CHAPTER 11

Occupational lung disease in women

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Workplace exposure to a variety of occupational agents can lead to diverse diseases, including most major chronic respiratory diseases (table 1) [1–3]. One agent may cause several disorders, while one disorder may have several occupational causes. Workers have marked differences in susceptibility to occupational substances (*e.g.* beryllium, diisocyanates, complex platinum salts), due to genetic polymorphisms, which can produce variations in the rate and pathway of metabolism. Other factors, including atopic predisposition, nutrition and other host factors, as well as home and nonwork related exposures, may explain the occurrence of other diseases in certain individuals and not others. Gender clearly plays a role in distribution of occupational lung disease, since there are gender differences in specific occupations and therefore differences in prevalence of exposure to agents causing occupational lung diseases. In addition, there are gender differences in overall reported prevalence of adult asthma, with a higher rate in women [4, 5], and there is a suggested increased susceptibility of women to smoking-related chronic obstructive lung disease (COPD) [6]. Similarly, there could potentially be gender differences in response to the same workplace exposures, but to date, this difference has not been clearly shown. Identification of a workplace-related cause of disease is important because it can lead to prevention of significant morbidity and mortality, not only for the affected individual, but also for other workers in the same environment.

Occupational lung diseases include bronchitis, bronchiolitis, asthma and other obstructive lung disease, interstitial lung disease, pneumoconiosis and lung cancer. The incidence of disease caused by mineral dust has declined in many countries, although is still a significant problem in developing countries [7]. Mining-related lung disease has remained the most common occupational lung disease in South Africa [8] and silicosis has been noted to be common among workers in slate pencil factories and agate workers in India [7]. Asbestos exposure is also common in developing countries [7], although there is little published information on the prevalence of occupational lung diseases in women in these countries. However, asthma has emerged as the principal occupational lung disease in many industrialised nations, as reflected by other surveillance programmes (Surveillance of Work Related and Occupational Respiratory Disease (SWORD), Physician-Based Surveillance for Occupational Respiratory Diseases (PROPULSE)) [9, 10]. Since women remain a minority in mining-related occupations and some other occupational areas, such as welding and construction, but have relatively frequent exposure to workplace asthmagens, most of the focus of this chapter will be on occupational asthma (OA).

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Table 1. – Examples of lung diseases in occupations relatively common for women and some causative agents

Selected disease examples and some associated occupations	Some causative agents
Occupational asthma	
Healthcare workers	Natural rubber latex
	Psyllium and other pharmaceutical agents
	Glutaraldehyde
	Formaldehyde
	Spills of cleaning products
Animal care workers (*e.g.* laboratory workers, farmers, veterinarians)	Animal proteins
	Natural rubber latex
	Pharmaceutical compounds
Food industry workers (*e.g.* bakers, farmers, food processors)	Flour
	Enzymes
	Storage mites
	Eggs and other foods
Hairdressers	Natural rubber latex
	Persulphates
	Phenylenediamine
Textile workers	Reactive dyes
	Textile dust (maybe from endotoxins)
Cleaners	Common indoor allergens (dust mites, cockroaches, animals, fungi)
	Cleaning agents
	Irritant mixtures
Industrial chemicals	Diisocyanates
	Amines
	Colophony
	Acid anhydrides
	Epoxy compounds
Byssinosis	
Textile workers	Textile dust
	Endotoxin
Bronchitis	
Industries/occupations with dusts, smoke and fumes	Irritant dusts
	Fumes
	Smoke
Inorganic dust diseases (*e.g.* silicosis, asbestos-related diseases, chronic beryllium disease)	
Ceramic and vitreous enamelling workers	Silica
Former asbestos workers	Asbestos
Metal alloy workers, aerospace/electronic/metallic goods workers	Beryllium
Hypersensitivity pneumonitis	
Farmers	Thermophyllic actinomycetes
Avian workers	Avian antigens, fungi
Office workers	Contaminated humidifiers
Machinists	Contaminated metal working fluids
Lung cancer	
Asbestos-exposed workers	Asbestos
Paint/dye manufacturers, tanners	Hexavalent chromium

Workplace exposures

Women make up a significant percentage of the workforce. In developing countries women (and children) may dominate the workforce of traditional handicraft industries,

with subsequent exposure to textiles, metals and stone polishing [7]. In developed countries, there is also the existence of certain occupations that are female dominated (*e.g.* healthcare workers, textile workers and domestic/office cleaners), but women are increasingly entering professions that were previously male-dominated. SETA *et al.* [11] have reported relative exposure of women to potential asthmagens as determined from an older survey, The United States National Occupational Exposure Survey database. This database collected workplace exposure data in the USA in 1981–1983 from 4,490 facilities representative of nonagricultural, nonmining and nongovernmental businesses covered under the Occupational Health and Safety Act of 1970. Female employees accounted for 29% of all employees exposed to potential asthmagens. They accounted for <50% of exposed employees in most categories of asthmagen exposure, *e.g.* 16% of all employees estimated to be exposed to diisocyanates. However, women represented >50% of the employees with workplace exposure to textiles (68%), pharmaceuticals (65%), flavours/condiments (63%), tobacco (58%) and animal enzymes (55%). Among women with exposure to a potential asthmagen, the most commonly identified exposures were textiles (15%), metals (12%), foods or animal-derived proteins (8%), woods (7%), vegetable gums (6%) and amines (3%).

A more recent analysis of workers' compensation data in Ontario, Canada showed a significant increase in the proportion of women among accepted claims for OA in 1987–1993, as compared with the previous 7 yrs, perhaps reflecting changes in proportions of women in exposed workplaces [12]. The percentage of women increased from 28 to 45% for claims accepted for OA related to diisocyanates ($p=0.001$), and from 20 to 36% for OA related to all other causes ($p=0.001$). Although information from compensation sources is limited to those who are eligible and apply for compensation, there is not known to be a gender bias in these factors.

A Canadian survey undertaken in 1993–1994 indicated that 56% of men and 34% of women reported dust exposure at work and 45 and 24%, respectively reported gas and fume exposures [4]. The percentage of men and women who changed or left work because it affected their breathing was 4.5 and 3.4%, respectively, the gender difference possibly reflecting the difference in reported exposures.

Asthma and the workplace

Estimates of the extent of the role of the workplace in adult asthma have varied with the methods used to assess this. Problems in cross-sectional studies of workers include the "healthy worker effect", wherein those who have stopped working due to their asthma are not included in statistics. Many studies have not distinguished between OA and workplace aggravation of asthma. Prevalence studies have estimated the workplace to be responsible for ~5–10% of all adult-onset asthma and ~16% of adult asthmatics report that their asthma is worse at work [13, 14]. Using different methods, a recent incidence study in Finland estimated the occupational attributable fraction for persistent adult-onset asthma to be 29% in men and 17% in women [15]. When adjusted for the assumed confounding effect of cigarette smoking, the attributable fractions for men and women were 23 and 20%, respectively. More than 250 substances found in the workplace have been implicated in OA and each year new substances are added.

OA can be classified as irritant induced (with no latency period) or asthma caused by a sensitising agent with a latency period of exposure and a demonstrated or presumed immunological mechanism. Single or multiple exposures to a potent nonspecific respiratory irritant in high concentrations can cause reactive airways dysfunction syndrome (RADS), otherwise known as irritant-induced asthma. Irritant-induced

asthma results in extensive desquamation of the epithelium, with epithelial cell ciliary abnormalities, smooth muscle hyperplasia and subepithelial fibrosis and increased numbers of inflammatory cells. Initial reports of RADS and irritant-induced asthma were predominantly in men [16, 17]. However, there are also some reports in women and in a recent survey of compensation claims, five of 12 claims accepted were in women [18]. The diagnosis is circumstantial, depending on the onset of asthma symptoms within 24 h of a high, usually accidental, irritant chemical exposure, persisting for at least 3 months, with objective documentation of asthma, in a patient with no known underlying respiratory disease. It appears to account for a minority of cases of OA (~7–15%) [9, 15, 17, 19]. The apparent lower proportion of women in several reports of irritant induced asthma may reflect less exposure to industrial spills/accidents or might reflect gender differences in smoking history and/or differences in inhaled aerosol distribution, as discussed later. The risk of asthma from nonmassive irritant exposures is unclear at present. LEUENBERGER *et al.* [20] chose never-smokers randomly from eight areas in Switzerland and tested nonspecific bronchial reactivity using methacholine challenge. Methacholine slopes were found to be 19% higher for never-smokers with exposure to dusts, fumes, vapours, gases and aerosols, than for the unexposed group. The effect was more significant among atopic subjects.

Sensitiser-induced OA accounts for ~90% of OA and is often induced by high molecular-weight biological proteins (*e.g.* animal or plant proteins) that stimulate production of specific immunoglobulin (Ig)E. Some low molecular-weight agents can act as haptens, *e.g.* complex platinum salts and epoxy compounds, which also induce OA due to a specific IgE-mediated mechanism [21, 22]. Specific allergens bound to IgE cause degranulation of mast cells, with release of preformed and newly generated mediators causing immediate asthmatic responses. In addition, cytokine activation results in an influx of inflammatory cells and further release of inflammatory mediators resulting in the late asthmatic response. Low molecular weight substances, such as diisocyanates (found in polyurethane foam production, spray paints and glues) and plicatic acid from Western red cedar, can also act as clinical sensitisers causing OA, but specific IgE antibodies have usually not been identified. The mechanism of response to these agents is presumed to be immunological and the inflammatory airway response in such patients is similar to those with IgE-mediated responses [23]. Since the best prognosis from OA has been clearly shown to relate to an early diagnosis with early removal from ongoing exposure to the causative agent, at a time when asthma is relatively mild [24, 25], it is very important that this diagnosis is considered in all working women with asthma and that appropriate objective investigations be initiated early [26].

The third manner in which asthma can relate to the workplace is the transient aggravation of non-OA by workplace irritant exposures. An example would be a woman with asthma since childhood, who works as a house cleaner and notes worsening of her asthma when using irritant cleaning agents, such as oven cleaners and bleach. Although this form of asthma is not usually considered to be OA, it is a true work-related respiratory effect, which may in some cases have an impact on the ability of the worker to continue to work in such an environment, despite adequate asthma management. There are relatively few studies on the prevalence of this form of asthma in contrast to OA. In Ontario, where workers' compensation claims have been accepted for transient aggravation of asthma at work, the number of accepted claims has been similar to those of OA [27]. Claims accepted for transient aggravation of asthma related to a specific accidental irritant exposure at work were over five-times as common as accepted claims for RADS, but symptoms attributed to the exposure were of significantly shorter duration [18].

Level of exposure is an important factor for development of sensitiser-induced OA; the higher the exposure level, the greater the proportion of exposed workers who will become

sensitised, as has been demonstrated for wheat proteins (in bakers), animal proteins (in laboratory workers) and diisocyanates (in spray paints and polurethane foam). In addition, host factors, such as atopy, increase the risk for sensitisation to high molecular-weight allergens and smoking increases the risk of sensitisation to certain agents, such as complex platinum salts and epoxy compounds. Associations between certain agents that cause OA (*e.g.* diisocyanates [28], complex platinum salts and animal protein) and HLA have been reported, although these associations have not been strong and remain to be confirmed. For example, studies of laboratory animal workers with occupational allergies/asthma have found two-times the prevalence of HLA-DR4 and B15 compared with healthy control subjects in one study and an excess of HLA-DR4, HLA-DR11 and HLA-DRW17 in another study [29, 30].

Epidemiological studies and surveillance programmes of several large populations have been useful in identifying occupations and industries at high risk of causing OA [15, 31–33]. Surveillance of work-related and Occupational Respiratory Diseases in South Africa (SORDSA) monitored the nature, extent and distribution of occupational respiratory diseases through voluntary reporting by physicians and nurses [8]. After pneumoconiosis and associated respiratory conditions, OA was the second most reported disease. Latex was the most frequently reported agent for OA, followed by diisocyanates and platinum salts.

The SWORD project in the UK identified OA as the most commonly reported occupational lung disease [9]. The project examined trends in estimated population-based incidence of OA by age, sex, occupation, geographical region and causal agents. Overall, 33% of all suspected causes of asthma were organic, 33% were chemical, 6% were metallic and the rest miscellaneous. The incidence of OA was higher in men than women, with the disparity especially marked in the population aged $\geq$45 yrs, where rates for men were at least twice those for women. Although the cause of this trend is not known, it might reflect a more marked male-domination in earlier years of jobs considered more hazardous (which also involved exposure to many substances known to cause OA). Except for laboratory technicians, most high-risk occupations were concerned with manufacturing and processing that used chemicals, metals and organic materials, previously male-dominated occupations.

Kovevinas *et al.* [33] assessed data from 15,637 randomly selected people aged 20–44 yrs from 12 industrialised countries. Asthma was assessed by a questionnaire determining symptoms and use of medication and in a subset of >9,000, methacholine challenge was also performed. The highest risk of asthma was shown for farmers (odds ratio (OR) 2.62), painters (OR 2.34), plastic workers (OR 2.20), cleaners (OR 1.97), spray painters (OR 1.96) and agricultural workers (OR 1.79). They found that the prevalence of asthma attributable to work among younger women had been underestimated. The risk of asthma attributable to occupational exposures was slightly higher in women than men. Approximately 5% of asthma risk in women could be explained by household exposures, but the attributable risk from "high-risk occupations", excluding housewives, remained high, at 11.5% for women. Studies of respiratory symptoms in the UK also identified a high-risk of OA among women [19]. Many occupational groups at high risk for asthma, such as textile workers, cleaners and farmers, include a substantial proportion of female workers.

Many agents can cause OA. Biological allergens, such as animal, plant and food derived proteins, are common sensitisers. Chemical-sensitiser exposures, which are not uncommon for women in manufacturing and processing, include diisocyanates (polyurethane foam manufacture and use of polyurethane glues or spray paints) and acid anhydrides (epoxy adhesives and paints, coatings, circuit boards, polymers, polyesters and plasticisers), aldehydes and acrylates (paints and adhesives). As these were male-dominated industries in the past, women had less exposure, but as they enter these

industries more commonly, an increasing prevalence of asthma in women from these agents may be expected.

In industries with a relatively higher proportion of female employees, exposures include animal proteins (laboratory animals, farming, veterinary medicine), dusts from flours and grains (bakers), dyes (textile workers) and persulphate (hairdressers). Healthcare workers are also predominantly women and exposures include natural rubber latex ((NRL) gloves), formaldehyde and glutaraldehyde (sterilising medical equipment). Spills of cleaning solutions, such as chlorine, bleach and strong acids, can cause RADS and irritant-induced asthma, or in lower concentrations, may aggravate underlying asthma and an irritant effect is likely to be at least a partial explanation of the increased prevalence of asthma reported in cleaners.

Women (and men) exposed to animal proteins are at high risk of developing occupational allergy and asthma. Common agents include animal dander, urine and serum (for pharmaceutical and research workers and breeders), bovine proteins (for dairy workers and farmers), chicken proteins (for poultry workers) and egg proteins (for egg-processing workers). While a history of atopy is associated with risk of symptom development, it has poor predictive value for any given individual. Prevalence of sensitisation is associated with exposure levels and number and type of animal species handled [34].

There have been relatively few prospective studies of women exposed to occupational allergens. GAUTRIN and co-workers [35, 36] prospectively studied a cohort of 769 apprentices entering training in animal-health technology, pastry-making and dental-hygiene technology (exposed to latex gloves). The percentage of women in these programmes was 86, 76 and 98%, respectively. They were followed during the training programme, up to 44 months for the animal programme, 32 months for the dental programme and 16 months for the pastry programme. Results showed significant incident rates of sensitisation to the relevant occupational allergens: 21% for the animal programme, 6.4% for the dental programme and 4.3% for the pastry programme. Among those in the animal programme, 89% were also followed with methacholine challenges and 7.5% of these showed findings of probable OA, defined as a significant (3.2-fold) increase in airway responsiveness to methacholine and a positive skin test to the occupational allergen. The high incidence of these findings emphasises the need for primary preventive strategies in these and similar occupations. Changes shown to be effective in reducing allergen exposure or rates of sensitisation include a switch to low-protein, powder-free gloves for dental and other healthcare workers, measures to reduce animal aeroallergen levels, as reported by REEB-WHITAKER *et al.* [37], and reduction of airborne flour levels ideally to 0.5 $mg \cdot m^{-3}$, (as suggested by HOUBA *et al.* [38], to reduce the risk of sensitisation to wheat to negligible levels).

Veterinarians are exposed to a more diverse range of animals. Lutsky *et al.* [39] studied 257 active veterinarians compared with 100 unexposed controls, using history, spirometry, skin tests and total serum IgE determination. Asthma was significantly more prevalent in veterinarians (16.3%) than in controls (6%, $p<0.05$), although only 13 of 257 had respiratory symptoms that were related to animal contact. A survey of zoo veterinarians reported a 32.2% prevalence of animal allergy and 14.2% prevalence of insect allergy [40]. Gender, length of experience and practice types affected the number and type of incidents encountered. Females reported higher rates of insect allergy and adverse reactions to anaesthetic gas, formalin, disinfectants and sterilants.

Farming is associated with numerous occupational respiratory diseases, including asthma and hypersensitivity pneumonitis. Exposures include organic dusts, animal proteins and chemicals, such as ammonia. KIMBELL-DUNN *et al.* [41] examined the prevalence of symptoms of asthma and allergy in different farming groups using questionnaires. Women were more likely to report current asthma than men (OR 1.8,

95% confidence interval (CI) 1.3–2.5). They found the overall prevalence of asthma was 11.8%, with higher levels for horse breeders and grooms (16.5%), pig farmers (18.2%), poultry farmers (17.4%) and those working with oats (17.4%). Asthma was also significantly elevated among those working with cleaning powders (14.7%).

Proteins from cereals or insect contaminants can also cause asthma, as reported in 7–9% of bakers and other flour workers. The latency period that precedes onset of symptoms may last months or years and is usually preceded by nasal and ocular allergic symptoms. Serum-specific IgE responses have been detected against albumin, flour protein and gluten fractions, including globulin, gliadin and glutenin [42, 43]. Aspergillus and Alternaria fungal-spore contaminants and enzymes, used for dough conditioning and fermentation, have also been implicated as causative agents in baker's asthma [44, 45].

Both bakers and egg-processing workers can develop asthma from inhalation of egg proteins, such as conalbumin, ovalbumin, lysozyme and ovomucoid [46]. Other food-processing workers may be exposed to an alkaline hydrolysis derivative of gluten used as a food additive and spices, such as garlic, onion and cinnamon [47, 48]. Workers exposed to dust from handling unroasted castor, coffee, soy and cocoa beans can develop IgE-mediated asthma. ZUSKIN *et al.* [49] found 5% of cocoa workers and 5.7% of flour workers suffered from OA, compared with 0% of control workers [49]. Food dyes, such as carmine, made from insects, are also allergenic [50].

Female textile workers were identified by TOREN *et al.* [51] in a Swedish study as having a significantly increased likelihood of asthma (OR 2.1, CI 1.2–3.8) [51]. This increase could not be explained on the basis of byssinosis or endotoxin exposure, since the workers were weaving, not spinning. In addition, it could not be explained as being due to an allergic response to dyes, since dyes were not used. An increased ratio of asthma in textile workers was also found in the multinational study by KOGEVINAS *et al.* [33], although in that study, the increase was not statistically significant. An older study of textile workers have shown 20% to have positive results to inhalation testing to both natural and synthetic fibres and 30% to be positive to nasal provocative testing [52]. ZUSKIN *et al.* [53] studied workers in a textile factory producing synthetic-fibre hosiery and found a higher prevalence of all chronic respiratory symptoms in exposed, compared with control subjects. Dyspnoea, "sinusitis and nasal catarrh" were significantly higher in female workers and "nasal catarrh" was significantly higher in male workers. There was a high prevalence of acute symptoms during the work shift, which was greatest for cough, dryness of the throat, dryness of nose and eye irritation. Spirometry demonstrated decreased forced expiratory flow at 75% of forced vital capacity (FVC), compared with predicted. Fibres, such as jute and sisal, have also been implicated as causes of an asthma syndrome in textile workers [54, 55]. Workers employed in dying cotton and wool fibres were found to have a prevalence of OA of ~6% [56].

LEINO *et al.* [57] studied the occurrence and causes of hairdressers' occupational diseases. After occupational dermatoses, respiratory complaints were the second most common occupational disorder in this group. A prevalence of 1.7% was noted for occupational rhinitis and 0.8% for OA. Ammonium persulphate was considered to be the cause of 90% of respiratory diseases and less commonly, paraphenylenediamine and latex. Atopic diseases increased the risk for occupational respiratory disease by three-fold [58].

NRL, as a cause of OA, is more common in women, particularly in healthcare workers, as a result of NRL glove use. In studies of NRL sensitisation among healthcare workers, <94% of those sensitised were female [59]. Similarly, 92% of all individuals with accepted Ontario workers' compensation claims for latex-induced OA in 1984–1999 were women [60]. The likelihood that this relates to exposure and coverage by the compensation system, rather than a specific gender response, is supported by a study of 131 staff and students skin tested to NRL extract in a school of dentistry [61]. Women comprised 98% of the clinic staff, 39% of the academic staff and 45% of the students.

They represented 63% of skin-test negative participants and 62% of skin-test positive subjects. Changes in NRL examination gloves to low-protein powder-free gloves have been associated with marked reductions in rates of sensitisation and clinical allergic responses to NRL, including asthma [62].

Another group of predominantly female healthcare workers with a reported increase in work related respiratory symptoms are medical radiation technologists. In addition to the use of NRL gloves, older practices of radiograph processing led to potential exposures to respiratory sensitisers and irritants, such as glutaraldehyde and formaldehyde, as well as respiratory irritants, such as hydroquinone and acids. Therefore, these workers had the potential to develop sensitiser-induced OA, irritant-induced OA, aggravation of unrelated asthma or any combination of these. Although an excess of work-related respiratory symptoms, as compared with physiotherapists, has been found (7.2% had two or more asthma symptoms worse at work, *versus* 3.4% of physiotherapists), the cause of these has not been clarified and confirmed cases of OA have been limited to small case series [63].

Cleaners are another group of women commonly exposed to substances known to cause asthma, such as irritants like chlorine, ammonia, acids and detergents. Acute irritant exposure, as may occur when bleach and ammonia are accidentally mixed, can result in RADS. Although quaternary ammonium compounds may be present in some cleaning agents and have occasionally been shown to be respiratory sensitisers, for many cleaners, the relationship of their asthma to their work appears to be on an irritant basis (irritant-induced asthma after an acute exposure, or transient aggravation of underlying asthma with lower exposures). Zock *et al.* [64] interviewed Spanish indoor cleaners and found that asthma prevalence was 1.7-times higher compared with office workers, with the highest prevalence being found in private home cleaners. Although in this study asthma risk among home cleaners was mainly historically associated with the use of kitchen cleaning products, especially oven cleaners, and furniture polishing, cleaners also have potential exposure to common indoor aeroallergens, such as dust mites, animal allergens and fungal allergens, which may cause or exacerbate their asthma [65, 66].

While most cases of occupational lung disease have been associated with industrial exposures, women employed in administrative/clerical fields are not entirely protected from substances that may cause occupational lung disease. Teachers and office workers are often predominantly women. OA can arise from sensitisation to indoor allergens, such as fungal spores or dust mites. Less commonly, hypersensitivity pneumonitis from contamination of humidifiers or air-conditioners occurs as a building-related illness. Other building-related occupational lung disease is relatively uncommon, but includes respiratory infection, such as legionnaire's disease, or tuberculosis, and asbestos-related disease. More commonly, work-related respiratory symptoms occur as a component of sick-building syndrome. This unexplained syndrome is more common in sealed buildings and has been reported to occur more commonly in women [67]. It has been associated in different studies with several factors, including poor building maintenance, water damage, fungal contamination (including potentially toxigenic moulds), inadequate ventilation/heat/lighting, volatile organic compounds, job dissatisfaction and psychosocial stress.

Bronchitis and byssinosis

Chronic bronchitis is defined as a cough productive of sputum present on most days for 3 months per year over two consecutive years. Many workplace exposures have been associated with occupational bronchitis. Although significant exposure to inorganic dusts occurs mainly in more traditionally male occupations, exposure to organic dusts

with resulting endotoxin exposure, which has been associated with chronic bronchitis and byssinosis, is not uncommon for women in farming, laboratory animal facilities and textile milling [68, 69].

SIMPSON *et al.* [70] studied the prevalence of work-related upper and lower respiratory tract symptoms in workers exposed to organic dusts. They found the highest prevalence of work related lower respiratory tract symptoms (38.1%) and chronic bronchitis (15.5%) among poultry handlers. Women were more likely to report upper respiratory tract symptoms than men. In a 15 yr follow-up study of cotton workers in China, compared with silk workers, there was a significant loss of forced expiratory volume in one second (FEV_1) in the cotton workers associated with symptoms of byssinosis, chest tightness at work and endotoxin exposure [71]. Female cotton workers (54%) had a significant pulmonary function decline, although this was less than that of the men and appeared to be explained by the almost complete lack of smokers among the women. SILVERMAN *et al.* [6] recently suggested that women may be more susceptible to the induction of COPD from smoking, as compared with men. If confirmed, this susceptibility may suggest that lung function changes, such as those from cotton dust which in men were enhanced in smokers, could be more pronounced as the proportion of female smokers increase.

BECKETT *et al.* [72] also administered questionnaires to female Chinese cotton textile-mill workers regarding standard respiratory history and symptoms. The ORs for prevalence of current frequent symptoms in those working in production, after adjustment for home exposure to passive tobacco smoke and coal heating, were 2.23 for frequent cough, 3.24 for frequent phlegm, 4.54 for shortness of breath and 2.96 for wheeze. Of the 973 surveyed women, nine had grade-I byssinosis.

Other irritant-induced lung diseases

There are several other occupational lung diseases which can result from occupational irritant exposures as has been reviewed recently [64]. In addition to irritant-induced asthma, these include bronchiolitis obliterans, bronchiolitis obliterans organising pneumonia, acute respiratory distress syndrome, as well as acute bronchitis, tracheitis and laryngitis. Relatively common causes include accidental workplace exposure to gases, such as chlorine, nitrogen oxides, acetaldehyde, ammonia (used in farm-crop preservation), hydrogen fluoride, hydrogen sulphide (used in oil refining) and phosgene (chemical manufacturing) [73]. Some of the determining factors for the resulting effects include the concentration and duration of exposure and the presence of underlying lung disease. There are gender differences in airways diameter; women have smaller diameter airways than men and have been described as having a different pattern of inhaled particle distribution due to this, with more tracheobronchial and less alveolar distribution than men. However, the authors are unaware of studies showing gender differences following equivalent "real life" exposures to high-level respiratory irritants.

Second-hand smoke in the workplace

Personal cigarette smoking is the predominant cause of COPD. Second-hand cigarette smoke can become an occupational hazard in places where smoking is prevalent and ventilation is poor, as in restaurants, bars and casinos. Women often make up the bulk of workers in these industries (waitresses, bar maids, cleaners), and therefore are at risk for lung diseases caused by such exposure. Studies have shown an exposure-response reduction in pulmonary function of workers associated with passive smoking, mainly

from work [74]. Long-term regular exposure to occupational environmental tobacco smoke is also associated with increased lung cancer risk in never-smoking women [75, 76].

Inorganic dusts

Occupational inorganic dusts *e.g.* silica and coal dust, can also cause or contribute to chronic airflow limitation, as well as causing pneumoconiosis. With many substances, the disease may progress for decades even after exposure has ceased. Women are not likely to have exposure in the mining, quarrying or foundry environment, but can have exposure to silica dust in other occupations, such as ceramics or vitreous enamelling which may lead to silicosis. Women may also have exposure to kaolin (clay used in china, ceramics and pharmaceuticals), and talc (paint, ceramics, leather, fabric and paper industries). Significant asbestos exposure is now uncommon, but changes resulting from former exposure including pleural changes, mesothelioma, asbestosis and lung cancer can be seen >20 yrs later. Significant asbestos exposure and asbestos-related disease is less common in women than men. In Denmark, the incidence of malignant mesothelioma in men in 1943–1993 was more than double that of women [77]. Deaths from mesothelioma in women, from a study in the UK, have been ~25% of the male rates [78]. However, mesothelioma can occur after even minor exposure, and especially in women, mesothelioma of the peritoneum may be misdiagnosed due to the range of potentialities of cells in the female pelvis [79].

LEMASTERS *et al.* [80] reported on an industry-wide pulmonary morbidity study to evaluate respiratory health of employees manufacturing refractory ceramic fibres at five sites in the USA over 2 yrs. The risk of working in the production of refractory ceramic fibres and having one or more respiratory symptoms was estimated by adjusted OR and found to be 2.9 for men and 2.4 for women, compared with nonproduction workers. Men showed a decline in FVC for current and past smokers and decline in FEV_1 was significant for current smokers. For women, the decline was greater and significant for FVC among nonsmokers as well. These findings also indicate that there may be important sex differences in responses to occupational exposure.

Beryllium exposure even at relatively low levels can induce chronic beryllium disease in genetically predisposed individuals. Beryllium is being used in an increasing number of processes to which women may have exposure. In addition to some of the more traditional uses, such as atomic energy applications, aerospace components, metal working and dental alloys, it is also used in making sporting goods, such as bicycle frames and golf clubs and in pen clips. Therefore, it should be considered in the differential diagnosis of both women and men who present with apparent sarcoidosis.

Organic dusts

Hypersensitivity pneumonitis, or extrinsic allergic alveolitis, is caused by an immunological reaction to one of a variety of inhaled organic antigens. Histology reveals diffuse mononuclear cell infiltrate of alveolar wall, alveoli, terminal bronchioles and interstitium. Inflammation is usually followed by granulomas, which can progress to fibrosis. It may be acute, subacute and chronic, depending on the degree, duration of exposure and the susceptibility of the patient. Many workplace substances have been identified as capable of causing this response: animal proteins (birds, rodents), fungi, metalworking fluid aerosols (metal parts machining shops), thermophilic bacteria, other bacteria (bacillus, pseudomonas), diisocyanates (paints and foams), trimellitic anhydride

and phthalic anhydride (epoxy resins, coatings and paints). Most of these exposures would be expected to occur more frequently in men, but farmers' lung and hypersensitivity pneumonitis from contaminated humidifiers in workplace buildings may be more commonly expected than other sources of this condition in women.

Cancer

At least 12 substances found in the workplace are classified as human lung carcinogens. Occupational exposure is estimated to account for ~5% of lung cancers in the USA [81, 82]. The majority of these cancers are caused by asbestos (boiler and pipe insulation), radon, silica (produced by stone cutting, drilling and tunneling), chromium (alloys and metal plating), cadmium, nickel, arsenic (pesticide sprays) and beryllium. Homozygous deletion of the glutathione *S*-transferase M1 (GSTM1) gene or an *N*-acetytransferase 2 (NAT2) slow acetylator genotype may confer additional risk of lung cancer among subjects exposed to asbestos.

Lung cancer is rapidly becoming the leading cause of cancer mortality in women. Ives *et al.* [82] conducted interviews with women with and without lung cancer. Data was stratified according to employment in a high-risk industry or occupation. Although not statistically significant, OR for employment in high-risk categories support earlier estimates that attributed 5% of lung cancer mortality in women to employment in hazardous occupations. Employment of the husband or a household member in selected industries and occupations yielded significantly increased OR, suggesting second-hand exposure may also be relevant to development of lung cancer in women.

Conclusions

Occupational lung disease in women, as in men, includes a wide range of diseases. The differences in relative prevalence of various occupational lung diseases in women, as compared with men, appears likely to relate in large part to ongoing differences in the prevalence of specific job descriptions and therefore differences in exposures to aetiological workplace agents. Many of the differences have lessened as women have entered more traditionally male-dominated work. However, the most commonly identified occupational lung disease in women continues to be work-related asthma, commonly associated with work in healthcare, cleaning and baking. Workplace respiratory effects, which relate in part to additional cigarette smoking in conjunction with workplace exposures, may also account for some relative increases in prevalence of occupational airways diseases in women compared with the era when women were less likely to smoke. Women may also, in some circumstances, have a different response than men to the same work exposure due to differences in airway size, which can affect inhaled particle/aerosol distribution in the lungs. Recent findings suggest a greater risk of chronic bronchitis from cigarette smoke in women and the need for extension of such studies to the effects of workplace irritant and toxic exposures.

Summary

An increase in occupational lung disease in women has been identified in several studies, especially relating to occupational asthma (OA) and airway diseases. This may

reflect increasing participation by women in occupations which were previously predominantly male and may also in part reflect the increasing prevalence of cigarette smoking in women. For example, in one study, the proportion of women among accepted claims for OA related to diisocyanates increased from 28 to 45% over the 7-yr periods before and after 1987, reflecting changes in exposure. There is also evidence that airway aerosol deposition may be greater in larger airways in women than in men and that women may be more susceptible to developing chronic bronchitis, though to date this potential to increased susceptibility has not been assessed in relation to work exposures. Predominantly female occupations with exposures relevant to occupational lung diseases include healthcare, laboratory animal workers, domestic cleaners, textile workers and pastry makers. Women in office buildings may develop building-related lung disease, including hypersensitivity pneumonitis and asthma, as well as respiratory symptoms as a component of sick-building syndrome. Approximately 5% of lung cancer mortality in women has been linked to employment in occupational exposures. Employment of the husband or a household member in selected industries and occupations yielded significantly increased odds ratio suggesting second-hand exposure may also be relevant to development of lung cancer in women, and women are frequently employed in casinos, bars and other areas with second-hand tobacco smoke exposures. Less common occupational lung diseases can also occur in women, and both current and former workplace exposures should be considered when diagnosing lung disease in women as well as in men.

Keywords: Asthma, gender, occupational asthma, occupational lung disease, women.

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