22 Asthma exacerbated at work

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WORKPLACE SCENARIOS

A hospital began renovating patient rooms in one wing of the surgical floor. The improvements included removing all interior walls, erecting and painting new walls, applying new floor coverings, and replacing the electrical wiring, plumbing, and ventilation ducts. Many staff members working nearby were upset by the noise, and the cleaning staff complained about the increased demand on them to remove dust and grime coming from the renovation activities.

1. Renovation work can result in exposures such as dusts, paint fumes, and cleaning products that may exacerbate asthma symptoms.
2. A nursing aide with stable asthma cared for post-operative patients in the hospital. He was normally able to conduct his duties without breathing difficulties and required only occasional (<1×/week) use of a quick-relief inhaler in addition to his oral bronchodilator. During the past month, he started to experience more symptoms that required additional uses of his inhaler during the day. At one point, he felt his symptoms were escalating in frequency and severity and scheduled an urgent appointment with his physician. The physician was familiar with the patient's history of adolescent-onset, normally stable asthma, having previously performed a comprehensive work-up and periodic follow-up examinations. During the clinical interview, the physician asked about changes in the patient's environment or activities at home, work, and elsewhere. The patient described no changes at home or in daily activities, but noted construction crews had recently started to renovate space on his floor of the hospital.
3. The physician knew that identifying and minimizing workplace symptom triggers could help both her patient and other workers with asthma, as well as hospital in-patients and visitors. After obtaining permission from the patient, the physician contacted the hospital's Director of Health and Safety, being careful to protect her patient's confidentiality, and asked the Director to confirm that the area being renovated was adequately isolated from the rest of the hospital. Health and safety staff determined that shrouding and ventilation of the renovation area were inadequate and implemented changes to correct these problems. This greatly decreased the "bystander" exposures of staff working near the renovations, and the symptoms of the nursing aide returned to baseline over the following week. Since construction activities and personnel can change frequently in the course of a project, the physician urged her patient to monitor the situation and offered to assist again if the exposures recurred.

INTRODUCTION

Exacerbation of asthma can result from exposures at home, at work, in the outdoor environment, and in public buildings. There is a general agreement in clinical practice that troublesome home environmental exposures should be avoided; physicians generally advise asthma patients to rid their homes of carpets, drapes, and other furnishings that might be repositories for allergens. Asthma-related exposures in the work environment are less frequently addressed, because exposures are often beyond the control of employees and employers may or may not accept their responsibility or have the ability to control exposures. The issue of an affected employee's right to workplace accommodation or compensation further clouds the issue.

Work-related asthma (WRA) comprises occupational asthma (OA) that is caused by conditions at work and work-exacerbated asthma (WEA), in which preexisting or concurrent asthma is worsened by workplace conditions (1,2). While it is still true that WEA has received less attention in terms of research and prevention than OA, the number of articles that address WEA has increased considerably since the last version of this chapter was published in 2005. There has been a noticeable shift from studying only OA or all WRA cases (i.e., OA and WEA cases combined) to considering WEA as its own legitimate standalone outcome. An indication of the growing information about and interest in WEA was the publication in 2011 of an "Official American Thoracic Society Statement: Work-Exacerbated Asthma" (1). This chapter covers various topics related to WEA, including definitions, frequency, agents, characteristics of cases, clinical approach, prevention, and future research directions.

DEFINITIONS OF WEA

A clear definition of WEA can help clinicians and policy makers refine approaches to prevention, treatment, and compensation,

and is necessary for the continuing scientific investigation of the spectrum of WRA.

WEA describes a worsening from baseline respiratory health resulting from workplace exposures or conditions in any individual with asthma. WEA is the result of an interaction between an individual with asthma and the environment in which the individual works. As discussed in the 2011 statement from the American Thoracic Society (ATS) (1), the term WEA does not denote the underlying cause of the asthma or limit the candidate causes of exacerbation. The ATS appropriately defined WEA as a "worsening of asthma due to conditions at work ..." (1). For individuals with asthma at risk for WEA, their underlying asthma might have been caused by nonwork exposures or by work (either allergic or irritant-induced asthma). The etiology of the asthma is a separate and infrequently relevant consideration to understanding and responding effectively to WEA. As a rule, the triggers for the exacerbations are more relevant than the original asthma category or cause.

The ATS committee recognized the prime importance of temporality of symptom occurrence in their proposed case definition for WEA. The case definition includes the following considerations:

- Preexisting or concurrent asthma. Asthma onset may have either predated current work or may have first occurred while in the worksite of interest but was not caused by specific exposures in that workplace.
- Increased frequency of asthma symptoms, medication use, or health-care utilization is temporally associated with work. Medical test results may document more frequent abnormality.
- Workplace exposures or conditions exist that can exacerbate asthma.
- OA (asthma caused by a specific, identified workplace exposure) is unlikely.

A somewhat similar case definition has been used in the USA since the 1990s for public health surveillance in the Sentinel Event Notification System for Occupational Risks (SENSOR) (3). The SENSOR criteria for work-aggravated asthma are (*i*) health-care professional's diagnosis consistent with asthma, (*ii*) an association between symptoms and work, (*iii*) asthma symptoms or treatment with asthma medication within the 2 years before entering a new occupational setting, and (*iv*) increased asthma symptoms or increased asthma medication use upon entering a new occupational setting. There is a longitudinal component to this definition, stipulating that asthma onset and the presence of asthma symptoms or related medication use must come before entering the new occupational exposure setting, and the condition must worsen after entering. Thus, the clinician or researcher must obtain, either prospectively or retrospectively, the knowledge of asthma status before and after subjects enter a new occupational exposure setting. The SENSOR definition of work-aggravated asthma has a critical difference with definitions of WEA offered by the 2011 ATS statement and by a 2008 consensus document of the American College of Chest Physicians (ACCP) (2). Specifically, the later definitions include exacerbations of "concurrent" asthma, namely asthma that is first recognized after work begins in the workplace of interest but is not caused by conditions at work. The ATS and ACCP definitions recognize the reality that asthma may develop in working adults with or without documentation of specific workplace exposures and clinical testing that confirms OA, and may be exacerbated by exposures or conditions in that same workplace.

Medical records may be useful to document an asthma patient's change in status. For example, in a study of recruits who entered the Israel Defense Force at the age of 18–21 years, baseline asthma status was established at the time of induction into the military and repeated clinical evaluations documented changes in asthma status over time (4). However, in the absence of medical records, determination of the progression of disease will often depend, at least in part, on subject or patient recall. This is evident in the next section on the frequency of WEA, in which nearly all of the studies summarized in Table 22.1 used self-reported data gathered by questionnaire in clinical or population-based settings to determine WEA status. The specific definitions used in the literature reviewed in this chapter vary somewhat by investigation, but reflect common efforts to understand the causes, consequences, and frequency of workplace exposures and conditions that adversely affect the health of people with asthma.

FREQUENCY OF WEA

The committee that prepared the ATS Statement on WEA used PubMed to conduct a systematic search for relevant literature that incorporated terms for several topics (i.e., asthma, occupation, and exacerbation), covered the time period January 1980–August 2009, and yielded 1292 references of potential interest (1). The same search strategy was extended to January 15, 2012, and provided an additional 219 references. Review of abstracts for all 1511 references and full-text articles for selected references provided information summarized in the current section on frequency of WEA and in the following section on exposures.

To arrive at an overall estimate of WEA frequency, a review of references published in peer-reviewed journals between January 1980 and January 2012 identified 15 articles reporting on studies that determined WEA status on a case-by-case basis, made it possible to express the frequency of WEA as a prevalence in adults with asthma or in working adults with asthma, and was conducted in general population or general health-care settings (5–19). The 15 references included the same 12 references that were published in 1995–2007 and used in the 2011 ATS Statement on WEA to summarize prevalence, and three more references that were published in 2010 and provided five additional prevalence estimates. The five new estimates included one from a multinational study (13) and four based on Behavioral Risk Factor Surveillance System surveys conducted in specific states in the USA (16,19).

Table 22.1 Prevalence of Work-Exacerbated Asthma from Studies Conducted in the General Population or General Health-Care Settings

References	Country (and State if in the USA)	Study Setting and Number of Participants (% of Eligible)	Criteria for Asthma	Number of Asthma Cases	Age (yr)	Time Frame for WEA	Criteria for WEA (Self-Reported on Questionnaire Unless Indicated Otherwise)	WEA Prevalence	
								In all Adults with Asthma	In Working Adults with Asthma
Abramson 1995 (5)	Australia	FU 589 with asthma symptoms from G pop survey (74%)	SR asthma dx	159	Mean = 43	Ever	Respiratory symptoms at work associated with particular job	20%	NA
Blanc 1999 (6)	Sweden	FU 1562 in G Pop study (ECRHS) (65%)	SR asthma and BHR	160	20–44	Ever	Being at work ever makes chest tight or wheezy	38%	NA
Bolen 2007 (7)[a,b]	Massachusetts, USA	FU 95 employed asthma cases in HMO (25%)	Asthma dx by medical record	95	18–45, mean = 34	Current, tested 3 wk	Researchers judged pattern of serial peak expiratory flow rate consistent with WEA	NA	14%
Caldeira 2006 (8)[a]	Brazil	FU 1922 in birth cohort (93%)	SR asthma symptoms and BHR	227	23–25	Ever	Preexisting asthma worsened by exposure at work, based on interview information	13%	NA
Goh 1994 (9)	Singapore	802 asthma cases in large primary care clinics (63%)	Asthma dx by medical record	802	20–54	Current	Work environment is asthma trigger	27%	NA
Henneberger 2002 (12)	Colorado, USA	1461 asthma cases enrolled in HMO (71%)	Asthma rx or care by medical record	1461	18–44	Current job	Current work environment makes asthma worse	25%	NA
Henneberger 2003 (10)	Maine, USA	664 from random sample survey of G Pop (62%)	SR asthma dx and current rx	42 (28 employed)	18–65, mean = 42	Last 12 mo	Coughing or wheezing is worse at work than away from work	14%	21%
Henneberger 2006 (11)[a,b]	Massachusetts, USA	598 asthma cases identified in HMO records (61%)	Asthma care and dx by medical record	598 (557 employed)	18–44	Last 12 mo	Combination of relevant exposure as judged by researchers and self-reported work-related symptoms or medication use	23%, or 21% if more stringent criteria[c]	24%, or 22% if more stringent criteria[c]
Henneberger 2010 (13)	11 European countries and the USA	FU 9812 in G Pop study (ECRHS) (59%)	SR asthma dx and current in the past 12 mo	966 (employed)	29–56, mean = 42	Last 12 mo	Job held in past 12 mo made chest tight or wheezy	NA	22%
Johnson 2000 (15)[a]	Canada	FU 2974 in G Pop study (ECRHS) (39%)	SR asthma dx	106 (adult onset)	20–44	Current job	Wheezing or dyspnea at or after work in current job	34% wheezing and 31% dyspnea	NA
Johnson 2006 (14)[a]	Australia	5331 in G Pop study (ECRHS) (37%)	SR asthma dx	694 (employed)	18–49	Current	Asthma better on weekends or holidays	NA	18%

(Continued)

Table 22.1 Prevalence of Work-Exacerbated Asthma from Studies Conducted in the General Population or General Health-Care Settings (*Continued*)

References	Country (and State if in the USA)	Study Setting and Number of Participants (% of Eligible)	Criteria for Asthma	Number of Asthma Cases	Age (yr)	Time Frame for WEA	Criteria for WEA (Self-Reported on Questionnaire Unless Indicated Otherwise)	WEA Prevalence	
								In all Adults with Asthma	In Working Adults with Asthma
Lutzker 2010 (16)	MI, MN, and OR, USA	G Pop study–2005 BRFSS Adult Asthma Call-Back Survey (MI = 54%, MN = 67%, and OR = 63%)	SR asthma dx and SR current asthma	MI = 642; MN = 330; OR = 694	18 and older	Current job	Asthma made worse by chemicals, smoke, fumes, or dust in current job	MI = 21%; MN = 24%; OR = 18%	NA
Mancuso 2003 (17)	New York City, USA	Prospective study of 230 persistent asthma cases in primary care practice (39%)	Asthma dx by medical record	102 (employed)	18 and older, mean = 39	Current job	Asthma made worse by workplace conditions	NA	58%
Saarinen 2003 (18)[a]	Finland	1925 asthma cases in national health insurance system (74%)	Asthma dx by medical record	969 (employed)	20–65, mean = 43	Past month	Asthma symptoms caused or worsened by work at least weekly in the past month	NA	20%
Tice 2010 (19)	New York State, USA	G Pop study–2006 and 2007 BRFSS Adult Asthma Call-Back Survey (% of eligible not indicated)	SR asthma dx and SR current asthma	750	18 and older	Current job	Asthma made worse by chemicals, smoke, fumes, or dust in current job	16%	NA

[a]OA was determined unlikely when cases of WEA were identified.

[b]The participants in Bolen 2007 (7) were a subset of the study sample in Henneberger 2006 (11), but different methods were used to determine WEA status in the two studies.

[c]Thirteen study participants with asthma were judged not to have had relevant exposures at work, but were still considered to have WEA because they had reported an association between asthma and work in three different items on the questionnaire. With the application of more stringent criteria that required evidence of exposure, the prevalence of WEA was 21% (instead of 23%) among all adults with asthma and 22% (instead of 24%) among working adults with asthma (11).

Abbreviations: BHR, bronchial hyperresponsiveness; BRFSS, Behavioral Risk Factor Surveillance System; dx, diagnosis; ECRHS, European Community Respiratory Health Survey; FU, follow up; G Pop, general population; HMO, health maintenance organization; MI, Michigan; MN, Minnesota; NA, not applicable; OA, occupational asthma; OR, Oregon; rx, medications; SR, self-reported; WEA, work-exacerbated asthma.

Characteristics of the 15 studies with prevalence estimates are summarized in Table 22.1. One study was based on a common protocol implemented in 11 European countries and the USA (13), and each of the other studies was located in one of seven countries. Each reference provided one estimate of WEA prevalence except for the study by Lutzker and colleagues (16) in the USA, which reported three state-specific estimates. Few studies shared the same methods, but the definition of asthma was typically doctor-diagnosed asthma based on self-reports or review of medical records. Two studies included bronchial hyperresponsiveness (BHR) in the criteria for asthma (6,8). WEA was usually defined as a self-reported association between asthma symptoms and work, but three studies used more objective criteria (7,8,11). The 15 studies calculated prevalence as the percentage of all adults with asthma or all working adults with asthma. Since the second risk set was considered preferable for WEA, the prevalence estimate based on that denominator was used for two studies (10,11) that calculated estimates using both types of denominators. The 17 estimates of WEA prevalence from the 15 studies had a minimum of 13%, maximum of 58%, median of 21%, and an interquartile range from 18% to 26%.

These summary estimates for WEA prevalence varied little by several characteristics. For example, the median value for the nine estimates from the USA was 21% (7,10–12,16,17,19), the same as the median for all other countries (5,6,8,9,13–15,18). The median WEA frequency from the six studies conducted in general health-care settings (7,9,11,12,17,18) was only somewhat greater than from the general population studies (5,6,8,10,13–16,19) (23.5% vs. 21%, respectively; $p = 0.40$, Wilcoxon rank-sum test). The size of study cohort seemed to have little impact on the summary estimates, with medians of 21% for the nine samples with at least 500 asthma cases (9,11–14,16,18,19) and 22.5% for the smaller samples (5–8,10,15–17).

The three studies that used more objective criteria for WEA status yielded lower prevalence estimates (7,8,11). The researchers in one investigation interviewed young adults and reviewed the data collected to decide which participants with preexisting asthma had experienced worsening of symptoms due to exposures at work (8). In another study, the criteria for WEA specified a work-related pattern of serial peak expiratory flow rate (PEFR) (7). The third study defined WEA using a combination of self-reported work-related symptoms or medication use and a decision from an expert panel that the person had been exposed to workplace asthma agents (11). The prevalence estimates for these three studies with more objective WEA criteria were 13% (8), 14% (7), and 22% (11), respectively. The median of these three values was 14%, which was less than that of 21.5% from the other 12 studies, although the difference was not statistically significant ($p = 0.09$, Wilcoxon rank-sum test).

EXPOSURES ASSOCIATED WITH WEA

The medical literature was reviewed to identify the types of exposures most commonly associated with WEA (Workplace Scenario [1]). The literature search for the ATS Statement on WEA was extended to January 2012 (as explained in the earlier section on frequency of WEA) (1), and articles based on studies conducted in clinics or general population settings were selected with the goal of capturing the range of WEA triggers across different occupations and industries. Two types of investigations reported putative occupational agents for WEA or exacerbation of asthma. In one type, the authors compiled agents for individual WEA cases that had been identified in clinics, surveillance systems, or workers' compensation programs. In the other type of study, the authors used a risk set approach, modeling exacerbation or work-related exacerbation of asthma, and testing associations with occupational exposures while controlling for potential confounders.

Ten articles from the literature search reported on studies based in clinical or general population settings and identified triggers for individual WEA cases. Nine of the investigations were conducted in North America in the following settings: a primary care practice in New York state in the USA (17); an asthma clinic in the province of Ontario in Canada (20); occupational health clinics in the US states of New York (21), Massachusetts (22), and Washington (23); WRA surveillance systems in four US states (3) and in the province of Ontario (24); and workers' compensation programs in Ontario (25) and the US state of Washington (26). The final investigation was based on WEA cases from a tertiary asthma referral clinic in Belgium (27). The 10 articles summarized agents for 1034 WEA cases. Table 22.2 presents the 17 most common categories of agents among these cases, with each agent associated with at least 20 WEA cases. Taken together, the 17 agent categories in Table 22.2 account for 73% of the 1170 exposures attributed to the cases.

The WEA agents in Table 22.2 are arranged in descending frequency, and at the top of the list is a general category for chemicals ($n = 181$). This nonspecific label could denote uncertainty about the exact agent, or that the agent was known but the authors created this inclusive category to provide a concise summary of results. This category included 145 exposures to "miscellaneous chemicals and materials, referenced by use" from WRA surveillance in Washington state in the USA (26), 17 WEA cases exposed to "chemicals, not otherwise specified" from WRA surveillance in four states in the USA (3), 14 cases in a primary care practice in New York state attributed to "chemical smells" (17), and 5 cases with exposure to "highly reactive chemicals" from surveillance in Ontario in Canada (24). The second most common agent in Table 22.2 is dusts ($n = 114$), followed by smoke, pyrolysis products, and exhaust ($n = 60$), paints ($n = 57$), and cleaning products ($n = 51$). Many of the exposures in Table 22.2 are respiratory irritants, but there are also several agents capable of causing sensitization, with the most common being isocyanates and diisocyanates ($n = 44$), plant materials ($n = 36$), microorganisms ($n = 33$), wood dust ($n = 31$), and flour and grain ($n = 31$). However, exacerbation associated with these types of agents was not necessarily due to a sensitization response. Several nonchemical workplace factors reported as

Table 22.2 Common Categories of Agents for Cases of Work-Exacerbated Asthma[a]

Agent	Number of Cases	References
Chemicals[b]	181	(3,17,24,26)
Dust[c]	114	(3,17,20–22,24,25)
Smoke, pyrolysis products, and exhaust	60	(3,21,24,26)
Paints	57	(3,20,21,25,27)
Cleaning products[d]	51	(3,20,21,24,25,27)
Indoor air pollutants	46	(3,17,21,22)
Hydrocarbons	44	(23,26)
Isocyanates and diisocyanates	44	(3,24–27)
Solvents	37	(3,21–23,25)
Plant materials	36	(3,26)
Microorganisms	33	(26)
Wood dust	31	(24,25,27)
Flour and grain	31	(20,24,25,27)
Molds	25	(3,21,22,24,25)
Cigarette smoke	22	(3,17,20,22,25)
Animals and animal materials	20	(3,25,26)
Welding fumes	20	(3,21,22,25,27)

[a]From the 10 articles identified in the peer-reviewed literature.
[b]See text for comments on the chemicals category.
[c]Dust category includes construction, cement, and cardboard dust.
[d]Cleaning products include bleach and ammonia.

responsible for WEA in the 10 articles occurred relatively infrequently and are not included in Table 22.1. These included exercise (n = 13) (26), temperature (n = 5) (17), physical factors (n = 5) (26), and emotional stress (n = 2) (20).

Review of references from the literature search yielded two articles that reported studies conducted in general population settings that used a risk set approach to identify occupational exposures associated with exacerbation or work-related exacerbation of asthma. The findings from these two articles regarding agents are consistent with the findings for individual cases of WEA. In one of the two studies, the investigators used data from 969 working adults with asthma that were identified in the records of the national health insurance system in Finland (18). The outcome was the self-report that asthma symptoms were caused or made worse by work at least weekly in the past month. Workplace exposures were either self-reported or based on expert evaluations of occupational categories, and the regression models included covariates to control for age, sex, smoking, medication use, and adult versus childhood onset of asthma. Positive findings were reported for several self-reported exposures: dusts [odds ratio (OR) = 3.1, 95% confidence interval (CI) 1.9–4.9], poor indoor air quality or abnormal temperatures (OR = 2.2, 95% CI 1.5–3.2), physically strenuous work (OR = 2.0, 95% CI 1.4–2.8), and chemical agents or factors (OR = 1.5, 95% CI 1.1–2.2) (18). Also, from expert evaluation of occupational exposure, workers with probable (OR = 2.0, 95% CI 1.4–2.8) or possible (OR = 1.5, 95% CI 1.1–2.1) daily occupational exposure to dusts, fumes, or gases had elevated risk for work-related exacerbation of asthma symptoms compared to those who were rated as unlikely to have such exposure (18).

The other study that used a risk set approach was an international population-based study of respiratory health, conducted in 11 countries in Europe and the USA (13). The 966 participants were working adults with current asthma, and the outcome was self-reported severe exacerbation of asthma in the past 12 months. Occupational exposures included in the regression models were based on a job–exposure matrix, and the covariates included to control for potential confounding were age, sex, and smoking status. An association with severe exacerbation of asthma was reported for high gas and fumes exposure [relative risk (RR) = 2.5, 95% CI 1.2–5.5], high exposure to mineral dust (RR=1.8, 95% CI 1.02–3.2), and both low (RR=1.7, 95% CI 1.1–2.6) and high exposures (RR=3.6, 95% CI 2.2–5.8) to biological dust (13). Severe exacerbation of asthma was also associated with a summary category of high dust, gas, or fumes exposure (RR = 3.1, 95% CI 1.9–5.1).

The ATS Statement on WEA reviewed selected papers on the types of jobs and exposures associated with WEA and offered several observations (1). First, asthma can be exacerbated by a variety of workplace factors. Second, exposures capable of exacerbating asthma in non-occupational settings may also be relevant in occupational settings. The contents of Table 22.2 are consistent with both observations. Examples in Table 22.2 of the second observation include dusts, cleaning products, plant materials, molds, and cigarette smoke. The final observation concerned the lack of information about quantitative exposures related to WEA and what workplace exposure levels are safe for workers with asthma, suggesting the need for further investigation (1).

DISTINCTIVE FEATURES OF ADULTS WITH WEA

Clinical Characteristics

A few studies have compared workers with WEA to adults with non-WRA. The clinical characteristics of workers with WEA did not differ greatly from adults with non-WRA. Some studies reported that workers with WEA tended to be older (28,29), and others found an increased proportion of smokers in subjects with WEA (28,30).

Workers with WEA are often very difficult to differentiate from asthmatic subjects with OA, especially in cases who report a new onset of asthma while in the current workplace. The studies that compared subjects with WEA and OA report discrepant findings that can be explained by the different populations studied (general population vs. tertiary clinics). Based on cases in the USA that fulfilled SENSOR surveillance case definitions, Goe et al. (31) found that subjects with WEA were more likely to be female, young, nonwhite, and nonsmokers compared with those with work-related new-onset asthma. These findings were not confirmed in the studies where WEA cases were from a referral clinic and defined by a worsening of

Table 22.3 Distinctive Demographic, Clinical, Functional, and Inflammatory Characteristics of Subjects with Work-Exacerbated Asthma Compared to Those with Non-Work-Related Asthma or Occupational Asthma

Characteristics	Compared to Adults with Non-Work-Related Asthma	Compared to Adults with Occupational Asthma
Gender	Similar (28,29) or predominance of men in subjects with WEA (30)	Similar (30) or greater number of women in subjects with WEA (31)
Age	Older (28,29)	Similar or younger (31)
Race	More nonwhite (28)	More nonwhite (31)
Education	Less (28)	N/A
Smoking habits	More likely to have ever-smoked cigarettes (28)	More smokers (30)
Asthma severity	More asthma exacerbations requiring ER visits or hospitalizations in workers with WEA (30); More days with asthma symptoms; more severe asthma based on self-report (28)	Same number of asthma exacerbations requiring ER visits or hospitalizations (34); Greater need of ICS in subjects with WEA (34)
Functional characteristics	Similar FEV_1 and PC20 (30)	Higher PEF variability when at work in subjects with OA compared to those with WEA (34); PC20 may be lower in subjects with WEA (32)
Airway inflammation	Neutrophilic inflammation inconsistently found depending on the study (33,45)	Eosinophilic airway inflammation in subjects with OA when at work (33,34)

Abbreviations: ER, emergency room; FEV_1, forced expiratory volume in one second; ICS, inhaled corticosteroids; N/A, not applicable; OA, occupational asthma; PC20, provocative concentration of methacholine causing a 20% fall in FEV_1; PEF, peak expiratory flow; WEA, work-exacerbated asthma.

asthma symptoms when at work and a negative specific inhalation challenge (SIC) to the suspected agent(s) (32,33).

Lemière et al. (34) found that after adjusting for age, asthma control, and forced expiratory volume in one second (FEV_1), the diagnosis of WEA was associated with more frequent prescriptions of inhaled corticosteroids, a non-eosinophilic phenotype, and a trend toward a higher proportion of smokers than the diagnosis of OA (34).

The timing of the onset of asthma with respect to the start of employment at the workplace of interest does not necessarily differentiate WEA from OA. For example, from a clinical investigation conducted in Belgium, Larbanois et al. defined WEA by the presence of WRA symptoms and a negative SIC, and showed that only 7% of the 71 WEA subjects had asthma before employment (32). Also, onset of asthma prior to employment in the workplace of interest does not preclude the diagnosis of OA. Workers with previously diagnosed asthma can become sensitized to a new agent at their workplace and develop OA. An increase in asthma symptoms or severity is usually noticed at this time.

In both cases of WEA and OA, the workers complain of a worsening of their asthma symptoms when at work with an improvement when removed from exposure. Serial peak expiratory flow (PEF) monitoring can show a greater variability during periods at work compared to periods away from work in both types of cases, and the PEF variability is greater in subjects with OA than with WEA (35). However, the difference in the magnitude of PEF variability does not allow differentiating WEA from OA in clinical practice.

SIC testing can be performed to diagnose OA, with a positive result considered indicative of OA. Although false-negative tests can occur, a negative SIC favors the diagnosis of WEA. In several clinical studies, the definition of OA and WEA relied on the positivity or negativity, respectively, of SIC (33). However, those tests are not available in the majority of settings.

An eosinophilic phenotype is more frequently found in subjects with OA compared with those with WEA. Workers with OA usually show an increase in eosinophilic inflammation when exposed to the agents to which they are sensitized. In contrast, workers with WEA had no increase in eosinophilic inflammation when at work compared with periods away from work or during exposure to the suspected agents in the laboratory (33).

Table 22.3 summarizes demographic, clinical, functional, and inflammatory differences between subjects with WEA and subjects with non-WRA or OA.

Some risks factors have been associated with the diagnosis of OA rather than with the diagnosis of WEA. Atopy has been shown to be associated with sensitization to high-molecular-weight agents in subjects with OA (36,37). Smoking may also play a role in association with atopy in the risk of developing OA to some specific agents such as laboratory animals (38) and tetrachlorophthalic anhydride (39). Although some predisposing factors have been suggested for OA, no specific risk factors have been clearly identified for WEA.

Socioeconomic Impact

Data reporting the high costs of OA have been previously published (40,41). The health-care utilization of subjects with WRA has been previously reported and is much higher than the health-care utilization of non-WRA (30,42). Lemière et al. (34) recently investigated health-care utilization by WEA and OA cases compared to asthmatic controls. The health-care-related costs were similar between OA and WEA but were 10-fold

greater than the costs related to non-WRA (34). Although the health-care-related costs of the subjects with OA significantly decreased during the year following the diagnosis, this was not the case for the subjects with WEA. In a few studies in which the work disruption of subjects with WEA was evaluated, it was reported to be similar to OA (32,43). However, there are few studies that have looked at these outcomes. There is a high rate of unemployment in workers with WEA (30–50%) (32,44), which is equivalent to subjects with OA. Job changes occur also very frequently in subjects affected with WEA. The reduction in earnings also seems to be similar in WEA and OA (32).

Overall, WEA exerts a large socioeconomic impact on workers and society by using a large amount of health-care resources and inducing substantial disruption of work.

CLINICAL APPROACH TO WEA

Work-exacerbated asthma should be suspected in all patients whose asthma is difficult to control and in patients who complain of a worsening of their symptoms or who require an increase of their asthma medication when at work (2) (Workplace Scenario [2]).

Before establishing a diagnosis of WEA, the diagnosis of asthma needs to be confirmed by objective measures. Most asthma guidelines recommend the performance of spirometry, including the measurement of FEV_1 both pre- and post-bronchodilator in order to show a FEV_1 reversibility of 12% with an absolute increase in FEV_1 of at least 200 mL (46). In the absence of a reversible airflow limitation, the measurement of airway hyperresponsiveness can confirm the diagnosis of asthma. The lack of objective confirmation of the diagnosis of asthma can lead to misdiagnosis in 30% of cases (47). Furthermore, nonspecific respiratory symptoms are frequent and can mimic asthma in workers exposed to a dusty or irritant environment (48).

The diagnosis of WEA relies on the demonstration of a relationship between occupational exposures and the occurrence of asthma exacerbations, or poor asthma control during periods at work, combined with the determination that OA is unlikely. Asthma exacerbations or loss of asthma control can be documented by a change in the frequency and severity of asthma symptoms or by the need for an increase in asthma medications. Asthma exacerbations can also be documented by the occurrence of emergency visits or hospitalizations or by changes in respiratory function at work. Serial PEF monitoring can show increased variability during periods at work compared to periods away from work (35). Identifying the factors that trigger asthma symptoms is important not only to confirm the diagnosis of WEA but also to decrease or remove the adverse environmental conditions at the workplace. Identifying multiple triggers is common, since the workers are frequently exposed to several agents concomitantly.

Although there is limited data concerning the management of WEA, professional organizations have advised minimizing exposures at work and optimizing standard medical management for asthma (e.g., pharmacologic treatment and avoidance of symptom triggers) (1,2). Differentiating WEA from OA may be useful for asthma management. The approach used to differentiate one type of WRA case from the other should depend on the expected benefit to the patient and is likely to reflect the standards of practice where the patient resides. Although there is clear evidence that a persistent exposure to the occupational agent that caused their asthma is detrimental for workers with OA (49), the impact of continuing exposure to triggers for WEA has not been well studied. There is limited evidence that workers with OA may have a greater improvement in their lung function and asthma control than those with WEA when removed from exposure (34,50).

PREVENTION OF WEA

Exacerbations of asthma from workplace exposures or conditions can be prevented by modification of the work environment to reduce the frequency or intensity of exposure to triggers (Workplace Scenario [3]). This requires an understanding of what the work-related asthma triggers are combined with the knowledge, motivation, and opportunity to make changes that result in improved control or elimination of WEA. Standard industrial hygiene practices should be employed to control exposures to offending agents such as dust, fumes, and vapors. There is a conceptual "hierarchy of controls" guiding workplace interventions that focus on environmental change (eliminating, containing, or diluting toxic exposures, temperature controls), administrative change (job rotation or redesign), and, least effectively, personal protective equipment such as respirators.

In general, reduction of dusts, fumes, and vapors and other toxic exposures in the workplace, good housekeeping practices, control of ambient temperature and humidity, and maintaining a work organization that supports employee health and wellbeing and controls unnecessary stressors can benefit all workers, particularly those with asthma. A comprehensive respiratory protection program (involving proper selection, fit testing, and maintenance of respirators, as well as user training) is valuable where respirator use is a necessary or desirable supplement to environmental control of respiratory hazards.

Since WEA is the result of the interaction between the individual with asthma and their work environment, optimal medical management, including but not limited to pharmacologic management, is also appropriate. Unfortunately the dearth of long-term outcome studies comparing different management strategies limits confidence in any single approach. In particular, use of bronchodilator and anti-inflammatory medications may control symptoms and enable exposure to higher levels of triggering agents, but the long-term consequences of symptom control without environmental control of triggers have not been investigated adequately.

In reality, specific approaches to prevention of exacerbations in an individual with asthma through environmental interventions at work are often easier to describe than to achieve in practice. Prevention relies upon the following:

- Recognition by the affected individual, the health-care provider, and/or the employer that the work environment is triggering asthma in a susceptible individual

- Belief that changes in the work environment are possible
- Willingness of the affected individual to communicate health concerns to the employer and a pathway for this communication
- The willingness and ability of an employer to make the changes in the work environment needed to control or eliminate triggers

Clinicians are often instrumental in helping patients with asthma to recognize the connection between workplace conditions and exposures, and exacerbations. Careful inquiry may identify specific triggers and the patient may be able to act on the possibility of eliminating or controlling them.

Employers in large measure, both legally and in reality, are responsible for workplace practices and exposures that may trigger asthma exacerbations. They may, however, lack the knowledge, resources, or motivation to make changes in work processes, job assignments, or workplace organization, or not believe or understand that it is their responsibility to do so. In some instances, especially for small employers, flexibility to reduce or eliminate triggers may be limited.

Patients, particularly the most economically vulnerable, may be reluctant to request changes in work assignments or exposures. While there may be some level of legal protection for a worker with asthma requesting accommodation through work reassignment or redesign, for example, by the American with Disabilities Act (ADA) in the USA, the results of ADA litigation are inconsistent. Legal consultation with an attorney familiar with this area may be useful.

DIRECTIONS OF FUTURE RESEARCH

- Accurate exposure assessment is essential to estimating exposure–response relationships in clinical and epidemiologic studies. Improved methods are needed to characterize workplace exposures responsible for WEA. Identification of what exposure levels are safe for most workers with asthma would greatly assist prevention efforts.
- Additional research should elaborate whether subsets of people with asthma are at increased risk for workplace exacerbation. For example, are those who respond to specific identifiable triggers such as aeroallergens at increased risk for exacerbation in particular work environments?
- Prospective surveillance of newly hired workers (preferably apprentices) with histories of currently controlled asthma or asthma in remission in workplaces where asthma triggers are likely to be encountered would contribute to understanding the development and natural history of WEA. Outcomes of interest would include (*i*) the number and frequency of asthma flares, (*ii*) the effects of workplace exposure on asthma control or severity—both short term and long term, (*iii*) the extent of temporary or permanent time lost from work as a result of exposure, (*iv*) the health consequences of continuing employment at such worksites, (*v*) the responses to various interventions, and (*vi*) the amount of time required to resolve and reestablish control of asthma.
- General health surveillance programs should fine-tune annual incidence data by including the means to identify WEA among working participants with asthma.
- Additional studies are needed to exam the economic, social (e.g., family), and productivity impact of WEA over time.
- Evaluating the effectiveness of different interventions would help determine which strategies for reducing or eliminating exposures and for maximizing asthma care have the best chance of achieving primary prevention of WEA among those at risk and minimizing adverse outcomes among existing WEA cases.
- Further research is needed to determine whether having workers with WEA leave their workplace is more effective than maintaining workers with WEA at their workplace with optimal asthma care and reduction of exposures for achieving an adequate asthma control. The socioeconomic consequences of both approaches should be assessed and compared.

CONCLUSIONS

Exacerbation of asthma can result from exposures at home, at work, in the outdoor environment, and in public buildings. Asthma-related exposures in the work environment are less frequently addressed, because exposures are often beyond the control of the individual patient and an employer may or may not accept the responsibility or have the ability to control exposures. The issue of an affected employee's right to workplace accommodation or compensation further clouds the issue. Research demonstrates that WEA is an important source of work disability and economic loss, and is an appropriate target for prevention. Additional outcomes research can help define how to address this problem more effectively.

DISCLAIMER

The findings and conclusions in this chapter are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

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