Sensitisation to mites in laboratory animal workers with rhinitis

P Ruoppi, T Koistinen, S Pennanen

Occup Environ Med 2005;62:612–615. doi: 10.1136/oem.2004.015685

See end of article for authors' affiliations

Correspondence to: Dr P Ruoppi, Department of Otorhinolaryngology, Kuopio University Hospital, Kuopio, Finland, PO Box 1777, SF-70211 Kuopio, Finland; pirkko.ruoppi@kuh.fi

Accepted 4 March 2005

Aims: To determine the frequency of sensitisation to mites among rhinitic laboratory animal workers and to clarify whether sensitisation could be occupational.

Methods: Skin prick tests (SPT) were performed in 40 subjects who were working with laboratory animals in Kuopio University research units and who had been referred to Kuopio University Hospital for work related rhinitis. The SPT panel consisted of three storage mites, two house dust mites, 11 other common environmental airborne allergens, latex, and 2–4 individually relevant laboratory animals. To determine signs of mites in animal facilities, guanine was determined in 22 dust samples taken from feedstuffs or bedding material used for laboratory animals and from rooms where these materials were stored and handled.

Results: Positive SPT results were found in 35 out of 40 workers: in 14 for storage mites, four for house dust mites, 25 for other common aeroallergens, as well as positive reactions to laboratory animals in 19 individuals. The guanine test was positive, indicating the presence of mite derived material in 21 out of 22 dust samples.

Conclusions: This study suggests that subjects who are occupationally exposed to laboratory animals are also exposed to mite derived allergens. Sensitisation to mites is common and may be work related.

Work related respiratory symptoms are an important health problem among laboratory animal workers and rhinoconjunctivitis is the most common complaint.¹ Rhinoconjunctivitis may be caused by laboratory animal allergy (LAA), which is a well known occupational hazard. The prevalence rate of LAA is between 20% and 40%.¹ In cases where no specific sensitisation to laboratory animals has been revealed in clinical examination, the work related symptoms have been considered as resulting from non-specific hyperresponsiveness to animal derived or other agents, such as dust, disinfectants, or ammonia that also are present in laboratory animal facilities.²

When a group of laboratory animal workers were examined in our clinic for work related rhinitis, our attention was drawn to numerous positive skin prick test (SPT) results for at least one of the three storage mites that were included in the routine test panel. This provided the impetus to determine the actual frequency of sensitisation to mites, especially to storage mites, among rhinitic laboratory animal workers. Another aim was to clarify whether this sensitisation could be occupational. There are no previous reports of sensitisation to mites in animal work.

MATERIAL AND METHODS

The study subjects consisted of 40 rhinitic animal workers. They were exposed to laboratory animals in the research units of the University of Kuopio, where about 250 people are working with animals at any given time. In a questionnaire study, 65 out of 254 employees reported work related rhinitis and 47 of them had been examined for LAA.³ Those 40 rhinitic animal workers, who in that connection were also tested for mites, constitute the subjects of the present study.

There were 24 researchers, 10 laboratory technicians and six animal handlers; 26 of the 40 were women; subjects were aged 24–56 years with a mean age of 35 years. The duration of exposure before the onset of rhinitis varied from one month to 18 years, mean 2.2 years. (table 1).

The patients completed a questionnaire that is in routine use in the clinic, which inquired about history and symptoms of rhinitis and history of previous atopic symptoms such as allergic rhinitis, asthma, and atopic eczema. A question about possible moisture damage in the workplace or at home was included in this inquiry. The type of protective gloves used in animal work was also asked. One or other of the two otolaryngologists in the study group performed a clinical examination that consisted of an anterior and posterior rhinoscopy, mirror laryngoscopy, and otoscopy. If there were signs indicative of sinusitis, a paranasal sinus x ray was taken and the subjects were treated accordingly for infection rhinitis or sinusitis before further examination.

SPTs (ALK-Abelló A/S, Hørsholm, Denmark) were performed with three storage mites (*Acarus siro*, *Lepidoglyphus destructor*, and *Tyrophagus putrescentiae*), two house dust mites (HDM) (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), pollen allergens (birch, alder, timothy, meadow foxtail, meadow grass, meadow fescue, orchard grass, mugwort, and dandelion), four domestic animals (cat, dog, cow, and horse), latex, and 1–4 individually relevant laboratory animals. The tests were interpreted according to the recommendations of the European Academy of Allergy and Clinical Immunology.⁴ Positive and negative controls were histamine hydrochloride (10 mg/ml) and allergen diluent, respectively. A weal diameter of at least 3 mm and half of the histamine control was considered as positive provided that there was no reaction from the negative control.

To detect signs of mites, a quantitative determination of guanine was performed in 22 dust samples. The dust sample sources in the research units were litter, straw, feedstuffs, and dust from storages of animal food. The determination of guanine was carried out according to Le Mao *et al*⁵ with slight modifications. Briefly, 50–150 mg of dust was washed twice

Abbreviations: HDM, house dust mite; LAA, laboratory animal allergy; SPT, skin prick test

Table 1 Characteristics of the 40 laboratory animal workers with rhinitis

	Researchers (24)	Laboratory technicians (10)	Animal handlers (6)	Total (40)
Female/male	13/11	9/1	4/2	26/14
Age (years)	24–47 (mean 30)	26–54 (mean 39)	36–56 (mean 46)	24–56 (mean 35)
Exposure time before rhinitis				
1–3 months	10	4	1	15
1–3 years	11	5	2	18
>3 years	3	1	3	7

in 20% methanol. After centrifugation, the supernatant containing the guanine, was mixed with a solution of 2 ml 0.16 M NaOH (in 20% methanol), and centrifuged. Fifteen µl of supernatant and 45 µl of methanol were added to the microtiter plate. Ninety µl of 16% Na₂CO₃ and 60 µl of colour reagent (0.25% sulphanilic acid in 1 N HCl; 5% NaNO₂, in a 1:1 ratio) was added. After 20 minutes, the intensity of the yellow colour was read at 490 nm. The concentration of guanine was determined by reference to a standard curve with guanine at 10–70 µg/ml. The coefficient of variation was 7.3% and limit of detection 10 µg/ml. A guanine level 0.6 mg/g or higher was considered as the sensitisation threshold as earlier proposed.⁶

Differences between patient groups were compared with the χ^2 test for independence. Fisher's exact probability test was used for small expected counts.

RESULTS

Thirty five out of the 40 rhinitic laboratory animal workers (88%) showed a positive reaction in SPT to at least one of the test allergens (table 2). Sensitisation to at least one species of mites was detected in 17/40 (43%)—that is, to storage mites in 14/40 (35%) and to HDMs in 4/40 (10%). Skin reactivity to both storage mites and HDMs was detected in one person (animal handler) who in addition exhibited positive SPT to dog. In two individuals, reactivity to storage mites was the only positive SPT result. There were positive SPT results to other common aeroallergens in 25 subjects (63%), from whom 20 subjects had concomitant reactivity to occupational

allergens, eight subjects to laboratory animals, nine subjects to mites, and three subjects to both.

Nineteen subjects (48%) showed reactivity to laboratory animals. There were positive SPT signs to mites in 6/19 subjects with sensitisation to laboratory animals and in 11/21 subjects with no sensitivity to laboratory animals. Mite sensitivity was detected more frequently in subjects with no sensitivity to laboratory animals but the difference was not statistically significant.

In sensitisation to mites there were no statistically significant differences in relation to exposure time before rhinitis but in 16 out of 17 mite sensitive workers, occupational rhinitis had started during the first three years of exposure. Regarding the three different occupations there was no significant difference in mite sensitivity; however, in researchers sensitisation to mites was less prevalent when they were compared with all other laboratory animal workers ($p = 0.037$). Pre-existing atopic respiratory symptoms (eight), skin symptoms (10), or both (seven) had been reported by 25 subjects, 18 out of 28 researchers, four out of 10 laboratory technicians, and three out of six animal handlers. In researchers, atopic constitution was more common than in other workers ($p = 0.048$). Mite sensitivity was detected more often in subjects with pre-existing atopic symptoms (13/25) than subjects with non-atopic constitution (4/15) but the difference was not statistically significant.

No reactivity to latex was found. The majority of protective gloves used were made of either polyvinyl chloride (vinyl) or acrylonitrile butadiene (nitrile), natural rubber latex gloves being available only in three out of 11 working units. All SPT results were negative in five subjects, two of whom were atopics.

A chamber challenge test was performed in 21 subjects, 19 with a positive SPT to at least one laboratory animal and two workers with negative animal SPT. Occupational LAA related disease was confirmed with a positive challenge test in 11 workers (rhinitis in two, allergic contact urticaria in four, and both diseases in five workers). In both subjects with negative SPT, the challenge test was also negative. The challenge test method has been described in detail previously.³ From the 14 subjects with a positive SPT to any of the three storage mites, three reported water damage in their homes. In one case, the moisture problem was current, in another case the damage had been repaired four years before this study, and in the third case, there was a suspicion of dampness but the home had not yet been examined.

Table 2 Sensitisation to storage mites, house dust mites, laboratory animals, and common aeroallergens in relation to the history of pre-existing atopic symptoms, exposure time before work related rhinitis, and occupation

	Positive SPT reaction									
	Storage mites		House dust mites		Laboratory animals		Common aero-allergens		At least one tested allergen	
	Yes (n = 14)	No (n = 26)	Yes (n = 4)	No (n = 36)	Yes (n = 19)	No (n = 21)	Yes (n = 25)	No (n = 15)	Yes (n = 35)	No (n = 5)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Pre-existing atopic symptoms										
Yes (n = 25)	10 (71)	15 (58)	4 (100)	21 (58)	11 (58)	14 (67)	20 (80)	5 (33)	23 (66)	2 (40)
No (n = 15)	4 (29)	11 (42)	0 (0)	15 (42)	8 (42)	7 (33)	5 (20)	10 (67)	12 (34)	3 (60)
Exposure time before rhinitis										
1–3 months (n = 15)	5 (36)	10 (38)	1 (25)	14 (39)	8 (42)	7 (33)	11 (44)	4 (27)	13 (37)	2 (40)
1–3 years (n = 18)	8 (57)	10 (38)	2 (50)	16 (44)	8 (42)	10 (48)	10 (40)	8 (53)	16 (46)	2 (40)
>3 years (n = 7)	1 (7)	6 (23)	1 (25)	6 (17)	3 (16)	4 (19)	4 (16)	3 (20)	6 (17)	1 (20)
Occupation										
Researcher (n = 24)	6 (43)	18 (69)	1 (25)	23 (64)	14 (74)	10 (48)	14 (56)	10 (67)	20 (57)	4 (80)
Laboratory technician (n = 10)	4 (29)	6 (23)	2 (50)	8 (22)	3 (16)	7 (33)	7 (28)	3 (20)	9 (26)	1 (20)
Animal handler (n = 6)	4 (29)	2 (8)	1 (25)	5 (14)	2 (11)	4 (19)	4 (16)	2 (13)	6 (17)	0 (0)

The guanine test was positive in 21 out of 22 dust samples (95%), confirming the presence of mite derived material. The guanine content varied from 2.4–5.3 mg/g (mean 3.5 mg/g, SD 0.81). In one dust sample (taken from a washing room), the guanine content was only 0.5 mg/g and this test result was interpreted as being negative.

DISCUSSION

Mites flourish in a warm and damp environment and feed on protein rich substances. As sources of food, HDMs can consume human and animal scales whereas storage mites live on agricultural products and fungi. Thus storage mites are found extensively in stored food products like grain, flour, and hay.⁷ Storage mite related occupational diseases were reported initially in farmers^{8–10} and subsequently in grain workers,^{11–12} bakers,¹³ and other food workers¹⁴ but occupational sensitisation to mites in laboratory animal workers has not been reported. Perhaps this phenomenon has been overlooked because all the bedding and feeding materials used in laboratory animal facilities are irradiated in order to destroy live organisms. In these materials, there are, however, remnants of mites and their excreta, which are also allergenic. In the present study, guanine, a metabolic excretion product of chelicerate arthropods, was used as a marker for mite faeces. A good correlation has been demonstrated between guanine concentrations and group I mite allergen (*Der p 1* and *Der f 1*) levels.^{15–16}

In the present study, the earlier proposed sensitisation threshold for the guanine level of 0.6 mg/g⁵ was exceeded in 95% of dust samples. This finding is in concordance with our earlier pilot study, where as many as 25% of the samples collected in facilities for laboratory animals contained mites which were so well preserved that they could be microscopically identified.¹⁷ In that study, most of the mites were storage mites belonging to the *Astigmata* and *Prostigmata* species. The appearance of mites in the working environment may explain the high prevalence of positive reactions to mites among the laboratory animal workers found in the present study. These results suggest that mites may be important allergenic agents in laboratory animal facilities and that there is a clear potential for occupational sensitisation, especially to storage mites in animal workers.

Storage mites seem to be also closely associated with damp housing conditions.^{18–20} An unusually high prevalence of positive SPTs for storage mite allergens has been reported in symptomatic employees working in a moisture damaged building.²¹ In this material, there were only three subjects in whom positive SPT to storage mites could be related to definite or suspected moisture damage in the home.

In the present study, sensitisation to storage mites was detected in 35% of laboratory workers. Previously reported prevalence rates of sensitisation to storage mites have been 11–33% in bakery workers but no difference has been found in comparison with controls.²² In a Swedish study in 55 asthmatic children, storage mites were found in 69% of the homes and sensitisation to storage mites was noted in 20% of the children.²³ There are great differences in the numbers and types of mites found in different climatic regions. There are also other studies where storage mites have been found to evoke sensitisation in urban populations with no relation to specific occupations.^{24–25} The magnitude of this sensitisation is enhanced when the climatic and environmental conditions have high relative humidity (about 80%) and temperatures close to 25–30°C.^{7–20} In our recent study, examining a random sample of 300 subjects of working age from Kuopio county (farmers not included), we found only 1.7% sensitisation to any of those three storage mites included in the SPT panel in the present study, and only 4.7% of individuals reacted to either of the two HDMs (unpublished data). When compared

with sensitisation figures in that random sample, sensitisation to storage mites was in this study approximately 20-fold and to HDMs twofold.

There are indications that the sensitisation to storage mites develops more frequently in patients already sensitised to HDM allergens.^{24–25} Sensitisation to storage mites in the absence of sensitisation to *Dermatophagoides* spp has even been proposed as being rare.²⁶ Part of the sensitisation to storage mites has been thought to be crossreactivity with HDMs^{27–28} although contradictory results have also been presented.^{7–29–30} Crossreactivity was not, however, the explanation for storage mite reactivity in the present study, because there was only one person with a positive SPT to both storage mites and HDMs.

In the present study, 25/40 (63%) of rhinitic laboratory animal workers reported pre-existing atopic respiratory or skin symptoms or both. Among researchers, a history of previous atopic diseases was positive more often than in other workers. There are at least two possible explanations for this clustering. Firstly, in order to avoid risky jobs atopic people are commonly encouraged to stay on at school, and that can mean that these individuals achieve academic degrees. Secondly, there may be a “healthy worker” effect among other laboratory workers. That means that symptomatic people in permanent occupations change their job whereas a great many university researchers, especially the younger ones, work on a temporary basis and finish their project, simply ignoring the possible symptoms.

In a cohort of 769 subjects working in pastry making, animal health, and dental hygiene technology, new occupational sensitisation was stated as a risk for development of sensitisation to common aeroallergens.³¹ In our study, sensitisation to common aeroallergens was detected in 25/40 of subjects of whom 19 subjects had a previous history of atopic symptoms. Concomitant sensitivity to occupational allergens was found in 20 of those 25 subjects but because in this study SPTs were performed only once, it is not possible to say what the sequence of allergens in the individual sensitisation process had been. Therefore it is not possible on the basis of the present study, to estimate the possible role of occupational sensitisation in relation to further non-occupational allergies. One interesting finding was the trend for there to be a negative association between mite sensitivity and laboratory animal sensitivity.

There were no statistically significant differences in mite sensitivity between three different animal worker groups; however, sensitisation to mites was less prevalent in researchers even though these workers more often had an atopic constitution than the other workers. Due to the nature of the job, researchers are not as extensively exposed to bedding and feeding materials than the other staff working in animal facilities, which may explain this trend. With regard to the exposure time before symptoms, in the great majority (16/17) of mite sensitive workers, occupational rhinitis had started during the first three years. That finding is in concordance with earlier findings concerning laboratory animal allergy.^{3–32}

Sensitisation to natural rubber latex was not detected and this gratifying finding is obviously due to a systematic switch from latex to protective gloves made of either polyvinyl chloride (vinyl) or acrylonitrile butadiene (nitrile) during the last decade.

The guanine test results indicate that animal workers are occupationally exposed to mite derived allergens. In our study, all the subjects experienced work related rhinitis and it is possible that the symptoms were mite induced in those animal workers who had been sensitised to mites. In laboratory work, mites as well as animals should be

Main messages

- In addition to being exposed to experimental animals, laboratory animal workers also seem to be occupationally exposed to mites.
- The possibility of sensitisation to mites to account for work related symptoms should be remembered and examined, at least in cases when laboratory animal allergy is not diagnosed.

Policy implications

- Animal workers should be aware of the risk of work related sensitisation not only when working with animals but also when handling their feeding and bedding materials.
- Proper ventilation, cleaning practices, and protection against mites with personal equipment, if necessary, are important in both animal and storage rooms.

considered as an occupational hazard and should also be included in allergy testing panels.

CONCLUSIONS

Work related respiratory complaints are common among laboratory animal workers and the risk for LAA is well known. If LAA is not diagnosed, the symptoms are usually considered as being non-specific. It seems that in addition to laboratory animal exposure, workers are also occupationally exposed to mite derived allergens. Occupational health personnel should be aware of the possibility of sensitisation to mites in laboratory animal facilities. When work related allergies are examined, mites should be included in the test panels. It is especially important to remember to test also for mites at least in those cases when LAA is not diagnosed. Adequate workplace health and safety education should not be overlooked. In the prevention of sensitisation, effective reduction of airborne allergen exposure is crucial.¹ In particular, symptomatic animal workers should wear personal protective equipment not only in the presence of animals but also when working in facilities where feeding and bedding material are handled and stored. In general, people with occupational allergy should be removed from regular exposure.

Authors' affiliations

P Ruoppi, T Koistinen, Department of Otorhinolaryngology, Kuopio University Hospital, Kuopio, Finland
S Pennanen, Kuopio Regional Institute of Occupational Health, Kuopio, Finland

REFERENCES

- Gordon S, Newman Taylor AJ. Animal, insect and shellfish allergy. In: Bernstein IL, Chan-Yeung M, Malo J-L, Bernstein DI, eds. *Asthma in the workplace*, 2nd edition. New York, Basel: Marcel Dekker, Inc, 1999:399-424.
- Hollander A, Doekes G, Heederik D. Cat and dog allergy and total IgE as risk factors of laboratory animal allergy. *J Allergy Clin Immunol* 1996;**98**:545-54.
- Ruoppi P, Koistinen T, Susitaival P, et al. Frequency of allergic rhinitis to laboratory animals in university employees as confirmed by chamber challenges. *Allergy* 2004;**59**:295-301.
- Dreborg S, Backman A, Basomba A, et al. Skin tests used in type I allergy testing. Position paper. *Allergy* 1989;**44**(Suppl 10):1-59.
- Le Mao J, Pauli G, Tekcia F, et al. Guanine content and Dermatophagoides pteronyssinus allergens in house dust samples. *J Allergy Clin Immunol* 1989;**83**:926-33.
- van Bronswijk JE, Bischoff E, Schirmacher W, et al. A rapid house-dust allergen test: preliminary results. *J Med Entomol* 1986;**23**:217-18.
- Tee RD. Allergy to storage mites. *Clin Exp Allergy* 1994;**24**:636-40.
- Cuthbert OD, Brostoff J, Wraith DG, et al. "Barn allergy": asthma and rhinitis due to storage mites. *Clin Allergy* 1979;**9**:229-36.
- Terho EO, Husman K, Vohlonen I, et al. Allergy to storage mites or cow dander as a cause of rhinitis among Finnish dairy farmers. *Allergy* 1985;**40**:23-6.
- van Hage-Hamsten M, Johansson SG, Höglund S, et al. Storage mite allergy is common in farming population. *Clin Allergy* 1985;**15**:555-64.
- Revsbech P, Andersen G. Storage mite allergy among grain elevator workers. *Allergy* 1987;**42**:423-9.
- Blainey AD, Topping MD, Ollier S, et al. Allergic respiratory diseases in grain workers: The role of storage mites. *J Allergy Clin Immunol* 1989;**84**:296-303.
- Revsbech P, Dueholm M. Storage mite allergy among bakers. *Allergy* 1990;**45**:204-8.
- Armentia A. Occupational asthma from storage mites contaminating foods. *J Invest Allergol Clin Immunol* 1997;**7**:407-8.
- Hoyet C, Bessot JC, Le Mao J, et al. Comparison between Der p I plus Der f I content determinations and guanine measurements in 239 house dust samples. *J Allergy Clin Immunol* 1991;**88**:678-80.
- Quoix E, Le Mao J, Hoyet C, et al. Prediction of mite allergen levels by guanine measurements in house-dust samples. *Allergy* 1993;**48**:306-9.
- Pennanen S, Harju A. Mites in facilities for laboratory animals. *Scand J Work Environ Health* 2003;**29**:314-16.
- Wraith DG, Cunningham AM, Seymour WM. The role and allergenic importance of storage mites in house dust and other environments. *Clin Allergy* 1979;**9**:545-61.
- Agha M, Gnanasakthy A. A cluster analysis of the effects of storage mites as allergens in relation to certain occupations and living conditions. *Clin Allergy* 1981;**11**:499-504.
- Iversen M, Dahl R. Allergy to storage mites in asthmatic patients and its relation to damp housing conditions. *Allergy* 1990;**45**:81-5.
- Roponen M, Kiviranta J, Seuri M, et al. Inflammatory mediators in nasal lavage, induced sputum and serum of employees with rheumatic and respiratory disorders. *Eur Respir J* 2001;**18**:542-8.
- Heederik D, Newman Taylor AJ. Occupational asthma in the baking industry. In: Bernstein IL, Chan-Yeung M, Malo J-L, Bernstein DI, eds. *Asthma in the workplace*, 2nd edition. New York, Basel: Marcel Dekker, Inc, 1999:377-97.
- Warner A, Boström S, Möller C, et al. Mite fauna in the home and sensitivity to house-dust and storage mites. *Allergy* 1999;**54**:681-90.
- Luczynska CM, Griffin P, Davies RJ, et al. Prevalence in specific IgE to storage mites (*A. siro*, *L. destructor* and *T. longior*) in an urban population and crossreactivity with the house dust mite (*D. pteronyssinus*). *Clin Exp Allergy* 1990;**20**:403-6.
- Ebner C, Feldner H, Ebner H, et al. Sensitization to storage mites in house dust mite (*Dermatophagoides pteronyssinus*) allergic patients. Comparison of a rural and an urban population. *Clin Exp Allergy* 1994;**24**:347-52.
- Müsken H, Fernández-Caldas E, Marañón F, et al. In vivo and in vitro sensitization to domestic mites in German urban and rural allergic patients. *J Invest Allergol Clin Immunol* 2002;**12**:177-81.
- Droste J, Myny K, Van Sprundel M, et al. Allergic sensitization, symptoms, and lung function among bakery workers as compared with nonexposed work population. *J Occup Environ Med* 2003;**45**:648-55.
- van der Heide S, Niemeijer NR, Hovenga H, et al. Prevalence of sensitization to the storage mites *Acarus siro*, *Tyrophagus putrescentiae*, and *Lepidoglyphus destructor* in allergic patients with different degrees of sensitization to the house-dust mite *Dermatophagoides pteronyssinus*. *Allergy* 1998;**53**:426-30.
- van Hage-Hamsten M, Johansson SGO. Storage mites. *Exp Appl Acarol* 1992;**16**:117-28.
- Griffin P, Ford AW, Alterman L, et al. Allergenic and antigenic relationship between three species of storage mite and house dust mite, *Dermatophagoides pteronyssinus*. *J Allergy Clin Immunol* 1989;**84**:108-17.
- Nguyen B, Ghezzi H, Malo JL, et al. Time course of onset of sensitization to common and occupational inhalants in apprentices. *J Allergy Clin Immunol* 2003;**111**:807-12.
- Krakowiak A, Szulc B, Górski P. Occupational respiratory diseases in laboratory animal workers: initial results. *Int J Occup Med Environ Health* 1997;**10**:31-6.