

Skin and respiratory symptoms among workers with suspected work-related disease

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Background	Many workers are exposed to chemicals that can cause both respiratory and skin responses. Although there has been much work on respiratory and skin outcomes individually, there are few published studies examining lung and skin outcomes together.
Aims	To identify predictors of reporting concurrent skin and respiratory symptoms in a clinical population.
Methods	Patients with possible work-related skin or respiratory disease were recruited. An interviewer-administered questionnaire collected data on skin and respiratory symptoms, health history, smoking habits, workplace characteristics and occupational exposures. Predictors of concurrent skin and respiratory symptoms were identified using multiple logistic regression models adjusted for age, sex and atopy.
Results	In total, 204 subjects participated; 46% of the subjects were female and the mean age was 45.4 years (SD = 10.5). Most subjects ($n = 167$, 82%) had possible work-related skin disease, compared with 37 (18%) subjects with possible work-related respiratory disease. Subjects with a history of eczema (OR 3.68, 95% CI 1.7–7.8), those from larger workplaces (OR 2.82, 95% CI 1.8–7.4) and those reporting respirator use at work (OR 2.44, 95% CI 1.2–4.8) had significantly greater odds of reporting both work-related skin and respiratory symptoms. Current smoking was also associated with reporting concurrent skin and respiratory symptoms (OR 2.57, 95% CI 1.2–5.8).
Conclusions	Workers reported symptoms in both systems, and this may be under-recognised both in the workplace and the clinic. The association between history of eczema and concurrent skin and respiratory symptoms suggests a role for impaired barrier function but needs further investigation.
Key words	Occupational disease; respiratory symptoms; skin symptoms; work-related symptoms.

Introduction

Many workers are exposed to chemicals that can cause lung and skin responses as a result of both inhalation and skin exposure. Although there has been significant work focused on individual lung or skin outcomes and their association with exposures, there are few published studies examining both airborne and skin exposures with lung and skin outcomes together. This is important clinically, as disease may be under-recognized when workers are assessed by physicians who are specialist in only one system. It is also important from a prevention standpoint, because opportunities for exposure control and prevention may be missed if research focuses on either airborne or skin exposure.

There is also increasing interest in the role that skin exposure may play in sensitization and the development of respiratory symptoms and/or disease [1,2]. In humans, skin exposure in the context of asthma development has been examined almost exclusively in workplaces with isocyanate exposure [3,4], though studies in animal models suggest this pathway may exist for other exposures [5,6]. Petsonk *et al.* showed that isocyanate-exposed workers who reported skin staining (a proxy for skin exposure) were more likely to report new-onset asthma symptoms at follow-up [3].

It is clear from animal studies that in order for the skin to act as a relevant route of sensitization in the development of asthma that both a skin and an inhalation

exposure are required [7,8]. In the occupational setting airborne and skin exposures may be correlated [9,10]. The skin exposure model proposed by Schneider *et al.* suggests that the airborne and skin exposure compartments may contribute to one another [11]. When the contribution of airborne exposure to skin exposure via deposition is high, the two exposures (airborne and skin) may be highly correlated. Furthermore, there is evidence that several common contact sensitizers are also associated with occupational asthma, and may cause both outcomes through independent exposure pathways [12].

Individually, exposure-response relationships have been reported between occupational exposure and skin symptoms [13,14], though studies of exposure-response for respiratory symptoms are far more common. There has been little research on causal exposures or risk factors for reporting concurrent skin and respiratory symptoms, despite case studies of workers with allergic contact dermatitis and occupational asthma in response to the same occupational exposure in the literature [15,16].

Given that some workers are likely to have both skin and inhalation exposures, and that these exposures may be correlated, it is plausible that some workers may experience both skin and respiratory symptoms. Aside from one clinical study and one occupational study, this issue has received little attention in previous research [16,17].

The primary objective of this study was to estimate the prevalence of concurrent skin and respiratory symptoms in a clinical population and to determine how workers with concurrent skin and respiratory symptoms differ from those with symptoms in only one system (skin or respiratory).

Methods

Subjects were recruited consecutively from a hospital-based outpatient occupational health clinic between July 2009 and June 2010. Patients with possible work-related respiratory disease were seen through the Allergy/Asthma (AA) clinical stream and those with possible work-related skin disease were seen through the Dermatology (Derm) clinical stream; both were eligible to participate. In both streams, patients were either referred through the public health care insurance system or through the workers' compensation insurance system.

Patients provided written informed consent. An interviewer-administered questionnaire was completed during the clinic visit by one of two trained interviewers. If there was insufficient time to complete the questionnaire, subjects were given the option of completing the questionnaire via telephone. The questionnaire contained questions on respiratory symptoms (modified ATS questionnaire [18]), skin symptoms, health history, smoking history, workplace characteristics and

workplace exposures. Following the clinic visit(s), the final physician diagnosis was abstracted from the subjects' medical chart.

The main outcome of interest was concurrent skin and respiratory symptoms. This was conceptualized as subjects who reported any respiratory symptom (any of cough, phlegm, wheeze, shortness of breath, or chest tightness) as well as current skin rash. Symptoms were considered work-related if they were reported to be worse at work, or better when away from work (days off or holidays).

Variables considered as possible predictors of concurrent symptoms included: history of asthma, history of eczema, workplace size, use of gloves at work, use of a respirator at work, occupation, insurance scheme (workers' compensation versus public system), clinical stream (asthma/allergy versus dermatology), presence of a union in the workplace, workplace education on personal protective equipment, workplace education on occupational disease(s) and a series of possible workplace exposures (cement, dander, dust, fumes, isocyanates, paints, pesticides, wet work and others).

Smoking included any reported tobacco smoking. Atopy was defined based on the subjects' positive responses to having allergies to dust, dust mites or other animals, or having had doctor-diagnosed hay fever [19]. A history of asthma and eczema were recorded as a positive response to both 'have you "ever" had asthma/eczema?' and, 'was it confirmed by a doctor?'

Workplace size was categorised into four groups based on the number of employees (<20, 20–99, 100–499 and >500) [20]. Self-reported job title and industry information was coded using the National Occupational Classification System (NOCS) [21]. Occupations were further condensed into six groups (trades, sales/service, office, manufacturing, health, other) due to small sample sizes in the major NOCS groupings. Workplace education variables included education on skin and/or respiratory personal protective equipment and occupational disease.

Differences between participants and patients who refused to participate were tested using chi-square test for categorical variables and Student's *t*-test continuous variables. Possible predictors of concurrent symptoms were first investigated using simple logistic regression. The outcome in these models was concurrent skin and respiratory symptoms; the comparison group was subjects who reported either skin or respiratory symptoms but not both. Predictors where the parameter estimate in simple logistic regression results had a $P < 0.20$ were offered into multiple logistic models. Multiple logistic regression models were adjusted for age, sex, smoking, atopy and interviewer. All analyses were completed in SAS version 9 software (SAS Institute Inc., Cary, NC, USA).

This study was approved by the St Michael's Hospital Research Ethics Board (Toronto, ON, Canada).

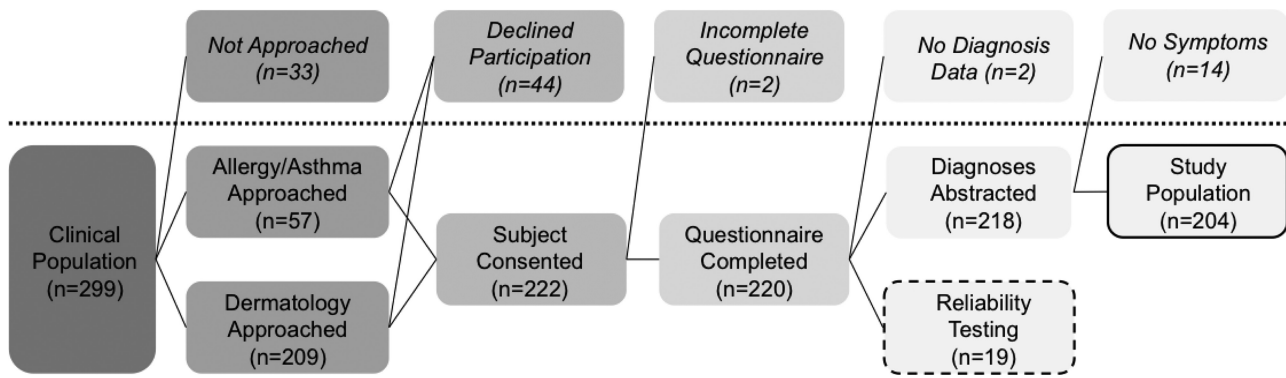


Figure 1. Flow chart of study progression, including sample sizes at each stage.

Results

In total, 218 subjects were successfully recruited with a response rate of 81%. Figure 1 shows a flow chart of the study progression with the sample sizes at each stage. Thirty-three patients were not approached at the discretion of the staff/physician (i.e. overly complex or contentious cases), or due to higher than normal volume in the clinic. Fourteen subjects were excluded from the analyses as they reported neither skin nor respiratory symptoms. The research objective was to determine how workers with concurrent skin and respiratory symptoms differ from those with symptoms in only one system, requiring all subjects to have symptoms in at least one system. The sample size for the reported analysis is 204 subjects.

Patients who refused study participation did not differ from the participants in terms of age or sex (results not shown) but were more likely to be from the AA clinical stream (26% versus 7%, $P < 0.001$). Subjects who declined participation also tended to be referred more often through the provincial worker's compensation system rather than the main public health care system (21% versus 13%), though this difference did not reach statistical significance.

Of the total 204 subjects, most ($n = 167$, 82%) had possible work-related skin disease and were seen through the dermatology (Derm) stream; only 37 (18%) subjects were seen in the asthma/allergy (AA) stream with possible work-related respiratory disease. This distribution of participants between the Derm and AA streams is reflective of the overall patient breakdown in the clinic. The participation rates were 86% and 68% for the Derm and AA streams, respectively. A total of 22 (59%) AA subjects and 117 (70%) Derm subjects were diagnosed with work-related disorders after their assessment. An additional 4 (11%) AA subjects and 31 (19%) Derm subjects were diagnosed with a possible work-related disorder. Just under half (46%) of the subjects were female and the mean age was 45.4 years (SD = 10.5) (Table 1). About 51% of subjects had a smoking history, either former or current. The distribution of smoking status (never,

former, current) did not differ significantly between AA and Derm subjects with 29% versus 22% current smokers, respectively ($P = NS$). Almost one-quarter ($n = 50$) of the study population self-reported a history of asthma (Table 1). Not surprisingly asthma was more common

Table 1. Demographic variables for all subjects

	Overall	Either skin symptoms only or respiratory symptoms only	Both skin and respiratory symptoms
<i>n</i>	204	121	83
Female	94 (46)	59 (49)	35 (42)
Male	110 (54)	62 (51)	48 (58)
Age in years, mean (SD)	45.4 (10.5)	45.7 (10.0)	45.1 (11.2)
Age <35 years	38 (19)	20 (17)	18 (22)
Age 35–49 years	88 (43)	55 (45)	33 (40)
Age ≥50 years	78 (38)	46 (38)	32 (39)
Never smoker	98 (48)	64 (53)	34 (41)
Former smoker	50 (24)	31 (26)	19 (23)
Current smoker	56 (27)	26 (21)	30 (36)
Interviewer 2	115 (56)	69 (57)	46 (55)
Interviewer 1	89 (44)	52 (43)	37 (45)
Telephone questionnaire	5 (2)	2 (2)	3 (4)
In clinic questionnaire	198 (98)	118 (98)	80 (96)
AA clinical stream	37 (18)	31 (26)	6 (7)***
Derm clinical stream	167 (82)	90 (74)	77 (93)***
Workplace insurance	91 (45)	59 (49)	32 (39)
Public insurance	113 (55)	62 (51)	51 (61)
Atopy	68 (33)	42 (35)	26 (31)
Doctor-diagnosed asthma	50 (24)	29 (24)	21 (25)
Doctor-diagnosed eczema	54 (26)	20 (17)	34 (41)***

*** $P < 0.001$.

All values reported as the row *n* (%) unless otherwise noted. Comparison between 'Both skin and respiratory symptoms' and 'Either skin symptoms only or respiratory symptoms only'.

Table 2. Symptom prevalence for all subjects, stratified by clinical stream

	Overall	Clinical stream	
		Dermatology	Asthma/ Allergy
<i>n</i>	204	167	37
General symptoms:			
Current skin rash	146 (72)	140 (84)	6 (16)
Hand/arm rash	134 (66)	130 (78)	4 (11)
Any respiratory symptom	141 (69)	104 (62)	37 (100)
Asthma-like symptoms	48 (24)	24 (14)	24 (65)
Work-related symptoms:			
Current skin rash	129 (63)	125 (75)	4 (11)
Hand/arm rash	120 (59)	117 (70)	3 (8)
Any respiratory symptom	83 (41)	50 (30)	33 (89)
Asthma-like symptoms	33 (16)	11 (6)	22 (59)
Concurrent skin and respiratory symptoms	83 (41)	77 (46)	6 (16)
Concurrent work-related skin and respiratory symptoms	40 (20)	36 (22)	4 (11)

Frequencies reported as *n* (%) for each column.

in the AA stream (54% (AA, *n* = 20) vs. 18% (Derm, *n* = 30), *P* < 0.001).

Among the study subjects, symptom prevalence was high, as expected in a clinical population (Table 2). General concurrent skin and respiratory symptoms were reported by approximately one-third of the subjects (Table 2) but work-related concurrent symptoms were only reported by 20% of subjects.

Among the subjects being assessed for possible work-related skin disease (Derm stream), 30% reported at least one work-related respiratory symptoms and 6% reported work-related asthma-like symptoms. Work-related skin symptoms were less common in the AA stream but were still reported (11% work-related rash, 8% work-related hand/arm rash) (Table 2).

Reported glove use at work was higher (90%) than the reported use of a respirator (39%) (Table 3). More than half of the subjects (53%) reported having had workplace education about personal protective equipment, but only 14% reported having education that addressed the topic of work-related disease.

Dust was the most commonly reported occupational exposure (68%); exposure to wet work (65%), fumes (55%) and paint (41%) were also common exposures (Table 4). None of the self-reported exposures were associated with reporting concurrent skin and respiratory symptoms.

Models were constructed to compare subjects with concurrent skin and respiratory symptoms to those with symptoms in only one system. The results of the multiple logistic regression models are shown in Table 5.

Table 3. Self-reported workplace characteristics for all subjects, stratified by subjects who reported both skin and respiratory symptoms

	Overall	Either skin symptoms only or respiratory symptoms only	
		Both skin and respiratory symptoms	Both skin and respiratory symptoms
<i>n</i>	204	121	83
Union in the workplace	98 (48)	62 (51)	36 (43)
<20 employees in the workplace	52 (25)	31 (26)	21 (25)
20–99 employees	57 (28)	38 (31)	19 (23)
100–499 employees	52 (25)	34 (28)	18 (22)
>499 employees	43 (21)	18 (15)	25 (30)
Gloves worn at work	183 (90)	10 (8)	78 (94)
Respirator worn at work	80 (39)	39 (32)	41 (49)*
Trades occupations	49 (24)	28 (23)	21 (25)
Sales and service occupations	42 (20)	25 (21)	17 (20)
Manufacturing occupations	38 (19)	25 (21)	13 (16)
Health related occupations	30 (15)	12 (10)	18 (22)
Office occupations	27 (13)	19 (16)	8 (10)
Other occupations	18 (9)	12 (10)	6 (7)
Education: PPE	108 (53)	59 (49)	49 (59)
Education: work-related disease	28 (14)	14 (12)	14 (17)

**P* < 0.05.

All frequencies reported as the row *n* (%) unless otherwise noted. Comparison between 'Both skin and respiratory symptoms' and 'Either skin symptoms only or respiratory symptoms only'.

Table 4. Self-reported occupational exposures for all subjects

	Overall	Either skin symptoms only or respiratory symptoms only	
		Both skin and respiratory symptoms	Both skin and respiratory symptoms
<i>n</i>	204	121	83
Cement exposure at work	41 (20)	21 (17)	20 (24)
Animal dander exposure at work	25 (12)	14 (12)	11 (13)
Dust exposure at work	139 (68)	85 (70)	54 (65)
Fume exposure at work	113 (55)	69 (57)	44 (53)
Isocyanate exposure at work	32 (16)	17 (14)	15 (18)
Paint exposure at work	84 (41)	52 (43)	32 (39)
Pesticide exposure at work	22 (11)	13 (11)	9 (11)
Wet work exposure at work	133 (65)	78 (64)	55 (66)

All frequencies reported as the row *n* (%) unless otherwise noted. Comparison between 'Both skin and respiratory symptoms' and 'Either skin symptoms only or respiratory symptoms only'.

Results showed that subjects with a history of eczema (OR 3.68, 95% CI 1.73–7.83) had significantly greater odds of reporting both work-related skin and respiratory symptoms. Additionally, subjects from larger

Table 5. Multiple logistic regression model results for predictors of reporting concurrent skin and respiratory symptom outcomes.

Predictor↓	Model description
	Both skin and respiratory symptoms
Never smoker	1.00
Former smoker	1.22 (0.52–2.85)
Current smoker	2.57 (1.15–5.76)
Atopy	0.86 (0.41–1.77)
History of eczema	3.68 (1.73–7.83)
<20 employees	0.96 (0.39–2.34)
20–99 employees	1.00
100–499 employees	1.00 (0.40–2.48)
>499 employees	2.82 (1.08–7.35)
AA clinical stream (versus Derm)	0.25 (0.09–0.70)
Respirator worn at work	2.44 (1.25–4.77)
Isocyanate exposure at work	–
Number of outcomes	83
Model <i>n</i>	204

Models adjusted for age, sex and interviewer.

(>499 employees) workplaces (OR 2.82, 95% CI 1.08–7.35) and those who reported wearing a respirator while at work (OR 2.44, 95% CI 1.25–4.77) were more likely to report concurrent skin and respiratory symptoms. Current smoking was found to be associated with reporting concurrent skin and respiratory symptoms (OR 2.57, 95% CI 1.15–5.76).

Discussion

Concurrent symptoms were more common among the Derm stream subjects (46%) compared with the AA stream subjects (16%), but both groups had a higher prevalence of concurrent skin and respiratory symptoms than previous studies [16,17]. In a clinical study, Moulin *et al.* reported on 234 patients with diagnosed contact dermatitis, of whom 10 (4%) had both work-related contact dermatitis and respiratory symptoms [16]. This is one-fourth the prevalence observed here in the Derm patients, 88% of whom were diagnosed with contact dermatitis. Lynde *et al.* studied working professional cleaners and still found that 7% reported both a current skin rash and two or more respiratory symptoms; 6% reported current skin rash as well as two or more work-related respiratory symptoms [17]. The lower prevalence in the Lynde *et al.* study may be due to the more stringent requirement of having to report two or more respiratory symptoms, instead of reporting any respiratory symptoms as in the current study.

Work-related symptoms were common, as would be expected in a clinical population being assessed for possible work-related disease. A large proportion of workers

also reported work-related symptoms in the system other than the one they were being assessed for; 30% of Derm stream subjects reported work-related respiratory symptoms and 11% of AA subjects reported work-related skin rash.

In models exploring the difference between subjects with concurrent symptoms (both skin and respiratory symptoms) and those with only one symptom (either skin or respiratory symptoms), none of the specific exposures investigated were significant risk factors for concurrent symptoms. A history of eczema was a risk factor for reporting concurrent skin and respiratory symptoms, but a history of asthma was not. Childhood eczema has been reported as a risk-factor for developing adult onset asthma [22], but the relationship between general eczema and concurrent symptoms is less clear.

Published studies offer some insight into the potential role of impaired skin barrier in skin exposure and disease. Vermeulen *et al.* (rubber workers) and Hino *et al.* (car spray painters) found that subjects with abnormal skin (mild dermatitis or hand eczema) had elevated biomarkers of exposure, suggesting that they had greater uptake of exposure through their skin [23,24]. In a clinical population with atopic dermatitis, Bremmer *et al.* reported that patients who also had ichthyosis vulgaris, a skin disease that disrupts the barrier function of the skin, were significantly more likely to report asthma symptoms [25].

The reported association between eczema and concurrent skin and respiratory symptoms suggests that impaired barrier function may play a role in modifying the uptake of exposures through the skin, and potentially also in the development of both skin and respiratory symptoms [26]. However, the data available in this study does not address the extent (if any) of skin barrier function impairment in the study subjects, or the location of the eczema and its relevance to occupational exposures.

Atopy was considered a possible confounder in the relationship between eczema and symptoms and was included in all models. The observed association between a history of eczema and concurrent skin and respiratory symptoms persists after adjusting for atopy (defined by questionnaire), suggesting that the association is not a result of confounding.

The association between large workplaces and reporting concurrent skin and respiratory symptoms is more challenging. There may be social factors (i.e. a lack of a personal relationship with their employer or greater communication between employees) that make workers from larger workplaces more likely to report symptoms as associated with their work, but these underlying factors cannot be determined from this study. Neither having a union in the workplace nor receiving occupational health and safety education (PPE or work-related disease) was associated with reporting concurrent skin and respiratory symptoms, though both are thought to

be more likely in larger workplaces.

No associations between workplace exposures and reporting concurrent skin and respiratory symptoms were observed. However, subjects reporting respirator use at work were observed to have significantly greater odds of reporting concurrent skin and respiratory symptoms. In this case, respirator use may serve as proxy for general exposure at work. The observed association may suggest an association between higher exposure, or perhaps higher risk exposure, and concurrent symptoms. It is also possible that, regardless of the other workplace exposures, the respirator itself is an important source of exposure (e.g. rubber components of a respirator). In cases of contact dermatitis and patch testing, gloves and the chemical components of gloves, are often implicated as causal occupational exposures, this is less common in the case of respirators, but it is still plausible [27].

Current smokers had increased odds of concurrent skin and respiratory symptoms. In a nested model (results not shown), comparing subjects with respiratory symptoms only to subjects with skin symptoms alone, smoking was not associated with reporting respiratory symptoms. This is surprising given that the association between smoking and respiratory symptoms is well established [28] and may be due to a lack of power in the nested model. However, there was no observed difference in smoking rates between the AA and Derm groups (even in the nested model), suggesting that it is unlikely that this lack of an association is due to lower rates of smoking among subjects with respiratory complaints.

The main limitation of this study is that it was cross-sectional and only able to describe association rather than causation. Secondly, this study was completed in a selective clinical population of patients with suspected work-related disease and may not be generalisable to all workers. The mechanism(s) underlying the reported symptoms cannot be ascertained from this study. The reported symptoms could be due to either allergic or irritant mechanisms; in the case of concurrent symptoms it is possible that one symptom is allergic in nature, while the other is irritant. Additionally, these results cannot say whether workers who report either skin or respiratory symptoms are likely to develop the other symptom, or the mechanism by which this may occur.

In conclusion, the association between a history of eczema and concurrent skin and respiratory symptoms, including the potential role of impaired barrier function in the development of concurrent symptoms needs further investigation. Future research should endeavour to include measures of both skin and respiratory exposures and outcomes in studies of occupational exposures that have effects in both systems. Prevention of both the skin and respiratory routes of exposure should be considered as part of primary and secondary prevention strategies in the workplace, and the possibility of disease in both systems should be considered in clinical practice.

Key points

- Among workers with suspected work-related skin and respiratory disease many also reported work-related symptoms in the other system.
- Workers who had a history of eczema, were current smokers, were employed in larger workplaces and reported respirator use were more likely to have concurrent skin and respiratory symptoms.
- Clinical investigations, exposure assessment and occupational health research should consider both the skin and respiratory systems as possible routes of exposure as well as sites of health effect.

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Conflicts of interest

S.M.T.'s clinical practice includes medical assessment for Ontario Workplace Safety and Insurance Board (WSIB). She has received peer-reviewed research funding from WSIB research advisory council and the research arm of British Columbia's Workers Compensation System.

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