

RADS and Its Variants

Asthma by Another Name

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KEYWORDS

- Reactive airways dysfunction syndrome • Work-exacerbated asthma
- Irritant exposures • Irritant asthma

KEY POINTS

- Acute high-level irritant exposures can cause asthma and exacerbate underlying asthma.
- Lower-level irritant exposures can at least exacerbate underlying asthma, although there is emerging consensus that recurrent lower-level exposures may also cause asthma.
- There is overlap between the exposures that have caused acute irritant-induced asthma and work-exacerbated asthma (WEA), many of which are also sensitizers.
- New-onset asthma in workers following lower-level irritant exposures, with no prior history of respiratory symptoms or asthma, may well be limited to a subset of “susceptible” hosts, such as those with asymptomatic airway hyperresponsiveness, atopy, and those who “outgrew” childhood asthma.
- The ATS statement on WEA has identified research needs to better define risk factors, biologic mechanisms, and outcomes in WEA, which should help facilitate necessary interventions in the medical system, as well as to formulate and apply strategies for prevention.

INTRODUCTION

Asthma is a chronic respiratory condition characterized by variable airflow obstruction, airways hyperresponsiveness, and airway inflammation. Approximately 7.7% of US adults of working age have asthma¹ and an estimated 16.3% of all cases of adult asthma have been attributed to asthma caused or exacerbated by workplace exposures.² Many other conditions and factors, such as rhinosinusitis, gastroesophageal reflux disease (GERD), vocal cord dysfunction, and cigarette smoking, may trigger symptoms that mimic asthma but are not, and these are covered elsewhere in this issue. Other, more serious conditions that mimic asthma include hypersensitivity

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pneumonitis, which can be caused by low molecular weight irritants that are also sensitizers,³⁻⁶ bronchiolitis obliterans,^{7,8} and irritant/odorant-triggered cough.⁹⁻¹¹ Whereas asthma caused by sensitization is well described and well accepted,¹²⁻¹⁶ it is not the primary focus of this article. On the other hand, reactive airways dysfunction syndrome (RADS) and other variants of irritant-induced or irritant-exacerbated asthma may not always initially appear as asthma, but are, in fact, alternate presentations of asthma. Therefore, occupational and environmental exposures that can cause or exacerbate asthma should be considered as well. Although unique conditions exist in the workplace that more often lead to the type of exposures that can cause or exacerbate asthma, exposure to sensitizers and irritants that exacerbate or cause asthma can also occur in the home, during avocational activities, and following accidental industrial releases into the environment. Thus, although the terms occupational and workplace are used in this article, environmental sources of these exposures should also be considered.

The role of irritants in the causation of asthma is now well established. RADS was originally defined in 1981 by Brooks and Lockey¹⁷ and detailed in case series of new-onset asthma syndrome within 24 hours following a single, high-level irritant exposure.¹⁸ Since that time, modifications to the case definition have been proposed, and more recently the term “acute irritant asthma” has been used, with good consensus that this is not just an asthma syndrome but indeed occupational asthma.^{14,16,19,20} Asthma has been reported after lower-level irritant exposures, with considerable controversy regarding whether or not the lower-level irritant exposure caused the asthma,^{21,22} was a result of concurrent immunologic sensitization,^{16,23} or caused an exacerbation of underlying asthma.^{14-16,24,25} Work-exacerbated asthma (WEA) is defined as “preexisting or concurrent asthma that is worsened by workplace conditions,”²⁵ in which there is a temporal association between asthma exacerbations and work in a place where conditions exist that can exacerbate asthma, but that asthma caused by work (immunologic asthma and acute irritant asthma) is considered unlikely. WEA is often not compensable under workers’ compensation.

This article covers the different clinical variants of irritant-induced asthma, specifically focusing on high level irritant-induced asthma and irritant-induced WEA reviews known causes, addresses the often adverse medical and socioeconomic outcomes of this complex condition, and considers issues of causation from an occupational and environmental medicine perspective.

CLINICAL VIGNETTE 1

John Adams is a 45-year-old city maintenance worker. He is a never-smoker and has no history of asthma or other medical problems. He performs maintenance inside city facilities, including the wastewater treatment plant. On one occasion, a regulator malfunction caused the sudden high-pressure release of 100% chlorine into the very small room where he was working. The sudden release caused him to take in a deep breath, and he experienced immediate cough, burning eyes and nose, chest burning and tightness, and shortness of breath. He was taken to the emergency department and placed on oxygen. He is not sure about what other treatment he received, but after a period of time he felt somewhat better and was discharged. Most of his symptoms continued to improve, but the dry cough persisted. He noted chest tightness and shortness of breath with exertion, such as walking in the mountains. His chest symptoms were also triggered by irritants, such as cigarette smoke, perfume, and dust, which had never bothered him before. He seeks medical attention for these symptoms 3 months later. Could this be asthma?

ACUTE IRRITANT ASTHMA

Yes, asthma should be considered as part of the differential diagnosis, and should be confirmed by methacholine challenge or bronchodilator responsiveness. The presentation is consistent with RADS, defined as asthma caused by a single, high level, irritant exposure hypothesized to cause acute bronchial mucosal damage leading to airways hyperresponsiveness. Whereas allergen exposures are well-documented causes of asthma, the role of irritants in the causation of asthma has been recognized only more recently. RADS was originally described as a “persistent asthma syndrome” after high-level irritant exposure.^{17,18} Brooks noted that although the illness clinically simulated bronchial asthma and was associated with airways hyperreactivity, it differed from typical occupational asthma because of rapid onset (within 24 hours) after a single high-level environmental exposure, and this period of time is too short for the development of sensitization.¹⁸ Although the validity of the syndrome as new-onset asthma was initially debated,^{26,27} numerous case reports have followed,^{9,28–32} and it is now widely accepted that acute high-level irritant exposures not only cause a syndrome that mimics asthma but can cause asthma itself.^{14–16,19,20} Tarlo and Broder introduced the term “irritant-induced asthma” in 1989 to include workers in their case series who had high-level irritant exposure on more than one occasion,³³ which has been subsequently reported by others.³⁰ Other studies included those with onset of symptoms up to 7 days after a well-defined spill; they identified additional cases that otherwise met the case definition.³⁴ The term “acute irritant-induced asthma” was recently proposed,^{16,20} and for workers without any prior history of asthma, the term is an accurate unifying descriptor. A list of some of the exposures reported to have caused acute irritant asthma, termed RADS and asthma after spills or accidental exposures, are shown in **Table 1**. The clinical criteria for RADS described by Brooks¹⁸ and modifications that have been proposed are shown in **Box 1**.

In many cases, the symptoms resolve within months, but they can persist in some.^{9,18,29–32,35,36} The long-term sequelae can be significant. One long-term follow-up study of workers (52% participation) with claims accepted by the workers' compensation agency in Quebec revealed significant ongoing respiratory impairment and psychosocial impact two years after initial symptoms. These patients presented with acute irritant-induced asthma due to a well-defined high-level accidental release (57% chlorine) and had symptoms that developed within 24 hours and persisted beyond 3 months. All subjects still had respiratory symptoms; 68% were on inhaled corticosteroids, there had been no significant improvement in forced expiratory volume in 1 second (FEV1) (mean FEV1 74.5% $\pm$ 19.5% predicted), and most still demonstrated airways hyperresponsiveness based on methacholine challenge or improvement after bronchodilator. There was a negative impact on quality of life, and about one-third had abnormal depression scores.³⁷ The long-term impact was similar to that reported in immunologic asthma.³⁸

CLINICAL VIGNETTE 2

Michael Janvier is a 54-year-old insulator in a large plant. He has a 5-pack-year history and had stopped smoking at age 30. He has no prior history of respiratory symptoms. He has performed installation, repair, and routine maintenance on the pipes in a chrome-plating shop on and off over the past 10 years. Some of the pipes were located 4 to 5 feet above the acid baths. Depending on the job, he could spend several weeks or even months at a time in that shop. He sometimes felt burning in his eyes, nose, and throat, as well as some cough, although these symptoms were fairly mild and typically resolved later that evening or the next day. About a year ago, he began

Table 1 Reported high-level irritant exposures associated with development of acute irritant-induced asthma, along with pH, potential for thermal injury, and sensitizer potential					
Author	Outcome	Reported Chemical	High or Low pH	Potential for Thermal Injury	Potential Sensitizer
Brooks et al, ¹⁸ 1985	RADs after single high-level exposure	Uranium hexafluoride			–
		Floor sealant			?
		Spray paint (3)			?
		35% hydrazine			
		Heated acid	+	+	
		Fumigating fog			?
		Metal coat remover	?		
Tarlo and Broder, ³³ 1989	RADs after 1 or more high-level exposures	Fire/smoke		+	?
		Acids	+		
		Calcium oxide			
		Chlorine, sulfuric acid, sulfur dioxide	+		
		HCl, phosgene	+		
		Calcium oxide, welding fumes			?
		Burnt paint fumes		?	?
		Spray paint no isocyanate			
		Chlorine			
		Toluene diisocyanate			+
Chatkin et al, ⁴⁵ 2007	Asthma after spills or accidental exposures	Diphenyl methane diisocyanate			+
		Isocyanates			+
		Paint			?
		Solvents			
		Chlorine			
		Ammonia	+		
		Calcium oxide	+		
		Acrylates			+
		Amines			+
		Epoxy resins			+
		Dyes			?
		Ozone			?
		Pesticides			
		Wood dust			?
		Methylmercaptan			

The “+” refers to the listed chemical exposures that have one or more of the other properties: high or low pH, potential for thermal injury and/or are potential sensitizers. The “?” refers to those chemical exposures that might have one of those properties, but there is insufficient information about the exposure to determine.

Abbreviation: RADs, reactive airways dysfunction syndrome.

to notice worsening shortness of breath while running and playing soccer. He also started awakening at night with chest tightness about once a week. A cardiac evaluation was negative, including a normal stress echocardiogram. His symptoms continue to worsen and he seeks further medical attention. Could this be this asthma?

ASTHMA FOLLOWING LOWER-LEVEL IRRITANT EXPOSURES

In 2005, Brooks³⁹ introduced the term “not-so-sudden onset” irritant-induced asthma to describe the exposures in a subgroup of subjects who had onset of asthma

Box 1**Clinical criteria for acute irritant-induced asthma^a**

1. A documented absence of preceding respiratory complaints.
2. The onset of symptoms occurred after 1 or more high-level exposures.^b
3. The exposure was to a gas, smoke, fume, or vapor that was present in very high concentrations and had irritant qualities to its nature.
4. The onset of symptoms occurred within 24 hours^c after the exposure and persisted for at least 3 months.
5. Symptoms simulated asthma with cough, wheezing, and dyspnea predominating.
6. Pulmonary function test may show airflow obstruction.
7. Methacholine challenge testing was positive.
8. Other types of pulmonary diseases were ruled out.

^a Clinical criteria for RADs defined by Brooks¹⁸ with minor modification as noted.

^b Exposure to high-level irritant exposure on one or more occasions not confined to a single workplace event.³³

^c Others have used symptom onset up to 7 days after exposure.³⁴

following longer and less intense irritant exposures. In a group of 71 subjects considered to be at moderate to high risk for RADs after repeated exposures to chlorine at a pulp and paper mill, 82% had persisting respiratory symptoms, 22% had evidence of reduced FEV₁, and 41% had nonspecific airways hyperresponsiveness based on methacholine challenge that persisted 18 to 24 months after the end of exposure without clear host predisposition.⁴⁰ In contrast, long-term decline in lung function was seen in a longitudinal study of workers exposed to “puffs” of chlorine at a metal production plant; these exposures caused mild symptoms in those with a smoking history of 20-pack-years or more.⁴¹ Kipen and colleagues²¹ described a series of 10 cases of adult-onset asthma following “low-dose” irritant exposures, as shown in **Table 2**. Four of the cases were reported due to exposure to acid mist, whereas 4 or 5 of the other irritant exposures potentially also could have been sensitizers. In this series, another 5 cases had been excluded because of a history of asthma before the exposure, although 41% of the cases did meet the investigators’ criteria for history of atopy (case history reviewed for seasonal allergy, rhinitis, atopic skin disease, or positive immediate hypersensitivity skin results). Host predisposition was also suggested as a mechanism in the subgroup with “not so sudden” irritant-asthma reported by Brooks and colleagues,²² in which 88% were atopic (defined as allergen skin testing or radioallergosorbent tests positive, personal history of allergic disease, elevated total immunoglobulin E level, or family history of allergy) and 40% had a history of childhood asthma or asthma that had been quiescent at least 1 year.

It is important to recognize that a single, high-level exposure to a sensitizing chemical with irritant properties may also cause irritant asthma, although it may be difficult to exclude concurrent sensitization when that exposure is not confined to a single event.^{18,33} Distinguishing between an immunologic and irritant mechanism can be difficult in the individual patient. This has been handled in a number of different ways: excluding those with exposure to irritants that were also sensitizers,^{39,42} analyzing the chemical composition to exclude the presence of sensitizers to determine irritant mechanism,⁴³ using a specific inhalational challenge (SIC) in the laboratory or workplace to distinguish the two,⁴⁴ or including all high-level exposures regardless of SIC

Author	Outcome	Reported Chemical	High or Low pH	Potential for Thermal Injury	Potential Sensitizer
Chiry et al, ⁴⁶ 2007	WEA with negative SIC	Flour			+
		Latex			+
		Isocyanates (3)			+
		Glutaraldehyde			+
		Triethanolamine			+
Lemiere et al, ⁴⁷ 2012	WEA with negative SIC	Ammonia	+		
		Engine exhaust fumes			
		Pyrolysis fumes		?	?
		Metal fumes			?
		Silica			
		Mineral fibers			
		Metal compounds			?
		Animal-derived aerosol			?
		Wood			?
		Flour			+
		Acrylates			+
		Paints, including industrial and motor vehicle			+
		Adhesives			?
		Degreasing stripping agents			
		Hardeners			+
		Isocyanates			+
		Solvents			
Kipen et al, ²¹ 1994	Low-dose RADS	Bisulfite+SO2			
		Chemistry teaching laboratory	?		?
		Acid mist (4)	+		
		Cutting oil			?
		Cleaning agents			?
		Perfume agents			?
		New carpet installation			?

The “+” refers to the listed chemical exposures that have one or more of the other properties: high or low pH, potential for thermal injury and/or are potential sensitizers. The “?” refers to those chemical exposures that might have one of those properties, but there is insufficient information about the exposure to determine.

Abbreviations: RADS, reactive airways dysfunction syndrome; SIC, specific inhalation challenge; WEA, work-exacerbated asthma.

results.⁴⁵ The latter is not inconsistent with the original criteria proposed by Brooks and colleagues.¹⁸ As shown in **Table 1**, many of the irritant exposures reported to cause acute irritant induced asthma are also potential sensitizers. Perhaps more important than establishing mechanism, establishing whether or not there is concurrent immunologic asthma has important implications for the degree of exposure control required for the worker to successfully remain in the workplace.

As described for high-level irritant exposures, lower-level exposures to sensitizing chemicals with irritant properties can also cause asthma either by an irritant or a sensitizing mechanism. Immunologic asthma has been differentiated from irritant-induced

asthma in some studies by results from SIC.^{46,47} As shown in **Table 2**, many of these irritant exposures in which sensitizers were not automatically excluded are very similar to the exposures reported with acute irritant asthma listed in **Table 1**. In a study by Kogevinas and colleagues,⁴⁸ occupations associated with excess risk of occupational asthma included farmers, painters, plastics workers, cleaners, spray painters, and agricultural workers; these are occupations in which there may be concurrent exposures to sensitizers. Overrepresentation of respiratory symptoms and asthma has been reported in workers repeatedly exposed to moderate to low-level irritant exposures that can also be sensitizers, such as cleaning workers^{49–51} and hair dressers.⁵²

CLINICAL VIGNETTE 3

Sandra Dalton is a 26-year-old woman with a prior history of childhood asthma and seasonal allergic rhinitis. Her asthma improved when she was an adolescent, and she used a bronchodilator only before exercise or for chest symptoms associated with an upper respiratory infection (URI). Six months ago she began a job with a company producing experimental semiconductors. She was responsible for loading panels of chips into a holder; this holder was then lowered into a nitric acid bath before the chips were removed and sent down the assembly line. Her job also involved refilling the nitric acid reservoir when levels were low. Although the bath was covered, it was opened to load and remove the computer chips. The room had an unpleasant acrid odor, and after about 3 months at work, she began to develop more frequent episodes of chest tightness that no longer completely resolved after using her bronchodilator. A recent URI triggered profound cough and wheezing, requiring a burst of oral steroids and the addition of a steroid inhaler to control symptoms. Is the patient's asthma exacerbation work related?

WORK-EXACERBATED ASTHMA

Yes, it is now widely accepted that low-level irritant exposures can exacerbate preexisting asthma.^{14–16,24,25} WEA was recently defined by the American Thoracic Society as “preexisting or concurrent asthma that is worsened by workplace conditions,” wherein the asthma either predates the exposure (preexisting) or is determined to have occurred independently, but concurrently with the workplace exposure (concurrent).²⁵ The diagnosis of WEA requires establishment of temporal association between asthma exacerbations and work in a workplace where conditions exist that can exacerbate asthma. WEA is common, reportedly occurring in 23% of adults within a health maintenance organization.⁵³

Temporary Exacerbation Versus Permanent Aggravation of Preexisting or Concurrent Asthma

There is an assortment of irritant workplace exposures that may temporarily increase symptoms due to underlying asthma, or indeed any other chronic lung disease. Such increases in symptoms are often mild, temporary, and respond well to simple measures to decrease or avoid exposure, with the occasional additional use of short-acting bronchodilators. Patients with severe underlying asthma may not be tolerant of low level irritants that are present in many different environments. The problem occurs when there are specific exacerbating conditions that exist in the workplace, but the worker does not have control over mitigating them; such workers are often unable to remain in the workplace. A letter to the editor described the long-term impact of WEA in 10 cases 1 to 4 years after a diagnosis of WEA. None had been able to remain in the workplace because of their respiratory symptoms, and

they also were unable to obtain any financial compensation from the Quebec Worker Compensation Board.⁵⁴ Although it is possible that medical treatment or enhanced ventilation or respiratory protection might have allowed these workers to remain in their jobs, outside of the workers' compensation system, such patients often do not have the authority to effect meaningful decreases in respiratory exposures in the workplace.

As a result, loss of employment, a need to change jobs, and other adverse socioeconomic effects,^{55–58} as well as increased use of health care resources and decreased quality of life,⁵⁹ have been documented by a growing number of studies of workers after a diagnosis of WEA. If the worker does not return to baseline status despite optimized medical therapy, and reasonable exposure control measures have been implemented, such worsening would be considered a permanent aggravation, rather than a temporary exacerbation.

Although there are considerable data on disability and adverse socioeconomic outcomes in WEA, there are few clinical outcome studies.²⁵ There are also no clinical outcome data on workers who receive optimized medication therapy and reasonable workplace exposure controls, and their long-term ability to remain within the workplace (ie, the extent to which such cases of WEA could be limited to temporary exacerbations that are not associated with job loss and other socioeconomic disadvantages).

More concrete consideration of permanent aggravation can be made in the context of an acute irritant injury in a worker with preexisting asthma. The original clinical criteria proposed by Brooks and colleagues¹⁸ excluded persons with preceding history of respiratory complaints. In most cases, it is impossible to verify a preexisting lack of airways hyperresponsiveness or airflow limitation. Multiple cases of high-level irritant exposures resulted in asthma that otherwise met the definition of RADS except for a prior history of mild asthma.^{22,36,60,61} There is nothing about underlying asthma that would be expected to confer immunity from airways injury following such irritant exposures that cause RADS in a worker with normal airways. Indeed, one might postulate that those with preexisting asthma are even more susceptible to airways injury and persistent effects from irritant exposures, as is suggested by the 76% of subjects with a preexisting history of asthma who had accepted claims for asthma by the Ontario Workers' Compensation Board following high-level irritant exposures.⁴⁵ In many cases, with treatment, workers with preexisting asthma will be able to return to their baseline status in the same way as those with no prior history of asthma. In others, the condition does not return to baseline, and there is objective evidence of permanent worsening, such as a change in FEV1, methacholine PC-20, medication requirements, and/or the need for permanent removal from exposure even after optimized medical treatment and implementation of exposure controls. In this setting, the term "acute irritant-aggravated asthma" could be considered to describe the permanent change from the patient's baseline condition.

CHALLENGES IN THE DIAGNOSIS OF IRRITANT-INDUCED VERSUS IRRITANT-AGGRAVATED ASTHMA FROM AN OCCUPATIONAL AND ENVIRONMENTAL MEDICINE PERSPECTIVE DISTINGUISHING WORKERS WITH PREEXISTING OR CONCURRENT ASTHMA FROM NEW-ONSET ASTHMA

There can be difficulty distinguishing between new-onset occupational asthma caused by work, and WEA. For example, in a group of 53 workers with documented reversible airflow limitation or airways hyperresponsiveness and WEA, defined by worsening asthma symptoms at work and a negative SIC, only 20% reported a history

of asthma before the exposure.⁴⁷ The investigators concluded that although it is often not possible to confirm by objective testing, a proportion of these subjects may suffer not from WEA, but from “low-dose irritant asthma” (ie, new-onset asthma). In another study, clinicians were not able to reliably differentiate the peak flow measurement pattern in workers with new-onset occupational asthma versus WEA on visual inspection or computer analysis.⁴⁶ In fact, the US National Institute for Occupational Safety and Health (NIOSH) Sentinel Event Notification Systems for Occupational Risks (SENSOR) program for surveillance of work-related asthma considered new-onset work-related asthma symptoms to be work-initiated asthma, even in the context of preexisting asthma that had been untreated or asymptomatic for at least 2 years before entering the workplace.⁶²

Preexisting asymptomatic airways hyperresponsiveness (AHR) is well described as one of the factors that can predispose to asthma, and some investigators have argued that the existence of preexisting AHR precludes a diagnosis of RADS as new-onset asthma. The prevalence of asymptomatic airways hyperresponsiveness has ranged from 4% to 35% of the population depending on the definition used.⁶³ It is described with⁶⁴ and without⁶⁵ correlation with eosinophilia, which along with atopy can also predispose to asthma. A prior history of asthma, including childhood asthma, is also defined as preexisting asthma. The extent to which these are preexisting conditions, or simply markers of host risk factors for asthma, remains to be determined.⁶⁶

In many of the US workers’ compensation systems, work-related conditions are defined on a medically probable (greater than 50% likely) basis that the need for treatment in a case is the result of a work-related exposure when certain factors are present. These factors include: (1) the work exposure causes a new condition; or (2) the work exposure causes the activation of a previously asymptomatic or latent medical condition to become symptomatic and now require treatment; or (3) the work exposure aggravates a preexisting symptomatic condition that now requires treatment that was not needed before. A helpful approach to determining whether a condition is work-related is recommended by the Colorado Division of Workers’ Compensation: would the patient need the recommended treatment if the work exposure had not taken place? If the answer is “no,” then the condition is most likely work related.⁶⁷ To establish that the worker had preexisting or concurrent asthma, the physician would need to verify an asymptomatic or well-controlled stable asthma pattern that had clearly changed due to a well-defined workplace irritant exposure. It is also incumbent on the physician to rule out the contribution of nonoccupational causes to the asthma exacerbation, such as GERD, infection, or rhinosinusitis.

Defining High-Level Exposure

What constitutes a high-level exposure may or may not be obvious. In cases of very high-level accidental releases where no respiratory protection had been worn, the high-level exposure is obvious. A good example is the massive exposure to airborne alkaline particulates following the World Trade Center collapse in 2001; this led to the development of asthma in many of the first responders.^{68–70} When explored, a dose-response has been noted,²⁸ but in most cases, no industrial hygiene monitoring data or dose reconstruction by an industrial hygienist are available. In less obvious cases, the physician can try to estimate the “dose” that was delivered to the lungs of the individual worker based on the intensity of the irritant exposure, the frequency, and the duration.

Intensity

Intensity is determined by the airborne concentration of the vapor, dust, gas, or fume, as well as the innate irritating properties of the chemical(s). Some chemicals are inherently more irritating than others.⁹ For example, those with very low, or worse, very high pH, are extremely irritating. When heated chemicals are inhaled, thermal injury may compound the damage.

A release may or may not be large. A worker very close to the source of a release may have a high concentration in his or her breathing zone that is not shared by others a little farther away, as the concentration of irritants can be fairly quickly dissipated through dilution with ambient air currents. Airborne concentrations will be much higher within a confined space because there is no such potential for dilution. Chemicals with very low vapor pressure can quickly volatilize in considerable quantity, particularly when heated. The size of the chemical particle and its water solubility will determine deposition within the respiratory tract, with the smallest and most water-insoluble chemicals having the greatest potential to reach the lower airways.

However, there does not need to be a release or other recognized event to signal exposure to high-level irritants. Not all workplaces will have appropriate engineering controls in place, such as enclosures and local exhaust ventilation, which can greatly minimize exposure to vapors, dust, gas, and fumes. Such controls need to have been installed and used correctly to be effective. Unrecognized failures of these control measures may result in unrecognized excess exposures, although such exposures may be limited to only a few individuals who work directly in the area. Air monitoring by an industrial hygienist can determine actual airborne concentrations, although if interim control measures have been implemented, these may not reflect the actual concentration at the time of the release or engineering control failure.

The amount of the vapor, dust, gas, or fume that reaches the lungs of the worker will be considerably decreased if respiratory protection is used, but only if it was used and worn correctly, and the exposure did not exceed the respirator's protective limits. A filtering respirator needs to have the correct cartridges for the exposure. For example, particulate filtering cartridges are highly effective in trapping airborne particulates but do not filter out irritant gases. Combined particulate (P100) and organic vapor cartridges are highly effective protection against many gases and vapors, as well as fumes and particulates. Filtering facepiece respirators are considered protective at concentrations up to 10 times the Occupational Safety and Health Administration (OSHA) Permissible Exposure Limit (PEL) for half-face respirators and up to 50 times the PEL with full-face respirators. However, the respirator will only have been effective to that level if it was worn properly sealed to the skin without facial hair, and the adequacy of the seal was confirmed by fit testing.

Frequency

The frequency of the exposure is relevant in considering exposures not confined to a single event, and should be considered along with duration.

Duration

The duration of the exposure before moving to fresh air is another important factor in determining "dose" in both high-level and lower-level exposures. Moderate to heavy physical exertion will increase tidal volume and respiratory rate, thus effectively increasing the amount of the irritant delivered to the lungs per unit of time.

SUMMARY

Acute high-level irritant exposures can cause asthma and exacerbate underlying asthma. Lower-level irritant exposures can at least exacerbate underlying asthma, although there is emerging consensus that recurrent lower-level exposures may also cause asthma. There is overlap between the exposures that have caused acute irritant-induced asthma and WEA, many of which are also sensitizers. What constitutes an excessive level enough to cause asthma from acute high-level or recurrent lower-level accidental releases is not currently defined. New-onset asthma in workers following lower-level irritant exposures, with no prior history of respiratory symptoms or asthma, may well be limited to a subset of “susceptible” hosts, such as those with asymptomatic airways hyperresponsiveness, atopy, and those who “outgrew” childhood asthma. But it is reasonable to consider asthma to more likely than not have been caused by such irritant exposures when previously asymptomatic workers develop symptomatic asthma following clearly defined workplace irritant exposures, the asthma is confirmed by objective testing, and other lung diseases and nonoccupational causes of the asthma have been excluded. This attribution of work-relatedness should also apply to workers with prior well-controlled stable asthma who sustain objectively documented changes in the pattern of their asthma.

Workers with irritant-induced and WEA should receive optimized asthma therapy. Equally important is the reduction and control of their exacerbating workplace exposures. Without the ability to receive this combination treatment, it is likely these cases of WEA will not be limited to temporary exacerbations, but will continue to experience the long-term disability and socioeconomic disadvantage that has been repeatedly observed. The ATS statement on WEA has identified research needs to better define risk factors, biologic mechanisms, and outcomes in WEA,²⁵ which should help to facilitate necessary interventions in the medical system, as well as to formulate and apply strategies for prevention.

The informed clinician should be prepared to identify and treat both new-onset and work-exacerbated asthma, and to partner with occupational and environmental medicine clinicians to address the challenges inherent in the diagnosis and treatment of irritant-induced and irritant-aggravated asthma.

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