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Immunological Status and Respiratory Findings in Furriers

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We studied 42 women occupationally exposed in the fur manufacturing industry (mean age: 34 years, mean duration of exposure: 11 years). The highest prevalence of positive immediate skin reactions to antigen of animal hair was found for marten (10%), followed by fox and lamb (7%), mink (5%), and Chinese lamb, domestic fox, and Chinese calf (2%). Precipitating antibodies were demonstrated for lamb (17%), astrakhan (14%), mink, domestic fox and skunk (12%), Chinese lamb (10%), and Chinese calf (7%). Increased total IgE was found in 9.5% of subjects. Chronic symptoms were consistently more prevalent among workers with positive skin tests and positive precipitins than among workers with negative tests. A high prevalence of acute symptoms during the work shift was found among furriers. The prevalence of these symptoms was higher among workers with positive precipitating antibodies than among those with negative studies but not for workers with positive skin tests. Mean acute reductions in ventilatory capacity over the work shift were recorded for most ventilatory parameters. In general, greater drops in respiratory parameters occurred in individuals with positive precipitins (e.g., FEV_1: -6.5% vs. -2.8%; positive vs. negative precipitins) but not in those with positive skin tests. Our study suggests that workers in the fur manufacturing industry develop acute and chronic respiratory problems often associated with specific indicators of atopy.

Key words: immunology, respiratory symptoms, pulmonary function, occupational allergy, furriers, animal hair reaction

INTRODUCTION

It has been documented that exposure to animals can cause impairment of respiratory function [Butcher et al., 1984; Brooks, 1985]. Previous epidemiological studies refer primarily to various syndromes grouped in the category known as "laboratory animal allergy" [Beeson et al., 1983; Cockcroft et al., 1981; Davies and McArdle, 1981; Lutsky et al., 1986; Slovak and Hill, 1981]. Only a few studies have specifically investigated the effect of occupational exposure in furriers. Pimentel [1970] described a granulomatous interstitial pneumonia in one furrier exposed to hair

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dust for 13 years. The same author experimentally reproduced interstitial lesions in the guinea pig by the inhalation of animal hair. More recently we have demonstrated that work in the fur industry may be associated with the development of chronic respiratory symptoms and impairment of ventilatory capacity in some workers [Zuskin et al., 1988].

The present study is an extension of our previous epidemiological study of respiratory function carried out in a group of furriers. There are no epidemiological studies of the effects of animal hair on the immunological status of workers employed in the fur manufacturing industry. In the present investigation we studied the relationship between respiratory dysfunction and immunological changes in workers occupationally exposed to different animal hair in the fur coat industry.

SUBJECTS AND METHODS

Subjects

A group of 54 women employed in fur manufacturing was initially studied (14 additional subjects were studied since the original report) [Zuskin et al., 1988]. The mean age was 34 years (range: 20–52 years) with a mean duration of employment in the fur industry of 11 years (range: 3–27 years). Only 8% of these workers were smokers. A group of 31 women employed in a fruit juice bottling company served as a control for respiratory symptoms and ventilatory capacity changes in the original study. A comparison of these two cohorts showed no significant difference in age or smoking habits. The control workers were not exposed to dusts or fumes. For details of these comparisons see our earlier descriptions [Zuskin et al., 1988].

Immunological Studies

Forty-two workers among the cohort of 54 furriers were skin tested with aqueous allergen of animal fur and standard allergens using intradermal testing. Occupational allergens were prepared from by-products collected from machines in the workrooms containing the hair of 14 different animal species. Only one fur is processed at a time in this industry and the machines are cleaned between processings. Thus, the by-products collected were specific for each animal species. These animal fur by-products included marten, domestic fox, polar fox, mink, Chinese lamb, domestic lamb, Chinese calf, astrakhan, nutria, skunk, bison, seal, wild cat, and squirrel. Allergens were prepared by the method of Sheldon et al. [1967]. Intradermal skin tests with these allergens were performed using a dilution of 1:500. Workers were also tested with standard extracts of house dust, molds, histamine base (0.1 mg/ml), and buffer as a control solution. Commercial mold antigen was prepared as a mixture of *Alternaria, Penicillium, Mucor, Cladosporium, Aspergillus niger,* and *Aspergillus fumigatus* as 0.2% w/v solution [Sheldon et al., 1967]. The skin reactions were read after 20 minutes. An intradermal skin test was considered positive if the diameter of the observed wheal was larger than 9 mm (corrected for the control reaction of buffer).

The Ouchterlony [1953] test for specific precipitating antibodies in the workers was used. Serum levels of total IgE antibody were measured by paper radioimmunosorbent test (PRIST), direct radioimmunological sandwich technique based on paper discs as a solid phase [Wide and Porath, 1966]. In addition, concentrations of immunoglobulins IgA, IgG, and IgM were determined by single radial diffusion on

agarose plates produced in the Immunological Institute, Zagreb. Levels of IgE below 125 kU/L were considered normal [Johansson, 1968]. We used standard reference values for IgG, IgA, and Ig (Behringewerke AG, Marburg-Lahn, Germany, 1986). Specific IgE tests for individual antigens were not available.

Respiratory Symptoms

Chronic respiratory symptoms were recorded by using a modification of the Medical Research Council Committee [1960] questionnaire with additional questions on occupational asthma (WHO, 1986). The following definitions were used: 1) chronic cough/phlegm: cough or phlegm production or both on most days for at least 3 months in the past year; 2) chronic bronchitis: cough and phlegm for a minimum of 3 months in a year and for not less than 2 successive years; 3) dyspnea grades: grade 3, shortness of breath when walking with other people on level ground; grade 4, shortness of breath when walking at one's own pace on level ground; 4) occupational asthma: chest tightness, cough, wheezing, shortness of breath, and acute decrease in ventilatory capacity (of the obstructive type) during exposure to dust at or following work.

The workers were asked additional questions about acute symptoms that developed while at work, such as cough, dyspnea, irritation or dryness of the throat, eye irritation, bleeding, secretion or dryness of the nose, or headache.

Ventilatory Capacity Measurements

Ventilatory capacity was measured by recording maximum expiratory flow-volume (MEFV) curves. The forced vital capacity (FVC), one-second forced expiratory volume (FEV_1), and flow rates at 50% and 25% of the vital capacity (FEF_{50}, FEF_{25}) were recorded. The MEFV curves were measured using a Pneumoscreen spirometer (Jaeger, Germany). The acute effect of exposure to fur dust on ventilatory capacity was studied by recording MEFV curves on a Monday before and after a work shift. The measured pre-shift values were compared with the expected normal values of the Commission des Communautés Européenes (CECA) [1971] for FVC and FEV_1, and those of Cherniack and Raber [1972] for FEF_{50} and FEF_{25}

Statistical Analysis

The results of ventilatory capacity measurements were analyzed using the Student's t-test for paired differences when comparing observed to predicted values or measuring across shift changes. Fisher's exact test was used for testing differences in the prevalence of respiratory symptoms; $p < 0.05$ was considered as statistically significant.

RESULTS

Immunological Studies

All tested furriers had typical skin reactions to histamine and none reacted to the buffer control solution. Seventeen percent of the workers reacted to house dust, but none to molds. Immediate skin reactions to different animal hairs are presented in Figure 1. The highest prevalences of positive immediate skin reaction were found for marten (10%), followed by polar fox and lamb (7%), mink (5%), and Chinese lamb,

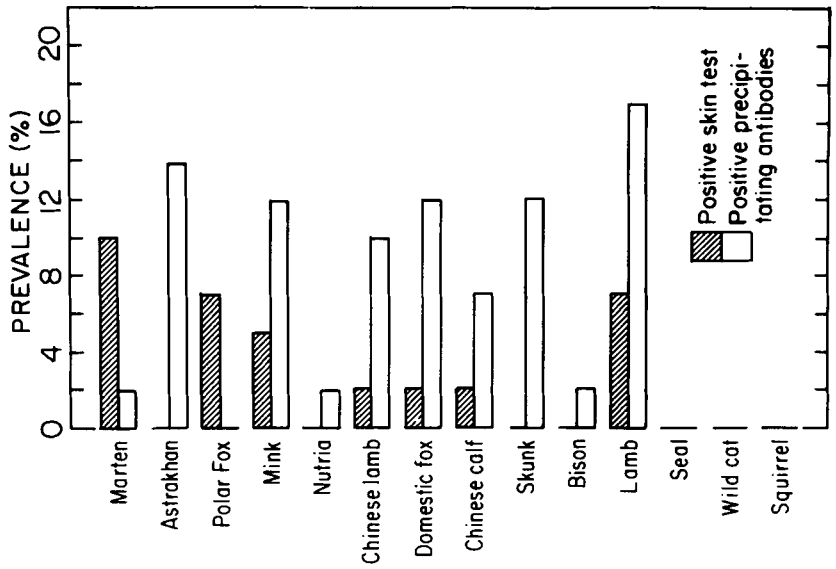

Fig. 1. Relative prevalences of positive skin tests and precipitins among 42 tested furriers.

domestic fox, and Chinese calf (2%). Negative skin reactions were obtained with the allergens of hair from astrakhan, nutria, skunk, bison, seal, wild cat, and squirrel.

The hair of some animals caused the development of precipitating antibodies in the furriers: lamb (17%); astrakhan (14%); mink, domestic fox, and skunk (12%); Chinese lamb (10%); Chinese calf (7%); and marten, nutria, and bison (2%). Precipitating antibodies did not develop to the hair of polar fox, seal, wild cat and squirrel. Only two workers had simultaneous positive skin and precipitin reaction. These were reactions to polar fox and Chinese lamb in both of the workers and additionally mink, marten, and bison in one. None of the workers had delayed skin test reactions.

Among the tested workers, four (9.5%) had increased serum levels of IgE. Previous studies (unpublished data) involving healthy subjects without occupational exposure have shown a lower frequency of elevated IgE (1/39; 2.6%). This difference in frequency does not reach statistical significance. Of these four workers with elevated IgE, one demonstrated immediate positive skin reactions to marten and lamb; two of these workers had precipitating antibodies to five different animal hairs. All four workers with increased IgE levels complained of respiratory symptoms. Serum levels of IgA, IgG, and IgM were within normal limits in all tested workers.

Respiratory Symptoms

Chronic symptoms. Table I presents the prevalence of chronic respiratory symptoms separately in furriers with positive and negative precipitating antibodies and in those with positive and negative skin tests to any of the animal hair. Chronic symptoms were more prevalent among workers with positive immunological tests. These differences reached significance for precipitin positive workers (nasal catarrh) and for skin test positive workers (chronic cough).

TABLE I. Prevalence of Chronic Respiratory Symptoms in 42 Furriers by Skin Tests and Precipitins

Group	N	Chronic cough (%)	Chronic phlegm (%)	Chronic bronchitis (%)	Asthma (%)	Dyspnea grades 3 and 4 (%)	Chest tightness (%)	Nasal catarrh (%)	Sinusitis (%)
Positive precipitins	13	3 (23.1)	2 (15.4)	2 (15.4)	1 (7.7)	3 (23.1)	10 (76.9)	6 (46.2)	8 (61.5)
p value[a]		NS[b]	NS	NS	NS	NS	NS	<0.05	NS
Negative precipitins	29	2 (6.9)	0 (0)	0 (0)	1 (3.4)	4 (13.8)	16 (55.2)	4 (13.8)	10 (34.5)
Positive skin tests	9	3 (33.3)	1 (11.1)	1 (11.1)	2 (22.2)	3 (33.3)	7 (77.8)	3 (33.3)	6 (66.7)
p value[c]		<0.05	NS	NS	NS	NS	NS	NS	NS
Negative Skin tests	3	3 (9.1)	1 (3.0)	1 (3.0)	0 (0)	5 (15.2)	20 (60.6)	7 (21.2)	14 (42.4)

[a]Comparisons are between workers with positive and negative precipitins.
[b]NS, difference not statistically significant ($p > 0.05$).
[c]Comparisons are between workers with positive and negative skin tests.

TABLE II. Acute Symptoms During the Work Shift in 42 Furriers According to Skin Tests and Precipitins

				Throat		Eye	Nose			
Group	N	Cough (%)	Dyspnea (%)	Irritation (%)	Dry (%)	Irritation (%)	Bleeding (%)	Secretion (%)	Dry (%)	Headache (%)
Furriers positive precipitins	13	7 (23.8)	9 (69.2)	9 (69.2)	11 (84.6)	13 (100.0)	3 (23.1)	2 (15.4)	8 (61.5)	9 (69.2)
		NS[a]	NS	NS	NS	NS	NS	NS	NS	NS
Furriers negative precipitins	29	7 (24.1)	12 (41.4)	10 (34.5)	16 (55.2)	16 (55.2)	3 (10.3)	3 (10.3)	13 (44.8)	14 (48.3)
Furriers positive skin tests	9	2 (22.2)	0 (0)	4 (44.4)	2 (22.2)	4 (44.4)	0 (0)	0 (0)	2 (22.2)	6 (66.7)
		NS	<0.01	NS	NS	NS	NS	NS	<0.05	NS
Furriers negative skin tests	33	11 (33.3)	19 (57.6)	15 (45.5)	23 (69.7)	22 (66.7)	5 (15.2)	5 (15.2)	20 (60.6)	17 (51.5)

[a]NS, difference not statistically significant ($p > 0.05$).

Acute symptoms. Table II presents the prevalence of acute symptoms during the work shift separately for workers with positive and negative precipitins and for those with positive and negative skin tests. The prevalence of acute symptoms was high for this group. Workers with positive precipitins had higher prevalences of acute symptoms. These differences did not, however, reach statistical significance. Comparison of skin test positive and negative workers did not show consistent differences and, in fact, two symptoms were significantly more prevalent among skin test negative workers (dyspnea and dry nose).

TABLE III. Ventilatory Capacity in 42 Furriers With Positive and Negative Skin Tests

	FVC			FEV_1			FEF_{50}			FEF_{25}		
	Before shift	Difference before-after		Before shift	Difference before-after		Before shift	Difference before-after		Before shift	Difference before-after	
Group	L	%	p[a]	L	%	p	L/s	%	p	L/s	%	p
Positive skin tests (N = 9)	3.32 ±0.81	−4.5	NS[b]	2.58 ±0.70	−0.4	NS	3.99 ±1.48	−1.5	NS	1.91 ±0.48	0	NS
p value[c]	NS			NS			NS			<0.05		
Predicted	3.66 ±0.52			2.80 ±0.43			4.47 ±0.33			2.38 ±0.26		
Negative skin tests (N = 33)	3.54 ±0.31	−5.4	<0.001	2.94 ±0.36	−5.8	<0.05	4.75 ±0.72	−9.1	<0.05	2.47 ±0.56	−1.2	NS
p value[d]	<0.001			NS			NS			NS		
Predicted	3.89 ±0.37			3.03 ±0.47			4.70 ±0.24			2.56 ±0.28		

[a]Comparison between before and after work shift lung function.
[b]NS, difference not statistically significant ($p > 0.05$). Ventilatory capacity tests are presented as mean ± SD.
[c]Comparisons are between workers with positive skin tests and their predicteds.
[d]Comparisons are between workers with negative skin tests and their predicteds.
L = liter; L/s = liter/second.

Ventilatory Capacity

As previously shown [Zuskin et al., 1988], significant baseline and across shift abnormalities exist compared to controls. Table III presents ventilatory capacity data in furriers with positive and negative skin tests and Table IV records lung function in furriers with positive and negative precipitins. The across shift reductions (measured as a percentage of baseline) were greater in workers with positive precipitins than in those with negative precipitins. By contrast, skin test negative workers had greater acoss shift changes than skin test positive workers. Predicted normal values were, in general, greater than measured for all ventilatory capacity tests particularly in workers with positive precipitins. However, significant differences were found only for FEF_{25} in furriers with positive and negative precipitins and positive skin tests. No consistent differences were found between the percent of predicted values for workers with positive and negative skin tests or between workers with positive and negative precipitins.

DISCUSSION

Our study demonstrates a high prevalence of chronic respiratory symptoms in furriers. In general, for respiratory symptoms, the subjects with positive precipitins and positive skin tests had a higher prevalence of symptoms, than those with negative precipitins and negative skin tests, although these did not usually reach statistical significance. Slovak and Hill [1981] described that laboratory workers with rhinitis-only symptoms and negative skin tests were unlikely to develop asthma. By contrast, they found that the group of workers with rhinitis and positive skin tests were likely to develop asthma. Similarly, in our study, furriers with positive skin tests had a

TABLE IV. Ventilatory Capacity in 42 Furriers With Positive and Negative Precipitins

	FVC			FEV_1			FEF_{50}			FEF_{25}		
	Before shift	Difference before-after		Before shift	Difference before-after		Before shifts	Difference before-after		Before shift	Difference before-after	
Group	L	%	p[a]	L	%	p	L/s	%	p	L/s	%	p
Positive precipitins (N = 13)	3.27 ±0.61	−8.0	<0.05	2.63 ±0.40	−6.5	NS[b]	4.25 ±1.04	−12.0	<0.02	1.78 ±0.33	−1.1	NS
p value[c]	NS			NS			NS			<0.01		
Predicted	3.62 ±0.45			2.85 ±0.47			4.40 ±0.23			2.30 ±0.27		
Negative precipitins	3.47 ±0.46	−5.2	<0.001	2.83 ±0.46	−2.8	NS	4.72 ±0.98	−6.4	<0.02	2.28 ±0.54	−1.8	NS
p value[d]	<0.01			NS			NS			<0.01		
Predicted	3.81 ±0.42			2.96 ±0.49			4.62 ±0.30			2.54 ±0.26		

[a]Comparison between before and after work shift lung function.
[b]NS, difference not statistically significant ($p > 0.05$). Ventilatory capacity tests are presented as means ± SD.
[c]Comparisons are between workers with positive precipitins and their predicteds.
[d]Comparisons are between workers with negative precipitins and their predicteds.

greater prevalence of symptoms than those with negative skin tests. In general, workers with positive precipitins in our study complained more frequently of acute symptoms than those with positive skin tests.

In our workers, significant reductions of ventilatory capacity over the work shift were frequently recorded. Workers with positive precipitins tended to have larger across shift decreases in lung function than those with negative tests; however, this was not the case for skin test positive workers. Other authors have described an increased prevalence of bronchial asthma, non-specific infectious respiratory diseases, and impaired pulmonary function in animal house workers compared to control workers [Lutsky et al., 1986]. The same authors described immediate wheal and flare reactions to epithelial and/or urinary antigens derived from laboratory animals, but did not find precipitating antibodies to inhalant antigens in these workers. We did not document differences in baseline lung function between workers with positive and negative immunological tests.

Immediate hypersensitivity reactions to animal dander of cats, dogs, horses, guinea pigs, hamsters, and rabbits are common and have been described for many years [Solomon and Mathews, 1983]. Recent immunochemical evidence has demonstrated that the major allergen from these animals is not a serum protein but may be salivary in origin [Ohman et al., 1974]. Several studies have demonstrated allergic symptoms in up to 30% of laboratory animal workers who were in contact with a variety of animal species [Lutsky and Neuman, 1975; Gross, 1980; Schumacher et al., 1981]. In persons sensitive to laboratory rodents, immunochemical studies (skin tests, radioallergosorbent test [RAST], and provocation studies) have demonstrated low molecular weight urinary proteins to be responsible for the observed symptoms [Newman Taylor et al., 1977]. Lutsky et al. [1984] described a significantly higher prevalence of reduced lung function measurements in veterinarians and laboratory

animal workers than among controls. By contrast, Cockcroft et al. [1981] described normal lung function in laboratory animal workers. Finally Neuman and Lutsky [1976] described that disodium cromoglycate (DSCG) afforded partial protection against laboratory animal-induced bronchospasm for susceptible individuals. In a previous study we found a similar degree of protection in our furriers pretreated with DSCG [Zuskin et al., 1988].

The dust samples from the work areas we studied showed that this dust was composed primarily of particles in the respirable fraction size [Zuskin et al., 1988]. For respirable fibers the concentrations varied from 0.1–4.0 fibers/cm^3 and for respirable dust particles the concentrations varied from 40–246 particles/cm^3. The clinical significance of these levels remains to be determined as there are no established maximal allowable concentrations for evaluation of safety in the fur industry.

Our previous observations on furriers [Zuskin et al., 1988] indicate that these workers are prone to an increased frequency of respiratory symptoms and lung function abnormalities. The current study demonstrates a trend of more frequent respiratory symptoms in skin test and precipitin positive workers but, presumably because of the small numbers of workers studied, these did not reach statistical significance. Workers with positive precipitins were noted to have larger across shift changes in lung function, but paradoxically it was the skin test negative workers who had greater drops across the work shift. While these results suggest some relationship between immunological findings and respiratory disease, additional clarification is necessary before making specific recommendations for preventive measures based on immunological methods.

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REFERENCES

Beeson MF, Dewdney JM, Edwards RG, Orr RG (1983): Prevalence of diagnosis of laboratory animal allergy. Clin Allergy 13:433–442.

Brooks SM (1985): Occupational asthma. In Weiss EB, Segal MS, Stein M (eds): "Bronchial Asthma." Boston/Toronto: Little Brown and Company, pp 461–493.

Butcher BT, Hammad YY, Hendrich DJ (1984): Occupational identification of agent. In Gee JB (ed): "Occupational Lung Disease." New York, Edinburgh, London, Melbourne: Churchill Livingstone, pp 111–117.

Cherniack RM, Raber MB (1972): Normal standards for ventilatory function using an automated wedge spirometer. Am Rev Respir Dis 106:38–46.

Cockcroft A, McCarthy P, Edwards J, Anderson N (1981): Allergy in laboratory workers. Lancet 1:827–830.

Commission des Communautés, CECA (1971): Aide-mémoire pour la pratique de l'examen de la function ventilatoire par la spirographie. Collection d'Hygiene et de Médecine du Travail. No. 11, Luxembourgh.

Davies GE, McArdle LA (1981): Allergy to laboratory animals. A survey by questionnaire. Int Arch Allergy Appl Immunol 64:302–307.

Gross NJ (1980): Allergy to laboratory animals: epidemiologic, clinical, and physiological aspects, and a trial of cromolyn in its management. J Allergy Clin Immunol 66:158–165.

Johansson SGO (1968): Serum IgND levels in healthy children and adults. Int Arch Allergy 34:1–4.

Lutsky II, Baum GL, Teichtahl H, Mazar A, Alzer F, Bar-Sela S. (1986): Respiratory disease in animal house workers. Eur J Respir Dis 69:29–35.

Lutsky II, Neuman I (1975): A laboratory animal dander allergy: I. An occupational disease. Ann Allergy 35:201–205.

Lutsky II, Toshner D, Bar-Sela S, Teichtahl H, Mazar A, Bum G (1984): Hypersensitivity lung disease in workers occupationally exposed to animals. In Gee JBL, Morgan WKC, Brooks SM (eds): "Occupational Lung Disease." New York: Raven Press, pp 251.

Medical Research Council Committee on the Aethiology on Chronic Bronchitis (1960): Standardized questionnaire on respiratory symptoms. Br Med J 2:1665.

Neuman I, Lutsky II (1976): Laboratory animal dander allergy: II. Clinical studies and the potential protective effect of disodium cromoglycate. Ann Allergy 36:23–29.

Newman Taylor A, Longbottom JL, Pepys J (1977): Respiratory allergy to urinary proteins in rats and mice. Lancet 2:847–849.

Ohman JL, Lowel FC, Bloch KJ (1974): Allergens of mammalian origin. III. Properties of a major feline allergen. J Immunol 113:1668–1677.

Ouchterlony O (1953): Antigen-antibody reactions in gel: types of reactions in coordinated system of diffusion. Acta Pathol Microbiol Scand 32:231–235.

Pimentel JC (1970): Furrier's lung. Thorax 25:387–398.

Schumacher MJ, Tait BD, Holmes MC (1981): Allergy to murine antigens in a biologic institute. J Allergy Clin Immunol 68:310–318.

Sheldon JM, Lower RG, Mathews KP (1967): A Manual of Clinical Allergy. Philadelphia, London: WB Saunders Company, pp 507–531.

Slovak AJM, Hill RN (1981): Laboratory animal allergy: a clinical survey of an exposed population. Br J Ind Med 38:38–41.

Solomon WR, Mathews KP (1983): Aerobiology and inhalant allergens. In Middleton E, Reed CE, Ellis EF (eds): "Allergy Principles and Practice." St Louis: CV Mosby, pp 1143–1202.

Wide L, Porath J (1966): Radioimmunoassay of proteins with the use of Sephadex coupled antibodies. Biochem Biophys Acta 130:257–260.

World Health Organization (1986): "Early Detection of Occupational Disease." Geneva.

Zuskin E, Skuric Z, Kanceljak B, Pokrajac D, Schachter EN, Witek TJ Jr (1988): Respiratory symptoms and lung function in furriers. Am J Ind Med 14:189–196.