

Correspondence

Reply

To the Editor:

We have read with interest the response of Walters et al¹ regarding our article.² We respectfully disagree with the comments made by Walters et al.

The authors mentioned that “Canadian Thoracic Society guidelines for occupational asthma (Tarlo et al, 1998) have stated that for practical purposes the absence of NSBR excludes the diagnosis of occupational asthma in asymptomatic exposed worker; this is likely to have significantly biased referrals for specific inhalation challenges toward those with significant NSBR.” We want to point out that the Canadian guidelines on occupational asthma (OA) were updated in 2009.³ This supposedly referral bias is not supported by both our current and previous studies; for example, we showed in a prospective observational study published in 2009 that among the 120 patients who were referred to our center over 1 year, 69 (57.5%) did not show evidence of asthma.⁴ Specific inhalation challenges (SICs) were performed in 74% (51) of the 69 subjects who had normal bronchial responsiveness. In the current study, 358 of the 1012 (35.3%) subjects investigated for possible OA had no evidence of asthma. Therefore, the performance of SICs or investigation of OA in our center is certainly not restricted to the patients who show functional evidence of asthma.

Walters et al state that “we perform challenges to a much wider range of agents that appear to fulfill the criteria for occupational asthma with sensitization.” This statement is not supported by the various cases that we see; our group has published several cases of OA to new agents. Although we seldom see workers exposed to diesel exhaust, we have seen workers with OA due to aluminum foundry fumes.⁵ Although we perform SICs in the laboratory when possible, when those test results are negative or when the exposure cannot be mimicked in the laboratory, we perform testing at the workplace, similarly to what Walters et al propose. Therefore, if the workers have true OA, we believe that we do not miss this diagnosis.

Walters et al state that OA to low molecular weight agents is less often associated with bronchial eosinophilia and thus, argue that nonspecific bronchial responsiveness is less often associated with OA caused by these agents. However, in the study quoted to support this statement,⁶ only 12 subjects underwent SICs and most subjects had peak expiratory flow rate (PEF) monitoring.⁷ It is thus surprising to see that Walters et al question the results of a large study of 1012 subjects, because it did not confirm the results of a small study of 38 subjects.⁶

Walters et al also argue that “This observation is supported by the meta-analysis of the value of NSBR in occupational asthma (Beach et al, 2007), which showed that pooled estimates of sensitivity are lower for low molecular weight agents than for high molecular weight agents.” Among the 24 studies included in this meta-analysis,⁸ only 2 studies included more than 100 patients (102 and 209). The sample size of the remaining studies varied from 4 to 75 subjects. The pooled number of subjects used for the meta-analysis represented only 64% of the sample size of our study. Furthermore, in contrast to our study, the work status of the workers was not taken into account in the meta-analysis.

Hence, the authors of the systematic review warned the reader regarding those results:

The general weaknesses associated with the quality and quantity of the research evidence suggests that caution should be used in interpreting these results. In the diagnosis review, the sensitivities and specificities varied widely for some of the comparison tests. We elected to pool heterogeneous data from individual studies, but would encourage clinicians to interpret these results cautiously and conservatively.

Finally, we want to emphasize that our study is the first to address the sensitivity and specificity of nonspecific bronchial responsiveness for diagnosing OA using a large sample size. Therefore, we can state confidently that in a setting without access to a full investigation of OA, excluding OA on the basis of a negative methacholine challenge is likely to misdiagnose only a very small number of patients. When in doubt, the investigation can still be completed by SICs, but relying only on “positive” PEF monitoring in a symptomatic patient with a normal airway responsiveness while at work is not sufficient to confirm the diagnosis of OA.

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