The role and interpretation of specific inhalation challenges in the diagnosis of occupational asthma

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Occupational asthma can result in a significant socioeconomic impact (1); however, correct diagnosis and management also results in a significant improvement in medical outcome and health care utilization (2). Specific inhalation challenge tests (SIC) with exposure to the suspected workplace sensitizer have been regarded as a reference standard for diagnosis of sensitizer-induced occupational asthma (OA) (3), although their role as a 'gold standard' has been questioned (4). Despite the recent publication of guidelines for performing SIC (5), and the recognition that there can be false-positive and false-negative responses, it is unclear how often false results occur. In North America, there have been relatively few centres performing SIC other than in Quebec, due, in part, to the need for specialized facilities with monitoring of exposures and responses and, in part, due to concerns about the possibility of severe reactions.

The report from Quebec by de Olim et al (6) (pages 341-347) in the current issue of the *Journal* is an important addition to the further understanding of factors affecting the interpretation of SIC. The study was performed by a group that included physicians with the greatest North American experience with SIC. Despite this, the study found that among 33 of the 53 (62%) patients who were deemed not to have OA on the basis of a negative SIC (ie, 25% of the total number of patients), there likely was at least one other sensitizer potentially present in their work environment that had not been identified by physician assessment and was not included in the SIC, but was subsequently identified by an occupational hygienist. Unfortunately, the authors state that they could not perform additional assessment with the workplace to assess the relevance of these additional agents, nor perform additional laboratory or workplace challenge tests as a result of this information. Nevertheless, these findings suggest the potential for significant underdiagnosis of OA by SIC based on expert physician assessment alone.

An implication of this study is that OA often cannot be excluded on the basis of a single negative SIC. Further investigation is needed: either input from an occupational hygienist to identify possible additional relevant exposures that could be followed-up with additional challenges or, alternatively, a trial of return to work with the same work conditions and objective monitoring to detect changes in asthma related to work. Most physicians who assess patients with OA would not have support from an occupational hygienist; however, in some larger centres, an occupational hygienist may be practical, and in a general occupational medicine clinic their input could also provide very useful exposure information for patients with other potential occupational diseases such as contact dermatitis, in which such information is highly relevant for patch testing. However, the results of such evaluations in OA assessments may also significantly increase the potential time involved for thorough SIC testing, especially if there are several different exposure agents because even a single agent may require up to multiple challenge days of increasing exposure (7).

Although the study by de Olim et al (6) focused on diagnosis using SIC, on a practical level, the results also highlight the importance of investigations other than SIC that can be performed by the respiratory physician or other specialist. Serial recordings of peak expiratory flow rates or spirometry, with recording of symptoms and short-acting bronchodilator use, as well as measures of airway responsiveness (and induced sputum cytology if available) during periods of work and repeated during periods away from work, can provide a 'real-life' measure of the relationship of asthma to work. Even in the absence of identification of the specific sensitizer, such information is often sufficient to reach a diagnosis of OA. These tests are most effective if performed when the patient is still employed in the same job suspected to have caused his/her asthma, and can again have the same type of exposure(s) as occurred near the onset of work-related symptoms. The specific sensitizer may be suggested from the history of exposure, review of safety data sheets and, in some cases, supported by demonstration of specific immunoglobulin E antibodies. However, even in the absence of an identified sensitizer, the diagnosis of OA can still be made. Of note, six of the 67 cases of OA in the study by Olim et al (6) had the diagnosis of OA reached without identifying the specific causative agent. The need to confirm the specific causative sensitizer by SIC may depend on the requirements of the relevant compensation system (eg, for compensation in Quebec, there is generally a need to undergo SIC to identify the specific agent but this is not generally a requirement in other Canadian provinces). Performance of SIC may also depend on the work options available (eg, if the worker has workplace and/or immunological evidence to support OA and can move into another work setting with no exposure to the agents that were present in the initial workplace, then it may not be necessary to identify the causative agent by SIC) (8).

Workplace studies do not require specialized testing, but do require early initiation of these tests by the respiratory physician or other specialist before the patient is advised to change jobs, and especially before advice to quit work. In addition, these tests require careful attention to the details of test performance and possible confounding factors such as concurrent infections, or a change in the work conditions compared with conditions at the onset of symptoms. These confounding factors could produce false-positive or -negative results. In the study by de Olim et al (6), note was made that 31 of the 53 with a negative laboratory SIC did not undergo workplace challenge: presumably these patients were no longer employed by the same company and/or could not return to the same work for additional tests. Again, this emphasizes the importance of performing workplace studies early while the patient is still employed and before development of severe asthma, while it is safe to do the tests at work.

It is hoped that additional prospective studies from this group will be performed to determine the frequency with which a more accurate final diagnosis is reached in patients after adding the input of the occupational hygienist.

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REFERENCES

1. Vandenplas O, Toren K, Blanc PD. Health and socioeconomic impact of work-related asthma. *Eur Respir J* 2003;22:689-97.
 2. Lemiere C, To T, de Olim C, et al. Outcome of work-related asthma exacerbations in Quebec and Ontario. *Eur Respir J* 2015;45:266-8.
 3. Tarlo SM, Balmes J, Balkissoon R, et al. Diagnosis and management of work-related asthma: American College of Chest Physicians Consensus Statement. *Chest* 2008;134(3 Suppl):1S-41S.
 4. Tarlo SM. Laboratory challenge testing for occupational asthma. *J Allergy Clin Immunol* 2003;111:692-4.
 5. Vandenplas O, Suojalehto H, Aasen TB, et al. Specific inhalation challenge in the diagnosis of occupational asthma: Consensus statement. *Eur Respir J* 2014;43:1573-87.
 6. de Olim C, Bégin D, Boulet L, Cartier A, Gérin M, Lemièr C. Investigation of occupational asthma: Do clinicians fail to identify relevant occupational exposures? *Can Resp J* 2015;22:341-7.
 7. Cockcroft DW, Cartier A, Jones G, Tarlo SM, Dolovich J, Hargreave FE. Asthma caused by occupational exposure to a furan-based binder system. *J Allergy Clin Immunol* 1980;66:458-63.
 8. Tarlo SM. When should specific occupational challenge tests be performed? *Chest* 2013;143:1196-8.
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