Respiratory Health Survey of Respiratory Therapists*

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Respiratory Health Survey of Respiratory Therapists*

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Study objectives: **The purpose of this study was to determine whether respiratory therapists (RTs) had an elevated risk of respiratory symptoms and to determine the association of work exposures with symptoms.**

Methods: **Mailed questionnaire responses from 275 RTs working in British Columbia, Canada, were compared to those of 628 physiotherapists who had been surveyed previously. Analyses incorporated logistic regression analysis with adjustment for age, sex, smoking status, and childhood asthma.**

Results: **Compared to physiotherapists, RTs had over twice the risk of being woken by dyspnea, having wheeze, asthma attacks, and asthma diagnosed after entering the profession. Among RTs, two work factors associated with asthma were sterilizing instruments with glutaraldehyde-based solutions and the use of aerosolized ribavirin. RTs who used an oxygen tent or hood had the highest risk of asthma diagnosed after entering the profession (odds ratio [OR], 8.3; 95% confidence interval [CI], 12.6 to 26.0) and of asthma attacks in the last 12 months (OR, 3.6; 95% CI, 1.2 to 10.9).**

Conclusions: **Our data suggest that RTs may be at an increased risk for asthma-like symptoms and for receiving a diagnosis of asthma since starting to work in their profession, possibly related to exposure to glutaraldehyde and aerosolized ribavirin.** ***(CHEST 2004; 126:1048–1053)***

Key words: aerosols; asthma; glutaraldehyde; respiratory therapists; ribavirin

Abbreviations: CI = confidence interval; OR = odds ratio; RSV = respiratory syncytial virus; RT = respiratory therapist; SPAG = small particle aerosol generator

Respiratory therapists (RTs), through their involvement in the diagnosis, treatment, and care of patients with respiratory and cardiopulmonary disorders, can potentially be exposed to a variety of agents that could impact occupational health. Respiratory hazards that may be encountered in the work environment include aerosolized agents and chemical sensitizers such as glutaraldehyde, which is used to disinfect bronchoscopes. Although there are many types of aerosolized substances, concerns have been raised about the potential health effects from occupational exposure to ribavirin or pentamidine.[1] Aerosolized ribavirin is used primarily to treat respiratory syncytial virus (RSV) infection in infants, while aerosolized pentamidine is used primarily for the treatment of *Pneumocystis carinii* pneumonia, which is often a complication for immunocompromised patients. Ribavirin and pentamidine are aerosolized in a particle size of < 5 μm to provide deep penetration into the lung of the patient.[2]

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Personal and area monitoring of airborne ribavirin and pentamidine, and the measurement of biological markers confirm that health-care workers can be exposed during the routine monitoring and care of patients.[3–6] The evaluation of respiratory health effects among workers exposed to these aerosolized substances in the hospital setting has been based on studies limited by small sample sizes.[6–9] For example, McDiarmid and colleagues[7] studied 11 nurses who administered aerosolized pentamidine and

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found no significant dose-response effect on lung function, although there were increased symptom complaints (*ie*, chest tightness and shortness of breath) in some of the nurses.

Two large epidemiologic studies have demonstrated that RTs have an increased risk for asthma.[10,11] For example, Kern and Frumkin[10] performed a mailout study of 315 RTs with control subjects consisting of physical therapists and radiology technologists working in Rhode Island. RTs had a higher prevalence of doctor-diagnosed asthma, recent asthma medication use, and wheeze attack with shortness of breath, and were four times more likely to have developed asthma after entering the profession than the control subjects.

The objectives of this study were to determine whether a population-based sample of RTs reported an excess of respiratory symptoms in comparison to control subjects and to evaluate the association of work exposures with symptoms.

Materials and Methods

Subjects

All registered RTs working in British Columbia were initially contacted by mail in October 2000 using the database of the professional registry. The mailout included a letter of invitation explaining the study, a self-addressed stamped return envelope, and a questionnaire. A second mailout was performed 1 month later with a support letter from their professional association, followed by a reminder note sent to those who had not returned a questionnaire.

From January to September of 1999, 628 physiotherapists participated in a mailout survey.[12] The protocol for this study was similar to that described above. Ethical approval to conduct the studies was granted by the Clinical and Behavioral Sciences Research Ethics Board at the University of British Columbia.

Questionnaire

The questionnaire included items on personal characteristics, symptoms, and work environment. Questions on job tasks were developed through consultation with professional RTs and through pilot testing. The section on aerosolized substances was open-ended, and included listing up to six of the most common aerosolized substances they had administered and questions about the method, duration, and frequency of administration.

The questions on respiratory symptoms were based on the American Thoracic Society-Division of Lung Disease[13] questionnaire on epidemiologic studies and the International Union Against Tuberculosis and Lung Disease.[14] The following terms were used for questions on respiratory symptoms occurring at any time in the last 12 months: *asthma attack* (had an attack of asthma); *wheeze* (had wheezing or whistling in chest when did not have a cold); *chest tightness* (woken up with a feeling of tightness in chest); *woken by cough* (been woken by an attack of coughing); and *woken by dyspnea* (been woken by shortness of breath). Terms for other respiratory symptoms or conditions included the following: *usual cough* (usually have a cough); *usual phlegm* (usually bring up phlegm from chest); *childhood asthma* (doctor-diagnosed asthma starting before age 16 years); and *reported asthma* (diagnosis of asthma since entering their profession).

Data Analysis

Descriptive analysis included χ^2 testing to evaluate the significance of differences in proportions, with $p < 0.05$ used as the level of significance (SPSS, version 10.0; SPSS; Chicago, IL). Logistic regression analysis (STATA, version 6; Stata Corporation; College Station, TX) was applied to obtain odds ratios (ORs) and 95% confidence intervals (CIs) after adjustment for potentially confounding factors (*eg*, smoking status, sex, age, and childhood asthma).

For RTs, the relationships among specific tasks, work environment characteristics, and methods of administering aerosolized agents were evaluated using χ^2 analysis. The use of pentamidine and ribavirin were chosen *a priori*, based on the literature review, to be included in the analysis. Exposure variables were selected for further analysis when one or more of the respiratory symptoms were positively related to the work factor ($p < 0.10$).

Results

Of the 527 RTs in British Columbia who were invited to participate and were sent questionnaires, 98 were excluded (Table 1), primarily because the contact information was incorrect, and 154 questionnaires were not returned, resulting in a participation rate of 64.1%. The response rate for physiotherapists was similar (68.6%).

As shown in Table 2, there were many differences in personal and work characteristics between the two groups of health professionals. All of the comparisons were statistically significant, apart from personal smoking or number of smokers living at home. A greater percentage of RTs were men, they were slightly younger on average, and a greater percentage worked at night or on rotating shifts. The prevalence of childhood asthma was higher among RTs. The percentage of current smokers was low (< 5%) for both groups.

The frequencies of the selected work exposure factors according to the percentage of RTs respond-

Table 1—*Participation Rate*

Variables	RTs	Physiotherapists
Population, No.	527	1008
Not returned, No.	154	287
Not included, No.	98	93
Undeliverable	66	65
Not in industry	24	2
Retired	2	10
Disability/unemployed	1	10
Leave of absence/maternity	0	6
Not living in province	5	0
Participants, No.	275	628
Participation rate, %	64.1	68.6

Table 2—*Personal and Work Characteristics of RTs and Physiotherapists

Characteristics	RTs (n = 275)	Physiotherapists (n = 628)
Age, yr	37.0 ± 7.7	43.2 ± 9.2
Female sex	58.5	91.2
Time profession, yr	11.3 ± 7.1	17.6 ± 9.6
Time worked per week, h	35.4 ± 8.7	31.2 ± 10.6
Day or afternoon shift	43.6	99.0
Employed at a hospital	94.2	75.0
Childhood asthma	9.1	5.1
Nasal allergies or hayfever	49.1	42.6
Smoking status		
Never	76.5	80.4
Ex-smoker	19.5	17.7
Current	4.0	1.6
Live with a smoker†	6.5	4.9

*Values given as mean ± SD or %.
†Nonsmokers only.

ing are given in Table 3. The most frequent aerosolized substances that were used were albuterol (81%) and ipratropium bromide (62.0%), among other reported agents (data not shown). The use of mist masks was the most common method of administering aerosolized agents. The administration of aerosolized substances by small particle aerosol generator (SPAG) or ribavirin units (exclusively used for administering ribavirin) and by oxygen tents or hoods was each performed by < 10% of the RTs.

As shown in Table 4, the respiratory symptoms of wheeze, woken by dyspnea, and asthma attacks were significantly higher for RTs compared to physiotherapists. RTs had over twice the risk for these symptoms and for reported asthma after adjustment for confounding factors (age, sex, smoking status, and childhood asthma). The relationships remained the same when the analysis was restricted to subjects without childhood asthma (data not shown).

Table 3—*Frequency of Work Exposures Among RTs*

Work Exposures	RTs, %
Work environment	
Work > 35 h/wk	74.0
On graveyard or rotating shifts	56.4
Been in profession > 10 yr	46.0
General ventilation in work area inadequate	41.6
Specific work tasks	
Performed chest physical therapy	58.4
Treated children under 6 yr of age once a week or more	56.2
Cold sterilized with glutaraldehyde-based solutions at least once a month	53.3
Aerosolized agents*	
Ribavirin (antiviral)	26.5
Pentamidine	15.6
Method of aerosolized agent administration*	
Mist mask	90.5
Ventilator	50.2
SPAG or ribavirin unit	8.0
Oxygen tent or hood	7.6

*Up to six possible agents and up to three methods of administration were given per subject.

Table 4—*Prevalence of Asthma and Respiratory Symptoms, Adjusted ORs, and 95% CIs Comparing RTs and Physiotherapists*

Symptoms*	RTs, %	Physiotherapists, %	OR*	95% CI
Woken by dyspnea	9.1	4.8	2.6	1.4–5.1
Asthma attack	13.1	6.1	2.6	1.4–4.7
Reported asthma†	6.9	4.6	2.4	1.2–4.7
Wheeze	21.9	13.5	2.3	1.5–3.5
Usual cough	9.8	7.2	1.6	0.9–2.9
Usual phlegm	9.1	6.6	1.4	0.8–2.7
Chest tightness	16.4	15.4	1.1	0.7–1.8
Woken by cough	37.2	37.1	1.0	0.7–1.4

*Adjusted for age, sex, childhood asthma, and smoking status (*ie*, current, ex-smokers vs never-smokers) using logistic regression analysis.
†Adjusted for age, sex, and smoking status (*ie*, current, ex-smokers vs never-smokers) using logistic regression analysis.

Personal protective respiratory equipment was worn at work by 67% of RTs. Of those, 35% reported frequency of use less than a few times per month; 24% at least once a week; and 41% daily. Almost 50% of the 275 RTs wore latex gloves, and 36% reported the use of glasses or goggles to protect their eyes.

As seen in Table 5, RTs who perceived that there was inadequate ventilation in their workplace had an increased risk of being woken by cough or by dyspnea. Working > 35 h per week was associated with wheeze and being woken by cough. RTs who reported sterilizing instruments with glutaraldehyde-based solutions once a month or more, in comparison to those who did not, showed elevated adjusted ORs for wheeze, woken by cough, and reported asthma. There was no association of respiratory symptoms or reported asthma with working a graveyard shift or rotating shifts, with ever performing chest physical therapy, or with treating children < 6 years of age at least once a week.

Table 6 shows the ORs for respiratory symptoms and conditions, related to the use of aerosolized agents and methods of administration. RTs who administered ribavirin showed a significantly higher risk of having an asthma attack in the last 12 months and of receiving a diagnosis of asthma since starting work in their profession. Administering pentamidine, on the other hand, showed no significant positive relationships. Those who used a ventilator as the method of administration had an increased risk of being woken by cough. The largest ORs were for the use of an oxygen tent or hood. RTs who used an

Table 5—*Adjusted ORs and 95% CIs for Respiratory Symptoms Among RTs Comparing Positive-to-Negative Responses to Work Exposures*

	Inadequate Ventilation		>35 h Worked per Week		Sterilized With Glutaraldehyde	
Symptoms*	OR	95% CI	OR	95% CI	OR	95% CI
Asthma attack	1.2	0.5–2.5	2.0	0.8–5.4	1.3	0.6–2.9
Wheeze	1.3	0.7–2.3	2.5	1.2–5.2	2.1	1.1–3.8
Reported asthma†	0.4	0.1–1.3	2.7	0.7–10.2	3.2	11.1–9.3
Chest tightness	1.7	0.9–3.3	2.1	0.9–4.9	1.4	0.7–2.8
Woken by cough	2.0	1.2–3.3	1.9	1.0–3.5	2.3	1.3–3.9
Woken by dyspnea	2.5	1.1–5.9	2.9	0.8–10.4	1.3	0.6–3.1
Usual phlegm	1.5	0.7–3.7	1.8	0.6–5.6	1.0	0.4–2.4
Usual cough	2.0	0.9–4.5	2.4	0.8–7.5	1.5	0.6–3.5

*Adjusted for age, sex, childhood asthma, and smoking status (*ie*, current or ex-smokers vs never-smokers) using logistic regression analysis.
†Adjusted for age, sex, and smoking status (*ie*, current or ex-smokers vs never-smokers) using logistic regression analysis.

oxygen tent or hood were eight times more likely to have reported asthma and over three times more likely to have experienced an asthma attack in the past year. The ORs relating use of a SPAG or ribavirin unit to respiratory symptoms were all < 1.0, but were not statistically significant (data not shown).

Discussion

Our survey of RTs not only confirmed previous findings of an elevated prevalence of asthma diagnosed after entering the profession, but also revealed an association of asthma-like symptoms and reported asthma with the administration of aerosolized ribavirin.

Over a decade ago, Kern and Frumkin[10] noted a previously unrecognized increase in the development of asthma after entry into the respiratory therapy profession. Christiani and Kern[11] conducted a large cross-sectional study of 2,086 RTs and 2,030 physical therapists working in the state of Massachusetts. The OR for asthma after entry into the profession was 2.5 (95% CI, 1.6 to 3.3) after adjustment for confounders. However, they did not find any relationship between the development of asthma and the work exposure questions of cold sterilizing with glutaraldehyde-based solutions, the number of various respiratory treatments administered, or treating children ≤ 5 years of age.

Our study showed a very similar increase in the risk of reported asthma for RTs who had received a diagnosis of asthma after entry into the profession (OR, 2.4; 95% CI, 1.2 to 4.7) in comparison to physiotherapists. However, we found that RTs who sterilized instruments with glutaraldehyde-based solutions once a month or more had an increased risk of developing asthma after entering the profession, as well as of wheeze and being woken by cough. Glutaraldehyde is known to be a sensitizer and is associated with occupational asthma.[15–17] Norback[18] concluded that even though exposures were well below the current occupational limits, 39 Swedish

Table 6—*Adjusted ORs and 95% CIs for Respiratory Symptoms Among RTs Comparing Positive-to-Negative Responses to Methods of Administration and Aerosolized Agents*

	Ventilator Method		Oxygen Tent or Hood Method		Ribavirin		Pentamidine	
Symptoms*	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Asthma attack	1.2	0.5–2.5	3.6	1.2–10.9	2.4	1.1–5.5	0.8	0.2–2.4
Wheeze	1.2	0.7–2.1	2.5	1.0–6.8	1.5	0.8–2.8	0.3	0.1–0.9
Reported asthma†	1.0	0.4–2.7	8.3	2.6–26.0	2.6	1.0–6.9	1.0	0.3–3.6
Chest tightness	1.5	0.7–2.9	2.4	0.8–6.7	1.4	0.7–2.9	1.0	0.4–2.5
Woken by cough	1.8	1.1–3.0	1.7	0.7–4.3	1.0	0.6–1.8	0.7	0.4–1.5
Woken by dyspnea	2.1	0.9–5.1	1.9	0.5–7.0	0.9	0.4–2.5	0.2	0.1–1.8
Usual phlegm	1.5	0.6–3.5	0.5	0.1–3.9	0.8	0.3–2.4	0.4	0.1–2.0
Usual cough	1.8	0.8–4.2	1.0	0.2–4.6	0.8	0.3–2.0	0.2	0.1–1.5

*Adjusted for age, sex, childhood asthma, and smoking status (*ie*, current or ex-smokers vs never-smokers) using logistic regression analysis.
†Adjusted for age, sex, and smoking status (*ie*, current or ex-smokers vs never-smokers) using logistic regression analysis.

hospital employees who used glutaraldehyde-based solutions for cleaning equipment had a relatively higher prevalence of airway symptoms, in comparison to an unexposed group. In contrast, Waters et al[19] found glutaraldehyde samples to be above limit values (*ie*, 0.10 ppm), despite the use of exposure control in five Australian health-care facilities, and found no significant differences in respiratory and airway symptoms between 38 exposed nurses and the control subjects.

According to our survey, RTs who had used aerosolized ribavirin, compared to those who had not, had 2.4 times the risk of asthma diagnosed after entering the profession and of having experienced asthma attacks in the past 12 months. The possibility that inadvertent exposure to aerosolized ribavirin may be a respiratory hazard is supported by a small pharmacokinetic study performed by Linn et al.[8] For the seven health-care workers with high exposure to aerosolized ribavirin, there were slight decreases in FVC and small variations in reported respiratory symptoms (*ie*, cough, phlegm, wheeze, dyspnea, and chest tightness), with significant overall increases in reported symptoms occurring during the exposure period relative to the pre-exposure period.[8] For patients treated with ribavirin, documented adverse drug reactions include acute worsening of asthma, deterioration of pulmonary function, and dyspnea.[20] By contrast, the study by Edell and colleagues[21] found that infants treated additionally with ribavirin at the early onset of severe RSV bronchiolitis had reduced incidence and severity of reactive airway disease after 1 year of follow-up. Ribavirin use may be a surrogate for exposure to viruses such as RSV in infants. However, we found that RTs who worked with children at least once a week were not at increased risk for respiratory symptoms or asthma.

Exposure to ribavirin among health-care workers has been demonstrated through measurements of personal breathing zones and through biological samples. Gladu and Ecobichon[4] detected ribavirin in all air samples and personal samples obtained over an 8-h period, while a volunteer simulated the administration and follow-up procedure. Personal breathing zone air samples were highest for six nurses and two RTs providing direct care to patients who received ribavirin through an oxygen tent.[3] According to Waskin,[20] for infants and children who were unable to utilize hand-held nebulizers, the SPAG unit nebulizing ribavirin could be connected to an oxygen hood, and oxygen tent, or a face mask. This type of open nebulization system could result in the release of ribavirin into the patient's room. Shults et al[22] found that the highest exposures to ribavirin, measured in personal breathing-zone air samples and in urinary samples, were found when ribavirin was administered through an oxygen tent alone or through an aerosol delivery hood. The lowest ribavirin levels were measured when an additional aerosol containment tent was used or when ribavirin was administered through a ventilator, which is a closed system. We found that use of an oxygen tent or hood had the strongest association with asthma diagnosed since starting to work in the profession (OR, 8.3; 95% CI, 2.6 to 26.0). On the other hand, reporting the use of a small particle aerosol delivery or ribavirin unit, which is exclusively used for ribavirin, was not associated with reported asthma or respiratory symptoms. If the ribavirin units had aerosol containment systems, this would be effective in reducing occupational exposures.[20]

The exposure of health-care workers to pentamidine has been evaluated primarily through urine sampling[23,24] and air sampling.[5,7] McDiarmid et al[7] evaluated the respiratory health of 11 nurses who administered aerosolized pentamidine over an 11-week period. Although there was no dose-response effect on lung function resulting from exposures, there were substantial declines in cross-shift peak expiratory flow rates, diffusion capacities, and increased symptom complaints (*eg*, dyspnea and chest tightness with shortness of breath) in a few of the nurses. We did not find any increased risk of respiratory symptoms or conditions among RTs who administered pentamidine.

An important limitation of our study is the cross-sectional design, in which both exposure and outcome data were derived from a mailout questionnaire. There were no objective measures for exposures, such as general ventilation, or for outcomes, such as skin prick testing for the determination of allergic sensitivity. Our investigation, like the previous epidemiologic studies, concerned the prevalence of asthma rather than the incidence. We cannot discount the possibility that exposure to aerosols may aggravate rather than cause asthma in susceptible individuals.

There is the possibility of selection bias since approximately one third of the eligible RTs did not return the questionnaire; however, the response rate was similar to that of the comparison group of physiotherapists. RTs may have been attracted to their profession as a result of personal or family history of respiratory problems (which was partly accounted for after adjustment for childhood asthma). Also, the knowledge of respiratory diseases that RTs would be expected to have may have introduced information bias. Recall bias may be another factor, such that those having respiratory difficulties were more likely to identify some aspect of their work environment, such as inadequate ventilation, as a causal factor. Finally, due to multiple

hypotheses testing there is the possibility of a statistically significant relationship occurring due to chance.

Despite the potential biases resulting from the cross-sectional design of the study, this survey of RTs raises the issue of whether there are respiratory health effects related to occupational exposures to aerosolized ribavirin. The method of administration (*ie*, by tent or hood) was highly associated with reported asthma among RTs. Further research on the occupational health risks due to exposure to aerosolized substances is needed. More importantly, in addition to ensuring adequate general ventilation, effective scavenger systems and aerosol containment devices should be installed and maintained to reduce the exposure of health-care workers to ribavirin and other aerosolized substances. The substitution of glutaraldehyde, a known etiologic agent for occupational asthma, is warranted. Paradoxically, it appears that RTs may be at risk for developing asthma and respiratory symptoms as a consequence of their work treating patients who experience respiratory problems.

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