                  | 8.9%                                                   | 25.0%                                                   | n.s.                            |
|                                             | History of allergic conjunctivitis                                 | 11.1%                                                  | 43.8%                                                   | $P < 0.05$                      |
|                                             | History of bronchitis                                              | 3.3%                                                   | 6.3%                                                    | n.s.                            |
|                                             | History of other respiratory disease                               | 4.4%                                                   | 0%                                                      | n.s.                            |
|                                             | History of neurodermatitis                                         | 15.7%                                                  | 6.3%                                                    | n.s.                            |
|                                             | History of flexural eczema                                         | 6.7%                                                   | 6.3%                                                    | n.s.                            |
|                                             | History of hand eczema                                             | 6.7%                                                   | 6.3%                                                    | n.s.                            |
|                                             | History of food allergy                                            | 10.0%                                                  | 6.3%                                                    | n.s.                            |
|                                             | History of drug allergy                                            | 5.6%                                                   | 0%                                                      | n.s.                            |
|                                             | SPT in the past                                                    | 44.4%                                                  | 56.3%                                                   | n.s.                            |
|                                             | SPT in the past with positive result                               | 24.4%                                                  | 37.5%                                                   | n.s.                            |
|                                             | <b>SPT in the past with positive result for laboratory animals</b> | <b>2.2%</b>                                            | <b>25.0%</b>                                            | <b><math>P &lt; 0.05</math></b> |
| Results                                     | $R_{\text{tot}}$ (percentage of threshold)                         | 55.4 (45.5; 72.2)                                      | 58.8 (42.2; 74.4)                                       | n.s.                            |
|                                             | SR (percentage of threshold)                                       | 61.0 (49.8; 76.5)                                      | 69.5 (50.8; 83.2)                                       | n.s.                            |
|                                             | FEV <sub>1</sub> /VC                                               | 84.0 (79.2; 86.6)                                      | 81.3 (75.3; 84.6)                                       | n.s.                            |
|                                             | FVC (percentage of threshold)                                      | 109.4 (101.5; 118.0)                                   | 110.7 (97.7; 124.0)                                     | n.s.                            |
|                                             | PEF (percentage of threshold)                                      | 101.4 (88.8; 116.0)                                    | 100.3 (87.6; 110.4)                                     | n.s.                            |
|                                             | MEF75 (percentage of threshold)                                    | 106.6 (91.1; 116.7)                                    | 93.7 (78.0; 118.8)                                      | n.s.                            |
|                                             | MEF50 (percentage of threshold)                                    | 89.2 (78.3; 106.9)                                     | 89.8 (65.8; 109.2)                                      | n.s.                            |
|                                             | MEF25 (percentage of threshold)                                    | 77.9 (66.2; 97.0)                                      | 66.7 (57.7; 91.8)                                       | n.s.                            |
|                                             | Airway hyper responsiveness                                        | 39.1%                                                  | 60.0%                                                   | n.s.                            |
|                                             | <b>Totale IgE (IU/mL)</b>                                          | <b>21.2 (10.4; 50.8)</b>                               | <b>300.0 (37.0; 920.0)</b>                              | <b><math>P &lt; 0.05</math></b> |
| Results from SPT<br>(% of positive results) | Grass pollens                                                      | 27.6%                                                  | 41.7%                                                   | n.s.                            |
|                                             | Tree 1                                                             | 17.1%                                                  | 33.3%                                                   | n.s.                            |
|                                             | Tree 2                                                             | 23.7%                                                  | 33.3%                                                   | n.s.                            |
|                                             | Mould 1                                                            | 6.6%                                                   | 0%                                                      | n.s.                            |
|                                             | Mould 2                                                            | 1.3%                                                   | 0%                                                      | n.s.                            |
|                                             | dog                                                                | 9.2%                                                   | 16.7%                                                   | n.s.                            |
|                                             | Cat                                                                | 14.5%                                                  | 33.3%                                                   | n.s.                            |
|                                             | <i>D. pteronyssinus</i>                                            | 13.2%                                                  | 25.0%                                                   | n.s.                            |
|                                             | <i>D. farinae</i>                                                  | 14.5%                                                  | 25.0%                                                   | n.s.                            |

Percentages and median values (25th and 75th percentile in parentheses). FEV<sub>1</sub>/VC, forced expiratory volume in one-second/vital capacity; FVC, forced vital capacity; MEF, maximum expiratory flow rate at 75, 50 and 25% of FVC (MEF 75, MEF 50, and MEF 25); PEF, peak expiratory flow;  $R_{\text{tot}}$ , total resistance; SPT, skin prick test; SR, specific resistance. Significant factors in the logistic regression analysis were marked in bold letters

scientists and technicians (Pacheco et al. 2003), but causes other than allergens or endotoxins might be responsible for symptoms in exposed workers (Lieutier-Colas et al. 2002). In our study, employees with symptoms but negative test

results had significantly lower total IgE in comparison to those whose complaints could be explained by positive test results. These findings are also indicative of a non-allergic cause of these symptoms.

In accordance with the data in the literature, we found that a history of rhinitis to ubiquitous allergens in the past medical history is a risk factor. Sensitisation against rat and/or mouse allergens was not found in persons occupationally exposed for less than 1 year, which indicates that occupational exposure is the main risk for mouse and rat allergy. From our cross-sectional data, it is not possible to deduce whether sensitisation against ubiquitous allergens is a cause or consequence of sensitisation against rat or mouse allergens. In the literature, exclusion of workers with atopy from working with animals has been considered as not justifiable. Neither factor investigated predicted the disease accurately, so the use of predictive factors should be restricted to the identification of people who may be more susceptible (Botham et al. 1995). Allergen exposure has been confirmed as the most important determinant of laboratory animal allergy (Cullinan et al. 1999).

Employees with and without complaints differ in their safety measures at the workplace. Reasonably those differences in safety measures are consequence and not cause of the complaints. It has to be pointed out that only 48.5% of those employees without complaints used respiratory protection at least on some occasions. Only in cases with complaints or a positive test result to rat and/or mouse allergens was the use of respiratory protection 63.9 or 75.0%, respectively. Furthermore, employees with complaints did use adequate respiratory protection (FFP2 mask) significantly more frequently. These results indicate that the risk of working with animals is often misjudged and adequate protection will only be used when the first complaints appear. In this context, doctors' advice on the occasion of a preventive medical check-up could be helpful in reducing exposure, by paying particular attention to the use of personal protective equipment. Many studies have shown a clear relationship between the development of work-related symptoms and intensity of exposure (Cullinan et al. 1994; Nieuwenhuijsen et al. 2003; Heederik et al. 1999; Hollander et al. 1997). It has been attempted to establish threshold limit values for allergens in the workplace (Baur et al. 1998). All of this supports the demand to minimise exposure in order to prevent the development of laboratory allergy. Nonetheless, we found that non-sensitised workers in particular do not recognise experimental animal dust as a hazardous substance, and they ignore measures for exposure reduction. Our data imply that more effort is necessary to educate employees regarding strategies to reduce work-related allergies. Studies have demonstrated that effective reduction of exposure to allergens can be achieved by several strategies, which together appear to minimise sensitisation to rodents (Thulin et al. 2002; Schweitzer et al. 2003; Gordon et al. 2001; Fisher et al. 1998; Korpi et al. 2007).

In summary, we consider periodic preventive medical check-ups for persons with occupational contact to labora-

tory animal dust as mandatory. Workers tend to ignore occupational risks, especially in the context of contact with animals. Nevertheless, we favour giving individual advice for a safer work environment over rigorous exclusion of all workers with atopy, sensitisation or work-related complaints. Most employees working with laboratory animals, both scientists and technicians, are primarily specialised in animal experiments and a suspension from duty would be a very rigorous restriction. As a consequence, the acceptance of medical check-ups, mainly in scientists with work-related complaints, may be poor, possibly from fear of the consequences for their future scientific careers. Therefore, we would primarily try to convince employees to assume responsibility for their own health instead of acting against their wishes by suspending them from their duties. In most cases, there are possibilities to reduce exposure and to increase the use of personal protective equipment. Under the condition of repeated medical monitoring, we would give these measures a chance to prevent employees from losing their job. Therefore, medical check-ups should be included in measures for primary, secondary and tertiary prevention, including education, engineering controls, administrative controls, use of personal protective equipment, medical surveillance, and vocational integration.

**Acknowledgments** The authors thank all participants for their co-operation. Parts of this paper have been included in the medical thesis (in preparation) of Meta Hager at the Medical Faculty of the University Erlangen-Nuremberg. Parts of this paper had been presented at the annual congress of the German Society for Occupational and Environmental Medicine (Mainz, Germany from 21st March to 24th March 2007) and at the Second World Congress on Work-Related and Environmental Allergy (13–16 June 2007, Weimar, Germany).

## References

- Baur X, Chen Z, Liebers V (1998) Exposure-response relationship of occupational inhalative allergens. *Clin Exp Allergy* 28:537–544. doi:10.1046/j.1365-2222.1998.00276.x
- Botham PA, Lamb CT, Teasdale EL, Bonner SM, Tomenson JA (1995) Allergy to laboratory animals: a follow up study of its incidence and of the influence of atopy and pre-existing sensitisation on its development. *Occup Environ Med* 52:129–133
- Bush RK, Stave GM (2003) Laboratory animal allergy: an update. *Occupational Health and Safety in Biomedical Research. ILAR J* V44(1):1–26
- Cullinan P, Lowson D, Nieuwenhuijsen MJ, Gordon S, Tee RD, Venables KM et al (1994) Work related symptoms, sensitisation, and estimated exposure in workers not previously exposed to laboratory rats. *Occup Environ Med* 51:589–592
- Cullinan P, Cook A, Gordon S, Nieuwenhuijsen MJ, Tee RG, Venables KM et al (1999) Allergen exposure, atopy and smoking as determinants of allergy to rats in a cohort of laboratory employees. *Eur Respir J* 13:1139–1143. doi:10.1034/j.1399-3003.1999.13e33.x
- Deutsche Gesellschaft für Arbeitsmedizin und Umweltmedizin e.V. (DGAUM) (2004) Leitlinie Lungenfunktionsprüfung in der Arbeitsmedizin. <http://www.dgaum.de>

- Fisher R, Saunders W, Murray SJ, Stave GM (1998) Prevention of Laboratory Animal Allergy. *J Occup Environ Med* 40:609–613. doi:[10.1097/00043764-199807000-00005](https://doi.org/10.1097/00043764-199807000-00005)
- Gordon S, Fisher SW, Raymond RH (2001) Elimination of mouse allergens in the working environment: assessment of individually ventilated cage systems and ventilated cabinets in the containment of mouse allergens. *J Allergy Clin Immunol* 108:288–294. doi:[10.1067/mai.2001.117258](https://doi.org/10.1067/mai.2001.117258)
- Hauptverband der gewerblichen Berufsgenossenschaften (ed.) Berufsgenossenschaftliche Grundsätze für arbeitsmedizinische Vorsorgeuntersuchungen. Gentner Verlag, Stuttgart 2004.
- Heederik D, Venables KM, Malmberg P, Hollander A, Karlsson AS, Renström A et al (1999) Exposure–response relationship for work-related sensitization in workers exposed to rat urinary allergens: results from a pooled study. *J Allergy Clin Immunol* 103:678–684. doi:[10.1016/S0091-6749\(99\)70242-3](https://doi.org/10.1016/S0091-6749(99)70242-3)
- Hollander A, Heederik D, Doekes G (1997) Respiratory allergy to rats: exposure–response relationship in laboratory animal workers. *Am J Respir Crit Care Med* 155:562–567
- Korpi A, Lappalainen S, Kaliste E, Kalliokoski P, Reijula K, Pasanen AL (2007) A multi-faceted approach to risk assessment of laboratory animal allergens at two facilities. *Am J Ind Med* 50:127–135. doi:[10.1002/ajim.20424](https://doi.org/10.1002/ajim.20424)
- Krakowiak A, Krawczyk P, Szulc B, Wisniewska M, Kowalczyk M, Walusiak J et al (2007a) Prevalence and host determinants of occupational bronchial asthma in animal shelter workers. *Int Arch Occup Environ Health* 80:423–432. doi:[10.1007/s00420-006-0152-1](https://doi.org/10.1007/s00420-006-0152-1)
- Krakowiak A, Wisniewska M, Krawczyk P, Szulc B, Wittczak T, Walusiak J et al (2007b) Risk factors associated with airway allergic diseases from exposure to laboratory animal allergens among veterinarians. *Int Arch Occup Environ Health* 80:465–475. doi:[10.1007/s00420-006-0153-0](https://doi.org/10.1007/s00420-006-0153-0)
- Lieutier-Colas F, Meyer P, Larsson P, Malmberg P, Frossard N, Pauli G et al (2001) Difference in exposure to airborne major rat allergen (Rat n 1) and to endotoxin in rat quarters according to task. *Clin Exp Allergy* 31:1449–1456. doi:[10.1046/j.1365-2222.2001.01180.x](https://doi.org/10.1046/j.1365-2222.2001.01180.x)
- Lieutier-Colas F, Meyer P, Pons F, Hedelin G, Larsson P, Malmberg P et al (2002) Prevalence of symptoms, sensitization to rats, and airborne exposure to major rat allergen (Rat n1) and to endotoxin in rat-exposed workers: a cross-sectional study. *Clin Exp Allergy* 32:1424–1429. doi:[10.1046/j.1365-2745.2002.01502.x](https://doi.org/10.1046/j.1365-2745.2002.01502.x)
- Nieuwenhuijsen MJ, Putcha V, Gordon S, Heederik D, Nenables KM, Cullinan P et al (2003) Exposure-response relations among laboratory animal workers exposed to rats. *Occup Environ Med* 60:104–108. doi:[10.1136/oem.60.2.104](https://doi.org/10.1136/oem.60.2.104)
- Ordinance on Hazardous Substances (Gefahrstoffverordnung; GefStoffV). Federal Gazette. Dezember 23th 2004: I S 3758
- Pacheco KA, McCammon C, Liu AH, Thorne PS, O'Neill ME, Martyny J et al (2003) Airborne endotoxin predicts symptoms in non-mouse-sensitized technicians and research scientists exposed to laboratory mice. *Am J Respir Crit Care Med* 167:983–990. doi:[10.1164/rccm.2112062](https://doi.org/10.1164/rccm.2112062)
- Platts-Mills TA, Longbottom J, Edwards J, Cockcroft A, Wilkins S (1987) Occupational asthma and rhinitis related to laboratory rats: serum IgG and IgE antibodies to the rat urinary allergen. *J Allergy Clin Immunol* 79:505–515. doi:[10.1016/0091-6749\(87\)90369-1](https://doi.org/10.1016/0091-6749(87)90369-1)
- Renström A, Malmberg P, Larsson K, Larsson PH, Sundblad BM (1995) Allergic sensitization is associated with increased bronchial responsiveness: a prospective study of allergy to laboratory animals. *Eur Respir J* 8:1514–1519
- Schweitzer IB, Smith E, Harrison DJ, Myers DD, Eggleston PA, Stockwell JD et al (2003) Reducing exposure to laboratory animal allergens. *Comp Med* 53:487–492
- Thulin H, Björkdahl M, Karlsson AS, Renström A (2002) Reduction of exposure to laboratory animal allergens in a research laboratory. *Ann Occup Hyg* 46:61–68. doi:[10.1093/annhyg/mef022](https://doi.org/10.1093/annhyg/mef022)