

IN-DEPTH REVIEW

Prevention of occupational asthma—practical implications for occupational physicians

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Background Occupational factors have been estimated to contribute to ~10% of adult-onset asthma and occupational asthma (OA) is one of the most common occupational lung diseases in industrialized areas. Persistent asthma frequently occurs with significant socio-economic impacts.

Methods A literature search was performed using PubMed. The key term searched was occupational asthma combined with prevention.

Results Primary prevention has been effective for OA related to natural rubber latex, and may have reduced the incidence of diisocyanate-induced asthma. Medical health surveillance has been effective in settings such as the detergent enzyme industry, workers exposed to complex platinum salts and likely for diisocyanate workers in Ontario. Tertiary prevention is still required for workers with OA and can improve prognosis.

Conclusions OA is potentially preventable. Sufficient studies have demonstrated the rationale and benefit of primary preventive strategies. Medical health surveillance programs combined with occupational hygiene measures and worker education have been associated with improved outcomes but further studies are needed to understand the optimum frequency and measures for such programs and to identify the separate contribution of the components. Until primary and secondary prevention is better understood and implemented, there will also remain a need for tertiary preventive measures.

Key words Medical surveillance; occupational asthma; prevention.

Introduction

In many industrialized areas of the world, occupational asthma (OA) is one of the most common chronic occupational lung diseases and workplace factors have been estimated to contribute to ~10% of all adult-onset asthma [1,2]. A subset (~10% or less of all OA) can be caused by an acute irritant exposure [3–5]. This has been termed irritant-induced asthma [5] and includes reactive airways dysfunction syndrome [3,4]. The majority of OA (80–90%) is caused by specific sensitization to a workplace agent [6]. For many specific sensitizers, especially

high-molecular-weight agents, such as animal, plant, insect or fungal agents, and also some low-molecular-weight chemical agents, such as complex platinum salts or acid anhydrides, this is often associated with specific IgE antibodies to that agent [7,8]. For other low-molecular-weight chemical sensitizers, such as diisocyanates, plicatic acid (present in red cedar dust), colophony and acrylic compounds, sensitization and OA are less clearly IgE antibody mediated and may be produced by other specific, presumed immunologic mechanisms [9–12].

Once OA has developed in a worker, outcome is best with early diagnosis, early removal from further exposure to the causative agent and milder asthma at the time of removal from further exposure [13–15]. Nevertheless, asthma may persist even after removal from exposure to the causative workplace agent and the socio-economic consequences of OA have been poor in reports from several different countries [15–17]. Given the burden of illness and potential for adverse outcomes, prevention of this relatively common occupational disease is therefore of importance. This paper will review studies which have assessed primary, secondary and tertiary preventive measures in OA (examples given in Table 1).

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Table 1. Examples of studies of OA prevention (not comprehensive)

	Target	Intervention	Industry
Primary prevention			
At the source			
Elimination	NRL	Change to non-NRL gloves	Health care [32]
Substitution	NRL	Change to low-protein, non-powdered NRL gloves	Health care [33–37]
Along the path			
Enclosure	Detergent enzymes Diisocyanates	Encapsulation Robots in enclosed areas	Detergent enzyme industry [44,45] Foam-making plants
At the worker			
Personal protective equipment	Farm allergens	Air supply respirator use	Dairy farmers
	Diisocyanates	Air supply respirator use	Spray painters
Secondary prevention			
Medical surveillance	Complex platinum salts	Skin prick tests, questionnaire, spirometry	Platinum workers [53]
	Diisocyanates	Questionnaire, spirometry	Foam-making and other diisocyanate workers [47,51]
	Enzymes	Skin prick tests, questionnaire, spirometry	Detergent enzyme industry [44,45,52]
Tertiary prevention			
Removal from further exposure	All with sensitizer-OA	Work in a separate building from that where the sensitizer is used	Any occupation using the specific agent
Marked reduction in exposure	NRL	Avoid personal contact, and co-workers use low-protein, low-powder NRL gloves	Health care workers [32]
	Farm allergens	Air supply respiratory use	Dairy farmers, laboratory animal workers [62,63]
Medical monitoring	All with sensitizer-OA and possible re-exposure	Symptoms, medication needs, peak flows, spirometry and airway responsiveness	Any occupation using the specific agent [59]
Asthma management	All OA patients	Environmental control, pharmacologic management	[59,60]
Immunotherapy	NRL-OA	Specific immunotherapy	Latex-sensitized workers [64]

Method of literature search

A literature search was performed using PubMed databases. The key terms searched were OA alone and combined with prevention. The latter identified 168 references from 1961 to 2004.

Results

Primary preventive measures

These measures can potentially include:

- (i) Identification of highly susceptible workers and locating them to areas without exposure to known sensitizers.
- (ii) Limitation of exposure to potential respiratory irritants among those with pre-existing asthma to reduce work-related aggravation of asthma.
- (iii) Use of engineering controls, such as elimination of a responsible agent, substitution with a safer sub-

stance/chemical, ventilation, process or equipment modification, process enclosure, dust reduction techniques, housekeeping and work practices.

- (iv) Administrative controls to reduce number of workers exposed or duration of exposure, e.g. job rotation, rest periods, shift or location changes where fewer people are working with sensitizers or irritant exposures.
- (v) Personal protective equipment (at the worker), which includes respirators, gloves, goggles and coveralls.

Irritant-induced OA

Irritant-induced asthma as currently understood results from acute exposure to an expected respiratory irritant [3,5]. This is usually an accidental workplace occurrence, as in a spill or fire. Appropriate measures of occupational hygiene such as containment measures 'at the source' (isolation/enclosure), ventilation measures 'along the path to the worker' and appropriate respiratory protective

devices 'at the worker' may prevent some cases of irritant-induced asthma. As an example, the lack of usage of appropriate respiratory protection among firefighters working at the site of the World Trade Center collapse has been suggested to be a significant factor contributing to the relatively high prevalence of irritant-induced asthma and airway hyper-responsiveness in these workers following inhalation of high concentrations of alkaline respirable dust [18,19].

Lowering exposure to concentrations of respiratory irritant agents, benefits workers with coincidental asthma by reducing the likelihood of work-related aggravation of asthma. The induction of asthma by chronic moderate or low exposures to respiratory irritants is suggested by epidemiologic studies but to date is unproven. If confirmed, there would be an additional potential primary preventive role for limiting such exposures.

Sensitizer-induced OA

Host factors. Since sensitization and OA from occupational agents occurs in a minority of exposed workers (5% or less in many studies), there clearly are host susceptibility factors. These include specific genotypes for which to date there is limited information [20], atopy and smoking history, as previously reviewed [21]. The importance of underlying atopy appears to be greatest in those who become sensitized by an IgE antibody-mediated response, particularly to high-molecular-weight allergens such as animal proteins and plant products [21–23]. However, the high prevalence of atopy in the general population (~20% or higher in some studies), compared with the relatively low risk of occupational sensitization, precludes this from being a useful determinant of employment, i.e. there is a low predictive value and it would exclude many who would not develop OA. Similarly, although smoking has been a significant risk factor for laboratory animal asthma [24], and the most significant associated host factor in sensitization to some occupational agents such as complex platinum salts [25] and acid anhydrides [26], the high proportion of the working-age population who still smoke precludes this from usefulness in pre-employment screening to determine employment. Thus, these factors cannot be justifiably used to prevent individuals from working in jobs that may lead to OA. Nevertheless, physicians caring for older children with asthma and allergic diseases may offer useful advice to their patients regarding careers in which underlying allergy increases the risks for work-related sensitization, e.g. to natural rubber latex (NRL) or to animal proteins [27].

Exposure factors. In order for immunologic sensitization to a specific workplace agent to occur, there clearly has to be exposure to that agent. In addition, it has been shown for some agents, as recently reviewed by Baur *et al.* [28] and by Bush and Stave [29], that the higher the exposure

levels to a sensitizer, the greater the proportion of exposed workers who will become sensitized [29–31] (i.e. there are dose–response relationships). As an example, we reported that among diisocyanate-using companies, those companies with workers who had claims accepted for OA due to diisocyanates, were more likely to have measured concentrations of diisocyanates >0.005 ppm than companies who did not have workers with claims over a 4-year period [30].

An effective primary prevention measure would therefore be to avoid the use of known sensitizers in a workplace (i.e. elimination), or to reduce the exposure levels to a minimum (e.g. by isolation/control at source), aiming for levels which are not likely to induce sensitization except in those with the strongest genetic susceptibility. Unfortunately, this may not be possible in many workplaces.

An example where this strategy has been very effective is in the case of sensitization and occupational allergy including OA, from NRL [32–37]. This was recognized to be common in health care workers and other workers with exposure to powdered NRL gloves in the early 1990s [38–43]. Factors thought to have increased the risk for sensitization at that time include increased glove usage with universal precautions to prevent infection with blood-borne pathogens in health care workers, resulting in an increased production of NRL gloves with increased tapping of rubber trees which may have altered proteins in the rubber latex, reduced leaching out of proteins from gloves during manufacture, and possibly earlier usage of gloves after manufacture. The NRL proteins became airborne in association with glove-donning powder in particles of a size which could be inhaled and could lead to respiratory allergic manifestations in addition to the mucocutaneous contact allergic manifestations. These factors may have contributed to increased exposure to NRL proteins by those wearing NRL gloves, and recognition of NRL allergy and asthma increased markedly during this time.

Following understanding of the problem, recommendations were made to change to non-NRL gloves where possible and to reduce the powder and the NRL protein content of NRL gloves if these needed to be used. Such changes have been associated with significant reductions in airborne glove powder and protein concentrations and declines in the incidence of NRL allergy and asthma as reflected in hospital series, compensation data and national figures, reported from Ontario (Canada) and Germany [34–37].

Removal of a sensitizer from the workplace and substitution with a non-sensitizing and non-toxic agent is an ideal approach which may not often be practical. The experience with NRL has shown, however, that if complete removal is not feasible, then changes to reduce exposure to a minimum, such as that currently occurring in many areas with NRL glove use (by use of minimal

powder and low-protein gloves), are likely to reduce, if not completely eliminate, sensitization [34,35].

A further example of primary prevention is the encapsulation of detergent enzymes (i.e. process modification; isolation) to reduce exposure [44,45]. This was very successful when first introduced and as recently reviewed in a large company with associated medical surveillance measures [45]. In contrast, introduction of new enzymes into a plant and failure of preventive measures led to further 'outbreaks' of sensitization and OA [46]. The use of robots (automation) in addition to separated and ventilated areas, as well as appropriate respiratory protective devices for workers with unavoidable intermittent potential exposures, in plants manufacturing polyurethane foam has coincided with declining rates of sensitization to diisocyanates as suggested by compensation rates in Ontario [47]. However, there is no direct evidence to determine whether these changes or other temporally associated interventions have been responsible.

Substitution of occupational sensitizers with newer chemicals, which may not cause sensitization, might be effective but there is currently no accurate method of determining the potential of new agents to cause human sensitization, despite the ability to obtain suggestive information from animal studies [48,49]. The introduction of less volatile or more complex forms of some sensitizers such as diisocyanates requires further investigation to determine relative rates of human sensitization.

Although primary prevention by complete avoidance of respiratory sensitizers is an ideal intervention, it is clearly not feasible in many settings, such as bakeries and animal care facilities. However, even in these settings, reduction of exposure sufficient to significantly reduce risks of sensitization can be feasible as described in laboratory care facilities [29] and suggested for bakeries [50]. The aim in these settings is to reduce the exposure to the lowest feasible level, but currently there is no known exposure concentration (other than zero) which will prevent sensitization in all susceptible workers. The introduction of a surveillance program for diisocyanates in Ontario in 1983 included monitoring of diisocyanate concentrations in the workplace with a maximum allowable 8-h time-weighted average (TWA) concentration of 5 ppb. The combination of this monitoring of workplace exposures in addition to a medical surveillance program (see Secondary Preventive Measures) was associated with a decline in new diisocyanate-related OA compensation claims [47]. However, it could not be determined from the information available whether the decline was due to reduced exposure (primary prevention—from compliance with exposure monitoring or from increased use of robots and better worker education as to appropriate protective respirator use) or to detection by the surveillance program of early reversible asthma in workers who were then moved away from diisocyanate exposure.

Secondary preventive measures

Secondary preventive measures are aimed at detecting indicators of early sensitization or early changes of sensitizer-induced OA before there is permanent disease. This identification and early intervention with removal from further exposure can prevent permanent asthma. There is no equivalent process for irritant-induced asthma since disease starts with one or more very high irritant exposures.

Medical surveillance programs for OA typically include a symptom questionnaire, skin prick testing (if the sensitizer is a high-molecular-weight allergen for which skin testing can detect specific IgE antibodies) and spirometry. Although there is some support for the effectiveness of such programs in some settings [44,45, 47,51], it is often difficult to determine which component of the program is effective and what is the optimum frequency of delivering such programs. In addition to serving as secondary prevention, such medical surveillance programs may lead to better control measures in the workplace, resulting in primary prevention for co-workers who are not yet sensitized and for future workers.

An example of such a program for which skin testing has been feasible and which appears to have been very successful is in the detergent enzyme industry [44,45,52]. The medical surveillance program that has been recommended for people who work with enzymes includes periodic questionnaires, skin prick tests with a dilute solution of the enzyme and spirometry every 6 months for 2 years and then yearly [52]. As with other high-molecular-weight occupational allergens, upper respiratory allergic symptoms often precede the onset of allergic asthma from the sensitizer. Workers who developed symptoms suggestive of an allergic upper or lower respiratory response at work and who had a positive skin prick test to the enzyme solution were moved away from further exposure in one company and rates of OA in this setting significantly declined in temporal association with this program [45].

Similarly, a medical surveillance program for workers exposed to complex platinum salts has been reported to be very effective [53]. A positive skin prick test to complex platinum salts has been found to be highly predictive of the development of later OA if exposure is continued (100% developed work-related symptoms in some studies). Therefore, those found to have a positive skin prick test on surveillance have been removed early from further exposure. Limitations of these programs are that the outcomes are usually compared to historical experience, rather than a concurrent setting not undergoing medical surveillance, so one cannot separate the role of parallel hygiene and engineering control measures.

In the case of low-molecular-weight sensitizers such as diisocyanates, the immunologic mechanism is less clear. Only a minority of those with OA from sensitization to

diisocyanates have been demonstrated to have serum IgE antibodies to diisocyanates with currently available methods of detection [54]. In addition, the development of work-related nasal symptoms is not known to be a sensitive or specific marker of development of OA in this setting. Therefore, medical surveillance programs for diisocyanates to date have relied on symptom questionnaires and spirometry, with referral for more specific testing based on these results. The program which was mandated by the Ontario Ministry of Labour in 1983 in the province of Ontario, Canada, required exposure monitoring and also a medical questionnaire administered every 6 months and performance of spirometry if indicated by the questionnaire or at least every 24 months. Referral for further medical assessment was to be made if asthma-like symptoms were reported or if the spirometry showed that the FEV₁ or FVC had declined at least 15% from previous results. No medical surveillance programs are mandated in Ontario for other asthmagens.

Unfortunately, there was no prospective evaluation of this program when it was introduced. Retrospective evaluation has suggested benefit from some component of the program. Review of workers' compensation data has shown that in the period after introduction of the program, annual claims accepted for diisocyanate-induced asthma initially rose, consistent with increased case finding, then fell below baseline, suggesting a true reduced incidence [47], while claims due to other causes also rose and then remained stable. In addition, the compensation claimants with accepted diisocyanate-induced OA during the period before the program was likely to have been fully in effect had a longer duration of work-related symptoms before diagnosis was made, and had markers of more severe asthma [47], showing a temporal relationship between earlier diagnosis of asthma at a milder stage with introduction of the medical surveillance program. Also, as compared with OA due to other causes, OA due to diisocyanates had a shorter duration with symptoms before diagnosis, and these workers had milder asthma [47] and were less likely to be hospitalized [55].

However, it remains possible that the earlier diagnosis may have resulted from other factors such as better knowledge of OA by family physicians and pulmonary physicians during the later time period or better education of workers with potential diisocyanate exposure so that they may have sought medical attention for work-related symptoms at an earlier stage. An analysis of companies known to be in compliance with the program showed an earlier diagnosis of OA (mean 1.7 years) compared with those not known to be in compliance (mean 2.7 years), and a trend to better outcome [30].

Although these studies have suggested a benefit from the program, it was difficult to determine which component was responsible. A small analysis of the relative role of spirometry as part of this surveillance program in one polyurethane foam-making company [56] showed a high

proportion of false-positive responses among those who had apparent spirometric changes in the absence of asthma symptoms on questionnaire (and surveillance spirometry did not add benefit to the questionnaire). However, conversely, in a medical surveillance program of a bakery [57], screening questionnaires were found to have a significant number of false-negative reports and the addition of an objective test has been advised where possible. The difference in these two reports may in part reflect the lack of job security among those reporting symptoms in the bakery in contrast to the foam-making company [56] where transfer to areas away from diisocyanate exposure was feasible.

Tertiary preventive measures

Tertiary prevention is aimed at limiting medical impairment among those with established OA.

- (i) For those with irritant-induced asthma, it has been suggested that early treatment with oral corticosteroids may improve long-term prognosis [58]. However, this is based only on a few case reports. For patients with persistent asthma induced by irritants, standard asthma management modalities, such as patient education, limitation of non-occupational irritant exposure and relevant allergen exposure as well as pharmacologic management as for non-occupational asthmatics, should be utilized [59, 60]. Depending on the severity of asthma, subsequent job modification and/or occupational hygiene measures may be needed to reduce exposure to potential respiratory irritants in order to avoid resulting aggravation of asthma symptoms.
- (ii) For workers with sensitizer-induced OA, the best prognosis generally requires complete avoidance of re-exposure to the sensitizing occupational agent and any immunologically cross-reacting agents, in addition to standard asthma management. Very low levels of NRL allergens may be tolerated by health care workers with NRL-induced OA [61], such as those achieved by avoidance of personal use of NRL products and use by co-workers when needed of only low-protein, powder-free NRL gloves. Residual powder should be removed from floors, furniture surfaces and ceiling plenums. However, the continuing presence of potential low exposures to airborne NRL allergen requires ongoing individual monitoring of the sensitized worker to ensure that there is no further work relationship of asthma.

In general, the sensitized worker is advised to completely avoid further areas of exposure to the sensitizer. For those who cannot leave exposure completely, a few reports have indicated that use of an air supply helmet respirator for occasional work in areas of potential exposure may prevent asthma exacerbation [62,63].

At this time, specific allergen immunotherapy is not a standard treatment for occupational asthma. Early reports have suggested that it might be of some effect for allergy to NRL [64], but more studies with larger groups are needed. Medical outcome is best when workers have an early, objective diagnosis of OA, soon after the onset of work-related symptoms; have mild asthma at the time of diagnosis and are removed early from further exposure [15,65]. Overall, a significant proportion of patients have ongoing asthma and suffer significant socio-economic consequences from the diagnosis [17], emphasizing on the preference for primary preventive measures.

MCQ questions

A set of MCQ questions on this article can be found at the back of the journal.

Conflicts of interest

None declared.

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