

Can medical surveillance measures improve the outcome of occupational asthma?

Occupational asthma (OA) has been reported to account for 3% to 20% of all asthma cases in studies that have included populations in Europe, North America, Australia, New Zealand, and Japan.¹ Even after the diagnosis has been confirmed and the worker removed from ongoing exposure to the causative work agent, it can still be associated with ongoing asthma, significant morbidity,² and even mortality.³

For some workplace sensitizers the risk of OA in the workplace can be reduced by primary prevention, particularly control of workplace respiratory exposure. It has been shown for several workplace sensitizers⁴⁻⁶ that the population risk of sensitization relates to the airborne exposure level. Reduced inhalation exposure levels have been achieved as a result of process or product changes (eg, for detergent enzymes by encapsulation of the enzymes⁷ and for natural rubber latex by powder-free low-protein glove use⁸). Other measures may include use of alternative nonsensitizing agents (elimination/substitution), occupational hygiene measures of ventilation, robots in high-exposure areas, and appropriate respirators. Regulations to control and monitor airborne concentrations of common sensitizers such as diisocyanates may enhance the likelihood of reducing work exposures to safer levels.

An additional method for primary prevention of OA would be to identify workers at risk of sensitization to specific workplace agents at the time of pre-employment and exclude their exposure to these agents. Unfortunately, at present those at risk cannot be predicted with sufficient sensitivity and specificity for this to be practical: although risk markers for those exposed to sensitizers, such as genetic markers, atopy, and smoking history⁹ have been recognized, they are not currently sufficiently sensitive or specific to justify exclusion of an individual from exposure.

Abbreviation used

OA: Occupational asthma

Thus measures for primary prevention are currently often not sufficient to prevent sensitization. As a secondary preventive measure, medical surveillance to detect OA at an early stage and remove sensitized workers has been implemented in some workplaces where there is exposure to known workplace sensitizers. The aim is to detect immunologic sensitization or OA early, before it becomes severe or irreversible. The rationale is the observation that the best prognosis and greatest chance of clearing OA is associated with a shorter duration of symptoms and milder asthma before diagnosis and complete removal from further exposure to the causative work agent.^{10,11}

However, the association noted above, that prognosis is related to early diagnosis, constitutes only indirect evidence that medical surveillance itself accomplishes this aim. Although widely recommended and implemented, until recently, there was little or no evidence that groups under surveillance actually had better outcomes, as compared with groups that were not under surveillance.^{11,12} We reported a better outcome for workers compensated for OA due to isocyanates versus those with OA due to other causes. Among those with isocyanate OA who worked at companies at which medical surveillance programs were in place, there was a shorter duration of symptoms and tendency to better outcomes versus those from companies without a program.¹¹ However, it is not possible to determine whether this was due to better industrial hygiene (lower exposures at the plants with programs), increased awareness on the part of the workers or physicians, or the surveillance program itself.

Medical surveillance programs for workplace sensitization and OA usually comprise a pre-employment or pre-exposure medical questionnaire that is repeated periodically during employment, commonly every 6 to 12 months.¹¹⁻¹⁴ Addition of skin prick tests may be feasible for workers exposed to high-molecular-weight allergens and for some chemical sensitizers such as complex platinum salts. In vitro assay of specific IgE antibodies may be used, particularly for low-molecular-weight allergens such as acid anhydrides, and for these, specific IgG antibody assay has also been shown to have predictive value.¹⁵

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Periodic screening spirometry has often been included in OA medical surveillance programs.¹¹⁻¹⁴ Unfortunately, the additional value of workplace spirometry to use of a questionnaire alone has not been demonstrated. Many "abnormal" results among isocyanate workers who denied work-related respiratory symptoms in a recent study could be explained on the basis of poor inspiratory or expiratory effort during workplace spirometry maneuvers.¹⁴ In that study spirometry did not appear to add to the effectiveness of the medical questionnaire in the medical surveillance program. On the other hand, 1 of the 3 cases of isocyanate OA in another study¹³ was identified initially by a decrease in FEV₁ only, with no respiratory symptoms.

In this issue of the Journal, Merget et al (p 707) report on a nested case-control study of workers exposed to complex platinum salts in catalyst production. This was a component of a 5-year prospective cohort study to assess the outcome of a medical surveillance program (6 monthly for the first year and then annually), using a symptom questionnaire as well as skin prick testing with the complex platinum salt. Workers developing a positive skin test reaction were removed from further exposure to complex platinum salts as soon as possible, irrespective of symptoms. In this report 14 skin test converters were matched with workers without skin test conversion and were then followed up for a mean of 19 months.

Symptoms consistent with work-related IgE-mediated allergic responses developed in 64% of skin test converters. Most, especially nonasthmatic symptoms, resolved during follow-up after removal from exposure. Seven (50%) of the skin test converters experienced asthma symptoms (3 work-related) by the time of or shortly after skin test conversion versus 9.5% of the group with negative skin test results. At follow-up 4 of the skin test converters had mild persistent asthma symptoms not requiring medication. In addition, skin test responses to platinum salt reverted to negative in all but 3 subjects on follow-up.

This study strongly suggests benefit from the medical surveillance program. However, the authors could not provide direct evidence of a reduction in development of OA in this study because there was no concurrent group without surveillance measures or reported incidence of OA before the program. Nevertheless, the platinum industry is known historically to have had a high incidence of OA and sensitization. The authors do not comment on how industrial hygiene measures and lower exposures may have changed over time during the 5-year prospective period of the study versus previous time periods.

In addition, although the slope of the histamine challenge test results in some of the skin test converters was within the range consistent with asthma, detailed clinical investigations for OA were not included in this study, and therefore it is difficult to identify the true incidence of OA in this cohort. However, Calverley et al⁴ have reported that all workers with positive skin prick test results to complex platinum salts will have symptoms of asthma at follow-up with continuing exposure, which suggests that the surveillance measures in the current study truly prevented OA in some sensitized workers. In this study only 2 skin test con-

verters had airway hyperresponsiveness at follow-up, again suggesting benefit in contrast to Merget's previous study, in which those who left exposure at a mean of 18 months after experiencing asthma symptoms had persisting nonspecific airway hyperresponsiveness.¹⁶

There was a striking reduction in work-related symptoms and skin test responses to complex platinum salts in this study after early removal from exposure. As the authors comment, in those in whom symptoms persisted, the duration of symptoms before removal was a mean of 8.5 months compared with 6.7 months in those who had clearing of symptoms. Thus even more benefit might be obtained from continued 6 monthly rather than annual screening, especially for the first 2 years of exposure, during which the risk of sensitization to complex platinum salts has consistently been shown to be highest, and particularly for those at particular risk (smokers^{4,17,18} and those with high exposure levels⁴). In contrast, for high-molecular-weight agents, work-related asthma, on average, takes longer to appear, so surveillance efforts should be spread out over longer time intervals.¹⁹

Because of the specificity of skin testing with platinum salts, it should be an excellent screening measure, as found in the current study. The rapid reduction in size of the skin test response in this study after workers were removed from exposure, as well as the reversion to negative responses in many workers at follow-up, does raise a note of caution. It suggests that when the skin test is used as a diagnostic test, there may be false-negative responses among patients who have discontinued exposure to complex platinum salts shortly after the onset of symptoms but before their clinical assessment.

Although the results of this study are clearly relevant for medical surveillance programs for workers exposed to complex platinum salts, the results may not necessarily be applicable to medical surveillance programs for other occupational sensitizers. For many sensitizers, especially low-molecular-weight sensitizers, the mechanism of sensitization is unclear and/or skin tests are not helpful at the current time. For other sensitizers the positive predictive value of the skin test for OA or rhinitis is lower or unknown. Many medical surveillance programs therefore continue to rely largely on medical questionnaires and pulmonary function measures. There is a need for further studies, ideally prospective randomized studies, to quantify the benefits and costs of surveillance programs and their components in other work environments. Finally, it should be emphasized that those conducting the medical surveillance must be ready to respond to the results of surveillance with appropriate interventions to reduce or eliminate asthma-inducing exposures.

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