Work related asthma

G M Liss, S M Tarlo

Difficulties in assessing relationships from population based surveys

Occupational asthma (OA) is the most frequently reported work related respiratory disease in Canada^{1,2} and other countries such as the United Kingdom,³ and a diagnosis of OA is associated with the potential for serious complications related to both health, such as excess hospitalisations,⁴ and economic consequences.^{5,6} In the United Kingdom, occupational lung disease surveillance data based on physician reports from the SWORD and SHIELD reporting schemes^{3,7} provide a valuable extensive picture of implicated industries. In the USA, the Sentinel Event Notification System for Occupational Risks (SENSOR) is also a source for physician reports of possible cases of OA asthma,⁸ but only from a limited number of states, without national estimates or reporting system. Thus, the report by Arif and colleagues⁹ in this issue helps in part to address this gap from a different perspective, based on a general population data source.

The authors analysed data from the Third National Health and Nutrition Examination Survey, 1988–1994 (NHANES III) to estimate the prevalence of participants reporting two outcomes, defined as work related asthma and work related wheezing, as well as which industries are at higher risk and could be targeted for future intervention.

They observed important proportions of asthma and wheezing that appeared to be attributable to work (based on the definitions utilised), with estimates of population attributable risk of 36.5% and 28.5%, respectively. To put these estimates in perspective, the authors noted that a recent analysis of previous studies by Blanc and Toren,¹⁰ regarding how much adult asthma might be attributable to occupational factors, including new onset and reactivation of preexisting asthma, found a range for attributable risk of 2–33% (median 9%). Among the 12 studies considered to be of higher quality, the median was 15%. Arif and colleagues⁹ acknowledged that their own estimate, which lies beyond the upper end of this range, could be higher as a result of differences in study populations and case definitions used to define work related asthma, the approach used to classify industries, or “may reflect true

differences in industrial and occupational exposures encountered in those regions”. Although there clearly can be regional differences in causes and rates of work related asthma, it is unfortunately difficult to assess the degree to which this may account for the findings in the current report because of other study limitations. We emphasise, however, that these caveats in interpreting their “point estimate”, which will be further addressed in this editorial, should not serve at all to minimise the importance of work related asthma.

“Wheezing may be present in other diseases such as acute or chronic bronchitis”

Firstly, as the authors acknowledge, components of their definitions of work related asthma (and wheezing) have not previously been validated. Their choice of definitions was determined by the structure of the NHANES questionnaire which was not designed specifically for the purposes of this study. Their definition of work related asthma was taken from positive responses to the combination of physician diagnosed asthma, and item HAL14D of the questionnaire, which combines lower respiratory symptoms (wheezing, whistling) “brought on by work environment” with “stuffy, itchy, or runny nose, watery, itchy eyes”. Therefore, it is very likely that a proportion of positive respondents had work related eye or nose but not lower respiratory symptoms, resulting in overestimation of asthma that appeared to be work related. The other item used, that of “wheezing” as a single symptom, similarly has not been validated as a sensitive or specific surrogate for asthma. It may be present in other diseases such as acute or chronic bronchitis, and may be absent in patients with objectively confirmed asthma. As an example, the health care group, which is known to have subgroups at risk for OA with exposures such as natural rubber latex (NRL) and glutaraldehyde, had a relatively high odds ratio (OR) of 2.18 for occupational asthma as defined in this study, but there was no increase in work related (WR) wheezing. This could be interpreted as

indicating a high rate of WR rhinoconjunctivitis in this population or a lack of sensitivity of wheezing as a reflection of asthma, or both. In addition, these definitions of WR asthma or wheezing do not ascertain whether this is “new” or whether similar symptoms preceded the individual’s workplace exposure.

Secondly, the definition of “exposure” (industrial group) in this report is self reported (thus, both outcome and exposure are subjective), unlike other studies which have used an exposure matrix or other methods to determine exposure. Furthermore, since “the longest industry worked in” was used as a surrogate for exposure, it is possible that the current or another previous job or industry was/is responsible for the WR respiratory problem, rather than the longest industry, and thus the attributed cause may be misclassified. Another related problem with exposure is that *within any broad industry*, there would be both “exposed” jobs (for example, involved with the guilty process) and “unexposed” jobs. Lumping these within one industry rather than a specific job process would usually tend to dilute risk estimates, with the result that some at risk subgroups or exposures within an industry may not appear.

Thirdly, as the authors recognise, the problem of the “healthy worker effect” or survival bias, which limits cross sectional studies in general, may result in underestimation because of symptomatic workers leaving the industry. In their study, Arif *et al* excluded approximately 3500 subjects who reported WR conjunctivitis, rhinitis, and asthma because they reported not working at the time of interview. They acknowledged that they may have stopped working because of asthma and may represent serious cases resulting in underestimation or failure to recognise “hotspots”. These excluded subjects might have served as a fruitful source of further exploration, but were not analysed by the authors; perhaps they could be included in a follow up paper.

Finally, a questionnaire based study such as this without objective documentation of asthma or the work relationship cannot distinguish between sensitiser induced versus irritant induced OA,^{11,12} versus work aggravation of preexisting asthma, or even unrelated coincidental asthma or other causes of symptoms. Although the importance of considering all work related asthma has been

Abbreviations: NHANES III, Third National Health and Nutrition Examination Survey; NRL, natural rubber latex; OA, occupational asthma; OR, odds ratio; SENSOR, Sentinel Event Notification System for Occupational Risks; WR, work related

emphasised,¹³ the treatment and intervention implications are quite different for the different types of WR asthma.¹⁴

What can we say about the associations that were highlighted? Despite the limitations, the study did confirm increased risks (for combined WR upper or lower respiratory symptoms) for some of the "expected" or previously reported industries such as agriculture, wood, and plastics, and highlighted the important burden of illness associated with these work related conditions. An additional positive contribution by this report is the attempt by Arif *et al* to assess which associations might be moved to the "causal" or "established" category from the "suggested" category, as did Becklake¹⁵ regarding occupational exposures as a contributor in the development of chronic obstructive pulmonary disease. This process of reaching the step of acceptance or agreement regarding the existence of the associations (in this case, of OA with a given exposure/industry) is important, so that the workplace parties and regulatory authorities can move to the next step to focus on intervention and prevention. Associations highlighted in this study include the greater than twofold risk, consistent for both "WR asthma" (OR 2.92) and wheezing (OR 2.25), in the electrical machinery, equipment, and supplies industry. As noted by the authors, causative exposures may include soldering fluxes, metal machining (metal working) fluids, adhesives, paints and coatings, and other chemicals.

Among the workers suggested by Arif and colleagues⁹ as needing further investigation are cleaners. Of interest, cleaners were also identified as having a significantly increased relative risk of asthma in other recent population based studies in Finland by Karjalainen and colleagues,¹⁶ and in a multinational study by Kogevinas and colleagues.¹⁷ Both of these studies included objective confirmation of asthma in at least a subset of the population. The cause of this increased risk has not been identified and merits further study as most case series of physician reported³ or investigated¹⁸ occupational asthma do not include a significant proportion of cleaners, or indicate that this occupational set is at increased risk. Educators were also identified in the present study as being a group at possible risk. One candidate agent to which this population may be exposed is mould, which has become a widespread concern in schools and public buildings in North America. Potential upper and lower respiratory symptoms which might relate to indoor environments contaminated with mould include not only allergic upper and lower respiratory symptoms, but also non-specific mucous membrane irritation from fungal components such as β 1,3

D-glucans, or associated poor indoor air quality, which may mimic several of these symptoms.

A final somewhat surprising finding in this study was the small number of workers in the repair industry meeting the authors' definition of WR asthma. Although the relative risk for WR asthma was increased (OR 2.83), this was based on only two cases and the confidence interval included unity; the OR for WR wheezing was 3.35 (95% confidence interval (CI) 1.35 to 8.33)). The authors point out that the exposures include spray paint which may contain isocyanates. We should emphasise that OA among spray painters (probably a result of associated isocyanate exposure) has been observed repeatedly in other databases. For example, in SWORD data for 1992–97, the very highest incidence rate was observed in coach and other spray painters (1464 per million/y, 95% CI 968 to 2173), compared with rates of 61 per million/y (95% CI 19 to 167) overall in the occupational order of painting, assembly, and packing, and 38 per million/y (95% CI 34 to 41) in all occupations.³

In summary, this study adds to the evidence supporting the magnitude of work related asthma, implicates some specific industries, and has the advantage of using an existing data source not requiring a great deal of resources. However, the various shortcomings of this design including the crude "lumped" exposure assessment, limit its utility for the identification of focused exposures/industries suitable for intervention, which was one of the objectives given by the authors. An alternative strategy, probably requiring more resources, might incorporate the use of a job exposure matrix reflecting exposure to biological or other dusts, gases, fumes, and vapours, as was used in the population based study by Kogevinas and colleagues,¹⁷ or an asthma specific job exposure matrix such as that described by Kennedy and colleagues.¹⁹ The exciting follow up design in the report by Karjalainen and colleagues,¹⁶ referred to previously, in addition to having the advantage of yielding incidence rates, also has the potential to identify associations with new occupations. By reminding us about the extent of work related asthma, the report by Arif *et al* underscores the related issues of asthma management, prevention of cases among coworkers, and education of health care providers to improve recognition of links between occupation and asthma, which in time may lead to successful intervention studies to prevent further disease, for example, as is now being shown with NRL.²⁰

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Authors' affiliations

G M Liss, S M Tarlo, Gage Occupational and Environmental Health Unit, University of Toronto, Canada

Correspondence to: Dr G Liss, Gage Occupational and Environmental Health Unit, 655 Bay Street, 14th Floor, Toronto, Ontario M5G 2K4, Canada; gary.liss@utoronto.ca

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