

Work-related chronic obstructive pulmonary disease

Occupational exposure, alone or along with smoking, is responsible for much COPD.

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Chronic obstructive pulmonary disease (COPD) is increasing worldwide, both in developed and developing countries. According to the 2001 World Bank/World Health Organization Global Burden of Disease report¹ COPD is the sixth leading cause of death in developing countries, responsible for 4.9% of deaths. Despite smoking being the most important risk factor for this disease, accounting for over 75% of cases of disease,¹ occupational exposures, alone or in combination with smoking, are responsible for a substantial proportion of disease.²

There are several factors that have been shown to increase the risk of developing COPD, and these may interact synergistically among themselves and with workplace exposures.

Inconsistencies in the definition may contribute to the widely differing reports of prevalence globally,³ but this shortcoming has been addressed somewhat by the Global Initiative for Chronic Obstructive Lung Disease (GOLD), which since 2001 has developed international consensus on a broad range of issues related to COPD.⁴ The GOLD defines the 'pulmonary component' of COPD as being 'characterised by airflow limitation that is not fully reversible'. This definition marks a shift in previous definitions, which included the conditions of chronic bronchitis and emphysema, as employed by the American Thoracic Society,³ or 'reduced maximal expiratory flow' as included in the definition of the European Respiratory Society.³ The disease includes the symptoms of chronic productive cough, airway hyperresponsiveness and breathlessness to differing degrees.

Work may have an impact on COPD in several ways, including having a causal relationship, and a synergistic effect with tobacco smoke, resulting in greater severity of disease, which in turn results

in greater disability or accelerates the rate of loss of lung function among those with the disease.⁵

Epidemiology

According to recent multicentre studies, the prevalence of COPD globally ranges from less than 5% among males and females in Mexico, to 16% and 22% among females and males respectively in South Africa.⁶ This variability could be partially ascribed to the inconsistency in the definition, as described above, as well as to the varying prevalence of risk factors in different countries. There are several factors that have been shown to increase the risk of developing COPD, and these may interact synergistically among themselves and with workplace exposures.

Smoking is a known risk factor, contributing to as much as 73% of the cause of COPD in high-income countries, and 40% in developing countries.¹ However, not all smokers develop the disease. It was previously thought that only 15% of smokers became symptomatic, but this figure has been challenged by recent research, with claims that up to 50% actually develop COPD.³ The evidence for interaction between smoking and workplace exposures in the aetiology of COPD is inconsistent, with some studies showing increased airway functional loss, and others showing no interaction.⁷

Indoor air pollution, particularly the use of biomass as a source of energy, has been shown to be strongly associated with COPD, with prevalence rates of disease 3 times higher among exposed never-smoking rural women, compared with non-exposed urban women in China.³ The cumulative inhalant exposure of indoor biomass fuels and occupational agents associated with COPD is likely to dramatically increase risk among newly urbanised workers living in informal housing and depending on alternative and cheaper sources of energy.

Ambient air pollution is reported to cause approximately 2% of COPD in developing countries.¹ Although the risk is substantially smaller than that of smoking or indoor air pollution, a recent report of approximately 1 500 adults in Durban found a substantially increased and statistically significant risk among adults who had an occupational exposure associated with COPD and living in an

industrially polluted community compared with those adults with similar occupational exposures, but living in less industrially polluted communities.⁸

Not everyone with similar exposures to smoking, environmental or occupational agents develops disease. This clearly suggests important genetic variability in risk. Deficiency of serine protease $\alpha 1$ antitrypsin is seen in 1 - 3% of patients with COPD. In addition, genes coding transforming growth factor $\beta 1$, tumour necrosis factor α , and microsomal epoxide hydrolase 1 have been implicated in COPD, but research findings to date are largely inconsistent.³ Having a genetic predisposition in the presence of another inhalant risk factor, such as smoking, environmental or occupational exposures increases the likelihood of disease.

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Other factors that need to be considered in a working population likely to affect the risk for COPD include ageing, sex, respiratory infections and socio-economic status. Older people are more likely to develop disease, or to have more severe disease. Historically, men have been at greater risk for the disease, probably due to smoking and work profiles. However, this pattern is changing in the high-income countries, with equal prevalence among men and women.⁴ It is

unclear whether women are more susceptible to disease given similar exposures to men.

The high prevalence of tuberculosis in South Africa has been suggested as the reason for some of the highest prevalence of COPD seen in the recent multicentre studies.⁶ Childhood infections are known to increase the risk of the development of COPD in adult life, probably related to increased airway responsiveness. Socio-economic status is probably a surrogate marker for a host of other factors, such as poor nutrition, indoor and outdoor pollution and working in riskier jobs.

Pathogenesis and pathology

COPD is an inflammatory response to noxious inhalants in the respiratory system. This process involves a variety of cell types, including neutrophils, macrophages, lymphocytes and airway epithelial cells, resulting in the release of proteolytic enzymes. An imbalance of proteases and antiproteases to counteract the lytic effects on the connective tissue in the lungs results in emphysematous changes.⁹ When activated, macrophages and neutrophils release endogenous oxidants, the reactive oxygen species (ROS). Smoking and noxious inhalants are key sources of exogenous oxidants. As with the proteolytic enzymes, an imbalance between oxidants and antioxidants results in oxidative stress, which results in tissue damage and stimulation of cytokines and chemokines, further aggravating the inflammatory process.¹⁰ These inflammatory processes result in airway remodelling through the release of pro-inflammatory, mitogenic factors. Among other effects, this remodelling causes airway hyperresponsiveness, a key predictor of COPD.¹¹

Remodelling results in mucous gland enlargement, airway wall thickening, lumen narrowing and destruction of the gas exchange tissue,¹¹ all of which account for the pathophysiological changes associated with COPD. Importantly, it seems that these inflammatory processes and pathological remodelling continue after cessation of the risk factor, such as smoking.⁴

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Occupational exposures

Since the seminal paper on chronic airflow limitation and occupational exposures by Margaret Becklake in 1989,¹² the evidence for work-related COPD has grown substantially. The current list for specific agents or specific work activities (Table I) is not exhaustive, and much more research is required. Nevertheless, occupational exposures such as vapours, gases, dusts and fumes present an important risk factor for the development of the disease, by itself and through interaction with other risk factors. A US study of over 10 000 adults concluded that COPD attributable to work was approximately 19% in the total population, and 31.1% among never smokers.⁴ The American Thoracic Society's consensus statement suggests that 10 - 20% of COPD is attributable to workplace exposures.² The effect of work exposures may be of a similar magnitude to that of smoking, or higher

Table I. Agents and occupations associated with COPD^{2,5,17}

| Agent | Occupation |
|---|---|
| Mineral dusts – silica, silicate, coal, asbestos, hard rock, cement, fibre, glass | Mine workers, quarry workers, construction workers, tunnel workers, transport workers, concrete/ cement manufacture, foundries, refractory brick workers, ship building |
| Metal fumes – cadmium, vanadium, aluminium | Metal workers |
| Hard metal dusts | Engineering, metal workers, car manufacturers, foundries |
| Chemical vapours or gases: isocyanates, sulphur dioxide, oxides of nitrogen | Painters, foundries, chemical processors |
| Organic dusts: cotton, grain, wood, animal feed, endotoxins, oil mist, tea | Wood and paper workers, mill workers, grain workers, bakers, fertiliser manufacture, food processors, farmers/agriculture, cotton textile workers, tea manufacture |
| Complex mixtures: welding fumes, engine exhaust, fire smoke, tobacco smoke | Welders, automobile industries – repairs, servicing, petrol stations, firemen/rescue services |
| Adhesives | Rubber, plastics |
| Tuberculosis | Health care workers, silica dust-exposed workers |

This table has been modified from the original developed by Dr Nadira Govender of the KwaZulu-Natal Provincial Medical Advisory Panel (PMAP) of the Compensation Fund, based on tables developed by Professor Mohamed Jeebhay and Dr Shahieda Adams of the Western Cape PMAP. This is reproduced with permission.

among heavily exposed workers,² and therefore warrants as much attention as smoking cessation programmes.

Clinical diagnosis and management

Establishing the relationship between COPD and work is not as easy as attempting to establish the relationship between a disease with acute presentation (such as asthma) and work. Because the onset of COPD is insidious, the disease progresses slowly and has a wide variety of possible causes, including smoking, genetic predisposition and indoor and ambient pollution, proof of work-causation is almost impossible. Apart from possible legal considerations, proving work-causation is probably not necessary. However, being able to show work-relatedness is essential. This identification of work-relatedness allows the clinician to intervene to prevent progression of the disease and to limit disablement arising from the disease. The clinician also has a public health responsibility in preventing disease among other exposed workers.

This assessment by the clinician depends on a detailed occupational exposure history and, because of the nature of the disease, requires a lifetime occupational history, including different jobs, activities within jobs and workplace exposures for each job/activity. It is necessary to characterise as many potentially associated agents as possible: duration and severity of exposure, control of exposures by engineering means, use of protective equipment and the presence of ventilation.

Once the clinical diagnosis of work-related COPD is made, there is an obligation on the part of the clinician and the necessary role players in the working environment to reduce the exposure of the patient. Removal from exposure in the early stages is not necessary for COPD¹³ (as compared to occupational asthma), providing exposure is reduced, preferably through workplace hazard control or, if not possible, by the provision of respiratory protective equipment. In the later stages of disease, removal from exposure may be necessary. This implies that regular medical assessment of the patient needs

to be conducted, and this will include symptom questionnaires and spirometry, including serial peak flow assessments. In addition, frequent assessment of the work activities to ensure that exposure levels are appropriately managed, is necessary.

Clinical management must consider the reduction of other risk factors, such as smoking, environmental pollution, particularly within the patient's home, and nutrition.

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) has provided a basis for the staging of the disease (Table II).⁴ Therapeutic guidelines for COPD are well documented, and are not reviewed here. The South African Thoracic Society guidelines provide a detailed approach for each stage of the disease.¹⁴

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Compensation for COPD in South Africa

COPD is a compensable disease under the Occupational Diseases in Mines and Works Act (Act 78 of 1973, as amended). However, for general industrial workers, exposed to known respiratory irritants, COPD is not a readily recognised compensable disease. Workers with COPD could be compensated if diagnosed as having a disease associated with certain exposures, some of which

are listed in Table I. Schedule 3 of the Compensation for Occupational Injuries and Diseases Act (Act 130 of 1993)¹⁵ lists 'any bronchopulmonary disease' arising out of working with metal carbides (hard metals) and 'any disease or pathological manifestation' due to cadmium exposure as compensable. For non-mining workers exposed to any of the other hazards or involved in work listed in Table I, developing work-related COPD is not presumptive according to the law – and requires motivation by the clinician for consideration as a work-related disease.

Under the Regulations for Hazardous Chemical Substances (Regulation 1179 of 1995) of the Occupational Health and Safety Act of 1993, workers exposed to hazardous substances, such as those listed in Table I, must be subjected to medical surveillance. There are similar provisions for medical surveillance for mineworkers under the Mine Health and Safety Act (Act 29 of 1996).

Workplace management of COPD-related hazards

As part of the clinical intervention to reduce exposures, the clinician needs to interact with the relevant management personnel, occupational hygienist and medical staff at the workplace. The approach to the control of hazardous exposure to respiratory tract irritants in the workplace is based on the 'hierarchy of hazard control'. This approach, supported by South African legislation (the Regulation of Hazardous Chemical Substances of the Occupational Health and Safety Act),¹⁶ stipulates that control must first consider elimination of the hazard, and if this is not possible, then engineering controls, such as ventilation or enclosure, must be investigated. If these primary steps are not possible, then administrative controls, which aim to reduce individual worker exposure by rotating workers through the hazardous environment for shorter periods of time during the working day, changing jobs, etc., must be introduced. The use of personal respiratory protective equipment is the last line in hazard control.

Workplaces depending on masks and respirators for the control of exposure

Table II. The GOLD staging of COPD

| Stage | Severity | Postbronchodilator lung function |
|-------|-------------|--|
| I | Mild | FEV ₁ /FVC ≤ 0.7; FEV ₁ ≥ 80% of predicted |
| II | Moderate | FEV ₁ /FVC ≤ 0.7; 50% ≤ FEV ₁ < 80% of predicted |
| III | Severe | FEV ₁ /FVC ≤ 0.7; 30% ≤ FEV ₁ < 50% of predicted |
| IV | Very severe | FEV ₁ /FVC ≤ 0.7; FEV ₁ < 30% of predicted or FEV ₁ < 50% of predicted with features of chronic respiratory failure |

must develop a respiratory protective equipment programme, which must ensure that the proper mask or respirator appropriate for the exposure is used, that proper fit testing is done, respiratory cartridges are replaced as per the manufacturer's guidelines, and maintenance of equipment is stipulated. Failure to implement such a programme is likely to cause exposure among users, and exacerbate symptoms.

Environmental monitoring by a trained occupational hygienist or accredited inspection authority is necessary as per the regulations. This provides quantitative feedback on the effectiveness of engineering controls.

Medical surveillance programmes

All workers exposed to respiratory irritants in the workplace should be subjected to a medical surveillance programme. Many of these substances are regulated under the Regulations for Hazardous Chemical Substances, and medical surveillance may be prescribed. This is a form of secondary prevention for exposed workers, allowing for early detection of disease, and implementation of measures to reduce disease severity and disability.

Medical surveillance should consist of a respiratory questionnaire – there are several standardised questionnaires available, based on international field studies, and field tested for South African working populations. Spirometry, conducted in

accordance with the standards stipulated by the South African Thoracic Society guidelines for office spirometry,¹⁴ should be done annually, and more frequently among those with suspected respiratory illness. Spirometric trends and comparisons with baseline, conducted at time of hire, should be done to detect any deviation from the expected. Serial peak flow recordings can be used to detect workers at risk of developing respiratory irritant-induced COPD.¹³

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In a nutshell

- COPD is a disease characterised by airflow limitation, which is generally irreversible, with the presentation of symptoms of productive cough and dyspnoea.
- COPD is a leading cause of morbidity and mortality in high-, middle- and low-income countries.
- Smoking is the most important cause of COPD, accounting for approximately 75% of the disease.
- Other risk factors include noxious inhalants from indoor and outdoor environments and the workplace.
- The pathogenesis of COPD is related to the inflammatory response to noxious inhalants, resulting in the release of destructive proteolytic enzymes from inflammatory cells, eventually resulting in airway remodelling.
- Research has shown that a variety of occupational vapour, gas, dust and fume exposures are strongly associated with COPD, together with certain occupations.
- Between 10% and 20% of the risk for the development of COPD can be attributed to occupational exposures.
- Establishing work-relatedness of COPD is essential for the ongoing management of the patient.
- Central to the management of a patient with work-related COPD is the reduction of exposure at the workplace, using occupational hygiene principles.
- COPD is compensable as an occupational disease for mineworkers, but in the case of industrial workers additional motivation is required on the part of the clinician.
- All workplaces where respiratory irritants are present should have a medical surveillance programme in place which allows for the early detection of respiratory disease and early intervention to prevent progression.