

Management of work-related asthma

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The physician managing work-related asthma (WRA) assumes many roles. The first is to confirm an accurate diagnosis, recognizing that WRA has multiple phenotypes, including sensitizer-induced occupational asthma (OA) caused by high-molecular-weight (HMW) proteins or low-molecular-weight (LMW) chemicals; irritant-induced asthma; and work-exacerbated asthma. Pharmacotherapy for WRA is identical to nonwork-related asthma and should be guided by current asthma guidelines emphasizing control of both asthma impairment and risk domains. It is well established that the majority of workers diagnosed with OA caused by sensitizers experience persistent asthma after leaving the workplace. However, the long-term risk of persistent unremitting asthma can be prevented in a minority of cases, particularly with OA caused by LMW sensitizers, by establishing an early diagnosis of OA and reducing or eliminating exposure. The physician consultant may advise employers on workplace interventions needed to minimize effectively an affected employee's exposure to a causative agent or condition, and what measures are required to prevent new cases of WRA (ie, primary prevention). Although allergen immunotherapy has a putative role in treating and preventing WRA caused by HMW sensitizers, further study is needed. (*J Allergy Clin Immunol* 2009;123:551-7.)

Key words: Work-related asthma, occupational asthma, work-exacerbated asthma, irritant-induced asthma

Recently, the term *work-related asthma* (WRA) has been widely adapted to encompass the entire spectrum of asthmatic conditions related to workplace exposures, including (1) occupational asthma (OA) induced by sensitizers or irritants at work; and (2) work-exacerbated asthma (WEA), referring to bronchospasm provoked by triggers at work in workers with concurrent or pre-existing asthma.^{1,2} OA and WEA are not mutually exclusive and may coexist in the same patient. Recent studies indicate that WRA is associated with increased medical resource use and health care costs.³

Occupational asthma has been defined as a disorder characterized by variable airflow limitation, airway hyperresponsiveness, and inflammation as a result of causes and conditions attributable

Abbreviations used

AIT:	Allergen immunotherapy
BDP:	Beclomethasone dipropionate
ETS:	Environmental tobacco smoke
HMW:	High-molecular-weight
IIA:	Irritant-induced asthma
LMW:	Low-molecular-weight
NRL:	Natural rubber latex
OA:	Occupational asthma
RADS:	Reactive airways dysfunction syndrome
SPT:	Skin prick test
WEA:	Work-exacerbated asthma
WRA:	Work-related asthma

to a particular occupational environment and not to stimuli encountered outside the workplace.⁴ This definition encompasses 2 distinct phenotypes of OA: (1) work-related asthma beginning after an asymptomatic latency period of exposure (or latency period) caused by either natural protein allergens or reactive chemical sensitizers and (2) irritant-induced asthma (IIA) associated with single or multiple exposures to high levels of irritants at work with no preceding latency period and no history of pre-existing asthma.

For occupational asthma, induction via IgE-dependent mechanisms may occur with respiratory sensitizers including natural proteins or certain low-molecular-weight (LMW) reactive chemicals acting as *in vivo* haptens (eg, phthalic anhydride). Many causative chemical sensitizers are not associated with demonstrable specific IgE responses, although immunologic mechanisms are suspected.⁵ Diisocyanate antigen specific IgE antibodies have been demonstrated in workers with diisocyanate asthma, although their etiologic significance remains controversial.⁶⁻⁸

The best defined phenotype of irritant induced asthma is reactive airways dysfunction syndrome (RADS), a syndrome characterized by acute lower respiratory symptoms (eg, cough, dyspnea, and/or wheezing) beginning within 24 hours after a single high-level exposure to a workplace irritant.^{9,10} The broader term IIA is used to refer to asthma induced by multiple irritant exposures in which the lag time between exposure and onset of symptoms is greater than 24 hours.¹⁰

Cogent examples of WEA include bronchospasm triggered at work by intermittent exposure to chemical fumes (eg, sulfur dioxide, chlorine gas, environmental tobacco smoke¹¹) or work-related bronchoconstriction elicited by fumes from bleach among cleaning workers.¹² Although the exact prevalence and incidence of work related asthma conditions are poorly defined, 10% to 25% of adult cases of asthma are estimated to be aggravated by occupational factors.¹³⁻¹⁵ Furthermore, WEA cases may represent between 10% and 50% of all workers identified with WRA.^{1,16,17} Considering that 1% to 18% of the global population is affected by asthma,¹⁸ it is likely that WEA is highly prevalent and underdiagnosed. Therefore, this review addresses management approaches for both OA and WEA.

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TABLE I. Management of WRA conditions

	Pharmacologic	Exposure intervention	Remain at former job?
OA—HMW allergens*	Treat to achieve asthma control‡	Prevent ambient exposure to allergens	No, unless exposure is controlled
OA—LMW chemical sensitizers	Treat to achieve asthma control‡	Prevent ambient exposure to chemical sensitizers	No
IIA; RADS†	Treat to achieve asthma control‡	Prevent high exposure to irritants§	Yes, with medical monitoring
Work exacerbation of pre-existing asthma	Treat to achieve asthma control‡	Prevent exposure to irritants, allergens, and relevant triggers§	Yes, with medical monitoring

Adapted with permission from Mapp et al.²⁵

*Includes natural proteins or glycoproteins from plant or animal sources.

†Occupational asthma induced within 24 hours after a single accidental exposure to an irritant at work.

‡Management with asthma medication should be directed by current asthma guidelines with the goal of achieving asthma control of impairment and risk domains.²³

§If appropriate, consider change in work area or personal protection including respirators.

||Some workers with OA caused by occupational protein sensitizers (eg, NRL) in whom ambient allergen exposures are controlled through interventions (eg, glove changes by worker and coworkers) may return safely to their former jobs with medical monitoring. Subsequent re-exacerbation of WRA would require removal from the job.

EVALUATION OF WORK-RELATED ASTHMA

Successful management and treatment depend on accurate diagnosis and characterization of WRA phenotypes. Diagnostic methods of OA and WEA have been reviewed elsewhere and in the recently published *American College of Chest Physicians Consensus Statement: Diagnosis and Management of Work-Related Asthma*.¹⁹⁻²¹ Potential respiratory sensitizers known to cause OA can be researched in published lists of etiologic agents (www.asmanet.com). Most of the approximately 400 known causes of OA are high-molecular-weight (HMW) protein sensitizers, and fewer than 30 reactive chemicals or LMW agents have been proven to cause OA.

It is ill-advised to base a diagnosis on medical history alone, a nonspecific diagnostic tool, without objective confirmation by measuring lung function at and away from work.²² Failure to establish an accurate diagnosis could have suboptimal consequences. For example, a diisocyanate-exposed worker with OA incorrectly labeled as WEA, if not advised to reduce or eliminate chemical exposure, can develop severe persistent asthma and asthma exacerbations. Conversely, workers with WEA misdiagnosed with sensitizer-induced OA could be improperly advised to quit their jobs in lieu of simple avoidance of asthma triggers at work, resulting in unnecessary social and economic hardships.

Successful management is predicated on comprehensive evaluation and correct diagnosis of WRA. The current diagnostic paradigm for establishing WRA includes 3 major components: (1) obtaining a compatible medical and occupational history, (2) confirming an asthma diagnosis, and (3) demonstrating decrements in lung function when exposed to a substance or condition at work with improvement away for a sufficient time from the work environment (or specific inhalation challenge, if appropriate). If available, skin testing and *in vitro* serologic tests can be used to recognize clinically relevant respiratory sensitizers encountered in the workplace.¹⁹ If present or suspected, concomitant medical conditions (eg, gastroesophageal reflux, chronic sinusitis) that may create barriers to asthma control should be investigated and treated. Workers should also be evaluated and treated for possible concomitant allergy and asthma triggered by nonoccupational common outdoor and indoor allergens, which could hinder successful management of WRA.²³ It is important to exclude conditions that could mimic WRA such as vocal cord dysfunction triggered by workplace irritants.²⁴

MANAGEMENT OF WORK-RELATED ASTHMA

There is not a single correct approach for managing WRA, and each worker presents with unique clinical manifestations and work exposure characteristics. Nevertheless, there are fundamental differences between approaches to managing sensitizer-induced OA, IIA, and WEA (Table I).^{19,25} Physicians must be aware of and sensitive to the impact of their management decisions on employment status. Almost 50% of workers have anxiety and feelings of depression after leaving a job and are duly concerned over potential economic consequences of interventions resulting from being identified with OA.²⁶ Surveys indicate that 42% to 78% of workers diagnosed with OA caused by sensitizers will have significant loss in income²⁷ resulting from job changes. Thus, final management strategies are almost always tempered by social and economic considerations.

Published asthma guidelines are directly applicable to management of WRA.²⁸ The recent National Asthma Education and Prevention Program Expert Panel Report 3 and Global Initiative for Asthma reports emphasize the overall aim of achieving asthma control through reduction of disease impairment and risk domains.^{18,23} Impairment is defined by daily and nocturnal symptoms, frequency of use of rescue inhaled bronchodilators, and spirometry measurements (eg, FEV₁ and FEV₁:FVC ratio). Risk reduction is achieved through efforts that decrease or eliminate unscheduled clinic and hospital visits for asthma exacerbations. In most cases, consultants experienced in management of occupational respiratory disorders recognize that pharmacologic interventions are rarely if ever adequate for controlling WRA. In contrast with nonoccupational asthma in which environmental factors may or may not be relevant, interventions that modify or eliminate exposure to respiratory sensitizers or workplace triggers are central to successful management.

Prevention

Specific goals of environmental control of harmful exposures must be tailored to the specific needs of each worker. A global proactive perspective emphasizes disease prevention. For example, removing a worker with established OA from exposure to a newly recognized occupational sensitizer is considered *tertiary prevention*; that is, efforts are directed at preventing progression to more severe asthma and progressive loss in lung function with continued exposure to offending agents at work. Justification for this approach is confirmed by a recent retrospective study in

more than 150 consecutive cases of OA that demonstrated a decelerated rate of decline in FEV₁ 6 months or more after removal from occupational exposure to causative agents.²⁹

Newly diagnosed or sentinel cases of OA provide the astute clinician a unique opportunity to assess a high-risk work environment and advise the employer to undertake control measures that may prevent new cases (*primary prevention*) among similarly exposed coworkers. Ideally, this may involve removing the causative agent and substituting a safer alternative substance in an industrial process. Often this is not feasible, but introduction of new engineering controls may substantially reduce human exposure to causative chemicals, preventing new cases of OA. For example, spray painting of hard metal surfaces using hexamethylene diisocyanate, an essential paint hardener, is now performed in most modern plants by robotic devices enclosed in independently ventilated paint booths. Diisocyanates, formerly used in monomeric forms for urethane production (eg, methylene diphenyl diisocyanate) or as paint hardeners (eg, hexamethylene diisocyanate), are now sold almost exclusively as prepolymerized products (eg, polyisocyanates), presumably reducing skin and respiratory exposure to active diisocyanate moieties. It is believed that the use of polyisocyanates may have reduced new cases of OA in diisocyanate-exposed workers. Awareness of the temporal periods of risk is also important. In 1 recent long-term prospective cohort study, apprentice laboratory animal workers exposed to HMW antigens exhibited the highest incidence of bronchial hyperresponsiveness in the first years of work, indicating a time at which increased control of exposure might modify risk.³⁰

Ideally, if threshold exposure limits could be defined at levels below which OA is unlikely to develop, prevention of new cases could be achieved.³¹ The best example of effective primary prevention is the successful control of allergy and OA achieved in health care workers exposed to natural rubber latex (NRL) gloves. Eight primary prevention programs were reviewed of health care worker populations in which powdered NRL gloves were substituted with low-protein powder-free NRL gloves and/or powder-free NRL gloves. These changes consistently resulted in reduced levels of measurable ambient NRL aeroallergens, reduced frequencies of NRL sensitization, and decreased new cases of OA in health care workers.³² Another good illustration of successful primary prevention is implementation of industrial hygiene programs in the detergent manufacturing industry. Specific measures include encapsulation of detergent enzyme protein granules in inert materials, engineering controls to minimize ambient enzyme dust, employee training to minimize personal exposure, and frequent ambient monitoring for enzymatic proteins. Such a program can be used to maintain ambient enzyme levels below 15 ng protein/m³, well below the American Conference of Governmental Industrial Hygienists Threshold Limit Value of 60 ng protein/m³, leading to dramatic declines in detergent enzyme sensitization rates and new cases of OA.³³

Significant reduction in ambient exposure to HMW allergens and early identification of workers with occupational allergic rhinitis may prevent development of new cases of OA (*secondary prevention*). The detergent enzyme industry has developed exemplary medical surveillance programs conducted annually in exposed workers by using medical questionnaires combined with skin prick testing with enzyme solutions (eg, *Bacillus subtilis* protease and *Aspergillus*-derived amylase).³³ Sensitized workers who develop allergic rhinitis symptoms are relocated away from potential high-exposure areas. After institution of surveillance and

industrial hygiene programs in 1 detergent company, the annual incidence of newly sensitized workers was maintained below 3%, with no new cases of OA reported over a 6-year period.³³ Atopic detergent workers are clearly at higher risk for sensitization to microbial enzymes, but this program has been conducted successfully without restricting employees presensitized to aeroallergens.

Exposure reduction is the cornerstone of prevention of sensitizer-induced OA. However, high serum-specific IgG₄ levels for mouse allergens have been reported to be associated with reduced risk of skin test sensitivity and allergic symptoms in a subset of laboratory animals workers. This suggests that workplace exposure may lead to natural tolerance and confer protection in some workers but cause sensitization in others.³⁴⁻³⁶ Whether these observations have an immunologic basis requires further study.

Pharmacologic management

Pharmacologic management of all 3 types of WRA is conducted according to prevailing asthma treatment guidelines.^{18,23} As mentioned, pharmacotherapy for OA should never be substituted for an effective exposure avoidance program. There are few controlled studies evaluating pharmacotherapy in workers with OA, and these have been undersized. One placebo crossover study evaluated the effect of 1 year of treatment with an inhaled corticosteroid (beclomethasone dipropionate [BDP]) versus placebo in workers with confirmed OA after they had been withdrawn from the workplace. Inhaled BDP exerted modest clinical benefit versus placebo in reduction of asthma symptoms and in improvement of quality of life measures.³⁷ In another trial, 15 workers with toluene diisocyanate asthma were treated with either BDP or placebo for 5 months after leaving the workplace. A decrease in methacholine responsiveness was observed in actively treated workers versus placebo. Bronchial sensitivity to TDI (determined by the PD₂₀) was reduced in both groups, but BDP treatment had no greater effect than placebo.³⁸ Thus, treatment with inhaled corticosteroids provided little additional benefit above what was achieved with effective reduction of ambient exposure to chemical sensitizers.¹⁸

Management of OA caused by sensitizers

Cessation of exposure to a causative agent is the treatment of choice for workers with proven sensitizer-induced OA (Table 1). In most cases, workers will be unable to return safely to their same job. If the worker cannot be accommodated by his employer with relocation to a job free of exposure to the sensitizing agent, a worker's compensation claim should be initiated to cover lost wages and medical expenses.

Persistent exposure to a causative agent (especially a chemical) after diagnosis of OA can lead to unfavorable clinical outcomes, including fatal asthma exacerbations triggered by HMW and LMW sensitizers at work, even in workers receiving asthma pharmacotherapy.³⁹⁻⁴¹ However, evidence suggests that asthma symptoms are likely to persist after leaving work in the majority of workers with OA caused by HMW and LMW sensitizers.⁴² A systematic review of 39 different studies evaluated clinical outcomes of workers with OA caused by HMW and LMW agents after cessation of workplace exposure. Only 32% reported complete recovery from asthma symptoms over a median follow-up time of 31 months.⁴³ Shorter durations of symptoms and exposure to causative substances were associated with symptomatic recovery.⁴³

Nevertheless, timely cessation of exposure can result in complete remission of clinical manifestations of asthma among individual workers with OA. In a follow-up survey in 40 individuals previously diagnosed with OA caused by sensitizers conducted at least 3 years after leaving work, 12.5% had no evidence of current asthma, reflected by absence of airway obstruction, airway hyperresponsiveness, or airways inflammation determined by induced sputum eosinophils or neutrophils.²⁶ In a medical surveillance study of MDI-exposed foam workers, all employees identified with OA within 1 year after initiation of diisocyanate exposure and onset of symptoms experienced complete asthma remission after removal from the work area.^{43,44} In another long-term follow-up study of 41 TDI-exposed workers with confirmed OA initially exposed for at least 5 years before leaving the workplace, 39% were reported to have experienced complete recovery from asthma, defined by a lack of symptoms and AHR to methacholine.⁴⁵ As in other studies, a lower duration of TDI exposure before intervention was associated with greater probability of asthma remission. These data suggest but do not prove that OA can be cured if a timely diagnosis is established soon after onset of symptoms and an affected worker is immediately removed from further exposure to a chemical sensitizer.

Despite improvement in lung function and symptoms with complete avoidance from a causative sensitizer, depression and anxiety are reported by approximately one half of workers with OA and at higher rates than observed in non-WRA.²⁶ Because of concerns over potential financial losses from job changes, certain workers may choose to remain exposed despite awareness of the short-term risks of exacerbations at work and the long-term risks of chronic persistent asthma.²⁶ Given the hardships of leaving a job, personal protective equipment could theoretically be an effective alternative method to prevent exposure to a causative agent. However, in a study of farmers with OA, use of respirators was only partially effective in preventing airway obstructive changes at work.⁴⁶ An estimated 80% reduction in the expected incidence of occupational respiratory disease was reported with the use of respiratory protective devices in a group of workers exposed to the respiratory sensitizer, hexahydrophthalic anhydride, for manufacturing an epoxy resin product. However, this preventive measure did not prevent new cases of OA.⁴⁷ For spray painters exposed to diisocyanates, negative pressure, air-purifying half-face piece respirators using organic vapor cartridges and prefilters have been reported to provide effective protection for spray painters, but these can leak if not properly fitted.⁴⁸ Industrial hygiene measures that maintain ambient chemical exposures in a factory below threshold limit values may still be inadequate for preventing new cases or for preventing symptoms in workers with established OA.⁴⁴ In the case of diisocyanate chemicals, new cases of OA may develop after intermittent accidental chemical exposures during maintenance procedures or from accidental spills of MDI or TDI, when exposure may escape detection by continuous monitors. Second, exposure to minuscule isocyanate levels (eg, 5 ppb) has been shown to elicit bronchoconstriction among highly sensitized workers with established diisocyanate asthma.^{44,49} Thus, it appears that measures that fall short of complete elimination of exposure are not usually effective.

Reduction of individual exposure without leaving the workplace may be effective in managing OA caused by HMW sensitizers. For example, many NRL-sensitized health care workers

with OA can continue to work in a facility after personal avoidance of NRL products and switch of coworkers to low-protein, powder-free NRL gloves.^{50,51} Such interventions may effectively reduce ambient NRL protein allergen exposure below that required to elicit asthmatic responses. Once an exposure modification has been implemented, workers with OA remaining at work should undergo periodic medical evaluations. Subsequent deterioration in asthma symptoms or lung function should prompt immediate removal from the work area and continued medical follow-up.

IIA

There is little published evidence to guide management of IIA or RADS. One report suggests that workers with IIA remaining in the current work environment exhibit worsening of AHR and persistent asthma symptoms despite inhaled corticosteroid treatment.⁵² Because RADS is asthma initiated by an unusual acute exposure to high levels of respiratory irritants, engineering controls are recommended to prevent future accidental exposures. Respiratory protective devices may be appropriate. After the latter measures are instituted and asthma is controlled with pharmacotherapy, workers with IIA or RADS are allowed to return to their former jobs.²⁵ Subsequently, continuous monitoring of the work environment and medical follow-up of patients with repeat lung function and methacholine tests are essential parts of long-term management. Although experts agree on this approach, there is little evidence defining how this strategy affects long-term disease outcomes (Table 1).

WEA

There is little published evidence pertaining to identification and management of WEA. As described in Table 1, asthma pharmacotherapy should be optimized. Workers can be allowed to return to their jobs provided that exposure can be reduced or eliminated to workplace irritants, environmental tobacco smoke (ETS), aeroallergens, or other relevant asthma triggers. Respiratory protective devices may be used to control future exposures, and frequent medical follow-up visits are required to monitor asthma control and lung function.

New insights have been provided in a recently published prospective cohort study of 77 bar workers evaluated before and after institution of a cigarette smoking ban. A subset of 10 of 77 workers with pre-existing asthma exhibited a 10% increase in mean FEV₁ and significant improvement in quality of life measures after institution of the smoking ban, effectively eliminating their exposure to second-hand ETS.¹¹ An estimated 25 million workers are exposed to ETS at work.⁵³ However, the contribution of various asthma triggers encountered on the job (eg, ETS, aeroallergens, exertion, and irritants) and their overall impact on the asthma disease burden are unknown.

ALLERGEN IMMUNOTHERAPY

As mentioned, the primary treatment for OA is elimination or reduction of exposure to the causative workplace allergens. A recently convened expert panel concluded that allergen immunotherapy (AIT) is a treatment option for sensitizer induced OA, although there is limited evidence to support efficacy of this modality.¹⁹ AIT can be considered in the following circumstances among affected workers with OA caused by certain HMW natural

protein allergens: (1) when avoidance of exposure to workplace allergens is not possible, (2) when the causative role of specific allergens to WRA has been established, and (3) when commercial allergen extracts are available for treatment.¹⁹

Workers with OA caused by HMW allergens (eg, cat, rodent proteins) wishing to minimize the potential economic impact of a job change frequently choose to continue working at jobs inevitably leading to continued exposure to occupational allergens. Although there is little supporting evidence, the physician could recommend in such cases a combined approach using personal safety measures (eg, room filtration, respirators, or masks), pharmacotherapy, and AIT, when appropriate.

There are rare chemical sensitizers proven to cause OA via specific IgE mechanisms. Acid anhydride chemicals (eg, trimellitic anhydride, phthalic anhydride), representing the prototypic class of reactive chemical haptens, can form allergenic determinants by combining *in vivo* with autologous respiratory proteins. However, AIT is not recommended for treating IgE-dependent OA caused by chemical sensitizers because of unknown risks of human toxicity from repeated injections of chemical antigens.¹⁹

Allergen immunotherapy is generally efficacious in treating patients with aeroallergen-induced asthma.^{54,55} Because there are minimal data evaluating efficacy and safety in worker populations and most studies are undersized, treatment decisions for individual workers may often be based on data from controlled clinical trials of AIT in nonoccupational study populations. However, limited data from trials of AIT for the treatment of work-related asthma are available for natural rubber latex, wheat flour, mammalian allergens, sea squirt, and house dust mite.

Natural rubber latex is a complex mixture of at least allergenic proteins that bind human IgE antibodies (Hev b allergens), derived from the sap of the rubber tree, *Hevea brasiliensis*.⁵⁶ Health care workers are commonly exposed to Hev b allergens in an occupational setting through the use of NRL gloves. Two double-blind, placebo-controlled trials of subcutaneous AIT with crude NRL extract have been reported. In the first study, 17 patients were identified with NRL allergy, defined as a clinical history of asthma, a positive skin prick test (SPT), and elevated NRL-specific IgE.⁵⁷ After 1 year of subcutaneous AIT with NRL, no effect on work-related asthma symptoms was demonstrated; 4 of 9 workers receiving active treatment experienced injection-related systemic allergic reactions. In the second study of 24 health care workers, 15 with asthma related to NRL exposure were identified.⁵⁸ After 3 months of a cluster build-up phase followed by 3 months of subcutaneous AIT with aluminum hydroxide-adsorbed NRL extract standardized with a US Food and Drug Administration reference antigen, no effects of treatment versus placebo were found in asthma medication or symptom scores or methacholine PC₂₀. However, improvement in respiratory symptoms during bronchial challenge testing with NRL powdered gloves was observed in NRL-treated but not placebo-treated subjects, nearly reaching statistical significance. As mentioned, systemic reactions to NRL injections were frequent, occurring with 9% of NRL injections.

Among bakery employees exposed to wheat flour, the prevalence of bakers' asthma is estimated to be 9%.⁵⁹ In 1 double-blind, placebo-controlled trial, 139 patients who worked with wheat flour were evaluated.⁵⁹ Of these workers, 30 were found to have asthma and a positive SPT with crude wheat flour extract or elevated *in vitro* specific IgE to wheat flour. By 20 months of

treatment with wheat flour extract AIT, the treated workers had a significant decrease in bronchial hyperresponsiveness to methacholine ($P < .0001$) and improvement in wheat flour-associated asthma symptoms ($P < .0001$). Although 1 patient developed transient urticaria with an injection, no severe systemic reactions were reported.

Of all animal workers, veterinarians are at the highest risk of developing work-related asthma, with 20% reporting asthma symptoms in the work environment.⁶⁰ The most commonly reported animals causing work related symptoms are cats (58%). There are no reported studies of animal allergen AIT tested in occupational settings. However, a small double-blind, placebo-controlled trial of AIT with cat pelt extract standardized for Fel d 1 supports the efficacy of AIT in animal workers.⁵⁴ Active treatment was associated with decreased pulmonary symptoms with cat exposure ($P < .03$), as well as a significant increase in PD₂₀ FEV₁ on specific bronchial provocation with cat allergen ($P < .05$). Treatment of workers with Fel d 1 AIT appears both safe and effective.

In a variety of occupations including domestic cleaners and janitorial staff, exposure to house dust mite allergens (Der p 1 and Der f 1) is unavoidable. Several small double-blind, placebo-controlled studies have evaluated dust mite AIT efficacy, although not specifically in occupational cohorts. In 1 study, 27 patients with mild asthma and a positive SPT result to Der p 1 and/or Der f 1 were followed for 3 years of treatment with AIT.⁶¹ Subjective symptom scores for asthma ($P = .016$), asthma medication use ($P < .033$), and nonspecific bronchial hyperresponsiveness by methacholine challenge ($P < .0001$) all improved with treatment. In a second study, 29 patients with asthma with Der p 1 SPT positivity were randomized to AIT or placebo.⁶² After 3 years of treatment, there was a significant decrease in the number of asthma exacerbations ($P < .01$) and a significant increase in the number of medication-free days ($P < .01$). A final study included 95 patients with asthma with a positive SPT result to Der p 1 and/or Der f 1.⁶³ After 3 years of treatment, there was a significant decrease in bronchodilator use in the treatment group ($P < .01$). No significant systemic reactions were reported in the review studies of AIT for dust mite-associated asthma.

ADMINISTRATIVE MANAGEMENT OF WRA

A physician consultant with expertise in WRA is expected to play a central role in all aspects of case management. The physician is the worker's principal advocate and charged with developing a management plan that protects the patient's respiratory health without compromising the worker's income or economic well being. The consultant is often asked to serve as an intermediary (with the worker's consent) between the worker and employer or the employer's representative (eg, risk manager). The employer may need to be informed of management options and of the necessity to accommodate the worker by instituting interventions to eliminate or reduce exposure to a causative substance or condition at work, thereby controlling risk to the worker and, in some cases, other coworkers.

Because asthma persists in most affected workers with OA after leaving the workplace, periodic medical evaluations for residual impairment and disability are recommended. These evaluations are addressed for OA in the American Thoracic Society *Guidelines for Evaluation and Impairment/Disability in*

*Patients with Asthma.*⁶⁴ Those workers advised to leave the current workplace to avoid further harmful exposure are considered to have 100% impairment for the current job and for other jobs where there exists exposure to similar causative agents. The American Thoracic Society Guidelines recommend the following options: (1) relocation to a new job in the same plant or in another site where there is no exposure, (2) rehabilitation of the worker to a new job, or (3) early retirement. If workers leave their jobs, financial compensation must be addressed through worker's compensation. The guidelines recommend that the clinician conduct an evaluation of impairment and disability in the patient at 2 years after leaving employment. Impairment ratings are graded on a class 0 to V scale and represent a composite score of: (1) postbronchodilator FEV₁ (% predicted), (2) percent improvement in FEV₁ after bronchodilator treatment or level of airway hyperresponsiveness (methacholine PC₂₀), and (3) asthma medication scores.⁶⁴

CONCLUSION

The clinician must first evaluate a worker with WRA and make a diagnosis of sensitizer-induced OA, IIA, or WEA before considering management options. An inaccurate diagnosis may lead to ill considered treatment recommendations that may have adverse consequences on affected workers' respiratory health and income. To treat a worker with WRA effectively, the physician must recommend environmental interventions combined with appropriate guideline-directed pharmacotherapy. Relocation to another job where exposure is entirely eliminated is often necessary to control and prevent progression to severe persistent asthma in patients with OA caused by chemical sensitizers (eg, diisocyanates). Pragmatically, because of the economic consequences of job changes, many affected workers are unwilling to leave their jobs to eliminate exposure to workplace allergens. Some workers with OA caused by HMW sensitizers may remain at their jobs if ambient exposure is controlled. If appropriate, and if commercial treatment HMW allergens are available, AIT should be considered for occupational allergic rhinitis and asthma along with appropriate avoidance and pharmacotherapy. Workers diagnosed with IIA or WEA can remain at work if engineering controls are in place assuring elimination of future exposure to irritants and various asthma triggers (eg, ETS, aeroallergens). Physicians recognizing new cases of sensitizer-induced OA at a work site should suggest introduction of environmental controls that may prevent new cases.

Future research

Standardized antigens must be developed and clinically validated for skin testing and *in vitro* specific IgE assays to identify accurately workers sensitized to occupational allergens. Clearly there is a need for larger, adequately powered controlled studies of AIT in worker populations that will also address long-term medical and cost outcomes. Because of the high prevalence of injection-related systemic reactions for some allergens (eg, NRL), less allergenic modified allergens may in the future be useful for these indications. Secondary prevention studies are needed to determine whether AIT can prevent development of OA among workers with occupational allergic rhinitis triggered by HMW allergens. The overall incidence, morbidity, and management of work-exacerbated asthma require further study.

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