International Journal of Occupational Medicine and Environmental Health, Vol. 10, No 1, 31–36, 1997

OCCUPATIONAL RESPIRATORY DISEASES IN LABORATORY ANIMAL WORKERS: INITIAL RESULTS

ANNA KRAKOWIAK, BOGDAN SZULC and PAWEŁ GÓRSKI

Department of Occupational Diseases
The Nofer Institute of Occupational Medicine
Łódź, Poland

Key words: Laboratory-animal allergy, Asthma, Rhinitis, Sensitization

Abstract. Laboratory-animal allergy (LAA) is a well-known occupational hazard to workers employed in biological or medical research institutes and in the pharmaceutical industry. The aim of this study was to focus on the problem of LAA and to assess factors predisposing to sensitization among subjects occupationally exposed to animals.

Sixty workers were examined in our study. They responded to a questionnaire and underwent spirometry (Vital Capacity, VC and Forced Expiratory Volume in one second, FEV_1). In addition, Peak Expiratory Flow (PEF) and the histamine provocation test were estimated in 5 subjects that had been hospitalized in the Department of Occupational Diseases. Skin prick tests with common allergens and with hair extracts from laboratory animals were performed, and total IgE levels and specific IgE antibodies were also measured.

Among 60 subjects who had been working with animals, 26 had positive skin prick tests for one or more of the common allergens. Five subjects supposed to have occupational bronchial asthma and four with occupational allergic rhinitis showed positive skin prick tests for one or more animal allergens, increased total IgE levels and specific serum IgE antibodies. All these subjects had smoked for years.

Conclusions: 1) Laboratory animal allergy develops within first years of exposure; 2) atopy and smoking predispose to laboratory animal sensitization and to a development of bronchial asthma and allergic rhinitis.

INTRODUCTION

Allergy to laboratory animals is common among workers employed in the pharmaceutical industry and biological or medical research institutes. This applies to both research workers and persons involved in animal breeding (4,5). Of those exposed to laboratory animals 10–30% become sensitized or report symptoms induced by their exposure to animals (2).

Address reprint requests to Prof. P. Górski, Department of Occupational Diseases, The Nofer Institute of Occupational Medicine, P.O. Box 199, 90-950 Łódź, Poland.

Rhinitis, bronchial asthma, conjunctivitis and contact urticaria belong to common manifestations of allergy to laboratory animals.

In many cases of laboratory-animal allergy (LAA), particularly in those involving asthma, specific IgE antibodies to responsible proteins are detected (7,10,11). Asthma is often associated with nasal symptoms of LAA and it generally develops within several months after the onset of other symptoms (18).

In this study the authors tried to focus on the problem of LAA among subjects occupationally exposed to animals and to assess factors predisposing to sensitization and development of allergic symptoms induced by exposure to laboratory animals.

MATERIALS AND METHODS

Sixty workers occupationally exposed to laboratory animals (animal breeders, technicians, scientists and zoo-keepers) participated in the study. They were aged from 22 to 56 years (mean – 39) and they had worked with laboratory animals (guinea pigs, rats, mice, rabbits, hamsters) for at least 1 year (the longest period of employment was 35 years). All the subjects responded to a questionnaire concerning allergic heredity, personal allergic and medical history, exposure to a number of irritants, smoking habits and animal exposure at home.

The study was approved by the Medical Ethical Committee and all the subjects gave their written consent.

Lung physiology

Chronic respiratory disease was diagnosed according to the criteria of the American Thoracic Society. Ventilatory function was measured by spirometry. The highest value of three forced expirations was taken as the forced expiratory volume in one second (FEV_1) and the highest of three forced and three slowest maximal expirations were selected as the vital capacity (VC) for each participated subject. In addition, Peak Expiratory Flow (PEF) and the histamine provocation test were estimated in 5 subjects that were hospitalized in the Department of Occupational Diseases.

Histamine in isotonic saline was inspired in increasing concentration (0.250; 0.5; 1; 2; 4; 8 and a maximum of 16 mg/ml). The cumulative inhaled dose of histamine which caused a 20% decrease in FEV_1 was calculated by interpolation on a log cumulative dose scale ($PC_{20}FEV_1$).

Skin prick tests

All workers were also tested with skin prick method with the use of eleven common allergens, such as: house dust mite (Dermatophagoides pteronyssinus), feathers, grass and tree pollens, and prick tests with hair extracts from: mouse, guinea pig, rat, rabbit, dog, cat and hamster (Beecham-Bencard Allergy Service).

Moreover, histamine chloride in concentration of 10 mg/ml was used as a positive reference and a 0.9% sodium hydrochloricum as negative control (standard test with phenol and glycerine, Beecham-Bencard Allergy Service). Reactions of a wheal $\geqslant 5$ mm in diameter were considered to be positive.

Total IgE levels were analyzed with EIA (Pharmacia). Sera from all workers exposed to laboratory animals were tested with RAST (Radioallergo Sorbent Test, RAST, Pharmacia, Uppsala, Sweden) to measure specific IgE levels.

Definitions

1. Laboratory animal sensitized subject – an individual was considered as sensitized to a laboratory animal if he/she had a positive skin-prick test or specific IgE in serum to the allergen.

2. Laboratory animal allergy subject – an individual showing symptoms (rhinitis, wheezing, thighteness of the chest, coughing or urticaria) clearly associated with laboratory animal work was considered to be an LAA subject.

3. Atopic – any person with a reaction of a wheal $\geqslant 5$ mm against any of common allergens in skin-prick tests or total serum IgE above 80 kU/L.

Statistics

All calculations were made with Microsoft[R] Excel. Values are expressed as means $\pm$ SD.

RESULTS

Acute episodes of dyspnoea classified as bronchial asthma were found in 8 subjects. The illness lasted from 2 to 7 years (mean 3 years). Out of eight subjects with bronchial asthma five confirmed exacerbation of their symptoms in their work-place. An 8-hour occupational exposure to laboratory animals intensified both cough and dyspnoea. Chest symptoms (asthma) developed within the first 2–3 years of employment and in all cases, they were concurrent with nasal symptoms such as: sneezing, itching, rhinorrhoea and congestion. Four workers had only nasal symptoms related to laboratory animal exposure. They were diagnosed as an isolated allergic rhinitis. All subjects that developed chest and nasal symptoms had smoked cigarettes for a least one year.

Lung functional values (VC and FEV_1) in the subject are shown in Table 1.

Table 1. Lung function in subjects occupationally exposed to laboratory animals

	All subjects N = 60	Asthmatic patients N = 8	Patients with rhinitis N = 4
VC (l)			
Mean $\pm$ SD	4.03 $\pm$ 0.5	3.6 $\pm$ 0.3	3.9 $\pm$ 0.9
FEV_1 (l/s)			
Mean $\pm$ SD	3.9 $\pm$ 0.8	2.9 $\pm$ 0.4	3.4 $\pm$ 0.5

Mean values of PEF and PC_{20} in the group of five asthmatic patients that had been hospitalized in the Department of Occupational Diseases were: 4.3 $\pm$ 1.2 l/s and 3.2 $\pm$ 0.7 mg/ml, respectively.

Twenty six of all laboratory animal exposed subjects developed a positive skin prick test (SPT) for one or more of the common allergens. Fourteen out of 26 subjects had also positive SPT for one or more of the animal extracts from animals they had been working with.

Total IgE levels in the group of 60 subjects were 56 $\pm$ 15 kU/l. Five subjects who had reported symptoms specific for occupational asthma had total IgE levels

> 100 kU/l, positive SPT for one or more of the common allergens and animal extracts and also specific serum IgE antibodies.

Total IgE levels of four subjects who had developed only nasal symptoms were 88 ± 20 kU/l, and they also had positive SPT for one or more of the common allergens and animal extracts and specific serum IgE.

All questionnaire responses concerning allergic heredity, personal allergic and medical history, smoking habits and animal exposure at home are shown in Table 2.

Table 2. Questionnaire responses among subjects occupationally exposed to laboratory animals

	All subjects N = 60	Asthmatic patients N = 8	Patients with rhinitis N = 4
Allergic heredity	4	2	2
Personal allergic history	12	8	4
Smoking habits	35	5	4
Animals at home	10	0	0
Medical history:			
corticosteroids	1	1	0
antihistamines	6	4	2
anti-allergic preparations	2	2	0
β agonists	2	2	0

DISCUSSION

Allergy to animals seems to be the most important occupational health hazard of laboratory animal workers. The number of employees whose work brings them into contact with animals in laboratory is not known in Poland. In the United Kingdom 21 cases among 554 diagnosed as occupational asthma resulted from sensitization to laboratory animals and insects (8). Several studies of laboratory animal workers have been reported in recent years (19,20). They examined the prevalence of allergic symptoms, the relationship of contact with animals, the evidence of immunologic response to extracts of animal excreta and the factors that may predispose to laboratory animal allergy, particularly atopy. In our study all subjects supposed to have occupational asthma (five subjects) and occupational rhinitis (four subjects) were atopics and had specific IgE against animal allergens. Atopy is a well documented risk factor for sensitization (9,17) and atopic subjects are much more likely to develop animal allergy (12). Renström noticed that high pre-exposure total IgE level predicted development of LAA. Subjects with an elevated total IgE level prior to work exposure were shown to have an approximately three times higher relative risk for sensitization and/or development of symptoms induced by the contact with laboratory animals (16).

Tobacco smoke is one of air pollutant which can be associated with an increased prevalence of atopic diseases, such as bronchial asthma and allergic rhinitis (3,22). All subjects participating in our study were active or passive smokers. A study performed in different regions of Bavaria revealed a significantly increased risk of atopic diseases or atopic sensitization in children born to mothers, who had smoked during pregnancy or lactation or whose parents smoked at home. Passive

smoking is by far the best identified risk factor for development of sensitization. This is particularly true in early childhood. Numerous epidemiological studies demonstrated the relationship between exposure to tobacco smoke and recurrent wheezing (15,21).

We also found that nasal and chest symptoms developed during the first years of employment.

Most studies have shown that the majority of subjects with laboratory-animal allergy developed symptoms between 6 and 36 months of exposure and that asthma usually develops after the onset of rhinitis (1,6). All five asthmatic patients participating in the study confirmed that nasal symptoms such as, sneezing, itching, rhinorrhoea and congestion had appeared before the development of chest symptoms (asthma), Asthma without rhinitis is rare. One can suppose that 4 subjects with isolated allergic rhinitis will develop bronchial symptoms if not removed from the occupational exposure. One can mention that asthma, at least initially, may only be manifested as increased airway responsiveness (e.g provoked by exercise or cold air) or it may develop only several hours after animal contact, making identification of the provoking agent more difficult (13,14).

From the initial results the authors conclude that atopic subjects and active smokers should not be employed under exposure to laboratory animals.

Final conclusions regarding factors predisposing to sensitization and the comparison of exposed and nonexposed workers for changes in the lung function, allergic symptoms and atopic status cannot be presented here as the study has not as yet been completed.

ACKNOWLEDGMENTS

This paper has been supported as a part of the Strategic Programme of the Polish Government — Strategy for "Poland 2000".

REFERENCES

1. Aoyama K, Ueda A, Manda F, Matsushita T, Ueda T, Yamauchi C. Allergy to laboratory animals: an epidemiological study. Br J Ind Med 49 (1): 41–47, 1992.
2. Bland SM, Levine MS, Wilson D et al. Occupational allergy to laboratory animals: an epidemiologic study. J Occup Med 28: 1151–1157, 1986.
3. Burrows B, Malonen M, Barbec RA et al. The relationship of serum immunoglobulin E to cigarette smoking. Am Rev Respir Dis 124, 523–527, 1981.
4. Gross NJ. Allergy to laboratory animals: epidemiologic, clinical and physiologic aspects and a trial of cromolyn in its management. J Allergy Clin Immunol 66: 158–165, 1980.
5. Held JR. Allergy to animals: a laboratory animal science perspective. N Engl Reg Allergy Proc 8: 179–182, 1987.
6. Hunskar S. Fosse RT. Allergy to laboratory mice and rats: a review of the pathophysiology, epidemiology and clinical aspects. Lab Animals 24: 358–374, 1990.
7. Lutsky I. Occupational asthma in laboratory animal workers. In: Occupational Asthma. CA Frazier (ed.), Van Nostrand Reinhold, New York, 1980.
8. Meredith SK, Taylor VM, MacDonald JC. Occupational respiratory disease in the United Kingdom 1989: a report to the British Thoracic Society and the SWORD project group. Br J Ind Med 48: 292–298, 1991.
9. Newill CA, Prenger VL, Fish JE, Evans R, Diamond EL, Wei Q, Eggleston PA. Risk factors for increased airway responsiveness to metacholine challenge among laboratory animal workers. Am Rev Respir Dis 146 (6): 1494–1500, 1992.

10. Platts-Mills T, Longbottom JL, Edwards J et al. Occupational asthma and rhinitis to laboratory rats: Serum IgE and IgG antibodies to rat urinary allergen. J Allergy Clin Immunol 79: 505–507, 1987.
11. Price JA, Longbottom JL. IgG antibodies in relation to exposure to laboratory-animal antigens. J Allergy Clin Immunol 84: 520–528, 1989.
12. Renström A, Malmberg P, Larsson K, Sundblad BM, Larsson PH. Prospective study of laboratory-animal allergy: factors predisposing to sensitization and development of allergic symptoms. Allergy 49: 548–552, 1994.
13. Renström A, Malmberg K, Larsson PH, Larsson BM. Allergic sensitization is associated with increased bronchial responsiveness: a prospective study of allergy to laboratory animals. Eur Respir J 8: 1514–1519, 1995.
14. Saloga J, Renz H, Larsen GL, Gelfland EW. Increased airways responsiveness in mice depends on local challenge with antigen. Am J Respir Crit Care Med 149: 65–70, 1994.
15. Schafer T, Dirschedl P, Pzybilla B et al. Maternal smoking (MS) and atopy manifestation (AM) in children are significantly correlated. A C I News 1: 221 (abstract), 1991.
16. Schumacher MJ, Tait BD, Holmes MC. Allergy to murine antigens in a biological research institute. J Allergy Clin Immunol 68: 310–318, 1981.
17. Sjostedt L, Willers S, Orbaek P. A follow-up study of laboratory animal exposed workers: the influence of atopy for the development of occupational asthma. Am J Ind Med 24 (4): 459–469, 1993.
18. Slovak AJM. Achieved objectives in laboratory animal allergy research: their significance for policy and practice. N Engl Reg Allergy Proc 8: 189–194, 1987.
19. Spitzauer S, Pandjaitan B, Soregi G et al. IgE cross-reactivities against albumins in patients allergic to animals. J Allergy Clin Immunol 96: 951–959, 1995.
20. Taylor K, Hardiman F. Laboratory animal allergy: an employer's responsibility. Occup Health Lond 45 (10): 338, 340–341, 1993.
21. Venables KM, Teed RD, Hawkins ER et al. Laboratory animal allergy in a pharmaceutical company. Br J Ind Med 45: 660–666, 1988.

Received for publication: October 1, 1996
Approved for publication: January 6, 1997