

Editorials

Practical implications of studies in occupational rhinoconjunctivitis

Susan M. Tarlo, MB, BS,^a and Gary M. Liss, MD^b Toronto, Ontario, Canada

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The natural history of occupational asthma has been the focus of multiple studies in the past 20 years.¹⁻⁴ One suggested risk factor is the development of occupational rhinitis, especially for high-molecular-weight sensitizers.⁵ Karjalainen et al,⁶ in a Finnish population study, recently reported that occupational rhinitis (defined on the basis of work-related symptoms, specific sensitization to a work substance, positive nasal challenge, and exclusion of other reasons for rhinitis) carried a crude relative risk of asthma of 4.8 (95% confidence interval, 4.3 to 5.4). The relative risk was highest among farmers and wood workers. The greatest risk of asthma was in the year after reported rhinitis, but increased risk persisted for several years.

Although allergic rhinitis and conjunctivitis have been well recognized to occur in similar occupations as those associated with occupational asthma, prospective incidence studies of occupational rhinoconjunctivitis (RC) have only recently been the focus of research.⁷⁻⁹ The study by Rodier et al¹⁰ in this issue of the Journal is the latest of several studies analyzing a large data set collected by this group in apprentices with exposure to high-molecular-weight allergens (in programs for pastry making, dental hygiene, and animal health technology), aiming to characterize the development of sensitization and allergic manifestations.⁷⁻¹¹ These are particularly important because they identify the incidence and natural history in these workers from the onset of their career training prospectively rather than from information gleaned from the more common cross-sectional study design.

Both cross-sectional (prevalence) studies and longitudinal (incidence) studies have advantages and disadvantages. Cross-sectional studies are generally easier to perform, less costly, and may allow assessment of a larger

Abbreviations used

RC: Rhinoconjunctivitis

group of workers, including those with many years of exposure as well as relatively newly exposed workers. However, because data on exposure and outcome are obtained concurrently, conclusions cannot be drawn about causality as may be possible with prospective cohort studies. Moreover, cross-sectional studies can have a bias, underestimating the true prevalence of disease due to the "healthy worker" effect; for example, those with work-attributed symptoms are more likely to leave that exposure, resulting in a survivor population with a lower prevalence of work-related symptoms. Identification and tracking of individuals who have left the workplace are often difficult in cross-sectional studies. Similar limitations can apply to prospective studies of workplaces where a proportion of workers may have had long exposure to the workplace sensitizer before the start of follow-up (a noninception cohort), and the workforce may have become selected for those less predisposed to sensitization, especially when sensitization is most common in the first few exposure years.

In contrast, prospective studies of newly exposed trainees (an inception cohort), such as the study by Rodier et al,¹⁰ include individuals relatively unlikely to have been previously exposed to the occupational allergens, potentially including all who may have development of sensitization and symptoms. Theoretically, this allows more accurate determination of rates of new sensitization and easier identification and follow-up of those leaving the program. In this study, the authors indicate that dropping out from the apprenticeship was not related to the incidence of work-related RC and that attrition probably did not result in substantial bias or the healthy worker effect. However, earlier analyses from the larger study assessing apprentices who quit the 3 training programs¹¹ found that specific immunologic sensitization and asthma symptoms in follow-up (in multivariate analyses) as well as certain baseline characteristics, including specific immunologic sensitization, hay fever, and shortness of breath (in univariate analyses), were the main determinants for quitting the training programs. Thus, underestimation and bias from the healthy worker effect may occur even in these prospective studies.⁷⁻¹¹

The current report¹⁰ focuses on development of RC in animal health technology apprentices, following similar

From Gage Occupational and Environmental Health Unit,^{a,b} Toronto Western Hospital,^a University of Toronto Departments of Medicine^a and Public Health Sciences,^{a,b} and Ontario Ministry of Labour,^b Toronto, Ontario, Canada.

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Reprint requests: Dr Susan M Tarlo, Toronto Western Hospital, EC4-009, 399 Bathurst St, Toronto, Ontario, M5T 2S8, Canada.

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analyses in the pastry-making and dental hygiene apprentices^{8,9} and analyses assessing development of occupational asthma.^{7,9} In this report,¹⁰ occupational RC symptoms included development of any single work-related symptom of rhinitis or conjunctivitis, a more liberal definition than generally used for clinical diagnosis of RC (usually requiring symptoms of both rhinitis¹² and conjunctivitis). It would be useful to conduct a "sensitivity analysis" to examine how the incidence of occupational RC varies with a more stringent definition of RC. Nevertheless, most subjects with occupational RC in this study had both rhinitis and conjunctivitis symptoms. The incidence was high, 24% over the 44-month study period from entry into the apprentice program. Not surprisingly, fewer (9.6%) had concurrent skin test responsiveness to a laboratory animal extract, illustrating probable inclusion of symptoms in the broader category that were nonspecific, non-work-related, or related to nonallergic exposures in animal care work such as dust, endotoxin, and ammonia. The high rate of nonallergic RC symptoms was similar to findings in pastry-making apprentices, where the incidence of occupational allergic RC was only a tenth of the rate of RC without specific sensitization.⁸

Animal care apprentices with specific sensitization associated with nasal or eye symptoms were more likely than those with RC without sensitization to report multiple symptoms suggesting an allergic response, as might be expected (most frequently sneezing, runny nose, and itchy eyes).¹⁰ In a significant proportion of subjects, symptoms appeared to remit during follow-up, but medication usage for upper respiratory symptoms was not documented and might account for at least some apparent symptom loss. Incidence of RC with skin sensitization to the occupational allergen was greatest in the first 20 months, indicating relatively short latency. Almost half of those with occupational allergic RC had study criteria for probable occupational asthma. Despite the relatively low (11.4%) positive predictive value of occupational RC for the development of occupational asthma as previously reported by this research group,⁷ these data suggest that including questions to assess RC symptoms in medical surveillance questionnaires for animal care workers may help to identify workers at increased risk of occupational asthma. Positive RC responses may require exposure modification or at least closer monitoring for asthma. The short latency indicates need for most intensive surveillance in the first few exposure years.

Although the association of probable occupational asthma was greatest in those with occupational allergic RC, there was an increased incidence (as defined by skin sensitization to a work allergen and bronchial hyperresponsiveness) among those with RC symptoms without sensitization (21.4% versus 7.8% in the whole cohort).¹⁰ Hours of rodent exposure was also associated with development of RC. Thus, the association of asthma with nonallergic RC might have reflected higher dust exposure and concurrent allergen exposure (although not measured in this study) among those who may have had irritant-related, nonallergic rhinitis. However, it is also possible

that irritant exposures may have increased nasal inflammation and epithelial permeability, leading to greater local exposure to allergens and subsequent respiratory sensitization. Alternatively, substances such as endotoxin may act as adjuvants, such has been demonstrated in animal studies with sensitization to natural rubber latex¹³; studies to clarify this would be useful.

Severity of RC was not addressed in this study but would be useful to address in the future, both for RC with sensitization and that caused by other mechanisms, assessing medication requirements and quality-of-life scales to determine whether such symptoms have significance mainly as an asthma risk factor or independently have significant morbidity.

As with previous studies, several underlying risk factors were identified among apprentices who had occupational RC, including preexisting nasal and lower airway symptoms, symptoms on contact with pets, and a positive skin test reaction to grass.¹⁰ Although relative risks with these factors are not sufficient (approximately 2-fold) to advise preentry screening of applicants for animal care work, the findings raise the question as to whether allergic high school children should be informed and educated by physicians or in school curricula regarding such increased risks to make informed career choices. There probably already is some self-selection by allergic and asthmatic young adults into careers with less respiratory irritant or allergen exposure, but there is little published information to assess this. A cross-sectional study¹⁴ found increased adult-onset asthma but less self-reported childhood asthma among medical radiation technologists exposed to irritant workplace developing chemicals (4.4%) than among physiotherapists (5.6%) (odds ratio, 0.78; 95% confidence intervals, 0.56 to 1.14). Similarly, Renstrom et al¹⁵ reported a trend to less baseline atopy among training laboratory technicians who later worked with animal exposure compared with those who did not ($P = .06$). Future research may provide insight as to career selection by allergic young adults and education needs.

Finally, this study did not include an exposure assessment measure other than hours of exposure. A relation has been clearly shown in several laboratory animal worker studies between degree of exposure and risk of occupational asthma.^{16,17} There are effective measures to reduce exposures in animal care facilities.¹⁸ Effectiveness has been suggested with a comprehensive preventive program including education, exposure control, and medical surveillance in an established animal care workforce.¹⁹ Preventive measures have been successful in dental students to reduce allergy to natural rubber latex.²⁰ The high incidence of symptoms in animal care apprentices emphasizes the need for prospective evaluation of intervention measures in such trainees.

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