

Prevalence and host determinants of occupational bronchial asthma in animal shelter workers

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Abstract

Objective We examined the risk factors for the development of airway allergy in animal shelter workers.

Methods The study population comprised 88 animal shelter workers occupationally exposed to cats and dogs. They responded to a questionnaire concerning the history of exposure to animal allergens and job characteristics and were subjected to skin prick test (SPT) to common and occupational allergens (cat and dog), and determination of total serum IgE level and specific IgE. In addition, SPT with rat and mouse allergens were performed. Bronchial hyperreactivity and peak expiratory flow rate were measured at work and off work only in workers with work-related symptoms suggestive of occupational asthma (OA).

Results The prevalence of OA was 9.1%. Sensitization to dog allergens was higher than to cats. The multivariate logistic regression analysis revealed a significant role of positive family history of atopy and having a dog as pet in the past for the development of occupational airway allergy (OR 5.9; 95% CI 1.76, 20.00; $P=0.003$; OR 6.47; 95% CI 1.90, 22.02; $P=0.002$, respectively). In the multivariate logistic regression analysis, the risk for developing OA was most clearly associated with growing up in the country (OR 7.59; 95% CI 1.25, 45.9; $P=0.025$).

Conclusions Allergic disease is a serious occupational health concern for subjects who have occupational contact with cats and dogs.

Keywords Allergy · Animals · Shelters · Occupational exposure

Abbreviations

SPT Skin prick test
OAA Occupational airway allergy
PEFR Peak expiratory flow rate
BHR Bronchial hyperreactivity
OA Occupational asthma

Introduction

Dog and cat allergy is an important health problem in the general population (Linnenberg et al. 2003; Waser et al. 2005). Thirty to thirty-five percent of atopic subjects displays type I allergic symptoms on exposure to dog and/or cat allergens (Spitzauer et al. 1994; Haah-tela and Jaakonmaki 1981; Schou 1993). Allergic sensitization to these animals may occur at home or in the workplace. Animal workers are in regular contact with these animals. In an epidemiologic study involving over 5,000 laboratory animal workers in Japan, symptoms were reported in 25% of workers in contact with dogs and 30% with cats (Aoyama et al. 1992).

A number of studies investigated the prevalence of atopy and allergic diseases among workers occupationally exposed to rodents (Cullinan et al. 1999; Agrup et al. 1986), and the prevalence of allergic diseases from the contact with pets in childhood and adulthood (Linnenberg et al. 2003; Waser et al. 2005), but there are

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only solitary reports on the development of occupational allergic sensitization and diseases from the exposure to dogs and/or cats (Aoyama et al. 1992). Occupational allergy to cats and dogs is generally less common than that to rats and mice, mainly because the former species are used less frequently in animal experiments. On the other hand, people have a more frequent contact with pets at home. Therefore, the process of diagnosing occupational allergic diseases may be more complicated.

In Poland, no epidemiological data have so far been available on the prevalence of occupational airway allergy (OAA) in subjects occupationally exposed to cat and dog allergens. The present study is the first attempt to evaluate the risk factors of allergic diseases in this population, which in our case are the workers at animal shelters.

Methods

Study population

The subjects were 88 animal shelter workers (57 males, 31 females, mean age 37.61 ± 13.02 , mean duration of occupational exposure 18.7 ± 8.2 years) who were occupationally exposed to cats and dogs. Their duties involved giving food and water to animals and cleaning their cages as well as performing some administrative tasks. The subjects were employed at different institutions located mainly in Central Poland and each of them spent 8 h a day in an animal shelter. The number of dogs was higher than that of cats, so the exposure to dog allergens was greater than that to cat allergens. The workers participating in the study had no occupational exposure to rodents. Those who reported ever having dogs and/or cats at home, or having allergic symptoms on contact with these animals before they started working in animal shelters, were excluded from the study.

None of the animal shelters examined possesses any ventilation system in use. Measurements of endotoxin levels have never been done by hygienic services in these shelters. Airborne endotoxin was not detected in the present study.

The study protocol had been approved by the local Biomedical Ethics Committee and all the subjects gave their written informed consent.

Questionnaire

The questionnaire was an adaptation of the instrument developed by the IUATLD (Burney et al. 1989). Apart from personal characteristics, the questionnaire inquired about general respiratory, nasal, ocular and skin symp-

toms, smoking habit, personal and family history of allergic diseases. The development of at least one symptom, a characteristic of bronchial asthma, rhinitis and conjunctivitis, was considered a positive diagnosis of respective diseases. The questionnaire items included also the job characteristics and the description of occupational exposure. A small animal shelter was defined as a shelter occupied by not more than 80 animals (cats and dogs).

Subjects reporting contact with animals in the past were either having a pet in their childhood or before they had an occupational contact with animals. In the part inquiring about the smoking habit, two categories were distinguished: smokers and non-smokers.

The category defined as smokers included current-smokers and ex-smokers. Current-smokers were defined as the subjects who reported smoking tobacco at present, while ex-smokers, as those who had smoked daily and quit at least a month before the survey. Non-smokers were the subjects who had never smoked.

The expression 'grown-up in the village' applied to animal shelter workers who lived in a village during the childhood (age: <18 years), while 'grown-up in the city' referred to the workers who spent their childhood in the city.

Skin prick tests

Skin prick tests (SPTs) with common environmental and occupational allergens were carried out. The allergens included tree pollens (alder, hazel, poplar, elm, willow, birch, beech, oak, plane) and grass pollens, *Dermatophagoides pteronyssinus*, *D. farinae*, moulds I (*Alternaria tenuis*, *Botrytis cinerea*, *Cladosporium herbarum*, *Curvularia lunata*, *Helminthosporium halodes*, *Fusarium moniliforme*) and moulds II (*Aspergillus fumigatus*, *Mucor mucedo*, *Penicillium notatum*, *Pullularia pullulans*, *Rhizopus nigricans*, *Serpula lacrymans*), feathers, cat and dog dander (Allergopharma, Reinbek, Germany).

SPTs were performed and interpreted according to the recommendation of the European Academy of Allergology and Clinical Immunology (Dreborg and Frew 1993). A wheal diameter of at least 3 mm was considered positive in the absence of a reaction to allergen diluent and in the presence of a positive reaction to histamine.

In addition, SPTs with rat and mouse allergens (Allergopharma) were performed following the scheme mentioned above. The negative control was a commercially available allergen diluent (containing 9 mg NaCl, 4 mg phenol and 63 mg glycerol/ml), and the positive one was a 1-mg/ml solution of histamine dihydrochloride. SPTs were performed according to a standardized

technique. The largest wheal diameter was assessed after 15 min.

Total and specific IgE

Specific Immunoglobulin E (sIgE) for the cat (e1) and dog (e2) epithelium was measured by enzyme immunoassay (Allergopharma) in all serum samples. The results were expressed quantitatively in kilo units per litre and considered positive at values higher than 0.35 KU/l. Moreover, the presence of serum sIgE against mouse (e71) and rat (e73) allergens was also evaluated (Allergopharma). The sIgE results were graded as follows: class 0 = 0.00–0.34; class 1 = 0.35–0.69; class 2 = 0.7–3.4; class 3 = 3.5–17.4; class 4 = 17.5–50.0 and class 5 > 50.0 IU/ml. Classes 1–5 were interpreted as positive.

Total serum Immunoglobulin (IgE) was determined in all blood samples, using UniCAP system (Pharmacia Diagnostics, Uppsala, Sweden).

Pulmonary function

In all the subjects, peak expiratory flow rate (PEFR) was measured on a day with occupational exposure to cats and dogs, and 24 h after the onset of work in contact with animals. Additionally, PEFR measurements were performed on a day—out of work (control day). The authors also performed histamine challenge testing according to Cockcroft et al. (1977), but only in the subjects who reported work-related symptoms suggestive of occupational asthma (OA). The test was carried out four times: before and after occupational exposure to cats and dogs, and before and after the control day.

Diagnostic criteria

Hypersensitivity to any allergen has been defined as at least one positive result of SPT or positivity of specific serum IgE assay (Johansson et al. 2001).

The symptoms were considered to be work-related, if they followed the contact with an occupational agent and improved during weekends or holidays (Johansson et al. 2001; Reininger et al. 2003).

Occupational allergic disease was diagnosed in a sensitised subject reporting work-related symptoms.

In our study, OA was diagnosed in the sensitised subjects reporting work-related chest symptoms, for whom a period of working with laboratory animals was found to induce an early or dual asthmatic reaction (a significant decrease in PEFR, or an increase in non-specific bronchial hyperreactivity (NSBH) (Perrin et al. 1992; Cote et al. 1990).

Statistical analysis

Continuous variables were expressed as mean values $\pm$ standard deviations (SD), while nominal variables as numbers and percentages. At first, a univariate logistic regression analysis was carried out to identify the risk factors for two outcomes: work-related symptoms suggestive of OA and OA and/or rhinitis—OAA. In all the risk factor analyses, the controls were animal shelter workers who did not report any symptoms. The analysis of OA risk factors concerned 8 cases, and the controls were 80 workers. For airway allergy, the risk factor analysis covered 19 persons with recognized OAA and 69 controls. The variables showing a significant association ($P < 0.05$) were then included in separate multivariate logistic regression models (Statistica 99). PEFRs measurements were expressed as mean values $\pm$ standard deviations (SD). PEFR values before and after the onset of occupational exposure in workers with no work-related respiratory symptoms suggestive of occupational allergy were compared using a paired Student *t* test. For the group of subjects with work-related respiratory symptoms suggestive of OA, the comparisons of PEFR and PC₂₀ values before and after the onset of occupational exposure were made with Wilcoxon matched pairs, signed-rank test. *P* values < 0.05 were considered statistically significant.

Results

In the animal shelter workers, the mean total IgE level was 90.07 ± 17.74 kU/l. The mean period of exposure to animals after which the subjects reported chest symptoms suggestive of OA was 6.4 ± 2.2 years and of nasal symptoms suggestive of occupational rhinitis 5.1 ± 1.8 years. Most subjects participating in the study had a positive history of smoking (Table 1). Positive SPTs to tree pollens were found most frequently in animal workers (Table 1). Sensitization to dog allergens (assessed by positive SPT and/or serum sIgE) was more frequently diagnosed among animal workers than sensitization to cat allergens 39.8 vs. 25%).

General ocular symptoms were found most frequently—in 29 (32.9%) out of the total of 88 subjects, while general skin symptoms were mostly rare; these were found in 7 (7.9%) workers (Table 2). General asthmatic symptoms were reported by 14 subjects (15.9%), nasal symptoms by 18 workers (20.1%) and asthmatic and nasal symptoms by 7 subjects (7.9%).

Work-related ocular symptoms were reported by 21 (23.9%), while the work-related nasal and asthmatic symptoms by 12 (13.5%) and 8 subjects (9.1%),

Table 1 Selected characteristics and immunological findings: study group

	Study group (N = 88)
Smoking	
Smokers	54 (61.4%)
Non-smokers	34 (38.6%)
Small shelter	49 (55.7%)
Family history of atopy	30 (34.1%)
Positive SPTs to	
At least one common allergen	60 (68.2%)
<i>Dermatophagoides pteronyssinus</i>	13 (14.7%)
<i>D. farinae</i>	18 (20.1%)
Tree pollens I ^a and II ^b	23 (26.1%)
Grass pollens	15 (17.1%)
Moulds I ^c and II ^d	16 (18.2%)
Feathers	8 (9.1%)
Sensitization to dog allergens (positive SPT and/or sIgE in serum)	35 (39.8%)
Sensitization to cat allergens (positive SPT and/or sIgE in serum)	22 (25%)
Sensitization to cat and dog allergens	13 (14.8%)
Sensitization to mouse allergens (positive SPT and/or sIgE in serum)	33 (37.5%)
Sensitization to rat allergens (positive SPT and/or sIgE in serum)	18 (20.1%)
Total IgE (kU/l) (mean ± SD)	90.7 ± 17.74

^a Alder, hazel, poplar, elm, willow^b Birch, beech, oak, plane^c *Alternaria tenuis*, *Botrytis cinerea*, *Cladosporium herbarum*, *Curvularia lunata*, *Helminthosporium halodes*, *Fusarium moniliforme*^d *Aspergillus fumigatus*, *Mucor mucedo*, *Penicillium notatum*, *Pullularia pullulans*, *Rhizopus nigricans*, *Serpula lacrymans*

respectively. Work-related skin symptoms were reported by four animal workers (4.6%).

Occupational allergic conjunctivitis was diagnosed in 19 (21.2%) subjects, occupational asthma in 8 (9.1%) and occupational allergic rhinitis in 11 subjects (12.5%). Occupational skin disease was diagnosed in four subjects, mainly on contact with cats.

There was no subject that would have work-related chest symptoms and would not be sensitized to cat and/or dog.

The authors found one worker with work-related nasal symptoms and two subjects with work-related ocular symptoms who presented no hypersensitivity to cat and/or dog allergens. Eight subjects out of 19 with the work-related symptoms suggestive of occupational allergy had abnormal PEFR value and 6 subjects out of 69 animal shelter workers with no work-related symptoms suggestive of occupational allergy (Table 3).

The prevalence of skin and serum sensitization to cat and dog allergens was higher in the group of subjects with work-related symptoms suggestive of OAA than in the group with no such symptoms, but we also

Table 2 Clinical symptoms: study group

Clinical symptoms	Study group (N = 88)
General asthmatic symptoms	14 (15.9%)
General nasal symptoms	18 (20.1%)
General asthmatic and nasal symptoms	7 (7.9%)
General ocular symptoms	29 (32.9%)
General skin symptoms	7 (7.9%)
Worsening or improvement of asthmatic symptoms at/off work	8 (9.1%)
Worsening or improvement of nasal symptoms at/off work	12 (13.5%)
Worsening or improvement of ocular symptoms at/off work	21 (23.9%)
Worsening or improvement of skin symptoms at/off work	4 (4.6%)
Work-related asthmatic symptoms in sensitized subjects (occupational disease)	8 (9.1%)
Work-related nasal symptoms in sensitized subjects (occupational disease)	11 (12.5%)
Work-related ocular symptoms in sensitized subjects (occupational disease)	19 (21.2%)
Work-related skin symptoms in sensitized subjects (occupational disease)	4 (4.6%)

Table 3 Immunological findings and PEFR in animal shelter workers with work-related symptoms suggestive of occupational allergy

	Cases with work-related symptoms suggestive of occupational allergy (asthma and/or rhinitis and/or conjunctivitis) (n = 19)	Cases with no work-related symptoms suggestive of occupational allergy (n = 69)
sIgE cat +/- sIgE dog +/-	11 (57.9%)	13 (18.8%)
sIgE cat -/ sIgE dog -	8 (42.1%)	56 (81.2%)
SPT cat +/- SPT dog +/-	10 (52.6%)	20 (29%)
SPT cat -/ SPT dog -	9 (47.4%)	49 (71%)
PEFR abnormal	8 (42.1%)	6 (8.7%)
PEFR normal	11 (57.9%)	63 (91.3%)

found 13 individuals who had positive SPT, and 20 workers who had serum sIgE to cat and dog allergens but were asymptomatic (Table 3).

Sensitization to dog and cat allergens (assessed by positive SPT and/or serum sIgE) was more frequently diagnosed among 19 workers with work-related symptoms suggestive of occupational allergy than among 69 animal shelter workers without these symptoms

(Table 3). Nine subjects out of 19 workers with work-related symptoms suggestive of occupational allergy had no skin reaction to cat and dog allergens and 8 subjects had no positive serum sIgE to these allergens. Sensitization to cat and dog allergens (positive SPT/serum sIgE) was also detected in asymptomatic workers (Table 3).

A significant decrease in PEFR was observed in eight subjects with work-related respiratory symptoms suggestive of OA during early and late allergic reaction on the day with occupational exposure to animals ($P < 0.05$) (Fig. 1). No marked changes in PEFR could be noted within the period of work abstinence (Fig. 1). Statistically significant differences in PC_{20} were found in eight workers with work-related symptoms indicating OA before and after working with animals (cats and dogs) (Fig. 2, $P < 0.05$). No significant differences in PC_{20} could be noted in eight workers with work-related symptoms suggestive of OA after the period of work abstinence (Fig. 2, $P > 0.05$).

The results of univariate logistic regression analysis indicated that such variables as sensitization to grass pollens and growing up in the country were significant

risk factors for developing work-related symptoms suggestive of OA due to cat and dog allergens (Table 4). The same analysis confirmed the protective role of growing up in the town/city for this outcome.

The authors did not find evidence that such variables as sensitization to mouse and rats were significant risk factors for developing work-related symptoms suggestive of OA due to cat and dog allergens (Table 4).

In the multivariate logistic regression analysis, the risk for developing OA was most clearly associated with growing up in the country (OR 7.59; 95% CI 1.25, 45.9; $P = 0.025$). This analysis also revealed the protective role of growing up in the town/city (OR 0.13; 95% CI 0.02, 0.79; $P = 0.02$).

Univariate logistic regression revealed that the positive family history of atopy and previous contact with dogs significantly determined the likelihood of developing work-related symptoms suggestive of occupational allergy (Table 5). Sensitization to mouse and rats did not prove to be a significant risk factor for developing work-related symptoms suggestive of occupational allergy (Table 5).

Fig. 1 PEFR values in animal workers with OA either during the period of working with animals or the period of work abstinence. * $P < 0.05$ (PEFR values after the onset of occupational exposure vs. baseline value; Wilcoxon matched pairs, signed-rank test)

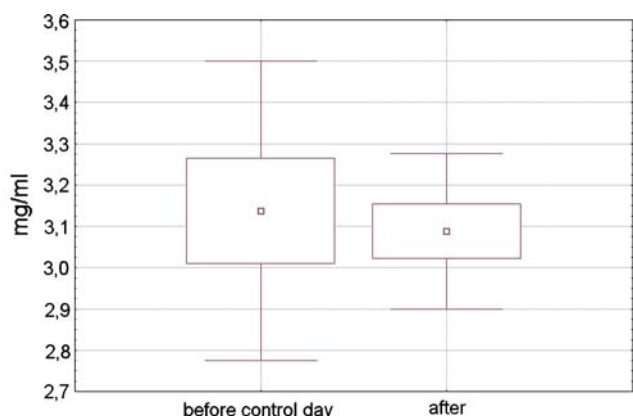
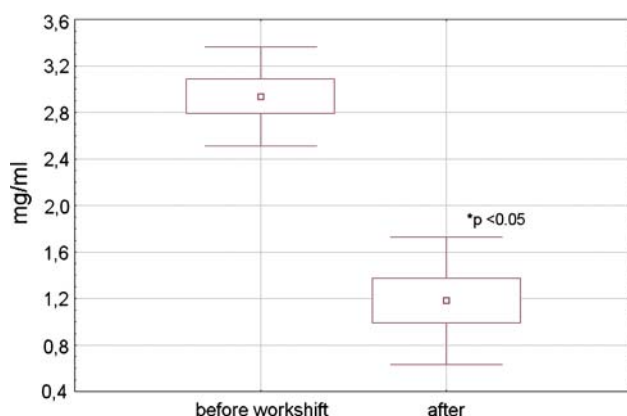
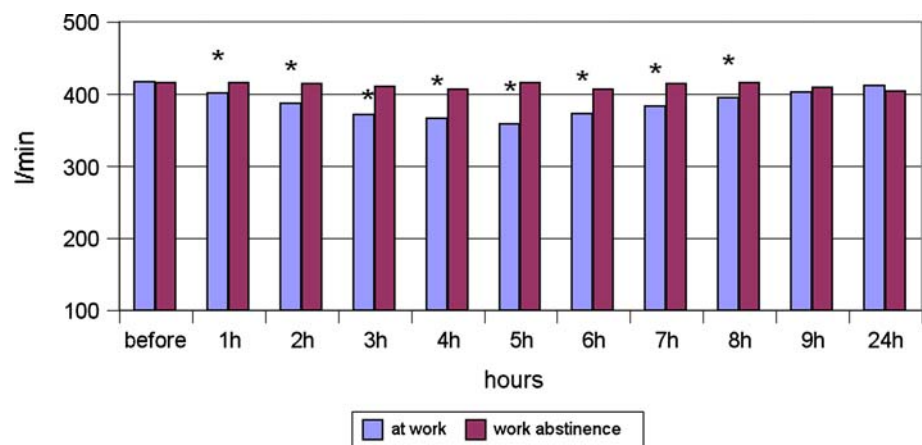


Fig. 2 PC_{20} values in animal workers with OA before and after the work shift and on a control day. * $P < 0.05$ (PC_{20} values after

the onset of occupational exposure vs. baseline value; Wilcoxon matched pairs, signed-rank test)

Table 4 Association of work-related respiratory symptoms suggestive of occupational asthma with host characteristics in animal shelter workers

Factor (univariate logistic regression analysis)	Cases with work-related respiratory symptoms suggestive of occupational asthma (<i>n</i> = 8)	Cases with no symptoms suggestive of occupational asthma (<i>n</i> = 80)	OR (95% CI)
Gender			
Male	7 (87.5%)	50 (62.5%)	4.2 (0.47, 36.9)
Female	1 (12.5%)	30 (37%)	0.2 (0.02, 2.09)
Smoking status			
Smokers	4 (50%)	50 (62.5%)	0.61 (0.13, 2.63)
Non-smokers	4 (50%)	30 (37.5%)	0.57 (0.10, 3.6)
Small shelter	6 (75%)	43 (53.8%)	2.58 (0.47, 13.89)
Family history of atopy	4 (50%)	26 (32.5%)	2.07 (0.47, 9.15)
Previous contact with animals			
Cat	1 (12.5%)	11 (13.5%)	0.89 (0.09, 8.26)
Dog	1 (12.5%)	21 (26.3%)	0.4 (0.04, 3.56)
Positive SPTs to			
At least one common allergen	7 (87.5%)	52 (65%)	3.77 (0.42, 85.64)
<i>Dermatophagoides pteronyssinus</i>	2 (25%)	11 (13.7%)	6.27 (1.33, 29.45)
<i>D. farinae</i>	3 (37.5%)	15 (18.8%)	2.6 (0.54, 12.3)
Either <i>D.p</i> or <i>D.f</i>	5 (62.5%)	26 (32.5%)	3.46 (0.65, 20.11)
Tree pollens I ^a and II ^b	1 (12.5%)	22 (27.5%)	0.37 (0.04, 3.34)
Grass pollens	4 (50%)	11 (13.7%)	6.27 (1.33, 29.45)*
Moulds I ^c and II ^d	2 (25%)	14 (17.5%)	1.57 (0.27, 8.82)
Feathers	0	8 (10%)	–
Residence in childhood			
Village	4 (50%)	11 (13.7%)	6.27 (1.33, 29.45)*
Town/city	4 (50%)	69 (86.3%)	0.15 (0.003, 0.74)*
Sensitization to mouse allergens (positive SPT and/or sIgE in serum)	2 (25%)	20 (5%)	1.00 (0.13, 6.22)
Sensitization to rat allergens (positive SPT and/or sIgE in serum)	1 (12.5%)	17 (21.3%)	0.52 (0.05, 4.74)

**P* < 0.05^a Alder, hazel, poplar, elm, willow^b Birch, beech, oak, plane^c *Alternaria tenuis*, *Botrytis cinerea*, *Cladosporium herbarum*, *Curvularia lunata*, *Helminthosporium halodes*, *Fusarium moniliforme*^d *Aspergillus fumigatus*, *Mucor mucedo*, *Penicillium notatum*, *Pullularia pullulans*, *Rhizopus nigricans*, *Serpula lacrymans*

The multivariate logistic regression analysis confirmed the significant role of the above-mentioned factors in the development of occupational allergy (OR 5.9; 95% CI 1.76, 20.00; *P* = 0.003; OR 6.47; 95% CI 1.90, 22.02; *P* = 0.002, respectively).

Discussion

Allergy to cats and/or dogs is a major occupational health problem. Our findings revealed the prevalence of asthmatic symptoms in animal shelter workers (15.9%) exceeding the prevalence of this condition in the adult population of Poland (3.6–7.6%) (Malolepszy et al. 2000). The rate of OA we found was similar to the results yielded by Aoyama's survey, which indicated that 9% of subjects occupationally exposed to laboratory animals had developed OA (Aoyama et al.

1992). Occupational conjunctivitis was the most frequently diagnosed disease among animal workers. Our findings are concordant with the results of other studies reporting on allergic conjunctivitis and rhinitis as the most common manifestation of allergy to laboratory animals (Elliott et al. 2005). We also observed a higher frequency of sensitization to dogs among animal shelter workers. This did not apply to cats. The workers employed at animal shelters more often reported having contact with dogs than cats, so we may presume this would explain the observed higher frequency of dog skin and/or serum reactivity in animal shelter workers.

According to literature reports, atopy has been identified as a risk factor for laboratory animal allergy (Cullinan et al. 1999). Different methods are used to demonstrate the presence of atopy, these including reports of positive family history of allergic diseases, positive SPT and indicative levels of total IgE in serum.

Table 5 Association of work-related symptoms suggestive of occupational allergy with host characteristics in animal shelter workers

Factor (univariate logistic regression analysis)	Cases with work-related symptoms suggestive of occupational allergy (asthma and/or rhinitis and/or conjunctivitis) (<i>n</i> = 19)	Cases with no work-related symptoms suggestive of occupational allergy (<i>n</i> = 69)	OR (95% CI)
Gender			
Male	14 (73.7%)	43 (62.3%)	1.69 (0.53, 5.33)
Female	5 (26.3%)	26 (37.7%)	0.59 (0.18, 1.86)
The smoking status			
Smokers	13 (68.4%)	41 (59.4%)	1.47 (0.49, 4.4)
Non-smoker	6 (31.6%)	28 (40.6%)	0.55 (0.17, 1.74)
Small shelter	14 (73.7%)	35 (50.7%)	2.72 (0.86, 8.5)
Family history of atopy	13 (68.4%)	17 (14.5%)	6.62 (2.14, 20.5)*
Previous contact with animals			
Cat	1 (5.3%)	11 (15.9%)	0.29 (0.03, 2.50)
Dog	11 (57.9%)	11 (15.9%)	7.25 (2.33, 22.48)*
Positive SPTs to			
At least one common allergen	14 (73.7%)	45 (65.2%)	1.49 (0.43, 5.44)
<i>Dermatophagoides pteronyssinus</i>	3 (15.8%)	10 (14.5%)	1.10 (0.26, 4.59)
<i>D. farinae</i>	6 (31.6%)	12 (17.4%)	2.19 (0.68, 7.04)
Either <i>D.p</i> or <i>D.f</i>	9 (47.4%)	22 (31.2%)	1.92 (0.61, 6.09)
Tree pollens I ^a and II ^b	3 (15.8%)	20 (28.9%)	0.45 (0.11, 1.78)
Grass pollens	5 (26.3%)	10 (14.5%)	2.1 (0.61, 7.27)
Moulds I ^c and II ^d	4 (21.1%)	12 (17.4%)	1.27 (0.35, 4.57)
Feathers	2 (10.5%)	6 (8.7%)	1.23 (0.22, 6.84)
Residence in childhood			
Village	4 (21.1%)	11 (15.9%)	1.40 (0.38, 5.13)
Town/city	15 (78.9%)	58 (84.1%)	0.71 (0.19, 2.59)
Sensitization to mouse allergens (positive SPT and/or sIgE in serum)	5 (26.3%)	17 (24.6%)	1.09 (0.33, 3.53)
Sensitization to rat allergens (positive SPT and/or sIgE in serum)	3 (15.8%)	15 (21.7%)	0.67 (0.17, 2.67)

**P* < 0.05^a Alder, hazel, poplar, elm, willow^b Birch, beech, oak, plane^c *Alternaria tenuis*, *Botrytis cinerea*, *Cladosporium herbarum*, *Curvularia lunata*, *Helminthosporium halodes*, *Fusarium moniliforme*^d *Aspergillus fumigatus*, *Mucor mucedo*, *Penicillium notatum*, *Pullularia pullulans*, *Rhizopus nigricans*, *Serpula lacrymans*

In our study, the multivariate analysis also revealed a higher frequency of positive family history of atopic diseases in animal shelter workers with work-related symptoms suggestive of OAA. Moreover, the univariate analysis indicated a higher frequency of positive SPT to grass pollens in subjects with work-related symptoms suggestive of OA. On the other hand, it is known that atopic diathesis may only be associated with frequent sensitization, which does not necessarily end up with the development of allergic symptoms.

The prevalence of skin and serum sensitization to cat and dog allergens was higher in the group of subjects with work-related symptoms suggestive of OAA than in the group with no such symptoms, but we also found individuals, who had positive skin and serum tests to cat and dog allergens but were asymptomatic. Hunskaar and Fosse (1990) found that 51–69% of

individuals with laboratory animal allergy had positive SPT to animal allergens, while Botham et al. (1987) found that only 40–64% of symptomatic animal workers had positive RAST tests.

The role of smoking in the development of both the sensitization and allergy to animals is still controversial (Cullinan et al. 1999). The present study did not confirm that smokers were more predisposed either to the development of occupational allergy or OA. Thus, we have no evidence for smoking as modifying the risk for OAA due to cat and dog exposure.

The prevalence of mouse and rat sensitization was similar in the group of subjects with work-related symptoms suggestive of OAA and the group with no such symptoms. It has been postulated that sensitization to dog and cat allergens may be related to rodent allergy. Both Heederik et al. (1999) and Hollander

et al. (1996) have shown that sensitization to rats was strongly associated with sensitization to cats and dogs. When looking at the structure of these allergens, it seems that the opposite situation is also possible—there may be associations between rodent and cat and dog sensitivities (Virtanen et al. 1999).

The cross-reactivity between these proteins was not demonstrated in our study, so we can presume that some subjects sensitized to rodents may not have reacted to the epitopes present in the cat and dog allergen solutions administered in our study or perhaps the association between rodent and cat and dog sensitization reflects a genetic predisposition.

We found only a few animal workers with work-related symptoms who were not sensitized to cat and/or dog. It is possible that the presence of these symptoms could be induced by endotoxin exposure (Pacheco et al. 2003)—of course this is only our suspicion, as we did not measure endotoxin levels. Respiratory challenge with endotoxin induces bronchial hyperreactivity (BHR) and reproduces nasal symptoms (Jagiello et al. 1996).

In the present study, previous exposure to dog allergens was significantly associated with the incidence of OAA among animal shelter workers. The above did not refer to having a cat as a pet animal. Numerous publications point to the keeping of cats and dogs as a factor protecting against sensitization and allergies (Hölscher et al. 2002; Hesselmer et al. 1999), but Lindfors et al. (1999) considered pet exposure to be a risk factor for allergic disease.

The most striking finding of this study is the significant role of growing up in the country. This was revealed by the univariate analysis for the development of OA and confirmed by the multivariate logistic regression analysis. Recent evidence suggests that farm residence in childhood is associated with a decreased risk of atopy and allergic diseases (Johnson and Alford 2002). It is thought that the protective effect of pet keeping in childhood on allergy may be caused by the induction of tolerance following high exposure and the induction of IgG4 (Platts-Mills et al. 2001), which may finally lead to a modifying TH2 response.

We suppose that the relationship between exposure to high concentrations of animal allergens at home in the childhood and/or youth, and the subsequent development of OAA, may be much more complex. It is widely known that pet keeping may increase exposure to bacterial components, such as endotoxin e.g. lipopolysaccharides (LPS) from gram-negative bacteria (Heinrich et al. 2001), which may favour a shift away from TH2 response (Eisenbarth et al. 2002). Some bacteria have molecules that interact with recognized receptors

present in antigen-presenting cells and epithelial cells (Imler and Hoffmann 2001). Polymorphisms in gene encoding Toll-like receptors (TLRs) may modulate the protective effects noted in farmers (Eder et al. 2004). Farmer's children carrying 1 or 2 T alleles in TLR2/-16934 were significantly less likely to have asthma, atopy, sensitization, but such relationship was not found for TLR4/+4434 (Eder et al. 2004). There are also publications showing that TLR4 receptors are responsible for optimal development of Th2 immune response (Dabbagh et al. 2002).

We can only suppose that the protective effect of growing up in the village in contact with animals on allergy might have been lost over time in our animal shelter workers as the influence of other environmental stimuli (smoking, air pollutions, starting more intensive exposure to occupational allergens in adulthood) or might have been induced by changes in polymorphisms in gene encoding TLRs.

Therefore, other studies should be performed in order to explain if the protective effect of childhood exposure to the agents encountered later on in occupational setting persists during the period of continuous exposure to these agents in adulthood or starting once again in adulthood.

We presume that pet exposure may influence the immune reactions via several pathways, in some persons acting as a protective factor, while in others as a risk factor for developing both sensitization and allergic diseases.

The findings of the present study refer to a relatively small number of cases; therefore, more extensive studies are necessary to clarify this issue. It is also possible that after an early contact with one or more aeroallergens, some individuals may not develop immune tolerance. Such observations have been made for food antigens (Holt et al. 1995).

The diagnosis of OA should be confirmed by objective methods. PEFR monitoring has the advantages of a commonly available and simple test; however, it has some limitations as well. It depends on the patient's cooperation and his/her recording of correct readings (Quirce et al. 1995).

In our study, a significant decrease in PEFR was observed in eight subjects with work-related respiratory symptoms suggestive of OA either during an early or late allergic reaction at the time of working with cats and dogs. PEFR results showing decrements during work under occupational exposure to cats and dogs and the subsequent increase on the control day supported the OA diagnosis.

Furthermore, we observed an increase in BHR to histamine after occupational exposure to shelter

animals. Histamine-challenge testing, the method used to measure non-specific bronchial hyperresponsiveness (NBR), has been proposed for the evaluation of OA (Johnson and Chan-Yeung 1999). It is a commonly expressed view that a negative result of this test helps the physicians exclude OA in those workers who present active symptoms (Hunter et al. 2002). The PEFR decrements observed in our study on the exposure day were consistent with a noticeable increase in NBR while at work. Therefore, results obtained either after a working day or on the control day support the OA diagnosis.

To conclude, allergic disease is a serious occupational health concern for subjects who have contact with cats and/or dogs. In the adult population of animal shelter workers in our study, the family history of atopy and having a dog previously were associated with an increased risk for developing OAA. Furthermore, growing up in the country was also positively associated with the development of OA. In view of the relatively small number of the examined cases of occupational allergy, further, more extensive research should be performed to clarify this association. Monitoring PEFR and NBH during periods at work may be useful in establishing the diagnosis of OA in individuals having contact with cats and/or dogs in workplace.

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