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EDITORIAL ARTICLE

OCCUPATIONAL EXPOSURES AS A CAUSE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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INTRODUCTION

Diseases have causes and consequences. The precise etiologic causes of lung diseases have received more attention than those of many other illnesses, partly because the response of the lungs to external agents can be monitored (with lung function tests) with more precision than that of many other organs and partly because most lung diseases can be initiated by substances inhaled and these substances can be measured in the air we breathe (Meldrum, et al., 2005). There are huge variations in the incidence of lung diseases around the world. For instance, asthma is more than 40 times as common in some countries as in others, and it has increased by more than 200% in our lifetime (GOLD, 2005 and Becklake, 1985). Similar variations occur for lung cancer, chronic obstructive pulmonary disease (COPD), tuberculosis, and pneumonia. All of these diseases can be caused by exposures at work (Burge, 2000).

Chronic obstructive pulmonary disease (COPD) is becoming an increasingly important cause of morbidity and mortality worldwide. In the United States, COPD is now the fourth or fifth leading cause of death in those over age 45 years, and by 2020, it is expected to be the fifth leading cause of the total burden of morbidity and disability in the world (GOLD, 2005). The socioeconomic impact of this disease burden is tremendous. While cigarette smoking is clearly the major preventable risk factor for COPD, there is strong evidence that occupational exposures are another key preventable risk factor. An American Thoracic Society (ATS) statement on the subject indicated that 15% to 20% of the burden of COPD could be attributed to occupational exposures (ATS, 2003).

Diseases as pneumoconioses and asthma have features that distinguish occupational from nonoccupational causes. Occupational exposures can also lead to COPD and lung cancer, both of which can be caused by occupational and nonoccupational factors that produce indistinguishable disease that can only be attributed to a particular cause using epidemiologically derived estimates of risk (Burge, 2000). This article will review the scientific knowledge that supports such a statement.

DEFINITION

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) has defined COPD as "a disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles and gases" (GOLD, 2005). Chronic airway inflammation is currently believed to lead to remodeling of the small airways (so-called obstructive bronchiolitis) as well as to destruction of alveolar attachments to the small airways and parenchymal destruction (emphysema). The chronic airflow limitation of COPD results from the airway narrowing and loss of elastic recoil that result from these pathologic processes. The relative contributions of airway remodeling and emphysema to airflow limitation vary from patient to patient. Spirometry before and after inhaled bronchodilator medication remains the main diagnostic tool for assessing the presence of chronic airflow limitation.

As the classic mineral dust–induced pneumoconioses decrease in frequency due to control of exposure, obstructive airway diseases (asthma and COPD) have emerged as the most prevalent category of occupational respiratory disorder (Meyer et al., 1999). Unlike the pneumoconioses, recognition of work relatedness in COPD is difficult. COPD does not have a clinical subcategory that is clearly identified as occupational, largely because the condition develops slowly and, given that the airflow limitation is chronic, does not reverse when exposure is discontinued (Boschetto et al., 2006). Also, in addition to the fact that COPD is a multifactorial disease strongly associated with non-occupational exposure to tobacco smoke, the occupational dose-response and temporal relationships for COPD are complex. Nonetheless, because COPD is common in the general population, even a small increase in prevalence due to occupational exposures would have major public health impact and should be prevented (John and Balmes, 2007).

Some work-related obstructive airway disorders have been classified as COPD but do not neatly fit into this category. For example, work-related variable airflow limitation may occur with occupational exposure to organic dusts such as cotton, flax, hemp, jute, sisal, and various grains. Such organic dust-induced airway disease is sometimes classified as an asthma-like disorder (Bernstein et al., 1999), but both chronic bronchitis and poorly reversible airflow limitation can develop with chronic exposure. Bronchiolitis obliterans and irritant-induced asthma are two other conditions that may overlap clinically with work-related COPD. (Burge, 2000).

HISTORICAL CONSIDERATIONS

The recognition that occupational exposures can lead to breathing disorders long preceded the modern use of terms such as asthma, chronic bronchitis, emphysema, or COPD. As importantly, the link between "dusty trades" and clinical syndromes consistent with obstructive airway disease was also observed many years before cigarette smoking was widespread. Thackrah (1832), the early 19th century British pioneer of occupational medicine, observed that exposure to organic dusts produced airway disease in many trades, including malt workers, coffee roasters, rag paper makers, flax workers, and grain millers. He even commented about the potential diagnostic imprecision of the use of the term "asthma" to refer to the respiratory symptoms of coffee roasters. In his opinion, coffee roasters often suffered from "chronic bronchitis" rather than asthma.

In the 19th century, inorganic dust exposure was even more clearly noted to cause respiratory disease. Even as the generic term "pneumoconiosis" came into use to refer to inorganic dust–induced interstitial lung disease on a pathologic basis, the airway component of the respiratory symptoms of miners, metal workers, and other inorganic dust–exposed trades was recognized and clinically accepted (Holland, 1843 and Greenhow, 1869).

In the early 20th century, acute irritant gas inhalation from the use of chemical gas weapons in World War I provided clear evidence that inorganic chemicals could cause not only asthma, but also chronic bronchitis (Gilchrest and Matz, 1933).

The modern era of occupational pulmonary medicine has established beyond question the causal link between a large number of specific exposures and work-related asthma. All of the tools of the research, including epidemiologic investigations, controlled human exposures, and experimental animal models, have been brought to bear on this issue,. In contrast, the question of chronic airway obstruction in relation to occupational exposures has received relatively little attention. This is probably in large part due to the ascendance of cigarette smoking as the primary preventable risk associated with COPD.

The attention that has been paid to occupational exposures and COPD in recent years was largely spurred by the pioneering work of Becklake (1985 and 1989), who convincingly demonstrated that multiple studies of dust-exposed workers had demonstrated an accelerated rate of decline in ventilatory function.

In the 1984 Surgeon General's report, only smoking and alpha-1-antitrypsin deficiency were accepted as being causally related to COPD (Becklake,1998).

The topic "Chronic Obstructive Pulmonary Disease" was first used in the chapter on "Occupational Lung Diseases" in the LaDou textbook in the 3rd edition, published in 2004. In the previous edition published in 1997, the topic was "Chronic Bronchitis." The same list, "Some agents causing chronic bronchitis" appeared in both editions.

The topic "Chronic Obstructive Pulmonary Disease and Chronic Bronchitis" was first used in the Rosenstock textbook in the section on "Diseases of the Lung and Pleura" in the 2nd edition, published in 2005. In the first edition published in 1994, the topic was "Irritant Bronchitis."

The American Thoracic Society Statement: Occupational Contribution to the Burden of Airway Disease was published in 2003 and stated, "Despite the difficulty of disentangling the effects of cigarette smoke from those of other exposures, and increasingly impressive body of scientific literature is available demonstrating the specific occupational exposures contribute to the development of COPD." The committee considered the clinical spectrum of occupational airway diseases to include asthma, COPD, and organic dust-induced asthma-like disorders. Agents considered were for occupational asthma (over 250 agents), COPD (vanadium for bronchitis and cadmium for emphysema), and asthma-like disorders (endotoxins in cotton and grain dusts).

OCCUPATIONAL EXPOSURES AND COPD EPIDEMIOLOGIC EVIDENCE

Epidemiologic studies of chronic disease in the workplace is notoriously difficult, as workers who develop a chronic disease generally leave employment and only those who are relatively resistant to the effects of the occupational exposure remain to be studied. Research sometimes shows that workers with the highest exposures have the highest lung function. This situation is compounded by the healthy worker effect in that those who are at work are selected for their above-average health. These factors result in younger workers with exposures likely to cause occupational COPD being healthier than their referents and those with the most severe disease having been removed from the cohort, leaving a survivor population (Murray and Lopez, 1996). To overcome these problems several groups have studied community-based cohorts, usually utilizing measurements made during a survey (Murray and Lopez, 1996 and Burge 2000).

At present the main strength of community-based studies is their inclusion of all those living, whether fit or unfit for work; their weakness is the occupational groupings, employed, which combine many people with dissimilar exposures,

e.g. Agricultural workers (Burge 2000).

In longitudinal epidemiologic studies, a dose-response relationship between the amount of cigarettes smoked and an observed accelerated decline in ventilatory function has been consistently found (Higgins et al., 1982 and U.S. Surgeon General, 1984). However, this effect has consistently been confined to a minority of smokers (approximately 15%). Cigarette smoke is analogous to a mixed inhalational exposure at a workplace because it is a complex mixture of particles and gases.

Based on the known effects of cigarette smoking, there is a priori biologic plausibility for a similar response to inhaled workplace irritants. In contrast to smoking, however, epidemiologic assessment of the association between occupational exposures and COPD has not been straightforward. The challenges of such epidemiologic studies are multiple. First, COPD is multifactorial in etiology with critical (and for the most part unknown) host as well as nonoccupational environmental determinants of risk. Second, unlike workers with pneumoconioses, for example, individuals with COPD due to occupational exposures cannot be distinguished pathologically from those with the disease due to other causes. Third, many persons with COPD have concurrent exposure to cigarette smoke (direct and/or secondhand) and workplace irritants. Fourth, exposed persons in the labor force at baseline tend to have better overall health and higher ventilatory function than the general population, the so-called "healthy worker effect." Fifth, workforce studies are often limited to a "survivor" population due to inability to assess or follow workers who leave their jobs, thereby underestimating the chronic effects of occupational exposures (John and Balmes, 2007).

Despite the difficulty of disentangling the effect of cigarette smoke from those of other exposures, there is growing evidence from large population based studies in the last 20 years suggesting that a sizeable proportion of the cases of COPD in a society may be attributable to workplace exposures to dusts, noxious gases/vapours, and fumes (DGVFs) (**Meldrum**, **et al., 2005)**. Table 1. For example, some reports have highlighted associations with mineral dusts (Coggon & Taylor, 1998), welding fumes (Nakadate et al., 1998), cadmium fumes (Davison et al., 1988), and sulfur dioxide (Piirila et al., 1996). There is also evidence that acute obstructive changes in the airways predict subsequent chronic (e.g., fixed) airways obstruction (Becklake, 1995). This has been observed with workers exposed to plant dusts, such as cotton, grain, red cedar, and coffee bean, and also chemicals such as diisocyanates, irritant gases, and inorganic dusts. Longitudinal studies of the effects of occupational exposures have been performed in coal miners (Attfield & Hodus, 1992 and Seixas et al., 1993), hard-rock miners (Holman et al., 1987), tunnel workers (Ulvestad et al., 2001), concrete manufacturing workers (Meijer et al., 2001), and several community-based populations (Xu et al., 1992 and Humerfelt et al., 1993).

Table 1. Some Agents Causing Chronic Bronchitis.

Smoke	Minerals	Metals	Organic dusts	Gases
Engine exhaust	Coal	Osmium	Cotton	Diisocyanates
Environmental tobacco smoke	Man-made vitreous fibers	Vanadium	Grain	Sulfur dioxide
Fire smoke	Oil mist	Welding fumes	Wood	
	Portland cement			
	Silica			
	Silicates			

From the point of biologic plausibility, however, the salient feature of these epidemiologic studies is that they demonstrate a consistent dose-response relationship across a variety of specific industries (Attfield & Hodus, 1992 and Becklake, 1995) as well as in population-based studies (Xu et al., 1992

and Humerfelt et al., 1993) in which occupational exposures are more generically defined. Furthermore, the magnitude of effect is also in a range consistent with biologic plausibility, assuming that cigarette smoking is used as a benchmark (Becklake, 1994). Finally, the time frame of effect (latency) is also consistent with the established time course of the clinical entities in question: chronic bronchitis, chronic airflow limitation, and emphysema.

Quantitative pathologic assessment of emphysema as an outcome variable has confirmed a relationship between dust exposure and degree of emphysema in several studies of coal (centrilobular emphysema) and hard-rock miners (panacinar emphysema). The relationship is stronger among smokers than nonsmokers (Ruckley et al., 1984) and easier to demonstrate when coal dust–induced fibrosis is present (Leigh et al., 1994).

The strongest evidence implicating occupational exposures in the pathogenesis of COPD comes from community-based studies. Community-based studies have demonstrated increased relative risks for respiratory symptoms consistent with COPD as well as for excess annual declines in forced expiratory volume in 1 second (FEV1) associated with occupational exposure to dusts or gases (Xu et al., 1992, Humerfelt et al., 1993, Fishwick et al., 1997, Post et al., 1994 and Sunyer et al., 1998).

The fraction of cases in a population that arise because of certain exposures is called the attributable fraction in the population or the population attributable risk (PAR). The American Thoracic Society (ATS) recently produced a consensus statement based on an evaluation of a number of large scale general population studies, and calculated that PAR for COPD was about 15% (Balmes et al., 2003). Several recent papers published since the completion of the ATS statement provide further evidence in support of a major contribution of occupational exposure to the burden of COPD. Hnizdo and coworkers in 2002, analysed the industries with increased risk including rubber, plastics, and leather manufacturing, utilities, building services, textile manufacturing, and construction. The PAR for COPD attributable to work was estimated at 19% overall and 31% among never smokers. A second US population-based study conducted by Trupin and coworkers (2003) showed that the PAR for COPD caused by the occupational exposures was 20%. In this study, the PAR for combined current and former smokers was 56%. Smoking and occupational exposures to dusts, gases, and/or fumes had greater than additive effects. A third cohort study from Sweden by Bergdahl et al., (2004)was designed to determine whether occupational exposure of male construction workers to dust, fumes, or gases, irritant chemicals, and wood dusts, especially among never-smokers, increased the mortality from COPD. An internal control group with "unexposed" construction workers was used, and the analyses were adjusted for age and smoking. There was a statistically significant increase in mortality from COPD among those with any airborne exposure (relative risk 1.12). In a Poisson regression model, exposure to inorganic dust was associated with an increased risk, especially among never-smokers. The fraction of COPD among the exposed attributable to any airborne exposure was estimated as 10.7% overall and 52.6% among never-smokers. Thus, occupational exposure among construction workers increases mortality due to chronic obstructive pulmonary disease, even among never-smokers.

The determination of the PAR% due to occupational exposure has been complicated until recently by the lack of standardization of definition for COPD. Moreover, relatively few studies have been conducted with the specific purpose of determining the occupational contribution to COPD in the general population. In the studies that have been performed, there has been no consistency in terms of a strict definition of COPD. Some have presented data on symptoms and diseases, others have presented data on lung function, and a few have done both. Although a certain degree of standardization has been accomplished for cough and phlegm, dyspnea has

been defined more variably among the studies.

While cigarette smoking and occupational exposures appear to account in combination for the major proportion of the population attributable risk of COPD, other influences are potentially important. The understanding of genetic susceptibility to this condition is still in its relative infancy, but certain data do suggest that genetics influences may be important (Molfino, 2004), when considering both the established disease and the accelerated annual decline in FEV1. Furthermore, interactions have been noted between α1 anti-trypsin deficiency and environmental exposures in the development of COPD (Balmes et al., 2003).

OCCUPATIONAL EXPOSURES AND COPD: EXPERIMENTAL EVIDENCE

Relevant experimental models of the pathologic processes, obstructive bronchiolitis, emphysema, and mucus hypersecretion, exist and can be used to evaluate the biologic plausibility of occupationally related COPD (Barnes, 2000).

Protease–antiprotease imbalance has long been hypothesized to be an important feature of the pathogenesis of COPD, especially with regard to the loss of elastin in lung parenchyma that is pathologically associated with emphysema. Neutrophil elastase, proteinase 3, and cathepsins have all been shown to produce emphysema in animal models (Stockley, 1999). These serine proteases are also potent mucus secretagogues and thus may contribute to the mucus hypersecretion that characterizes chronic bronchitis (Sommerhoff et al., 1990) metalloproteinases (MMPs) may have a role in emphysema (Finlay et al., 1997 and Ohnishi et al., 1998) and, in addition, may generate peptides that are chemotactic for macrophages. The role of macrophages may be more pivotal than previously appreciated, and there is increasing evidence of an important role for lymphocytes as well (Saetta et al., 1998 and Di Stefano et al., 1998; and Pesci et al., 1998).

The best human model of emphysema in relation to protease imbalance is that of α1-antitrypsin deficiency (Barnes, 2000). Because α1 anti-trypsin is the endogenous inhibitor of neutrophil elastase and neutrophil elastase is capable to cause alveolar destruction, it has long been considered the major player in the development of emphysema. Although smoking is the most potent and well-established cofactor in emphysema related to α1-antitrypsin deficiency, occupational exposures are clearly linked to such disease as well (Putulainen et al., 1997 and Mayer et al., 2000). As such, it appears entirely plausible that work-related exposures may impact protease–antiprotease balance.

The occupationally relevant agents, other than cigarette smoke, that can cause emphysema (cadmium, coal, endotoxin, and silica) in animals, all cause the centrilobular form of the disease rather than the panacinar form that is associated with α1 anti-trypsin deficiency so mechanisms other than uninhibited neutrophil elastase activity are likely operative. The recent evidence about Matrix metalloproteinases suggests a potential mechanism by which inhaled dusts or fumes could cause emphysema since macrophages have a primary role in the clearance of these materials from the terminal airways and alveoli (Boschetto et al., 2006).

Evidence suggests that oxidative stress plays a role in the development of COPD, perhaps through activation of proinflammatory cytokines (Barnes, 2000). Here again, there is ample biologic plausibility for a role in occupational exposures. Although inhalation of tobacco smoke generates increased oxidative stress in the airways and lung parenchyma, many occupational exposures (e.g., oxides of nitrogen, residual oil fly ash, transition metals) are also capable of causing oxidant injury (MacNee, 2000).

ORGANIC DUST–INDUCED OBSTRUCTIVE AIRWAY DISEASE

Some work-related airway disorders do not fit neatly into either asthma or COPD categories. Work-related variable airflow limitation may occur with occupational exposure to organic dusts such as cotton (byssinosis), flax, hemp, jute, sisal,

and various grains. Such organic dust–induced airway disease is often classified as an "asthma-like disorder" rather than as true asthma (Bernstein et al., 1999). The stated rationale for this distinction includes lack of airway eosinophilia, less frequent airway hyperresponsiveness, and, finally, a tendency to develop both chronic bronchitis (by clinical definition) and poorly reversible airflow limitation with chronic exposure.

Longitudinal studies of workers chronically exposed to cotton or grain dusts have shown these workers to have increased prevalence of cough and phlegm and accelerated annual decline in lung function (Glindmeyer et al., 1991, Chan-Yeung et al., 1992 and Niven et al., 1997). A dose-response relationship and a potential interaction with smoking have also been demonstrated for both cotton and grain dust–induced chronic airflow limitation (Tabona et al., 1984 and Glindmeyer et al., 1991). The concentration of endotoxin in the inhaled dust may be more critical to the development of respiratory symptoms and airway disease than the level of total cotton or grain dust (Kennedy et al., 1987 and Schwartz et al.,1995), although the role of other cofactors has not been excluded.

The airway response to organic dust inhalation appears to be primarily mediated by nonallergic inflammatory mechanisms (Tabona et al., 1984). The results of in vitro studies demonstrate that grain dust can activate complement and induce alveolar macrophages to release neutrophil chemotactic factors (Von Essen et al., 1988). Moreover, both animal and human studies have shown that inhaled grain dust can cause recruitment of neutrophils to the proximal and distal airways (Von Essen et al., 1988, Schwartz et al., 1994 and Jagielo et al., 1996). Animal studies have shown that responsiveness to endotoxin is critical to the development of grain dust–induced airway inflammation and airflow obstruction (Gordon et al., 1991). Human challenge studies with cotton dust also suggest that neutrophilic inflammation and endotoxin responsiveness are important components of acute "byssinosis" (Castellan et al., 1987). Although the mechanisms underlying the development of chronic bronchitis and poorly reversible airflow limitation in association with occupational exposures to grain or cotton dust are less clear, there is sufficient epidemiologic and experimental evidence to support the biologic plausibility of these exposures in the etiology of COPD.

OCCUPATIONALLY-RELATED COPD DIAGNOSIS

Cigarette smoking is by far the predominant risk factor for COPD. Till today, diagnostic assessments able to calculate the relative contribution of work exposures in a smoker with COPD are not available. However, adjustment of associations between occupational exposure and COPD for smoking status has been performed in epidemiological studies, showing that occupational risks likely play a role on their own. Thus, physicians must be aware of the potential occupational aetiologies for obstructive airway disease and should consider them in every patient with COPD. An occupational history should be the first step in the initial evaluation of the patient. A proper occupational history consists of a chronological list of all jobs, including job title, a description of the job activities, potential toxins at each job, and an assessment of the extent and duration of exposure. The length of time exposed to the agent, the use of personal protective equipment such as respirators, and a description of the ventilation and overall hygiene of the workplace are helpful in attempting to quantify exposure from the patient's history (Boschetto et al., 2006).

Additional information can be obtained from a visit to the workplace by experts in occupational hygiene, from material safety data sheets for workplace chemicals, and from the manufacturers of the workplace substances.

Identifying occupational risk factors on the individual level is important for prevention of disease before it is advanced and for modifying disability risk once disease is established (Petty and Weinmann, 1997). In addition, the clinician has a critical role in case identification for the

purposes of public health surveillance and appropriate work-related insurance compensation.

ENVIRONMENTAL AND OCCUPATIONAL EXPOSURES: DO THEY AFFECT CHRONIC OBSTRUCTIVE PULMONARY DISEASE DIFFERENTLY IN WOMEN AND MEN?

There is growing evidence that COPD mortality and morbidity is rising among women relative to men, and it has been hypothesized that this may be linked to an increase to tobacco exposure or susceptibility among women (Mannino et al., 2002 and Prescott et al., 1997). Other evidence indicates that smoking rates among adult women have declined in parellel with men since 1980s, at least in Western countries (US Department of Health and Human Services, 2001), suggesting that other factors must also be contributing to the apparent rise in COPD among women.

If it is true that women are more susceptible than men to the effects of one inhaled pollutant (i.e. tobacco smoke), it raises the question: Are women more susceptible than men to the effects of other inhaled pollutants, namely those found in work, residential, or community environments? Very few studies of the health impact of occupational or environmental exposures have investigated gender differences in the outcomes or in exposure.

A systematic literature review of a total of 73 articles (since 2000) reporting on occupational and environmental exposures and their impact on chronic obstructive pulmonary disease was performed, of which only nine provided gender-stratified results. In two mortality studies, results were contrary (one finding increased chronic obstructive pulmonary disease mortality in relation to traffic among elderly women compared with men, the other finding no gender difference). Two other environmental studies suggested small gender differences with slightly greater effect of biomass or traffic-related pollution among women. Four of five occupational studies also found increased effects of workplace pollutant exposure on measures of chronic airflow obstruction or bronchitis symptoms in women; again the differences were small. Preliminary findings from analysis of pooled data from six cross-sectional occupational surveys also indicated increased relative risk for airflow obstruction in relation to work in industrial or service jobs among women compared with men, but only when airflow obstruction was measured using a gender-specific approach to determining the lower limit of normal. The development of gender-sensitive tools is needed for conducting future research in this area as well as populations sufficiently large to permit gender-stratified analyses (Kennedy et al., 2007).

OCCUPATIONALLY-RELATED COPD: MANAGEMENT AND PREVENTION

Directions about the management and prevention of work-related diseases (Felton, 1982), can be applied to COPD as well. Prevention must be the primary tool for decreasing the incidence of and morbidity and disability from work-related COPD, which can become a severely disabling disease. Prevention must involve cooperation between employers, workers, and their representatives, regulators, and medical personnel (Friedman-Jimenez et al., 2000).

Guidelines for the identification and management of individuals with work-related asthma were published in 2000 and are relevant to work-related COPD (Friedman-Jimenez et al., 2000).

The treating clinician should attempt to understand the patient's occupational exposures and whether he or she has been adequately trained in the dangers of these exposures and how to avoid them. Effective clinical management requires efforts to reduce exposures and treatment with appropriate medications.

Unlike workers with sensitizer-induced asthma, workers with irritant-induced COPD may continue to work in their usual jobs if their exposure to the inciting agent is diminished via proper engineering controls or respiratory protective equipment, if engineering controls are not feasible. However, the effective use of personal protective equipment requires that the appropriate equipment be selected, properly fit tested,

maintained, and worn when there is potential for exposure. The failure to properly carry out any one of these essential tasks may cause failure of personal protective equipment to prevent exposure; thus, it is not surprising that data regarding the efficacy of such equipment is equivocal (John and Balmes, 2007).

Primary prevention is designed to abate hazards before any damage or injury has occurred. Primary prevention strategies include the same exposure controls (i.e., elimination, engineering controls, administrative controls, personal protective equipment) described for management of work-related COPD due to irritant exposures. As cigarette smoking is the main risk factor for COPD, smoking should be discouraged outside the workplace as well as inside the workplace (Balmes, 1991).

Another important component in the prevention of irritant-induced COPD is surveillance for these diseases in the workplace. Surveillance programs are a type of secondary prevention, in that their principal goal is the early detection of disease so that its duration and severity can be minimized. For medical surveillance of COPD, short symptom questionnaires can be administered before employment and repeated annually. They should include items such as improvement in respiratory symptoms on week-ends and holidays (Venables, 1994 and Tarlo et al., 1998). In addition, spirometry can be performed on an annual basis and compared to baseline spirometric testing at the time of hire. Review of peak expiratory flow rate records over several weeks can also detect workers at risk for developing irritant-induced COPD.

Tertiary prevention aims at the prevention of permanent COPD. It includes institution of appropriate health care. Furthermore, early recognition of the disease and early removal from, or reduction of, exposure, make it more likely that the patient will avoid permanent COPD (Tarlo et al., 1998).

Industrial hygienists can perform environmental monitoring to ensure that appropriate engineering controls are in place to protect worker safety. Reviewing and updating lists of agents used at a given workplace should be performed on a periodic basis to identify possible respiratory tract irritants.

Public policy needs to be better informed about the roles of occupational factors in obstructive airway disease. This will require active education and outreach on the part of the medical-scientific community. Specific public policy issues to be re-examined in light of the magnitude of the occupational contribution to the burden of airway disease include standard setting for exposure in and out of the workplace, attribution criteria for compensation, health care costs and their assignment, and health care resources allocation (Boschetto et al., 2006).

The clinician must be aware of the potential occupational aetiologies for obstructive airway disease and consider them in every patients with asthma or COPD. Identifying occupational risk factors on the individual level is important for prevention of disease before it is advanced and for modifying disability risk once disease is established (Petty and Weinmann, 1997) .In addition, the clinician has a critical role in case identification for the purposes of public health surveillance and appropriate work-related insurance compensation.

CONCLUSIONS

There is growing evidence that a sizeable proportion of the burden of COPD in the developed world is attributable to workplace exposures to irritating dusts, gases, fumes, and smoke (Fishwick et al., 1997). In the developing world, population data are less readily available, but because occupational exposures are often higher, it stands to reason that the risks are likely higher as well (Christiani, 2005). Morbidity and mortality from COPD are projected to increase worldwide over the next several decades (Burge, 2000). Given that one in five cases may have an occupational contribution, occupational health professionals and public health policy makers now need to consider actions to reduce exposures to inhaled irritants at the workplace. Research is also

needed to provide better understanding of both mechanisms by which irritant exposures cause COPD and to provide effective interventions to reduce such exposures to prevent the disease.

Besides epidemiological studies, further animal experimental studies can lead to a better understanding of the occupational hazards which may cause COPD and establish a stronger link between the severity of COPD and specific occupations. Experimental studies may actually serve as models from which to derive basic insights of COPD and to identify a cellular basis of the work-related disease.

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