

Reduction of Exposure to Laboratory Animal Allergens in a Research Laboratory

HANS THULIN^{1*}, MARIANNE BJÖRKDAHL², ANNE-SOPHIE KARLSSON³
and ANNE RENSTRÖM³

¹Pharmacia Corp., Consumer Healthcare, Box 941, 251 09 Helsingborg; ²Active Biotech, Box 724, 220 07 Lund; ³Respiratory Health and Climate, National Institute for Working Life, 112 79 Stockholm, Sweden

Received 23 October 2000; in final form 1 October 2001

Objectives: The purpose of this study was to determine exposure levels in the laboratory during different tasks and evaluate the effectiveness of safety equipment used to reduce personal exposure.

Methods: Personal and stationary air samples were collected during different tasks in a laboratory animal facility in which several allergen reduction strategies had been implemented. Mouse urinary allergen concentrations were measured using a polyclonal sandwich enzyme-linked immunosorbent assay. Sera from the personnel ($n = 29$) were analysed every 6 months for the presence of specific antibodies against mouse and rat urinary allergens, and the staff answered questionnaires on work-related symptoms, exposure and use of respiratory protection.

Results: The highest airborne mouse allergen levels were measured during manual emptying of cages, during changing of cages on an unventilated table and during handling of male animals on an unventilated table. Automatic emptying and cleaning of cages resulted in low airborne allergen levels in the working room. Using a ventilated cage-changing wagon reduced the allergen exposure level from 77 to 17 ng/m³. The housing of animals in ventilated cabinets, with air exhausted through the cabinet, effectively prevented the release of allergens into the ambient air. The handling of animals on ventilated benches and the use of a centralized vacuum cleaner resulted in a low exposure level. Only two subjects developed specific immunoglobulin E of >0.35 kU/l, of whom one was reduced to negative after increased use of respiratory protection.

Conclusions: Effective reduction of exposure to allergens can be achieved by several strategies, which together appear to minimize sensitization to rodents.

Keywords: laboratory animal allergy; exposure; mouse; task

INTRODUCTION

Allergy to mice in laboratory workers was described in 1957 (Sorell and Gottesman, 1957), and patients with allergies to guinea pigs, rats, rabbits and mice were reported in 1961 (Rajka, 1961). Since then, allergy to laboratory animals (LAA) has become a well-known occupational disease in personnel exposed to them (Hunnskaar and Fosse, 1990). The prevalence rate of LAA among laboratory animal workers is often reported to be 10–30% (Hunnskaar and Fosse, 1990; Renström *et al.*, 1995). The LAA syndrome has been defined as an allergic disorder characterized by conjunctivitis, rhinitis, urticaria and

asthma. The reaction is known to occur through either inhalation of or skin contact with animal allergens.

The major allergens from the mouse and rat are lipocalin proteins produced by the liver and excreted in the urine. Excretion is under hormonal control, and levels of the protein complex Mus m 1 is 4-fold higher in urine from mature male mice than from female mice (Hastie *et al.*, 1979; Lorusson *et al.*, 1986; Price, 1987).

The allergens are found on particles over a considerable size range, including those >10 µm in aerodynamic diameter (Platt-Mills *et al.*, 1986; Price and Longbottom, 1988; Sakaguchi *et al.*, 1989; Hollander *et al.*, 1998). Contact with contaminated bedding

*Author to whom correspondence should be addressed.

seems to be a major source of allergen exposure (Gordon *et al.*, 1992).

Personal exposure to rat and mouse urinary allergens differs between jobs, but more so between facilities, probably because of differences in task performance and technology (Hollander *et al.*, 1998). Reduction of exposure to allergen can be achieved by the use of ventilated systems both for housing and handling animals. The exposure is reduced 20-fold when the handling of rats is performed in a ventilated cabinet compared with handling on an open bench (Gordon *et al.*, 1997). The exposure is reduced when the cage changing is performed on a ventilated changing table (Kacergis *et al.*, 1996) and the ambient allergen level is reduced through housing mice in individually ventilated cages with negative air exhaust pressure (Reeb-Whitaker *et al.*, 1999).

An exposure-response relationship between the prevalence rate of sensitization to rat allergens and exposure intensity has been observed (Hollander *et al.*, 1997; Heederik *et al.*, 1999), and a 10-fold reduction of aeroallergen exposure has been proposed as clinically meaningful (Reeb-Whitaker *et al.*, 1999).

Prevention of LAA is crucial because of the potential for adverse impact on both health and career. Levels of allergen exposure are clearly task related, and changes in processes to reduce exposure to allergens can involve building layout, animal housing, cage changing and cleaning methods.

In an effort to prevent LAA, a comprehensive programme to reduce exposure to allergens was developed in a major pharmaceutical company. The programme included:

- building design;
- animal housing in ventilated cabinets;
- ventilated wagon for cage changing;
- centralized vacuum cleaner;
- machine for removal of contaminated bedding and cleaning of cages;
- handling of animals on ventilated benches;
- removal of contaminated exhaust filters directly into a plastic bag;
- medical examination of the staff every 6 months.

Objective

The purpose of this study was to determine exposure levels in the laboratory during different tasks and evaluate the effectiveness of safety equipment used to reduce personal exposure.

MATERIALS AND METHODS

Air sampling

Air samples were collected on 25 mm Teflon filters (FALP02500, 1.0 µm pore size; Millipore, Sundbyberg Sweden) in IOM filter cassettes (SKC, Blandford

Forum, Dorset, UK) using portable pumps at 2 l/min airflow. Airflow through the filter was measured before and after sampling.

Static samples (30–150 min sampling time) were collected:

- in the animal housing room beside (20–40 cm) the ventilated cabinets (90–120 min sampling time);
- in an airlock between two laboratories (30–150 min sampling time);
- near the cage emptying/cleaning machine (30–60 min sampling time).

Personal task samples were collected during:

- cage changing on trolley (78–92 min);
- cage changing using a ventilated cage-changing wagon (60–68 min);
- handling of animals on ventilated benches (32–90 min);
- handling of animals outside ventilated benches (45–70 min);
- cleaning of floor in animal rooms and laboratory (15–17 min);
- manual emptying of cages in ventilated funnel (8–34 min);
- removal of contaminated exhaust filters (25–45 min).

During these tasks, the personnel carried the pumps in a belt with the sampler head fastened in the breathing zone.

Extraction of material from air-sampler filters

The filters were eluted on the day sampled in 1 ml of 15 mM phosphate-buffered saline, 0.5% v/v Tween 20 (Kebo Lab, Lund, Sweden), 0.15% v/v Kathon CG (Rohm and Haas, Landskrona, Sweden) during rotation for 2 h. The filter was then discarded, 10 mg (1% w/v) of human serum albumin was added for protein stabilization, and the eluates were stored at –20°C until analysis.

Allergen analysis

Levels of mouse urinary allergen in the samples were measured as described previously (Renström *et al.*, 2001), using a polyclonal sandwich enzyme-linked immunosorbent assay (ELISA). Samples with low allergen content were analysed in the ELISA using assay signal amplification (AMPAK, Dakopatts AB, Älvsjö, Sweden) according to the manufacturer's recommendations.

The analytical limit of detection for the samples was 20 pg of mouse urinary allergen (MUA) per ml. For statistical reasons, samples below detection limit were given the nominal value 10 pg/ml. The

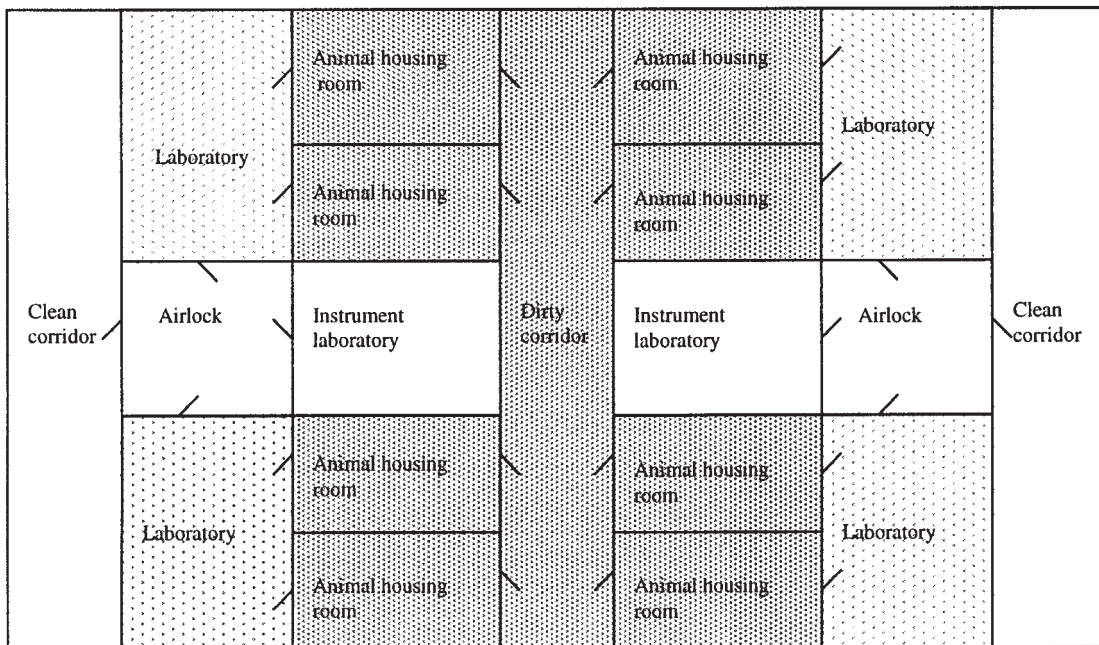


Fig. 1. Part of the facilities for activities that involve the use of laboratory animals.

geometric and the arithmetic mean detection limit of airborne allergen in the 67 samples was 0.2 ng/m^3 .

Building design

The design of buildings housing laboratory animals is an important element in attempts to reduce the spread of allergen and the incidence of allergy among staff working with animals and to prevent microbiological contamination of the animals within the facility.

The activities that involve the use of laboratory animals in the investigated company are isolated from the rest of the research facilities (Fig. 1).

- Changing rooms are provided with ventilated lockers specifically designed to reduce contamination of street clothes. The changing rooms also have adequate washing and showering facilities.
- The facilities are designed so that clean equipment (cages, cabinets) is transferred from 'clean' areas to 'dirty' areas.
- The airflow pattern has a distribution of air from clean areas into dirty areas to prevent the release of material into the clean areas.
- All personnel are required to change into laboratory trousers, shirt and shoes upon entering the facility. When entering a laboratory connected to animal housing rooms, personnel put on an additional coloured long-sleeved laboratory coat, hair covering, gloves and shoes dedicated for the area.
- Emptying and cleaning of cages and ventilated cabinets are done in dedicated areas.

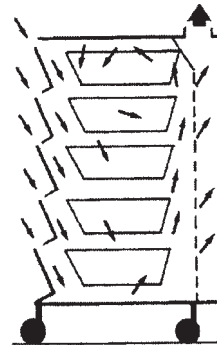


Fig. 2. Ventilated cabinet.

Animal housing room

The animals are housed in ventilated cabinets in an attempt to reduce the spread of allergens. In the ventilated cabinets, the animals are kept in plastic open-top cages (MAK III), with 10 mice in each cage. The bedding material consists of non-autoclaved aspen chip. The ventilated cabinets (B&K Universal, Nittedal, Norway) can hold a maximum of 20 MAK III cages, placed on open shelves in five rows, with four cages per shelf (Fig. 2).

The animal housing rooms are $5.45 \times 3.15 \times 2.65 \text{ m}$ (length $\times$ width $\times$ height), giving a volume of 45 m^3 and space for six ventilated cabinets. Air is supplied into the room in the middle of the ceiling and all exhaust air is taken out through the ventilated cabinets, $126 \text{ m}^3/\text{h}$ per cabinet, giving a room air

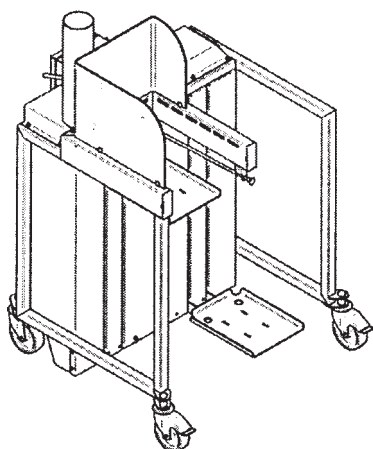


Fig. 3. Cage-changing wagon.

exchange rate of 16.8 per h. The exhaust is extracted from the cabinet directly into the building air exhaust system.

The relative humidity in the air was maintained at $50 \pm 5\%$, noted to reduce allergen levels in the air (Jones *et al.*, 1995), and the air temperature is maintained at $22 \pm 1^\circ\text{C}$.

Cage changing

Bedding was changed twice a week. Previously, personnel transferred mice from soiled to clean cages and stacked the used cages on an unventilated table. Every time a cage is stacked into another, contaminated air is pushed out from the cage underneath and changing of cages is therefore a task that generates high levels of exposure to allergens (Kacergis *et al.*, 1996).

To reduce exposure during changing of cages, a ventilated cage-changing wagon (Fredrikssons Verkstads AB, Vadstena, Sweden) was developed. The equipment is portable and can hold one stack with clean cages and one stack with soiled cages, with 24 cages in a full stack. The upper cages are adjustable to maintain the same height, in order to prevent musculoskeletal disorders. Air is extracted ($250 \text{ m}^3/\text{h}$) through a perforated frame around the top of the stack of soiled cages and the animal is thus placed in an airstream away from the operator (Fig. 3).

All animal housing rooms are equipped with an exhaust outlet to which the portable ventilated cage-changing wagon can be connected.

Cleaning of floors

Traditionally floor cleaning has been carried out by dry sweeping or by using a portable vacuum cleaner. Portable vacuum cleaners without high-efficiency particulate air filtration on the exhaust may contribute to airborne dust by leakage through the filter. Port-

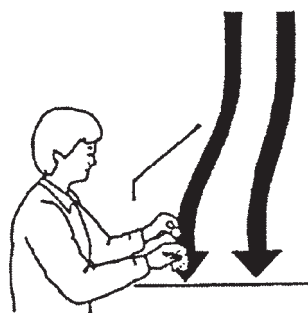


Fig. 4. Ventilated bench with downward airflow.

able vacuum cleaners may also contribute to airborne dust by disturbance of floor dust.

To minimize the spread of allergens, floors are first cleaned using a centralized vacuum cleaner that delivers dust into a closed pipe conveyor with deposition into a closed container. After vacuuming, floors are wiped using a moist mop.

Emptying and cleaning of cages

Dirty cages are transported to a dedicated emptying and cleaning area. Emptying and cleaning of dirty cages was traditionally carried out by manually tipping dirty bedding into a ventilated funnel. The funnel was connected to a closed transport system, delivering bedding to a sealed container. The cages were then washed, dried and filled with new bedding material.

To reduce personnel exposure during the removal of contaminated bedding and cleaning of cages, an automatic cage-handling machine (Fredrikssons Verkstads AB, Vadstena, Sweden) was developed. The machine removes cages from the stack of soiled cages and then empties, cleans and dries them, and finally fills the clean cages with new bedding material and stacks them on trolleys. The machine is placed behind a wall of glass in the emptying and cleaning area.

Handling of animals in laboratories

In an attempt to reduce the spread of allergens, animals are transported into the laboratory in ventilated cabinets. In all laboratories it is possible to connect the cabinet to an exhaust outlet. Cages are placed on a laboratory bench and animals are handled on a ventilated bench equipped with a safety hood.

Ventilated benches (e.g. from addVise AB, Malmö, Sweden) create a vertical downward principal flow field, with extraction through a horizontal perforated plate and airflow past the operator. If a high level of safety is required, the ventilated bench can be equipped with a safety hood open at the top in order to make the vertical flow field more stable (Fig. 4). The animal is thus placed in an airstream that passes away from the operator.

Removal of contaminated exhaust filters

The facilities for working with animals have no recirculation of extracted air. All exhaust air from laboratories and animal housing rooms are filtered before being emitted outdoors.

The exhaust air system has a large number of filters in need of regular maintenance. Service staff responsible for filter changes can be exposed to high levels of allergens, so to minimize the exposure, filters are withdrawn directly into plastic bags. Service staff also wear full-face masks and protective clothing during the removal of contaminated filters.

Analysis of specific immunoglobulin E (IgE) to rat and mouse urinary protein in serum

Staff ($n = 29$) were tested every 6 months from the commencement of the study in 1997 or from the beginning of employment, and until the end of the study or until leaving the company, from one to seven occasions (mean = 4).

Specific IgE against rat and mouse urinary allergen (RUA-IgE and MUA-IgE) was analysed in serum as described previously (Heederik *et al.*, 1999), with the following alterations: standards and sera were diluted in phosphate-buffered saline without the addition of normal human serum. For RUA-IgE, a pool of 38 sera with known specific IgE concentrations was used as a standard, and for MUA-IgE, a pool of 26 sera was used. Both pools were calibrated against the CAP FEIA® tests for rat and mouse urinary allergens, respectively (Pharmacia, Uppsala, Sweden), giving a final concentration of 13 kU/l for RUA-IgE and 6 kU/l for MUA-IgE. The standard curves ranged from 0.01 to 1 kU/l and sera were diluted 10-fold, giving a detection limit of 0.1 kU/l.

Questionnaire

All subjects answered questions every 6 months on their medical history, including details of any work-related symptoms that had occurred.

Subjects

Of the 29 subjects, seven were animal technicians, 13 were laboratory technicians and the rest were researchers, PhD students and service technicians.

The animal technicians change animal cages and clean the floors in animal rooms and laboratories twice a week. Occasionally they take part in animal examinations, which are performed on ventilated benches.

The laboratory technicians perform surgery and administration of medicinal products to the animals. Most of this work is performed on ventilated benches, but some specific work tasks are performed close to the breathing zone. PhD students have a similar exposure situation as the laboratory technicians.

Service technicians handle the automatic cage emptying/cleaning machine.

Most subjects were currently working with mice (27, median 40 h/month) and some with rats (16, median 8 h/month). Eighteen of the 29 subjects had been exposed to rodents prior to the start of the study.

RESULTS

The results of the airborne allergen analysis are shown in Table 1. The highest airborne mouse urinary allergen levels were measured during the manual emptying of cages, handling of male animals and changing of cages on an unventilated table.

Allergen levels were significantly lower: (i) during cage changing using the ventilated changing wagon (17 ng/m³) than during changing on an unventilated table (77 ng/m³), $P = 0.009$; and (ii) when the automatic cage-handling machine was used (0.5 ng/m³ in the working room, 6.8 ng/m³ in the loading zone) compared with manual emptying of cages (367 ng/m³).

The mean allergen exposure was low (2 ng/m³) during handling of 40–80 female animals on ventilated benches equipped with a safety hood and when the work was carried out close to the perforated plate. Allergen exposure during handling of 50–120 male animals outside of or 30 cm above the perforated plate in the ventilated bench without a safety hood was high (87–94 ng/m³).

The mean exposure to mouse allergen during removal of contaminated exhaust filters was 13 ng/m³, and was 5 ng/m³ during cleaning of floors using central vacuum cleaning and moist mopping.

The mean allergen levels were very low (0.2 ng/m³) in the airlock entrance to the laboratories and animal rooms, even when the levels in the laboratory were 45–212 ng/m³. The allergen levels were below the detection limit (<0.2 ng/m³) in undisturbed animal housing rooms, equipped with ventilated cabinets with air exhausted through the cabinet.

IgE against laboratory animal allergens

On a few serum sample occasions, two subjects had detectable levels of serum-specific IgE against MUA. However, the levels were <0.35 kU/l, which is the CAP-FEIA cut-off limit for sensitization. One of them had elevated levels twice and symptoms when working with male mice outside a ventilated bench. However, since starting to use respiratory protection (Dustmaster DM4, 3M), levels of specific IgE against MUA were negative and no symptoms have been seen.

Eight subjects had elevated serum-specific IgE against RUA on one or several occasions during the sampling period. However, only three of them were working with rats during this period, none of whom reported any symptoms. Only two subjects had IgE

levels (RUA) >0.35 kU/l. One subject has left the company and the other started using respiratory protection—a face mask with a P3 filter (3M 9332, 3M, Sollentuna, Sweden)—and had undetectable serum-specific IgE against RUA in the following serum sample.

Of the atopy tested subjects ($n = 27$), six subjects (22%) were positive in a Phadiatop test or had total IgE levels >100 kU/l.

Symptoms

Only five subjects (18%) reported symptoms when working with mice. Two of them were PhD students and the other three were laboratory technicians; among all of them, three regularly used respiratory protection, successfully avoiding symptoms. Respiratory protection (facial mask) was used regularly by 28% of the subjects and occasionally by 52%.

DISCUSSION

The results demonstrate that the introduction of a comprehensive programme has the potential to significantly reduce allergen levels.

The airflow patterns with distribution of air from a clean area into a dirty area has effectively prevented

the release of allergens from the dirty area (laboratory) into the clean area (airlock entrance).

An excellent barrier effect for allergens has been achieved by the housing of the animals in ventilated cabinets with air exhausted through the cabinet. The allergen level in undisturbed animal housing rooms was as low as in the airlock between laboratories.

Cage changing causes for a high level of exposure to allergens and is an ergonomic risk factor. The use of a ventilated cage-changing wagon reduced allergen exposure from 77 to 17 ng/m³ and also improved the ergonomic work posture. The personnel have reported a clear improvement and a reduced stress of the neck and upper extremities (data not shown). To prevent microbial cross-contamination, each laboratory with attached animal rooms is equipped with its own cage-changing device.

Cleaning floors by sweeping and vacuuming cause a major increase of particles in the air (Kacergis *et al.*, 1996). The use of a centralized vacuum cleaner, followed by moist mopping, resulted in a low exposure level during this operation.

The activity that generated the highest exposure level to allergens was the manual emptying of cages. The introduction of an automatic machine for emptying and cleaning of cages has eliminated the manual

Table 1. Levels of airborne mouse urinary allergen (MUA)

Area, situation, no. of samples	ng MUA/m ³ , geometric mean	ng MUA/m ³ , arithmetic mean	Below assay detection limit, n	ng MUA/m ³ , range	% male animals	No. of handled cages or mice
Airlock between two labs, $n = 8$, S	0.2	0.4	2	<0.2–1.1		
Animal housing, $n = 5$, S	<0.2	<0.2	3	<0.2–0.25	40–50	280–640 mice
<i>Cage changing</i>						
Unventilated table, $n = 5$, P	77.3	77.9	0	65.1–88.0	0	89–101 cages
In ventilated changing wagon, $n = 5$, P	17.2	17.4	0	14.0–20.8	0	81–97 cages
Cleaning of floors using central vacuuming, $n = 4$, P	4.4	6.5	0	0.7–11.8		
Manual emptying of cages, $n = 4$, P	367	472	0	111–931		121–355 cages
Automated emptying, loading and cleaning of cages, in the working room outside the machine's containment, $n = 5$, S	0.5	0.7	1	<0.2–1.8		20–160 cages
Automated emptying, loading and cleaning of cages, in the zone where stack of cages is loaded to the machine, $n = 5$, S	6.8	7.8	0	4.1–16.8		20–160 cages
<i>Handling of animals in laboratory</i>						
Close to the perforated plate in a vent. bench with safety hood, $n = 6$, P	2.1	3.3	0	0.6–9.8	0	40–80 mice
Outside vent. bench, animals 20 cm from breathing zone, $n = 9$, P	87.2	107	0	34.8–220	100	50–100 mice
30 cm above the perforated plate in a vent. bench without safety hood, animals 20 cm from breathing zone, $n = 5$, P	94.3	113	0	45.3–212	100	84–120 mice
Removal of contaminated exhaust filters, $n = 6$, P	13.1	14.7	0	5.8–29.0		

S = stationary samples; P = personal samples.

emptying of cages. The airborne allergen levels in the working room where the automatic cage-handling machine is placed were very low (0.5 ng/m^3) and in the machine's loading zone the level was 7 ng/m^3 . Also, the operator does not have to be present in the working room near the machine during the whole emptying and cleaning operation.

The machine also prevents occurrence of musculo-skeletal disorders, since the manual handling of cages is eliminated.

The highest exposure level after introduction of the comprehensive programme was found during the close handling of male animals. Note that the level of the protein complex Mus m 1 is 4-fold higher in urine from mature male mice than from female mice. Incidentally, the handling of female animals on ventilated benches equipped with a safety hood and with the work carried out close to the perforated plate resulted in a low exposure level.

It was not possible to handle male animals on a ventilated bench equipped with a safety hood, and because special examination of the animals was necessary, they had to be handled 30 cm above the perforated plate. One of the people performing this work had specific IgE below the detection limit in all six serum samples but was positive in a skin prick test for mouse allergens 1985, and therefore wears a protective filtered-air hood (Dustmaster DM4, 3M, Sollentuna, Sweden) that prevents expression of symptoms. This person can visit the clean area in the animal facilities without respiratory protection and without showing any symptoms.

Another person performing this work had detectable specific IgE against MUA on two occasions (0.15 and 0.16 kU/l), and reported rhinitis and irritation in the eyes. Serum-specific IgE against MUA was undetectable and no symptoms were reported after the worker started to use respiratory protection (Dustmaster DM4).

One subject with specific IgE levels (RUA) $>0.35 \text{ kU/l}$ reduced IgE levels to below the detection limit after starting to use respiratory protection (3M 9332).

These results indicate a possible effect of respiratory protection, and these individuals and similar future cases should be followed up carefully.

The possibility of detecting specific IgE levels at very low concentrations is important and may be used as an 'early marker' for the development of sensitization, perhaps even before any symptoms have become evident.

Service staff are often exposed to chemicals and other factors that may affect health. In this facility the working environment has been improved, e.g. filters are withdrawn directly into plastic bags during the removal of contaminated filters. The level of exposure to allergens during the removal of filters was in the same order of magnitude as cage changing using ventilated equipment.

CONCLUSIONS

Effective reduction of exposure to mouse allergens and an improved working environment can be achieved by the use of ventilated systems and equipment for housing and handling animals and for handling cages.

The use of automated removal of contaminated bedding and cleaning of cages has eliminated the manual emptying of cages that generates high allergen exposure, and the use of a ventilated cage-changing wagon has reduced the work exposure to allergens from 77 to 17 ng/m^3 .

The housing of animals in ventilated cabinets effectively prevented the release of allergens into the ambient air. The allergen exposure during handling of female animals close to the perforated plate in ventilated benches equipped with a safety hood was low, while close-range handling of male animals outside of or 30 cm above the perforated plate in a ventilated bench without a safety hood was associated with high levels of allergen exposure.

The design of the building, isolating the laboratory animal work and with the air flowing from clean areas into dirty areas, has prevented the release of allergenic material from dirty areas into clean areas.

REFERENCES

- Gordon S, Tee RD, Lowson D, Wallace J, Newman Taylor AJ. (1992) Reduction of airborne allergenic urinary proteins from laboratory rats. *Br J Ind Med*; 49: 416–22.
- Gordon S, Wallace J, Cook A, Tee RD, Newman Taylor AJ. (1997) Reduction of exposure to laboratory animal allergens in the workplace. *Clin Exp Allergy*; 27: 744–51.
- Hastie N, Held W, Toole J. (1979) Multiple genes coding for the androgen regulated major urinary proteins of the mouse. *Cell*; 17: 449–57.
- Heederik D, Venables KM, Malmberg P, Hollander A, Karlsson AS, Renstrom A, Doekes G, Nieuwenhijzen M, Gordon S. (1999) Exposure–response relationships for work-related sensitization in workers exposed to rat urinary allergens: results from a pooled study. *J Allergy Clin Immunol*; 103: 678–84.
- Hollander A, Heederik D, Doekes G. (1997) Respiratory allergy to rats: exposure–response relationships in laboratory animal workers. *Am J Respir Crit Care Med*; 155: 562–7.
- Hollander A, Heederik D, Doekes G, Kromhout H. (1998) Determinants of airborne rat and mouse urinary allergen exposure. *Scand J Work Environ Health*; 24: 228–35.
- Hunnskaar S, Fosse RT. (1990) Allergy to laboratory mice and rats: a review of the pathophysiology, epidemiology and clinical aspects. *Lab Anim*; 24: 358–74.
- Jones RB, Kacergis JB, MacDonald MR, McKnight FT, Turner WA, Ohman JL, Paigen B. (1995) The effect of relative humidity on mouse allergen levels in an environmentally controlled mouse room. *Am Ind Hyg Assoc J*; 56: 398–401.
- Kacergis JB, Jones RB, Reeb CK, Turner WA, Ohman JL, Ardman MR, Paigen B. (1996) Air quality in an animal facility: particulates, ammonia, and volatile organic compounds. *Am Ind Hyg Assoc J*; 57: 634–40.
- Lorsson JR, Moffat S, Ohman JL. (1986) Immunologic and biochemical properties of the major mouse urinary allergen. (Mus m 1). *J Allergy Clin Immunol*; 78: 928–37.

- Platt-Mills TAE, Heymann PW, Longbottom JL, Wilkins SR. (1986) Airborne allergens associated with asthma: particle size carrying dust mite and rat. *J Allergy Clin Immunol*; 77: 850–7.
- Price JA, Longbottom JL. (1987) Allergy to mice. I. Identification of two major mouse allergens. (Ag 1 and Ag 3) and investigation of their possible origin. *Clin Allergy*; 17: 43–53.
- Price JA, Longbottom JL. (1988) ELISA method for measurement of airborne levels of major laboratory animal allergens. *Clin Allergy*; 18: 95–107.
- Rajka G. (1961) Ten cases of occupational hypersensitivity to laboratory animals. *Acta Allergol*; 16: 168–76.
- Reeb-Whitaker CK, Harrison DJ, Jones RB, Kacergis JB, Mayers DD, Paigen B. (1999) Control strategies for aeroallergens in an animal facility. *J Allergy Clin Immunol*; 103: 139–46.
- Renström A, Malmberg P, Larsson PH, Sundblad B-M. (1995) Allergic sensitization is associated with increased bronchial responsiveness: a prospective study of allergy to laboratory animals. *Eur Respir J*; 8: 1514–1519.
- Renström A, Björing G, Höglund AU. (2001) Evaluation of individually ventilated cage systems for laboratory rodents: occupational health aspects. *Lab Anim*; 35: 42–50.
- Sakaguchi M, Inouye S, Miyazawa H, Kamimura H, Kimura M, Yamazaki S. (1989) Particle size of airborne mouse crude and defined allergens. *Lab Anim Sci*; 39: 234–6.
- Sorell AH, Gottesman J. (1957) Mouse allergy. *Ann Allergy*; 15: 662–3.