INVITED REVIEW

Coal mine dust lung disease in the modern era

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ABSTRACT

Coal workers' pneumoconiosis (CWP), as part of the spectrum of coal mine dust lung disease (CMDLD), is a preventable but incurable lung disease that can be complicated by respiratory failure and death. Recent increases in coal production from the financial incentive of economic growth lead to higher respirable coal and quartz dust levels, often associated with mechanization of longwall coal mining. In Australia, the observed increase in the number of new CWP diagnoses since the year 2000 has necessitated a review of recommended respirable dust exposure limits, where exposure limits and monitoring protocols should ideally be standardized. Evidence that considers the regulation of engineering dust controls in the mines is lacking even in high-income countries, despite this being the primary preventative measure. Also, it is a global public health priority for at-risk miners to be systemically screened to detect early changes of CWP and to include confirmed patients within a central registry; a task limited by financial constraints in less developed countries. Characteristic X-ray changes are usually categorized using the International Labour Office classification, although future evaluation by low-dose HRCT) chest scanning may allow for CWP detection and thus avoidance of further exposure, at an earlier stage. Preclinical animal and human organoid-based models are required to explore potential re-purposing of anti-fibrotic and related agents with potential efficacy. Epidemiological patterns and the assessment of molecular and genetic biomarkers may further enhance our capacity to identify susceptible individuals to the inhalation of coal dust in the modern era.

Key words: coal mine dust lung disease, coal mining, coal workers' pneumoconiosis, health surveillance, respirable dust.

Abbreviations: , CMDLD, coal mine dust lung disease; COPD, chronic obstructive pulmonary disease; CT, computed tomography; CWHSP, Coal Workers' Health Surveillance Program; CWP, coal workers' pneumoconiosis; DDF, dust diffuse fibrosis; FCMHSA, Federal Coal Mine Health and Safety Act; FDA, Food and Drug Administration; FEV_1, forced expiratory volume in 1 s; GBD, Global Burden of Disease; GWAS, genome-wide association study; HRCT, high-resolution computed tomography; IL, interleukin; ILO, International Labour Office; MDP, mixed-dust pneumoconiosis; MMP3, matrix metalloproteinase 3; NALP, NACHT, LRR and PYD domains-containing protein; NFkB, Nuclear factor kappa B; NILP, National Institute of Labour Protection; NIOSH, National Institute for Occupational Safety and Health; NLRP3, Nod-like receptor protein 3; PET, positron emission tomography; PMF, progressive massive fibrosis; RNS, reactive nitrogen species; ROS, reactive oxygen species; RPP, rapidly progressive pneumoconiosis; STAT, signal transducers and activators of transcription; TGFβ, transforming growth factor beta; TNF-α, tumour necrosis factor alpha; Wnt/β, Wnt/ beta catenin.

INTRODUCTION

Inhalation of dust generated by coal mining can lead to the development of coal mine dust lung disease (CMDLD). In addition to the classical coal workers' pneumoconiosis (CWP) and its severe and potentially fatal form, complicated or progressive massive fibrosis (PMF), CMDLD also includes mixed-dust pneumoconiosis with coexistent silica exposure, chronic bronchitis, emphysema and dust-related diffuse fibrosis (Table 1).[1–4] Furthermore, dust exposure can adversely affect the lung function of miners in a similar pattern to COPD, particularly for those who have ever-smoked. Thus, miners are a high-risk

Table 1 The spectrum of CMDLD

Lung function pattern	Diagnoses
Normal in most instances	Anthracosis[†]
	Chronic bronchitis
	Caplan's syndrome (rheumatoid pneumoconiosis)[‡]
Restrictive	CWP
	• Simple CWP
	• Rapidly progressive CWP
	• PMF
	Mixed dust pneumoconiosis (MDP)
	Diffuse dust-related fibrosis (DDF)
Obstructive	COPD, with and without smoking history
Mixed	Restrictive CMDLD with COPD

[†]Endoscopic and/or pathological diagnosis.
[‡]Also associated with mild restriction in some patients.
CMDLD, coal mine dust lung disease; COPD, chronic obstructive pulmonary disease; CWP, coal workers' pneumoconiosis; PMF, progressive massive fibrosis.

group for respiratory morbidity and premature death. Given the extent of coal mining globally and its potential for a large burden of disease, the respiratory health of coal miners remains an important consideration worldwide.

TRENDS AND DISTRIBUTION OF CWP

High-income countries

In response to an unacceptable burden of lung disease in coal miners, in 1969, the Federal Coal Mine Health and Safety Act (FCMHSA) of the United States established statutory recommendations for respirable dust exposure limits for underground and surface mines.[5] Under the order of the FCMHSA, the National Institute for Occupational Safety and Health (NIOSH) implemented the Coal Workers' Health Surveillance Program (CWHSP) to monitor the reduction in disease that almost certainly resulted from new dust control regulations. In the United States, this public health intervention effectively reduced the CWP prevalence to one-fifth for underground miners from 11.2% during 1970–1974 to 2.0% during 1995–1999,[6] and reduced mortality from more than 15 to under 5 deaths per million.[7] However, since 2000, there has been an observed increase in the number of CWP diagnoses for underground miners even for those aged less than 50 years who would have spent their entire employment under the modern dust control regulations of the FCMHSA.[8] This recent increase in prevalence has been attributed in part to increased coal mine dust levels, longer working hours especially at the face of the mine, increased exposure to crystalline silica and employment in a smaller mine.[8,9] Progressive mechanization with advancing mining equipment technologies has resulted in more respirable dust being produced by fewer miners.[10]

Unlike the surveillance for underground miners in the United States, the FCMHSA did not specify periodic

health surveillance for surface miners. Comparable prevalence data were lacking until a series of chest radiographs of surface miners was reviewed between 2010 and 2011.[11] Of 2257 miners with at least 1 year of surface mining experience, 2.0% (*n* = 46) were found to have CWP with 0.5% (*n* = 12) having PMF, of whom most of them had never worked underground and were from the central Appalachian region of southern West Virginia, eastern Kentucky and western Virginia.[6,8,10] Thus, surveillance is also important to this subgroup of miners.

In Australia over the past century, there has been a similar and dramatic decline in pneumoconiosis-related deaths from any cause, including CWP, which has plateaued to around five deaths per million since 1970.[12] In 2006–2007, 16% of pneumoconiosis-related admissions were attributed to CWP (*n* = 34),[12] which may have been related to long-standing disease. In contrast with the United States, CWP mortality in Australia has been negligible since the 1970s.[7] Recently however, coal miners have been unexpectedly diagnosed with CWP within the Queensland mining industry, where this state produces the majority of Australia's higher quality metallurgical (coking or black) coal from both underground and open-cut mines. These events have raised two issues. First, the recommended respirable dust exposure levels vary between Australian states (2.5 mg/m³ for New South Wales[13] vs 3 mg/m³ for Queensland[14]) compared with 2 mg/m³ in the United States that has been reduced to 1.5 mg/m³ since 1 July 2016. Second, doubts have been raised as to the effectiveness of the modern engineering dust controls in the mines to prevent overexposure of miners to respirable dust. Neither performance nor the effectiveness of these dust controls have been the focus of global regulatory requirements, in spite of a substantial increase in global production from all forms of mining.

Low-to-middle-income countries

In China, CWP is the main occupational lung disease and accounts for over half of the total new diagnoses of pneumoconiosis. This equated to 13 955 new diagnoses in 2013.[15] In a systematic analysis of 11 Chinese reports published between 2001 and 2011, the pooled prevalence of CWP was estimated to be 6.0%,[16] based on 10 821 people diagnosed with CWP from 173 646 dust-exposed Chinese workers. This was relatively higher in local mines compared with state-run mines, and approximately compared with a prevalence of 3.2% in the United States and 0.8% in the UK during a similar time period.

Although CWP is a serious health issue in other countries of the Asian Pacific region, there are few studies that describe the extent of the problem. A comprehensive report was published from Vietnam almost 20 years ago and this described very high rates of pneumoconiosis from 'special field studies' that were conducted by the Government of Vietnam. This contrasted with official statistics for silicosis from the National Institute of Labour Protection (NILP) which acknowledged these figures were an underestimate of the true frequency.[17] As coal miners with respiratory

symptoms were usually funded to have a chest radiograph, many miners with asymptomatic disease were not identified despite the potential benefits from earlier intervention. At the time, traditional manual work was the predominant mining technique, yet the respirable dust concentration in one underground coal mine was reported to be over 30 times higher than the national standard. Silica concentrations in open-cut mines were estimated to be between 12% and 28%,[17] so the affected individuals may have had mixed-dust pneumoconiosis which is an entity that is now formally recognized within the CMDLD spectrum.

The Global Burden of Disease (GBD) study estimated the age standardized death rate per 100 000 persons to halve from 0.8 in 1990 to 0.4 in 2013, largely for low-to-middle-income countries.[18] However, these mortality data were collected at two time points and may not have been substantially influenced by the recent upward trend in CWP prevalence.

CLINICAL, PATHOLOGICAL AND RADIOLOGICAL FEATURES OF CWP

Phenotypes

Over the years, CWP has been typically diagnosed in a coal miner who has had considerable dust exposure accompanied by compatible chest radiographical findings.[2] The latency period is usually more than 10 years, although it has been reported for miners working as few as 6 years in Vietnam.[17] The recent trend of a

Table 2 Epidemiological comparisons between traditional CWP categories that represent opposing ends of the spectrum of CMDLD

	Traditional CWP phenotypes	
	Simple CWP	Complicated CWP
Alternate taxonomy	Anthracosis	PMF
Age	Tends to affect older miners	Younger miners are overrepresented[19]
Symptoms	Few	Longstanding cough with or without exertional shortness of breath
Latency	Typically >10 years	Typically >10 years
FEV$_1$ decline	Minimal change	FEV$_1$ decline >60 mL/ year greater than miners without CWP[21]
Prognosis	No difference in mortality[19]	At risk of respiratory failure and premature death
Intervention	Adequate dust control and health surveillance	Adequate dust control and health surveillance

CMDLD, coal mine dust lung disease; CWP, coal workers' pneumoconiosis; FEV$_1$, forced expiratory volume in 1 s; PMF, progressive massive fibrosis.

longer latency in China may relate in part to more effective dust control protocols.[19] A large number of CWP patients are diagnosed after a miner ceases employment.[2] Even in the context of dust exposure at low levels, some miners can develop CWP from 15 to 20 years after exposure.[19,20]

From the series of 495 individuals diagnosed between 1963 and 2014 in Eastern China, compared with miners with early or stage 1 CWP, the mean age of diagnosis was earlier for miners with the most severe disease (43.3 years vs 52.3 years).[19] This was despite a similar duration of dust exposure. In this same series, the mean age of death for those diagnosed with CWP was less than the mean age of CWP survivors which was similar to the baseline population (56.8 years vs 71.6 years). This observation of differing lung function trajectories resemblances the traditional classification of simple and complicated CWP (Table 2), with a subgroup of younger and more susceptible miners having a worse prognosis. More recent data have shown consistent decrements in forced expiratory volume in 1 s (FEV$_1$) % of predicted across a range of radiographical profusion subcategories and this reflects the progressive nature of the disease.[22]

Of concern is the overrepresentation of younger miners in the subgroup with rapidly progressive CWP, defined by the development of PMF and/or an increase in small opacity profusion greater than one subcategory over 5 years.[9] Genetic predisposition as discussed below may play a role. Consistent with mixed-dust pneumoconiosis, recent evidence from histopathological specimens has found silica to be present in high concentrations in the lungs of workers with rapidly progressive pneumoconiosis.[23]

Pathological features of CWP

Coal dust accumulation in lung tissue leads to a variety of pathological findings from innocuous airway anthracosis to irreversible lung fibrosis and emphysema. Coal dust accumulates in the terminal bronchovascular bundle and is engulfed by alveolar and interstitial macrophages which result in the formation of pulmonary macules and nodules with deposition of dense collagen fibres.[24] Focal emphysema changes around respiratory bronchiole walls can also be observed. The stimulated release of pro-inflammatory cytokines including TNF-α is a potential biomarker of lung pathology,[25] and iron within coal dust may reflect the extent of exposure and be a marker of oxidative lung damage.[1,26]

Radiological features of CWP

Classical chest X-ray reticulonodular features are typically categorized according to the International Labour Office (ILO) International Classification of Radiographs of Pneumoconiosis and this was updated in 2011 to extend its applicability to digital images.[27] As distinct from the ILO classification system, the Chinese National Diagnosis Criteria of Pneumoconiosis (GBZ 70-2009) is used in China. The diagnosis can be made by consensus readings, expert panel readings, independent B reading and final determinations derived from multiple independent readings.

Both CWP and silicosis are typically characterized by small (<1 cm) nodular interstitial opacities in the upper zones. However, radiological features of CWP may not be typical. An evaluation of the U.S. CWHSP over 30 years found that 38% of coal miners with radiographical interstitial changes had predominantly irregular opacities, of whom 41% were largely confined to the lower lung zones.[28] These irregular opacities on plain films are also a feature of mixed-dust pneumoconiosis, as opposed to the predominance of rounded opacities in silicosis.[29] Dust diffuse fibrosis (DDF) is a specific form of CMDLD with radiological findings similar to those seen in idiopathic pulmonary fibrosis, including lower lobe interstitial opacities, honeycombing and traction bronchiectasis.[30,31]

Complicated CWP or PMF occurs in around one-third of coal miners who fulfilled criteria for rapidly progressive CWP,[9] and features the coalescence of smaller opacities to large nodules of at least 1 cm in size.[3] In patients of suspected lung malignancy, positron emission tomography (PET) scanning is of limited value because the majority of nodules more than 1 cm in diameter can be metabolically active.[32] This can lead to a false positive result as standardized uptake values can overlap with malignant nodules.[1]

Clinical features of CWP

The respiratory symptoms of CWP are non-specific and mostly overlap with other coal dust-related conditions such as chronic bronchitis, COPD and emphysema.[33] Black-pigmented sputum production (melanoptysis) can occur when large nodules necrotized and liquefied into the airways. Lung function patterns include chronic airflow obstruction, true lung restriction, mixed ventilatory defects and reductions in carbon monoxide diffusing capacity,[1,34] and these can vary according to the inhaled silica content, stage of disease and extent of tobacco smoke exposure. Even in the presence of radiologically confirmed pneumoconiosis, airflow obstruction seems to play a predominant role in coal workers' breathlessness.[35] Coal miners are frequently exposed to cigarette smoke, diesel exhaust and bio-aerosols and this can make it difficult to determine the role of coal mine dust in miners who develop COPD. In a series of 722 CWP autopsies, Kuempel *et al.* recently demonstrated that coal mine dust exposure was associated with a greater risk of developing emphysema compared with cigarette smoking in their population.[36] Furthermore, coal mine dust exposure is a predictor of chronic bronchitis and emphysema mortality even in non-smokers.[37,38]

HRCT of the chest should be performed in coal mine workers with either borderline interstitial findings on plain radiographical films or in whom other diagnosis such as neoplasm, vasculitis, hypersensitivity pneumonitis or mycobacterial infection need to be considered. Open lung biopsy or bronchoscopy sampling is usually not necessary in patients with significant exposure and typical imaging.

Cardiopulmonary exercise testing can be used to assess a patient's physical limitations and the impact of lung disease. In CWP patients, a high ventilatory equivalent ratio for oxygen (suggesting mismatch between ventilation and perfusion) has been found to be the best predictor of dyspnoea severity when compared with other functional indices.[35] An early and accelerated FEV_1 decline has been suggested to relate more closely to small airway disease than to either emphysema or fibrotic lung disease.[21] Interestingly, recently published results in a broader mild to moderate COPD population with functional assessment of small airways with expiratory and inspiratory computed tomography (CT) technique were consistent.[39] Early recognition of small airway disease might be beneficial in detecting workers at risk of COPD development; these observations need to be reproduced by a larger cohort with detailed functional and radiological assessment of the small airways.

Severe pulmonary fibrosis associated with significant impairment in gas exchange may lead to chronic hypoxaemia, pulmonary hypertension and right heart failure. Particularly for low-to-middle-income countries, CWP can be complicated by *Mycobacterium tuberculosis* infection, especially when associated with silica exposure and more advanced stages.[19,20]

ENVIRONMENTAL RISK FACTORS

The early development of simple CWP is regarded to be the most important risk factor for the development of complicated pneumoconiosis which is closely related to the intensity and duration of respirable dust exposure.[40] Modern mining technology used globally that has the capability to generate high volumes of coal per shift has been identified as a major determinant for the recent increase in CMDLD. In Australia, for example, the development of medium and thick seam mines has allowed the installation of bigger and more productive longwall equipment. Such longwall mining practices has been compared with other underground mining techniques in Table 3.

In terms of respirable coal (and silica) dust exposure, besides the type of mine, important factors to consider include the profile of the coal; tenure and hours of employment; job type ranging from rock driller to dozer operator; job duties such as tunnelling, set explosives or shovelling coal; and the pattern of respirator or mask use (Fig. 1).[2] Diesel-powered machinery can generate diesel exhaust particulates and transporting coal out of the mine can disperse particles further. Specific to underground mines, the type and effectiveness of the engineering dust controls, mining technique, coal seam height, time spent at the coalface, the use of powered air-purifying respiratory helmets and adequacy of dust control with water sprays and ventilation systems are highly relevant. For surface mines, factors to take into account include the amount of dust in open or enclosed cabs while operating heavy machinery and the time spent outside cutting, drilling or blasting rock.[2]

With the progressive mining of thinner coal seams by the industry, particularly in the United States, an increased coexistence of silica-related fibrosis can contribute to CWP.[7] This in part explains the higher

prevalence of CWP in the United States in spite of lower recommended respirable dust limits, where the 2 mg/m^3 limit was based on a 1.4% risk of PMF for miners working with medium to low rank coal.[41] The practice of roof bolting that is particularly frequent in the United States is closely linked to silica exposure as these miners work outside the coal seams in quartz-containing rock.[2,10]

PREVENTION

There is no cure for CWP, therefore prevention is crucial. CWP can be associated with reduced lung function, even prior to the development of chest radiographical changes.[42] This provides an opportunity to monitor lung function by means of serial spirometric measurements ranging from annually to 3-yearly, in addition to radiographs.[43] This is currently recommended for United States miners,[1] particularly if symptomatic of dry cough and/or progressive breathlessness on exertion. The early identification of CWP is essential to implement appropriate management and make potential changes to employment. However, even after dust exposure has ceased, PMF can appear or if present, progress as manifest by an accelerated decline in lung function and/or development of typical radiographical changes. A comprehensive and coordinated approach to regular screening is important to secondary and tertiary preventative strategies that can improve quality of life and life expectancy. This may be limited by financial constraints in low-to-middle-income countries, but this is especially important as respirable dust concentrations can be relatively high and pulmonary tuberculosis may complicate advanced CWP and/or mixed-dust pneumoconiosis in up to 6–7% of patients.[19]

Mining operators of all underground and surface mines have a responsibility to ensure that respirable coal dust and silica exposures remain below recommended or regulatory levels. In some countries, compliance sampling methods that average respirable dust concentrations may conceal instances of several random samples that are well above the limit,[7] which may otherwise be detectable by continuous monitoring. Between 2012 and 2014 in Queensland, Australia, the estimated mean respirable dust concentration for workers in longwall production
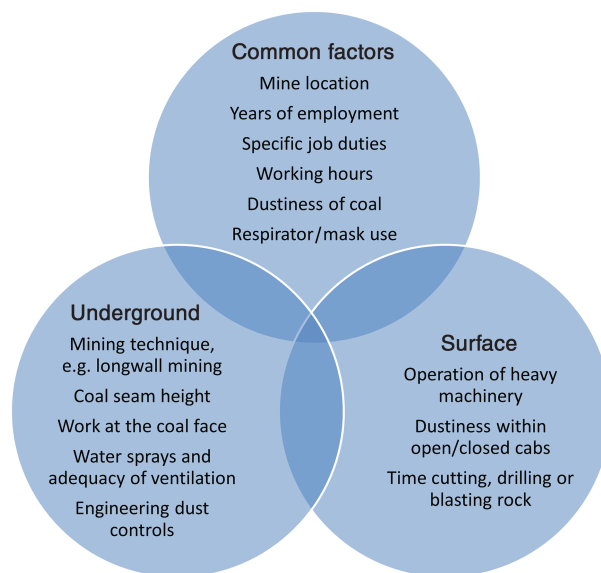
Figure 1 Job-specific environmental risk factors, common and specific to underground and surface mining.[2]

was below the recommended limit of 3 mg/m^3, but periodically this level peaked above 6 mg/m^3. These exceedances occurred particularly during 2014,[44] and in the absence of a change in monitoring ± measuring practices, this is consistent with progressive mechanization. Whilst engineering dust control equipment and processes are reasonably standardized throughout the world, the equipment and processes implemented can vary from mine to mine.[45] Wearing respiratory protection equipment can limit dust exposure, but a more comprehensive evaluation of the type and practices is needed.

From an Australian perspective, surface and underground coal miners are recommended to be part of a periodic surveillance system to identify early CMDLD,[11] At-risk miners who could be part of a more targeted intervention include those with early and more prolonged coal mine dust exposure, those with a greater exposure to silica dust and/or tobacco smoke and especially those with respiratory symptoms. Personal continuous dust monitoring devices is an option to

Table 3 Description of mining techniques and procedures[2]

Underground mining	**'Room and pillar' mining**	**Conventional mining**
	Coal is mined and remaining 'pillars' provide roof support	Holes are drilled and then blasted using compressed air or explosives
		'Continuous' mining
		Steel bolts placed in the mine ceiling to prevent collapse
	Longwall mining	
	A specialized machine cuts across the length of the coal face to extract coal	
	A hydraulic roof support system supports the mine ceiling, which is allowed to collapse as cutting advances	
Surface mining	Overburden (topsoil and rock) is removed by drilling, blasting and excavating	
Transport	Underground diesel-fuelled shuttle cars and conveyor belts transport coal to the surface → preparation plant	
Preparation plant	Coal is washed, crushed to size and separated from waste (rock and soil)	

more accurately document a worker's true exposure.[43] As a priority, the surveillance system requires a coordinated approach to the timely reporting of tests and effective communication of potential CMDLD to individual miners.

Although the use of low-dose conventional and HRCT scanning for screening purposes has not been accepted internationally,[1,46] it offers the advantage of being more sensitive at detecting reticulonodular patterns in early pneumoconiosis than plain films alone.[47] Further evaluation of this potential screening tool will need to encompass the management of potentially malignant pulmonary nodules, especially for miners with other known risk factors. At least in Australia, this evaluation would be extended to include the feasibility of conducting these investigations as some miners would need to travel up to 150 km to such a facility and whether it is cost-effective at a population level.

Patients with CMDLD should be offered best supportive care that includes exposure avoidance, smoking cessation, pulmonary rehabilitation, appropriate disease burden compensation, home oxygen and lung transplant evaluation when eligible.

FUTURE SCIENTIFIC APPROACHES

Epidemiology and public health
Prospective cohort studies of coal miners would ideally have serial lung function measurements and chest radiographs, which can correspond with the testing performed in periodic health surveillance programmes. Specifically, adverse respiratory health outcomes such as impaired lung function growth, accelerated lung function decline and/or compatible radiological findings can be used to identify risk factors for early-onset disease. To complement routine questionnaire data including personal smoking history, other epidemiological questions could be incorporated into the periodic health visits to help address formulated research questions. Establishing any evidence of reduced lung potential by comparing coal mine workers with non-mining workers may then influence the medical workforce, industry and government to guide public policy in the interests of coal miners.

For countries that have collected insufficient information about the health of coal miners and burden of pneumoconiosis, well-designed epidemiological studies should ideally be undertaken. The differing radiographical classification is an important consideration for international studies that collaborate with China. As working environments have become more heavily polluted with increasing economic incentives to mine coal, there should also be strong focus on assessing the adequacy of dust monitoring and controls in order to minimize dust exposure wherever possible.

Molecular biomarkers
The primary underlying mechanism of CWP relates to the release of pro-inflammatory cytokines by alveolar macrophages, which eventually lead to interstitial fibroblast formation and coalescing of fibrotic nodules into conglomerate masses. Compared with coal dust, dust from silica is highly fibrogenic and so silicosis as a single entity has been more extensively investigated in animal models and in human cell culture systems. Similarities with a murine-based model of bleomycin-induced fibrosis have been observed.[48]

Currently there are no reliable, validated biomarkers for CMDLD in human cohorts.[25] Many lack specificity or require invasive testing such as bronchoscopy or lung biopsy. There is, however, extensive preclinical in vitro and in vivo animal data. Early biomarkers that might correlate with the extent of exposure include those of oxidative damage, antioxidant enzymes, reactive nitrogen species (RNS) and reactive oxygen species (ROS) and the activation of downstream transcription factors such as NFkB and the STAT family that activate inflammatory and fibrogenic gene expression programmes. While most relate to silicosis, the oxidative damage marker of iron within coal dust appears to correlate well with rates of pneumoconiosis in different mining regions, especially the more bioavailable and complex forms.[1,26] TNF-α and its receptor are potential candidate biomarkers that might reflect lung pathology at a cellular level before the development of CWP and silicosis.[25] TNF-α and IL-8 are pro-inflammatory cytokines which have been associated with the presence and progression of CWP, although both still require validation using well-designed and adequately powered prospective cohort studies.[25,49,50]

Genetic testing and genomic biomarkers
Genetic-based research using case–control study data has largely been performed in China and has focused on the potential for genetic factors to predispose to CWP particularly in relation to inflammation and silicosis. No genomic markers, however, have been validated to date.[1] This includes potential susceptibility loci from genome-wide association studies (GWAS, rs73329476, rs4320486 and rs117626015),[51] and the T1559C/rs5368 polymorphism.[52] Regarding TNF-α, the TNF-α-308A allele has been linked to ever having CWP especially with nodules as opposed to PMF,[53] whereas TNF-α promoter TNF2 polymorphism has been associated with the development of large opacities.[54] Other identified polymorphisms include IL-4 C-590T;[55] cyclo-oxygenase-2 rs689466 and rs20417;[56] microRNA-149 rs2292832 TT;[57] a potentially protective effect of MMP3 rs522616 GG;[58] and NLRP3 rs1539019, especially in early disease.[59] The latter is of particular interest given evidence implicating the NALP inflammasome in silicosis, activation of the Nalp3 inflammasome by silicates,[60,61] in the context of mixed-dust pneumoconiosis. However, genetic candidate markers may be most relevant to future research that examines gene-by-environmental interactions as contributing factors for rapidly progressive CWP, while considering that racially restricted CWP susceptibility gene polymorphisms may exist.

Novel mechanism and drug discovery

Although limited to date, there is a great potential for filling the knowledge gap with regard to mechanisms and drug targets specific to CWP. Examples of recent work in murine models of silicosis include the demonstration that the Wnt/β-catenin pathway is required for activation of TGFβ and fibrosis.[62] Dasatinib, the Food and Drug Administration (FDA)-approved kinase inhibitor, has been shown to ameliorate structural changes in the lungs as well as changing macrophage phenotype in an intervention that commenced once disease had been established,[63] as have annexin A1 mimetic peptides.[64] The assessment of short-term responses of single cell populations in culture systems, known as high-throughput screening, is a particularly useful approach to drug discovery. However, silicosis and pneumoconiosis represent multicellular pathological processes that are likely to be more amenable to lower throughput of drug candidates using organoid-on-a-chip type technologies.[65]

COST AND COST-EFFECTIVENESS STRATEGIES

CWP is a progressive, debilitating and potentially fatal disease and the financial burden it forces onto patients, families, governments and the wider community is costly. The United States spends an estimated $US one billion annually in treatment and compensation. In China, which has a high prevalence of CWP, the future medical treatment, welfare and associated costs were estimated in 1986 and 1992 to approximate 0.4% of its gross domestic product, thereby placing a substantial burden on its economy.[66] Furthermore in China, there have been attempts to economically evaluate preventative strategies including the use of advanced protective equipment.[67]

Even in high-income countries, the increasing CWP prevalence is still of great concern. In Australia, there has been a call to standardize recommended exposure parameters and monitoring procedures, to implement a comprehensive screening programme and establish a centralized occupational lung disease register.[34] There is also a need to employ methods such as cost-effectiveness which have been used to evaluate other occupational health interventions such as silicosis.[68] Such an analysis could involve costing this programme of prevention and early diagnosis of CWP, PMF and other lung-related fibrotic diseases; benefits in terms of potential downstream cost-savings that may arise (reduced hospitalizations); as well as modelling the improvements in health outcomes. The potential benefits from the prevention of these diseases could also be quantified using quality-adjusted life years that capture the likelihood for gains in survival and quality of life from preventing the development of lung-related fibrotic diseases that are due to exposure to coal dust. The purpose of such an evaluation would be to measure the impact of these diseases and to look at the cost and cost-effectiveness of strategies for prevention. This would enable governments and industry to assess whether a greater commitment of resources is required

given the expansion in industry and re-emergence of some mining-related lung diseases in recent years.

CONCLUSION

CWP in its most severe form can lead to chronic respiratory failure and premature death. A high cumulative exposure to respirable coal and especially silica dust is central to the development of CMDLD and other possible susceptibility factors are still not well defined. With improved technology of mining equipment to maximize productivity in recent decades, there has been a resurgence of CWP that has attracted media attention and political interest in higher income countries. Globally, there is evidence to support the need for a greater emphasis on the efficiency and performance of the engineering dust controls in mines and stricter policy to facilitate early detection and timely treatment for miners in the coal industry. Recommendations include more stringent measurement and monitoring of respirable dust exposure levels, a more systematic screening programme and a centralized registry of CWP patients. Improved collection of epidemiological data may identify at-risk miners and, in doing so, provide information

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KEY POINTS

- CWP is a preventable and potentially fatal occupational lung disease without a clearly proven effective treatment that has been incorporated into the spectrum of CMDLD.
- After successful control of the disease in some high-income countries, there has been a reappearance or an increase in CWP diagnoses, in association with increased coal production and greater mechanization of mining techniques.
- Compared with Australia, a greater prevalence of CMDLD for mines that have higher respirable silica dust concentrations may reflect a rise in mixed-dust pneumoconiosis-related diagnoses.
- In addition to excessive exposure to respirable dusts, increased susceptibility that manifests as a more severe and progressive disease has been observed in younger miners and the predisposing factors have not yet been well defined.
- Effective dust monitoring and control are a crucial step to ensure employer adherence to the recommended respirable dust limits, which is a task that is especially challenging for low-to-middle-income countries.
- Early disease recognition together with efficient reduction/elimination of ongoing respirable dust exposure is central to minimizing the emergence of the severe form, progressive massive fibrosis.
- The rising prevalence in global burden creates an imperative for efforts to discover new and effective treatments.
- Future research into the potential use of HRCT chest scanning, epidemiological identification of at-risk miners and validation of candidate biomarkers will advance scientific knowledge that aims to improve the health of miners in the coal industry.

for health education strategies and a new platform to validate candidate biomarkers and develop experimental models including novel drug discovery. For some countries, there are substantial financial barriers to adequately address the health problems of coal mine workers.[17] However, the prevention of CMDLD is an important public health target and the quality of life cost utility may enable governments and industry to ultimately develop cost-efficient strategies for its prevention.

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