CHAPTER 7

Work-Related Asthma

Kenneth Rosenman[1,*]

[1] *Michigan State University, East Lansing, USA*

Abstract: Work-related asthma is a common condition that affects men and women who work in a wide range of industries. Adults can develop new-onset asthma after a latency period of months to years of exposure where they become immunologically sensitized or after an acute exposure that causes bronchial wall damage. Adults can also experience the aggravation of pre-existing asthma that may have developed in childhood but becomes worse after exposure at work to respiratory irritants. Exposure to over 300 substances., including chemicals, metals, insects, animals, plants, or fungi, have been identified that cause new-onset asthma. There are thousands of substances, as well as cold air or stress, that can aggravate pre-existing asthma. Guidelines have been developed for prompt recognition and diagnosis of work-related asthma because ongoing exposure after the onset of asthma symptoms is associated with a poorer prognosis. Both primary and secondary prevention have a role in reducing the occurrence and morbidity of the condition. The field has continued to advance with the recognition of an increased number of etiological agents, an understanding of the pathophysiology, an understanding of the prognosis and factors associated with a better prognosis, and the initiation of work on the interaction with genetic variability. Awareness of the disease by clinicians and the promulgation of allowable air standards by regulatory agencies that protect against the development of asthma at work will be essential to reduce the burden of this disease.

Keywords: Asthma, Diagnostic guidelines, Epidemiology, Prevention, Prognosis.

INTRODUCTION

Work-related asthma (WRA) is caused by exposure to a variety of substances in the workplace. For primary prevention, to reduce the occurrence of the disease, it is important to identify the various substances that cause WRA, and control exposure to these substances. For secondary prevention, to improve the prognosis of those who, despite primary prevention, develop WRA, it is important to conduct workplace medical monitoring for early diagnosis. This chapter will describe the pathophysiology, diagnosis, epidemiology, hazard control, diagnosis,

[*] **Corresponding author Kenneth Rosenman:** Michigan State University, MI, USA; Tel: (517) 353-1846; Fax (517 432-3606; E-mail: rosenman@msu.edu

Ki Moon Bang (Ed.)

and treatment of WRA. The chapter begins with a case report of a patient who died from WRA.

Case Report

A man in his mid-forties with a 10 year history of asthma had an acute asthma attack while at work. Normally he worked with an assistant, but on the morning of his acute asthma attack, he had sent his helper to do other work while he installed a spray-on truck bed liner in a van. His helper returned 20 minutes later to find the work completed, the equipment turned off and the individual was gasping for breath on his knees outside the building. The helper immediately took the individual to an urgent care clinic. The individual collapsed at the door of the urgent care clinic. A nurse at the clinic began cardiopulmonary resuscitation (CPR). An ambulance arrived nine minutes later. Despite CPR and transport to a nearby hospital, he was pronounced dead 46 minutes later. Wheezing was noted on auscultation while he was being bagged during resuscitation. On microscopic examination of his lungs at autopsy, there was mucus in his airways with numerous eosinophils in his airways and his mucosa. The bronchial basement membrane was thickened with hyperplasia of the mucus glands. There were aggregates of pigment laden macrophages in the peribronchial alveoli. He was also noted to have diffuse pan lobular moderate to severe pulmonary emphysema, and diffuse and heavy anthracosis. His heart showed coronary arteriosclerosis, calcification, myocardial hypertrophy, and perivascular fibrosis. The medical examiners cause of death was "Asthmatic reaction due to inhalation of chemicals." The deceased had a history of allergies. He had never been hospitalized for respiratory problems. He had had three medical visits in the year prior to his death: 1) a laceration of his hand; 2) low back pain; and 3) symptoms of shortness of breath and the medical record from that last encounter, when he had symptoms of shortness of breath, indicated he inhaled "chemicals" two days prior while working with a bed liner and wasn't wearing a breathing pack. He was exposed for ten minutes and, within 10-15 minutes, couldn't catch his breath. He received a nebulizer treatment and was given 40 mg of prednisone and antibiotics for seven days, cough syrup with codeine and an albuterol inhaler. His regular asthma medication consisted only of an albuterol inhaler. He had never had pulmonary function testing. He had smoked two packs of cigarettes per day but was tapering down. The deceased had worked as the manager at a small auto detailing facility, which included himself and two employees. The shop did vehicle detailing, rustproofing and spray-on truck bed liners. The deceased was the only individual who did the spray-on truck bed lining. After he died, his coworkers mentioned that the manager had had difficulty breathing after previous spray liner applications. The deceased used a positive pressure respirator with supplied fresh air while spaying on the bedliner [1].

The spray-on bedliner was a two component system of methylene diphenyl diisocyanate (MDI) and polyol. The components were mixed during the spray process. When mixed, polyurethane was formed, which provided abrasion resistance, insulation, and a watertight seal to the bed of the truck. The work was performed inside because no moisture can contact the bed liner during application. Isocyanates have historically been the most common cause of work-related asthma. This case report illustrates the most severe consequence of a healthcare provider not adequately addressing a patient's increased respiratory symptoms associated with work. The response by the health care provider after the visit for respiratory problems prior to the patient's death was limited to acute treatment. No action was suggested to the patient on managing future exposure. The results of studies on individuals who have developed asthma from exposure to isocyanates conclude that those individuals should no longer be exposed to isocyanates [2]. At the minimum, the manager should not have applied the bedliner and probably should no have worked at the facility.

Work-related asthma encompasses both new onset asthma and aggravation of pre-existing asthma from work exposures/conditions (Fig. **1**).

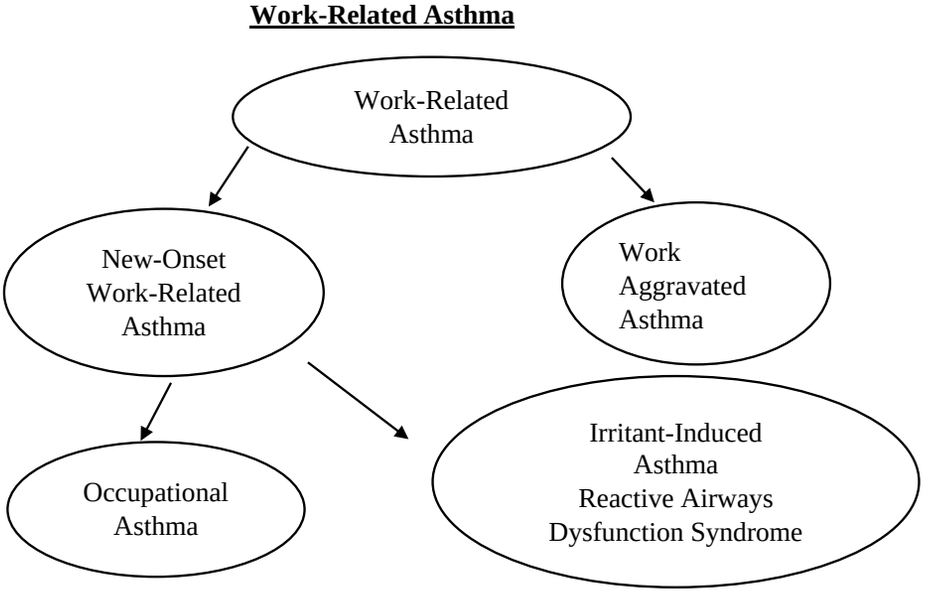

Fig. (1). Classification of work-related asthma (WRA).

New onset asthma can be caused by exposure to an irritant or a substance that causes sensitization. Over 300 substances have been identified where exposure at

work can lead to sensitization and asthma [3]. New-onset asthma from an acute single exposure is called Reactive Airways Dysfunction Syndrome (RADS) [4]. It should be noted that RADS is not the same as reactive airways disease. Reactive airways disease has been used by clinicians for patients with bronchospasm as an alternative diagnosis to asthma when it is difficult to diagnose asthma, children under five, or when it is suspected a patient's wheezing is an acute process perhaps related to an upper respiratory infection. However, since there is no International Classification of Disease (ICD) code for reactive airways disease, medical records with reactive airways disease as the diagnosis will be coded as asthma. New onset asthma from repeated chronic exposure to an irritant at work as a cause of asthma has also been described, but it is not as well an accepted entity as RADS [5]. Aggravation of pre-existing asthma by work can occur from exposure, including stress, physical activity, and temperature/humidity. Unlike work-related lung diseases such as pneumoconioses, which cause irreversible fibrosis, work-related asthma is potentially completely reversible if diagnosed soon after the onset of symptoms and the patient's exposure to the etiologic agent ceases [2]. Beginning in the early 1900's asthma from exposure at work to plant material and metals first began to be reported in the medical literature. In the 1970's, Dr. Jack Pepys from England markedly advanced the identification of etiological agents by developing a practical way to perform specific inhalation challenge testing [6]. In more developed countries such as Europe and the United States, which have implemented controls or banned the use of certain mineral dust (*i.e*. asbestos, silica) that have caused the most common pneumoconioses, work-related asthma, has become a more important cause of new-onset work-related lung disease than the more traditional pneumoconioses.

Consensus statements from the American Thoracic Society (ATS) that were based on the review of the medical literature have concluded that approximately 15% of new-onset asthma in adults is caused by work [7, 8]. A third ATS consensus statement concluded that 21% of adults with asthma had aggravation of their asthma by their work [9].

Multiple overviews have been written on work-related asthma, from the perspective of an allergist [10], from the perspective of a pulmonologist [11, 12], and in a comprehensive book [6].

PATHOPHYSIOLOGY

The chance of becoming sensitized to a substance is dose-related but also has a genetic component since typically, only a minority of the exposed workforce will become sensitized. Historically the highest percentage of individuals affected has been among individuals in research facilities working with mice or rats (as high as

30%) and lower in facilities using chemicals such as isocyanates (5-10%). Substances that cause work-related asthma have been grouped as high and low molecular weight antigens. Typically, animals and plants antigens are high molecular weight, and chemicals antigens are low molecular weight (Table 1).

Table 1. Examples of high and low molecular weight compounds and occupations/industries where exposures occur known to cause sensitization and new-onset asthma.

High Molecular Weight Compounds
Animals
Animal dander, insects, mold,
Animal Handlers
Antibiotic Workers
Detergent Enzyme Manufacturers
Entomologists
Plants
Grain, flour, flowers and pollens, woods
Bakers
Grain Elevator Operators
Wood workers
Low Molecular Weight Compounds
Chemicals
Anhydrides, chromium, diisocyanates, quaternary ammonium compounds, platinum,
Epoxy Resin Workers
Cleaners using disinfectants
Platinum Refiners
Polyurethane Foam Manufacturers

The mechanism for sensitization from high molecular weight material is typically IgE antibody mediated, and skin prick tests and specific IgE results are useful in the diagnostic workup. The mechanism for sensitization to low molecular weight chemicals can be IgE mediated with the chemical acting as a hapten and binding to a protein in the airways and/or the blood, which then interacts with IgE or a non-IgE mediated mechanism involving cytokinins and T-cells. Generally skin prick tests and specific IgE results have limited usefulness for low molecular weight chemicals, although there are exceptions such as work-related asthma from sensitivity to platinum. The mechanism for an irritant is hypothesized to involve damage and oxidative stress to the bronchial epithelium with the release of neuroactive molecules and reactive oxygen species and recruitment of neutrophils. A not uncommon irritant exposure is the mixture of cleaning products, one containing acid and the other bleach, which generates chlorine gas, or one containing ammonia and the other bleach, which generates chloramine gas (Fig. **2**).

Chlorine

Acid + Hypochlorite (Bleach) = Chlorine Gas

$4H^+ + 2OCl^- = Cl_2 + 2H_2O$

Chloramine

Ammonia + Hypochlorite (Bleach) = Monochloramine

$NH_3 + 2OCl^- = NH_2Cl + OH^-$

Dichloramine

$NH_3 + 2OCl^- = NHCl_2 + 2OH^-$

Fig. (2). Generation of chlorine or chloramine/dichloramine after mixture of cleaning products containing acid or ammonia and bleach.

Exposure to chloramines that are released in the air above pool water (produced from the mixing of ammonia in the sweat and/or urine of swimmers and chlorine compounds in the pool water) is the causal agent for asthma related to swimming pools that occurs among swimmers and pool workers [13].

Longitudinal studies of individuals first going to work in an occupation with exposure to an allergen such as flour in a baker apprenticeship program have found that an individual with a negative methacholine challenge test at baseline prior to exposure, who goes on to become symptomatic from the workplace exposure develops a positive methacholine challenge test prior to developing symptoms [14]. Conversely, the methacholine challenge test will require a higher dose of methacholine to be positive or will become negative in individuals who have become sensitized but who are removed from the position and their exposure ceases. Similarly, either skin prick or specific IgE tests may become positive prior to the development of symptoms and become weaker or negative after cessation of exposure.

Atopy (sensitivity to common environmental allergens such as pollen or dander) or a family history of allergies, both of which are clinical markers of genetic susceptibility, are associated with the development of work-related asthma from exposure to some high molecular substances. No specific gene or part of a gene has been associated with the development of work-related asthma. Rather, genetic

studies have identified multiple areas of the genome that are associated with the development of new-onset work-related asthma [15].

DIAGNOSIS OF WORK-RELATED ASTHMA

Asthma, including RADS, that is caused by work exposure, has the same symptoms, physiology, response to asthma medication, and pathology as non-work-related asthma. The recognition of work-related asthma requires the health care provider to ask about the history of onset and situation(s) that aggravate symptoms. Given the general tendency of health care providers not to ask about work exposures, it is not surprising that the results of epidemiological studies show that work-related asthma is markedly underdiagnosed. The underdiagnosis of work-related asthma is to the detriment of patients since removal from exposure is a key component of the treatment of work-related asthma.

A dramatic example of the effect of underdiagnosis or a delay in diagnosis of work-related asthma is illustrated in the death summarized in the case report at the beginning of the chapter. Data from the U. S. Behavioral Risk Factor Surveillance System (BRFSS) have reported a larger number of cases of work-related asthma in the general population than identified in surveillance systems [16]; that 75-79% of patients who think their work was making their asthma worse have never discussed this concern with their physician [17]; and that individuals with work-related asthma have increased morbidity, more severe asthma symptoms, higher healthcare utilization, and less well-controlled asthma than those individuals with non-work-related asthma [18].

To address the underdiagnosis of work-related asthma, a consensus statement from the American College of Chest Physicians (ACCP) recommended the following four key questions be asked of all adult patients with new onset asthma or whose asthma becomes more symptomatic [19]:

1. Were there changes in work processes in the period preceding the onset of symptoms?
2. Was there an unusual work exposure within 24 hours before the onset of initial asthma symptoms?
3. Do asthma symptoms differ during times away from work, such as weekends or holidays or other extended times away from work?
4. Are there symptoms of allergic rhinitis and/or conjunctivitis symptoms that are worse with work?”

The medical history provided by the patient is not specific for the diagnosis of work-related asthma but is a sensitive screening that, if positive, should lead to

follow-up diagnostic testing. Question 1 elicits whether there have been changes in the process such that a new chemical has been introduced or levels of exposure have changed. Question 2 asks about a previous acute exposure that immediately (within 24 hours) preceded the onset of symptoms. A positive response to question 2 is consistent with the development of RADS. Question 3 is the key question because it assesses improvement away from the workplace. The typical response obtained to question 3 with new onset asthma from a work exposure is an improvement of symptoms on weekends or vacations or even complete resolution after a more prolonged time away from work. This is particularly true early in the course of new-onset asthma. As the duration of exposure and symptoms increase, the patient is less likely to resolve their symptoms when away from work, to the point where there may be no improvement. Accordingly, it is important to ask about the temporal relationship of symptoms with work exposure at the time symptoms first began since temporal relationships may become less obvious or disappear with time. This clinical response is consistent with the pathological changes that occur in asthma over time; increased bronchial smooth muscle increased mucus producing goblet cells, and thickening of the bronchial basement membrane. The development of chronic pathological changes explains why a patient's risk will remain symptomatic after exposure to the etiological agent ceases increases with the time of exposure prior to cessation of exposure [20]. The known delay in diagnosing work-related asthma [21] is an important factor in why the majority of patients with new onset asthma from sensitization to exposure at work remain symptomatic even after exposure ceases [20]. This delay is also associated with fatal work-related asthma cases [22]. Even though most patients continue to have symptoms and require asthma medication after removal from exposure to the causal substance, they will have less morbidity than if they continued to be exposed. With reduction in symptoms and medication requirements, maximum improvement generally occurs two years after removal from exposure, and the patient’s status at two years best predicts their long-term prognosis.

The time between first exposure and development of symptoms may vary from weeks to years but is generally more common in the first two years after exposure. If a patient's asthma symptoms improve away from work, the patient should be asked to describe what they do and what activities or exposures are associated with their respiratory symptoms. Once an individual becomes sensitized to a substance, they can have different time intervals after exposure when they have their asthma symptoms. The four patterns are 1) within minutes, acute onset reaction; 2) 4-8 hours, late onset reaction; 3) both within minutes and also hours later, dual onset reaction; and 4) prolonged symptoms that occur periodically over multiple days. Asking the patient to draw a floor plan of the workspace may be helpful to better understand potential exposures since the patient may not work

directly with the substance causing their asthma but work near the substance. The use of personal protective equipment and the patient's perception of the ventilation should be assessed. Additional history should be obtained on other factors that increase the risk of sensitization; the frequency of the patient's exposure to spills and leaks, whether the patient was responsible for cleaning up the spilled material and whether they were provided with special protective equipment to perform the cleanup. Sensitization has been reported after a single acute spill or leak, but this is more commonly the history in a patient with RADS. When available, industrial hygiene reports of previous air sampling studies can be useful to document particular substances in the workplace and average exposure levels but generally miss higher levels during excursions. However, since the allowable air level standards for most workplace substances causing asthma were not implemented to prevent sensitization, measured levels that are below allowable OSHA standards are no assurance that the substance is not causing the patient's asthma. Similarly, physicians should be wary of safety data sheets (SDSs). There is no legal requirement that SDSs, which chemical manufacturers and formulators are required to prepare and accompany the products they sell, list workplace allergens as ingredients on the SDSs.

The fourth recommended question asks about the symptoms of allergic rhinitis and conjunctivitis since these symptoms commonly occur in subjects who have become sensitized to high molecular weight substances such as flour in a bakery or mice or rats in a research lab. Patients who first develop rhinitis or conjunctivitis from exposure to a high molecular weight substance are at increased risk of progressing on to develop new onset asthma.

Other relevant items in the history include non-occupational factors such as cigarette smoking, exposure to secondhand smoke, hobbies of the patient or members of the patient's household, presence of pets, and a personal or family history of allergies. The presence or absence of these factors does not preclude the diagnosis of work-related asthma. A long-term cigarette smoker is at increased risk of chronic obstructive pulmonary disease (COPD), and it is important to first determine the medical diagnosis of a patient. Different exposures are associated with COPD and asthma, so one needs to know the diagnosis before determining whether work may contribute to the condition. Irritants at home from secondhand smoke, hobbies or other irritants may cause respiratory symptoms that mask the temporal association with work. The acquisition of a pet or the initiation of a hobby coincidental with a new job or work exposure may confound the evaluation of work-related asthma. In addition, some workplace exposures also occur at home.

For example, veterinarians can become allergic to both their own pets and their animal patients or individuals can be exposed to cleaning products and or disinfectants, which contain a number of asthma-causing agents (Table **2**), in both their home and workplace.

Table 2. Known sensitizers in cleaning agents/disinfectants.

bleach	chloramine T
chlorhexidine	formaldehyde
glutaraldehyde	isothiozolinone
quaternary ammonium compounds	
Aliphatic polyamines	
ethylene diamine	
diethylene triamine	
triethylene tetraamine	
Ethanolamines	
monoethanolamine	
triethanolamine	

Multiple diagnostic flow diagrams for work-related asthma have been developed. The most comprehensive diagram is in a recent book on work-related asthma [6]. All diagnostic flow diagrams for work-related asthma begin with confirmation that a patient with asthma symptoms has asthma by the documentation of hyperreactivity with a positive pre/post bronchodilator or methacholine challenge test. If the patient is still at work, then a negative methacholine challenge test has a high predictive value (95%) that the patient does not have work-related asthma. The predictive value of a negative methacholine drops to 82% if the patient is no longer at work [23]. A positive methacholine challenge test, regardless of current work status, has a low specificity. Breathing tests performed in relationship to work are needed to confirm the diagnosis of work-related asthma.

The differential diagnosis of work-related asthma includes vocal cord dysfunction, irritant bronchitis, chronic obstructive pulmonary disease (COPD) that may be difficult to distinguish from asthma, especially in the asthma-COPD overlap (ACO), metal fume fever, hypersensitivity pneumonitis, and bronchiolitis obliterans. Symptoms that begin immediately or within days after initiation of work are not consistent with work-related asthma unless the patient already had asthma prior to the initiation of this job or had been exposed to asthma causing agent in a previous job. Symptoms that begin so soon after initiation of work are more likely secondary to pre-existing asthma or to upper airway irritation in the absence of asthma. If the symptoms involve loss of voice, then vocal cord dysfunction should be highly considered, and the patient should be evaluated by

an otolaryngologist, who can assess vocal cord movement [24]. All these other conditions, which may present with asthma like symptoms, can be related to work exposures but have different prognoses and treatment approaches. In diagnosing work-related asthma, the physical examination is of secondary importance to the history. A chest radiograph is generally sufficient to exclude non-asthma causes of respiratory symptoms. A high-resolution CT scan may be indicated when considering conditions such as hypersensitivity pneumonitis or bronchiolitis obliterans. Pulmonary function testing, which meets the ATS criteria for quality control, including an inspiratory loop, lung volumes, diffusing capacity, and a determination of hyperreactivity, is important in working through the differential diagnosis [25].

After confirmation that the patient has asthma, diagnostic guidelines recommend skin testing or specific IgE testing, when available for high molecular weight substances. See Table 3 for examples of commercially available IgE tests. IgE testing for high molecular weight compounds has a high enough sensitivity and specificity to be useful in the diagnostic evaluation. For most low molecular weight compounds such as the isocyanates, IgE testing is not available but when it is available, the results have low sensitivity and specificity and are only useful when the results are positive, and then the positive tests only confirm exposure.

Table 3. Examples of commercially available specific IgE tests.

Animals	Plants
Cats, Cows, Dogs,	Grains
Guinea Pigs, Horses,	Grasses
Mice, Pigs, Rats	Latex
	Woods

Chemicals

Formaldehyde

Isocyanates -Toluene Diisocyanate (TDI), Diphenylmethane Diisocyanate (MDI), Hexamethylene Diisocyanate (HDI)

Phthalic Anhydride

Breathing tests performed in relationship to work or the suspected exposure are the final step in the diagnosis of work-related asthma. The gold standard for diagnosing occupational asthma is specific inhalation challenge testing [26], which is only available in a limited number of specialized centers in Europe and Canada. In the United States, the history of a temporal association of asthma symptoms in association with work exposure to a known cause of occupational asthma is the typical approach to diagnosing work-related asthma. Although the history of symptoms in association with work has a high sensitivity, it has a low

specificity and all guidelines recommend confirmation with breathing tests. Alternatives to specific antigen challenge testing are spirometry, serial methacholine challenge testing and peak flow measurements at and away from work [27]. Peak flow testing is the most cost-effective approach and has a good correlation with specific inhalation challenge testing [28, 29]. Free software is available to facilitate review of the peak flow results, which ideally are obtained every two hours while the patient is awake over a period of two weeks at work and two weeks away from work [30]. There are situations, however, where the patient can no longer return to work, *e.g*., has been fired or is too symptomatic, where the diagnosis may need to be made by history after confirmation that the patient has asthma.

TREATMENT

The medications used to treat work-related and non-work-related asthma are the same. What differs is that removal from exposure is a key component of the treatment of work-related asthma. Although patients will typically feel better after initiation of asthma medication even as they remain exposed to the causal substance, patients with ongoing exposure will over time require more medication and have more symptoms and health care usage than those who cease exposure. Given the economic/social consequences of work restrictions and or job loss [31], it is important that clinicians are confident in the diagnosis of work-related asthma before writing restrictions or giving advice to their patients to leave work. It is also important to have objective documentation of the diagnosis (*i.e*., peak flow testing or, at the minimum a measure of hyperreactivity) beyond the clinical history to ensure that the patient can receive workers' compensation for wage replacement and medical coverage. With reduction in symptoms and medication requirements, maximum improvement generally occurs two years after removal from exposure, and the patient's status at two years best predicts their long-term prognosis. There are situations where the patient doesn't want to/can't afford to cease exposure (*e.g*., worker close to retirement, a graduate student working with lab animals while finishing their thesis research). Alternative approaches such as mandatory use of a respirator (generally would require the more protective and easier to tolerate powered air purifying respirators (PAPR)) or the re-assignment of specific tasks may sufficiently reduce exposure to allow the patient over a short period to maintain their job but still reduce morbidity. There are some older case reports of allergy desensitization for high molecular weight compounds that allowed the patient to work symptom free with ongoing exposure [32].

HAZARD CONTROL AND DISEASE PREVENTION

The risk of developing work-related asthma increases with an increasing level of

exposure, either measured as a time weighted average (TWA) and/or as the number of spills/leaks in the workplace. OSHA permissible exposure limits (PELs), the allowable workplace legal air concentrations, for many materials were not developed to prevent sensitization and asthma but rather to prevent an acute irritant or toxicological effect. The best examples of substances where the PEL is based on an irritant effect are flour and wood dust which are regulated in the United States as inert dusts (TWA - 15mg/m^3) rather than at a level to protect against sensitization. In addition, the possibility of sensitization through dermal exposure has not been incorporated into exposure standards (*e.g*., isocyanates). A comprehensive, regularly updated list of substances that cause occupational asthma is maintained on the internet by the Association of Occupational and Environmental Clinics [3]. Components of primary prevention include approaches that limit exposure through engineering controls, education of workers about the potential hazards, administrative controls to limit access to areas where sensitizing agents are used, and provision of personal protective equipment for workers performing high exposure tasks or during excursions such as clean up after spills/leaks [33 - 35]. Additional approaches have been the substitution with polymers (*i.e*. isocyanates), which are less volatile, or encapsulation (*i.e*. enzymes), which are less dusty. An increased risk of developing occupational asthma from selected workplace substances has been identified for atopic individuals (those with a history of allergies and/or skin prick tests to common environmental agents), or cigarette smoking. However, the risks associated with atopy or cigarette smoking are not sufficiently predictive of who will get occupational asthma to use this information on a pre-placement exam to exclude new employees from a workplace.

It is the general consensus that individuals who work with substances that cause occupational asthma should be provided periodic medical surveillance to increase the likelihood of early diagnosis and subsequent prompt removal from exposure to reduce morbidity [36]. There is agreement that a questionnaire to assess respiratory symptoms should be part of the surveillance. The inclusion of allergy testing for high molecular weight substances may provide even earlier recognition of those who will go on to develop asthma. There is no consensus on the inclusion of spirometry in periodic monitoring. Spirometry may supplement a respiratory questionnaire, particularly where workers may be reluctant to report or do not recognize work-related respiratory symptoms when their symptoms may be mild or when they are afraid of the economic consequences of their diagnosis of work-related asthma.

New causes of work-related asthma are identified each year; argan powder used in the cosmetic industry is an example of a recent report [37]. Generally, these reports come from medical centers in Europe, or Quebec, which use specific

inhalation challenge testing as part of the diagnostic workup, or medical centers in Great Britain, which use peak flow measurements every two hours over multiple weeks both at and away from work to document the new causal agent.

Depending on the jurisdiction, the surveillance systems of work-related asthma rely on voluntary reports from physicians, mandatory but non-enforced reporting laws and/or worker compensation records [38, 39]. The work-related asthma systems in the United States also include data from hospitals, emergency departments, and poison control centers [22]. These surveillance systems as well as workers' compensation data in the United States are known to markedly underestimate the true incidence of work-related asthma. Although the existing surveillance systems markedly underestimate the true incidence of work-related asthma, there is no indication that this underestimate has changed over time, so trend data in these systems are presumed to be useful to examine how the epidemiology of work-related asthma has changed over time. The number of cases from well-recognized causes of occupational asthma such as the isocyanates, latex and enzymes have decreased while cases related to cleaning agents have either increased or remained unchanged. Work-related asthma cases are sentinel cases of a larger public health problem. Reporting of work-related asthma by health care providers in the community to public health and/or workplace regulatory authorities identifies trends and new causal agents. Inspection of the workplace where a reported case has worked has been shown to be effective in identifying ongoing problematic exposures and additional symptomatic workers [22]. In order to reduce the burden of work-related asthma, regulatory standards that encompass more protective PELs, administrative controls, medical screening, and education are needed.

CONSENT OF PULICATION

Declared none.

CONFLICT OF INTEREST

The author confirms that the author has no conflict of interest to declare for this publication.

ACKNOWLEDGMENTS

Since 1988, the author has received funding from the National Institute for Occupational Safety and Health to conduct surveillance for work-related asthma.

REFERENCES

[1] Chester DA, Hanna EA, Pickelman BG, Rosenman KD. Asthma Death after Spraying Polyurethane Truck Bedliner 2005.

[http://dx.doi.org/10.1002/ajim.20183]

[2] Vandenplas O, Dressel H, Nowak D, Jamart J. What is the optimal management option for occupational asthma? Eur Respir Rev 2012; 21(124): 97-104.
[http://dx.doi.org/10.1183/09059180.00004911] [PMID: 22654081]

[3] Rosenman KD, Beckett WS. Web based listing of agents associated with new onset work-related asthma. Respir Med 2015; 109(5): 625-31.
[http://dx.doi.org/10.1016/j.rmed.2015.03.004] [PMID: 25863522]

[4] Brooks SM, Weiss MA, Bernstein IL. Reactive airways dysfunction syndrome (RADS). Persistent asthma syndrome after high level irritant exposures. Chest 1985; 88(3): 376-84.
[http://dx.doi.org/10.1378/chest.88.3.376] [PMID: 4028848]

[5] Dumas O, Le Moual N. Do chronic workplace irritant exposures cause asthma? Curr Opin Allergy Clin Immunol 2016; 16(2): 75-85.
[http://dx.doi.org/10.1097/ACI.0000000000000247] [PMID: 26914673]

[6] Asthma in the Workplace; 5th edition. Tarlo S, Bernstein DI, Malo JL, Vandenplas O, Eds. Boca Raton, Florida: CRC Press 2021.

[7] Balmes J, Becklake M, Blanc P, *et al.* American Thoracic Society Statement: Occupational contribution to the burden of airway disease. Am J Respir Crit Care Med 2003; 167(5): 787-97.
[http://dx.doi.org/10.1164/rccm.167.5.787] [PMID: 12598220]

[8] Blanc PD, Annesi-Maesano I, Balmes JR, *et al.* The Occupational Burden of Nonmalignant Respiratory Diseases. An Official American Thoracic Society and European Respiratory Society Statement. Am J Respir Crit Care Med 2019; 199(11): 1312-34.
[http://dx.doi.org/10.1164/rccm.201904-0717ST] [PMID: 31149852]

[9] Henneberger PK, Redlich CA, Callahan DB, *et al.* An official american thoracic society statement: work-exacerbated asthma. Am J Respir Crit Care Med 2011; 184(3): 368-78.
[http://dx.doi.org/10.1164/rccm.812011ST] [PMID: 21804122]

[10] Dao A, Bernstein DI. Occupational exposure and asthma. Ann Allergy Asthma Immunol 2018; 120(5): 468-75.
[http://dx.doi.org/10.1016/j.anai.2018.03.026] [PMID: 29580845]

[11] Tarlo SM, Lemiere C. Occupational asthma. N Engl J Med 2014; 370(7): 640-9.
[http://dx.doi.org/10.1056/NEJMra1301758] [PMID: 24521110]

[12] Lau A, Tarlo SM. Update on the Management of Occupational Asthma and Work-Exacerbated Asthma. Allergy Asthma Immunol Res 2019; 11(2): 188-200.
[http://dx.doi.org/10.4168/aair.2019.11.2.188] [PMID: 30661311]

[13] Jacobs JH, Spaan S, van Rooy GB, *et al.* Exposure to trichloramine and respiratory symptoms in indoor swimming pool workers. Eur Respir J 2007; 29(4): 690-8.
[http://dx.doi.org/10.1183/09031936.00024706] [PMID: 17107995]

[14] Gautrin D, Ghezzo H, Infante-Rivard C, Malo JL. Incidence and determinants of IgE-mediated sensitization in apprentices. A prospective study. Am J Respir Crit Care Med 2000; 162(4 Pt 1): 1222-8.
[http://dx.doi.org/10.1164/ajrccm.162.4.2001023] [PMID: 11029321]

[15] Bernstein DI, Lummus ZL, Kesavalu B, *et al.* Genetic variants with gene regulatory effects are associated with diisocyanate-induced asthma. J Allergy Clin Immunol 2018; 142(3): 959-69.
[http://dx.doi.org/10.1016/j.jaci.2018.06.022] [PMID: 29969634]

[16] Knoeller GE, Mazurek JM, Moorman JE. Work-related asthma among adults with current asthma in 33 states and DC: evidence from the Asthma Call-Back Survey, 2006-2007. Public Health Rep 2011; 126(4): 603-11.
[http://dx.doi.org/10.1177/003335491112600419] [PMID: 21800756]

[17] Lutzker LA, Rafferty AP, Brunner WM, *et al.* Prevalence of work-related asthma in Michigan, Minnesota, and Oregon. J Asthma 2010; 47(2): 156-61.
[http://dx.doi.org/10.3109/02770900903509073] [PMID: 20170322]

[18] Dodd KE, Mazurek JM. Asthma medication use among adults with current asthma by work-related asthma status, Asthma Call-back Survey, 29 states, 2012-2013. J Asthma 2018; 55(4): 364-72.
[http://dx.doi.org/10.1080/02770903.2017.1339245] [PMID: 28704107]

[19] Tarlo SM, Balmes J, Balkissoon R, *et al.* Diagnosis and management of work-related asthma. Chest 2008; 134(3) (Suppl.): 1S-41S.
[http://dx.doi.org/10.1378/chest.08-0201] [PMID: 18779187]

[20] Rachiotis G, Savani R, Brant A, MacNeill SJ, Newman Taylor A, Cullinan P. Outcome of occupational asthma after cessation of exposure: a systematic review. Thorax 2007; 62(2): 147-52.
[http://dx.doi.org/10.1136/thx.2006.061952] [PMID: 17040933]

[21] Fishwick D, Bradshaw L, Davies J, *et al.* Are we failing workers with symptoms suggestive of occupational asthma? Prim Care Respir J 2007; 16(5): 304-10.
[http://dx.doi.org/10.3132/pcrj.2007.00064] [PMID: 17934677]

[22] Reilly MJ, Wang L, Rosenman KD. The Burden of Work-related Asthma in Michigan, 1988-2018. Ann Am Thorac Soc 2020; 17(3): 284-92.
[http://dx.doi.org/10.1513/AnnalsATS.201905-401OC] [PMID: 31682471]

[23] Pralong JA, Lemière C, Rochat T, L'Archevêque J, Labrecque M, Cartier A. Predictive value of nonspecific bronchial responsiveness in occupational asthma. J Allergy Clin Immunol 2016; 137(2): 412-6.
[http://dx.doi.org/10.1016/j.jaci.2015.06.026] [PMID: 26220529]

[24] Graham BL, Steenbruggen I, Miller MR, *et al.* Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. Am J Respir Crit Care Med 2019; 200(8): e70-88.
[http://dx.doi.org/10.1164/rccm.201908-1590ST] [PMID: 31613151]

[25] Hull JH, Backer V, Gibson PG, Fowler SJ. Laryngeal Dysfunction: Assessment and Management for the Clinician. Am J Respir Crit Care Med 2016; 194(9): 1062-72.
[http://dx.doi.org/10.1164/rccm.201606-1249CI] [PMID: 27575803]

[26] Vandenplas O, Suojalehto H, Aasen TB, *et al.* Specific inhalation challenge in the diagnosis of occupational asthma: consensus statement. Eur Respir J 2014; 43(6): 1573-87.
[http://dx.doi.org/10.1183/09031936.00180313] [PMID: 24603815]

[27] Vandenplas O, Suojalehto H, Cullinan P. Diagnosing occupational asthma. Clin Exp Allergy 2017; 47(1): 6-18.
[http://dx.doi.org/10.1111/cea.12858] [PMID: 27883240]

[28] Burge CBSG, Moore VC, Pantin CFA, Robertson AS, Burge PS. Diagnosis of occupational asthma from time point differences in serial PEF measurements. Thorax 2009; 64(12): 1032-6.
[http://dx.doi.org/10.1136/thx.2009.120923] [PMID: 19850961]

[29] Burge PS, Moore VC, Robertson AS, Walters GI. Do laboratory challenge tests for occupational asthma represent what happens in the workplace? Eur Respir J 2018; 51(6)1800059
[http://dx.doi.org/10.1183/13993003.00059-2018] [PMID: 29748310]

[30] Oasys. Available from: http://www.occupationalasthma.com/occupational_asthma_pageview.aspx?id=4443

[31] Ayres JG, Boyd R, Cowie H, Hurley JF. Costs of occupational asthma in the UK 2011.
[http://dx.doi.org/10.1136/thx.2010.136762]

[32] Dille JR, Gibbons HL, Spikes GA. Allergicproblems in screwworm fly eradication program personnel. Aerosp Med 1968; 39(10): 1116-9.

[PMID: 5678089]

[33] Feary JR, Schofield SJ, Canizales J, *et al.* Laboratory animal allergy is preventable in modern research facilities. Eur Respir J 2019; 53(6)1900171
[http://dx.doi.org/10.1183/13993003.00171-2019] [PMID: 30956209]

[34] Henneberger PK, Patel JR, de Groene GJ, *et al.* Workplace interventions for treatment of occupational asthma. Cochrane Database Syst Rev 2019; 10CD006308
[http://dx.doi.org/10.1002/14651858.CD006308.pub4] [PMID: 31593318]

[35] Occupational Safety and Health Administration Fact Sheet. Do You Have Work-Related Asthma? A Guide for YOU and YOUR DOCTOR.. 2014.Available at: https://oem.msu.edu/images/annual_reports/OSHAAsthmaFactSheet.pdf

[36] Fishwick D, Forman S. Health surveillance for occupational asthma. Curr Opin Allergy Clin Immunol 2018; 18(2): 80-6.
[http://dx.doi.org/10.1097/ACI.0000000000000424] [PMID: 29461276]

[37] Paris C, Herin F, Penven E, *et al.* First evidence of occupational asthma to argan powder in a cosmetic factory. Allergy 2016; 71(4): 550-5.
[http://dx.doi.org/10.1111/all.12811] [PMID: 26606505]

[38] Logar-Henderson C, MacLeod JS, Arrandale VH, *et al.* Adult asthma among workers in Ontario. Results from the occupational disease surveillance system. Ann Am Thorac Soc 2019; 16(5): 563-71.
[http://dx.doi.org/10.1513/AnnalsATS.201810-701OC] [PMID: 30682323]

[39] Seed MJ, Carder M, Gittins M, *et al.* Emerging trends in the UK incidence of occupational asthma: should we be worried? Occup Environ Med 2019; 76(6): 396-7.
[http://dx.doi.org/10.1136/oemed-2018-105414] [PMID: 30936407]