Occupational Interstitial Lung Diseases

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KEYWORDS

• Occupational lung disease • Interstitial lung disease • Asbestosis • Silicosis
• Hypersensitivity pneumonitis

KEY POINTS

- Silicosis, asbestosis, and coal worker's pneumoconiosis are commonly encountered in pulmonary clinics, and are related to dust and asbestos exposure.
- Wood dust, gases, vapors and fumes, silica, and agricultural dusts, are associated with idiopathic pulmonary fibrosis.
- Silica, welding fumes, solvents, heavy metals, and particulate matter, are associated with connective tissue disease-associated ILD.
- Bird, mold, and agricultural exposures are associated with hypersensitivity pneumonitis.
- There are limited treatment options; reduction of exposure is essential to reduce disease progression.

INTRODUCTION

Interstitial lung diseases (ILDs) are a heterogeneous group of parenchymal lung diseases, some of which arise as a result of genetic susceptibility, as well as external noxious stimuli, of which occupational and environmental exposures contribute. Such exposures may by directly causal, such as in the case of dust-related pneumoconioses, or partly contributory, such as in the case of idiopathic pulmonary fibrosis (IPF) and connective tissue disease associated interstitial lung diseases (CTD-ILDs) (**Table 1**). This review will outline our current understanding of the occupational burden of common ILDs, highlight limitations of our current knowledge, and propose future research directions.

OCCUPATIONAL INTERSTITIAL LUNG DISEASES

Pneumoconioses

The pneumoconioses are parenchymal lung diseases that arise from the inhalation of inorganic dust particles. It comprises a heterogenous group of parenchymal lung

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Table 1
Common interstitial lung diseases and associated occupational exposures

ILD	Relevant Occupations
Silicosis	Miners, artificial stone benchtop fabrication, sandblasting, and jewelry polishing
Asbestosis	Miner, asbestos production, insulation, lagging, cement production, boilermaker, shipyard and railway workers, car mechanics, demolition, and WTC first responders
Coal worker's pneumoconiosis	Coal miners and coal production
Chronic beryllium disease	Aerospace and defense industries, alloy and automotive industries
IPF	Silica-related industries, vapors, gases, dusts, fumes, wood dusts, and agricultural dusts
CTD-ILD	Silica-related industries, petrochemical industries, motor vehicle production, dry cleaning, particulate matter, welding fumes, and heavy metals
Sarcoidosis	Agriculture, bakers, food production workers, silica-associated industries, firefighters, WTC first responders, dental technicians, machine operators, and aerospace industry
Hypersensitivity pneumonitis	Farming, food production workers, bird breeding, and poor ventilation/contaminated water systems

Abbreviations: CTD-ILD, connective tissue disease-associated interstitial lung disease; ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis; WTC, World Trade Center.

diseases, whose pathogenicity and disease sequelae vary depending on the dust composition, the degree of exposure, and associated comorbidities.

Silicosis

Prevalence

Silicosis is a fibrotic lung disease resulting from the inhalation and deposition of respirable crystalline silicon dioxide. Recognition of silicosis emerged in in the 1st century with Pliny the Elder, again in 1716 by Bernadino Ramazzini, and in the early 1900s in South Africa and elsewhere.[1] Historically, those at most risk of silicosis were workers who encountered silica in its natural environment, including miners, tunnel, and quarry workers. Although a greater understanding of the risks of silica and the development of dust control measures had resulted in a decline in silicosis morbidity and mortality, rates remain unacceptably high and are increasing in some areas. More recently, there has been an increase in pneumoconiosis attributable to silica exposure in Central Appalachian coal miners.[2] This highlights that constant dust control vigilance is required. Rates have also increased in newer industries including artificial stone benchtop fabrication, denim jean production (sandblasting),[3] and jewelry polishing,[4] where silica has been introduced without recognition or control of its hazards. Artificial stone is formed from finely crushed rocks (predominantly quartz), with added constituents including colored glass, shells, metals, and adhesives, all of which are bound by a polymer resin, molded into shape, and heat-cured.[5] Artificial stone contains up to 95% crystalline silica, far higher than any other commonly used stone.[6] Stone slabs are most commonly cut and shaped for benchtop fabrication using high powered hand tools that generate extremely high levels of respirable crystalline silica dust. The current permissible crystalline silica exposure limit in the United States is 0.05 mg/m^3 over an 8-h work period.[7]

By way of example, dry cutting artificial stone generates silica dust levels of 44 mg/m^3 over 30 minutes; over 300 times the permissible limit.[8] More than 500 workers with silicosis have been identified from the artificial stone benchtop industry in Australia,[9] and cases are rapidly emerging in North America,[10] Spain,[11] and elsewhere. In Israel where much of the artificial stone is produced, at least 82 workers with silicosis were identified, and at least 18 workers having undergone lung transplantation for this condition, representing a 15-fold increase in the expected rate of transplantation.[12]

Pathogenesis

The development of silicosis is related to factors specific to silica exposure including the concentration of silica dust, fibrogenicity of silica particles, additional constituents of the silica-containing products, as well as other contributory factors such as smoking, infections, and genetic and autoimmune susceptibilities.

Silica mediates interstitial damage both directly and indirectly through the upregulation of inflammatory and fibrotic pathways. When silica particles are inhaled in the lungs, they are engulfed by alveolar macrophages, which stimulate pro-inflammatory and pro-fibrotic pathways. Dust-laden macrophages enter the interstitium both directly and via the hilar lymph nodes, and a perpetual cycle of inflammation and fibrosis ensues. Silica particles also enter the interstitium directly, and freshly fractured silica, which is generated through newer industries, is more likely to directly penetrate the epithelium. These silica particles are more likely to generate free radicals, leading to oxidative stress and stimulation of cytokine transcription factors, which further stimulates a pro-inflammatory and pro-fibrotic response[13,14] (**Fig. 1**).

Persistent silica uptake and its associated immunologic effects leads to the formation of parenchymal silicotic nodules, tending to occur around respiratory bronchioles in the subpleural and paraseptal areas. Over time, these nodules conglomerate and obliterate the surrounding small airways and pulmonary vessels, and results in progressive massive fibrosis (PMF).[11,12]

Diagnosis

Diagnosis of silicosis requires a history of silica exposure, concordant radiological findings, and exclusion of other diseases that mimic silicosis. Additional investigations including bronchoalveolar lavage (BAL), and lymph node or lung biopsy may be required (**Table 2**).

Plain chest x-ray (CXR) using the International Labour Classification (ILO) has traditionally been used in screening and diagnosis of silica-affected workers. However, the higher resolution of computed tomography (CT) makes it superior to CXR in the detection and characterization of disease and has supplanted the use of CXR for diagnosis in high-resourced countries. Simple silicosis tends to be characterized on CT by diffuse centrilobular nodules (up to 1 cm in size), usually in an upper lobe predominant distribution. As silicosis progresses, nodules coalesce to form conglomerate masses (>1 cm in size) with central cavitation. Distortion of the surrounding lung parenchyma and peribronchial vessels occurs and is often associated with pleural thickening. Lymphadenopathy with or without calcification may be seen (**Fig. 2**). Rarely, in silicoproteinosis, crazy paving with septal thickening and airspace consolidation may be identified.[15,16]

Additional tests include BAL fluid analysis, where a predominance of macrophages may be seen in the cell count differential (though nonspecific), and birefringent silica particles may be visualized and quantified. Histopathology shows well-demarcated fibrotic nodules containing birefringent silica particles, histiocytes, and interstitial fibrosis.[11,12]

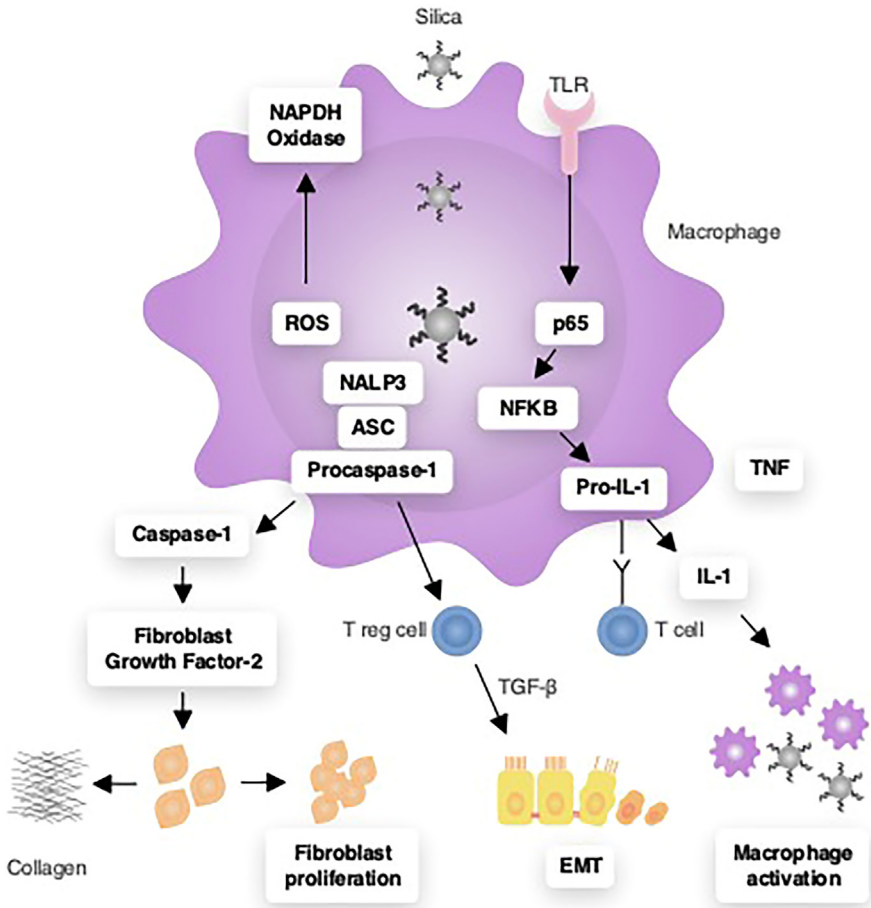

Fig. 1. Biological pathways in silicosis. NALP3 (NACHT, LLR, and PYD domains containing protein 3), ASC (apoptosis-associated speckle-like protein containing a CARD), and procaspase-1 form the inflammasome. EMT, epithelial mesenchymal transition; IL, interleukin; NADPH, nicotinamide adenine dinucleotide phosphate; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; ROS, reactive oxygen species; TGF-β, transforming growth factor beta; TLR, toll-like receptor; TNF, tumor necrosis factor. (*From* Barnes H, Goh NSL, Leong TL, Hoy R. Silica-associated lung disease: An old-world exposure in modern industries. *Respirology.* 2019;24(12):1165-1175.)

Disease Behavior and Treatment

Outcomes range from subclinical pathologic changes on imaging, to lung damage, reduced ventilatory capacity, diminished quality of life and reduced life expectancy.

The mainstay of management of silicosis is reduction or elimination of the exposure, according to the hierarchy of controls (**Fig. 3**), as persistent exposure is associated with disease progression. However, it is also important to note that some will continue to progress even after exposure cessation.[3] Workplace reporting and compensation programs vary between states and countries, and clinicians should make themselves and their patients aware of the options for workplace remediation and ongoing support.

Table 2
Common interstitial lung diseases and associated imaging and histopathological findings

ILD	Imaging Findings	Additional Tests
Silicosis	Simple silicosis—diffuse centrilobular nodules in an upper zone distribution Complicated silicosis—conglomerate masses with cavitation and distortion of the surrounding parenchyma Mediastinal and hilar lymphadenopathy	BAL—macrophage predominant, birefringent silica crystals Histopathology– well demarcated fibrotic nodules containing silica crystals, interstitial fibrosis
Asbestosis	Bilateral lower zone fibrosis, parenchymal bands, traction bronchiectasis, honeycombing, subpleural dot-like opacities, pleural plaques, diffuse pleural thickening, pleural effusions	Histopathology—peribronchiolar and subpleural fibrosis, asbestos bodies
Coal worker's pneumoconiosis	Small round reticular nodular opacities, upper zone predominant. Progressive massive fibrosis with conglomerate masses and parenchymal distortion Mediastinal and hilar lymphadenopathy	Histopathology—nodules containing dust-filed macrophages, with adjacent fibrosis and collagen, and surrounded by a halo of emphysema

Abbreviations: BAL, bronchoalveolar lavage; CTD-ILD, connective tissue disease-associated interstitial lung disease; ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis.

Whole lung lavage is an experimental therapy considered in carefully selected patients. Although there are no clearly established criteria, radiological presence of diffuse ground glass nodules with minimal evidence of PMF is likely to confer the greatest benefit. Given that some patients improve after exposure cessation, whole lung lavage is generally reserved for those who continue to progress despite cessation. There is limited evidence of reduction in radiological and physiologic progression in the short term,[17,18] though the long-term effects are still unknown. Anti-fibrotic therapy in those who display a progressive-fibrosing phenotype may be indicated, though not specifically studied in this population.[19] Lung transplantation may be indicated for end-stage disease in otherwise suitable patients. In addition to specific therapies, smoking cessation and treatment of coexisting infections including mycobacterial infections are important.

Asbestosis

Asbestosis is an ILD caused specifically by exposure to asbestos fibers. Other respiratory effects of asbestos include benign pleural plaques, diffuse pleural thickening, mesothelioma, and lung cancer.

Asbestos is a naturally occurring mineral, and is used to strengthen, insulate, and fireproof materials. Asbestos is still used in the United States, and although its use is now banned in many other countries, its lag time in developing disease makes it a still relevant occupational risk factor. Asbestosis may develop 20 to 40 years after exposure, and risk of disease is dose dependent.[20] Those most at risk include

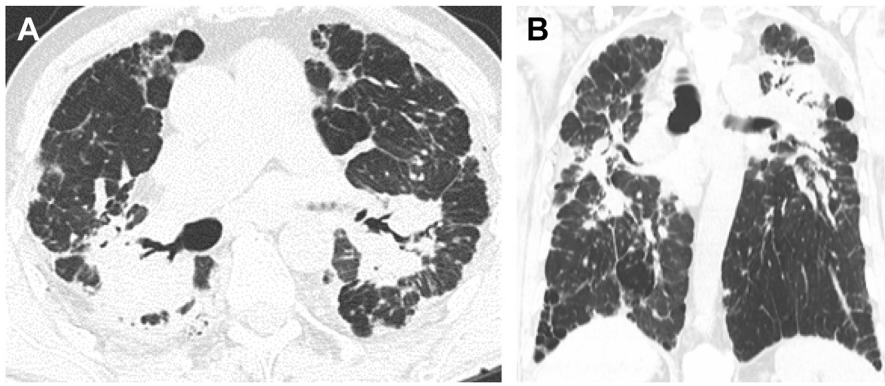

Fig. 2. Axial (*A*) and coronal (*B*) HRCT images of silicosis with progressive massive fibrosis. Numerous perilymphatic nodules are present, and coalesce in the upper lobes with marked upper volume loss and masslike fibrosis.

miners of asbestos, boilermakers, those working with insulation and cement, shipyard and railway workers and those involved in demolition. In addition, first responders of the World Trade Center had significant asbestos exposure (see Table 1).[21]

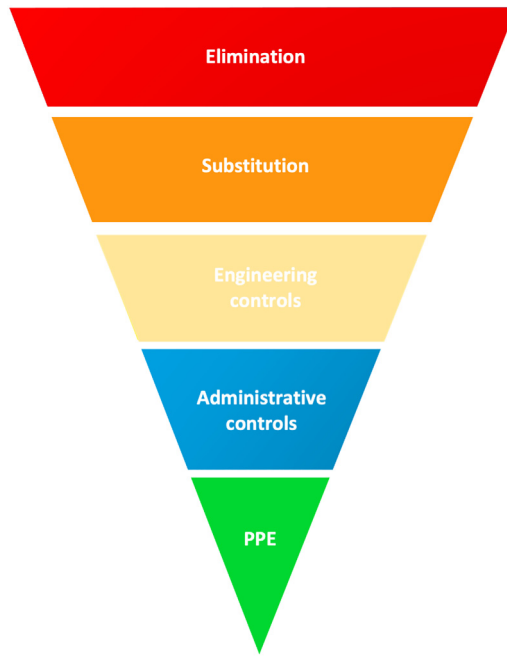

Fig. 3. Hierarchy of workplace controls. Elimination (including physical removal of the hazard) and substitution (including replacing the hazardous material) are the most effective hazard reduction measures, though then tend to be the most difficult to implement. Administrative controls include changing the way people work and engineering controls which includes isolating people from the hazard. Personal protective equipment (PPE) includes respirators, masks, gloves, ear plugs, and other equipment which the employee wears to reduce the risk of exposure. PPE tends to reduce but not eliminate risk.

Pathogenesis

Asbestosis results from inflammation and fibrosis that occurs both directly from asbestosis fibers and indirectly from the activation of the innate immune system. When asbestos fibers are inhaled into the lung, they are engulfed by alveolar macrophages, which subsequently lyse, releasing cytokines that attract further macrophages, CD4+ T lymphocytes, and mast cells, perpetuating an inflammatory response. Ingestion of asbestos fibers by alveolar macrophages also stimulates the NLRP3 (NACHT, LRR and PYD domains-containing protein 3) inflammasome to produce interleukin-1 (IL-1) and recruit fibroblasts. Persistent inflammation and stimulation of pro-fibrotic cytokines increases fibrogenesis. Hypertrophy and hyperplasia of type II epithelial cells promote fibrogenesis, and the upregulation of proto-oncogenes, leading not only to fibrosis but an increase in the risk of lung cancer[22,23] (**Fig. 4**).

Diagnosis

A detailed occupational history is essential to confirm sufficient exposure to asbestos. Common sources include brake pads, insulation products, and mined material. In addition, patients may be indirectly exposed through regular household contacts in the relevant industries.[24]

Imaging. High-resolution computed tomography (HRCT) chest findings include bilateral fibrosis, predominantly lower zone and subpleural in distribution, with parenchymal bands, traction bronchiectasis, and honeycombing (**Fig. 5**). Features which differentiate asbestosis from IPF can be subtle or absent and includes the presence of subpleural dot-like or branching centrilobular opacities and associated pleural disease (see **Table 2**).[25]

Histopathology. Lung biopsy specimens show an initially peribroncholar and subpleural fibrotic pattern, which advances beyond the pleural in the later stages. Asbestosis may share similar histopathological properties to usual interstitial pattern (UIP), though asbestosis tends to lack significant inflammation, and is collagenous rather than fibroblastic.[26] Asbestos bodies may be detected through light microscopy or electron microscopy.[26] Two or more asbestos bodies per 1 cm^2 of a 5 mm thick lung section, plus associated findings of pulmonary fibrosis, are required to confirm diagnosis.[26]

Disease Behavior and Treatment

Asbestosis tends to be less rapidly progressive than untreated IPF, although cases of progressive asbestosis do occur.[27] There are no specific treatments for asbestosis. Avoidance of ongoing exposure is essential to reduce further progression. Monitoring for pleural disease including mesothelioma and lung cancer is important. Patients who meet criteria for progressive-fibrosing ILD may be candidates for anti-fibrotic therapy.[19] A small single-arm exploratory study examining the use of pirfenidone in those with asbestosis found no significant safety signals.[28] There was a stability in FVC in the 24 weeks of treatment, but the study was not powered to detect differences in efficacy. Supportive treatments including oxygen supplementation, pulmonary rehabilitation, and palliative care referral should be used where indicated.

Coal Worker's Pneumoconiosis

Coal worker's pneumoconiosis (CWP), also known as 'black lung', is an irreversible ILD resulting from chronic inhalation of coal dust. In addition to CWP, coal dust can also cause silicosis, chronic obstructive pulmonary disease (COPD), and chronic

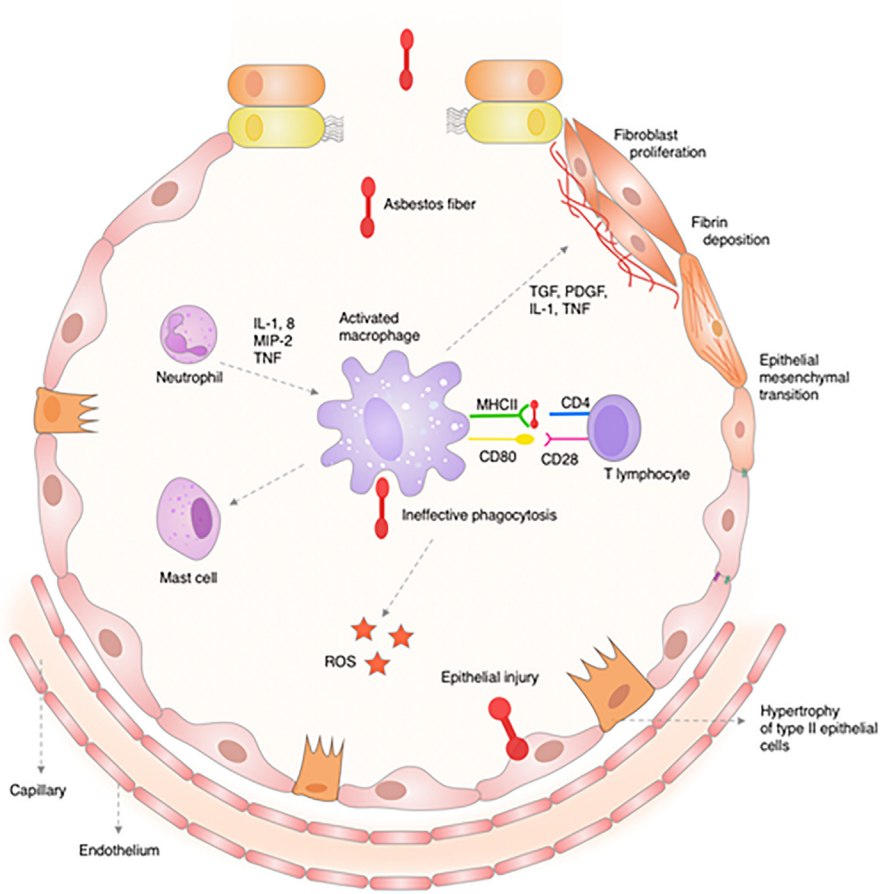

Fig. 4. Immunopathogenesis of asbestosis. Asbestos fibers are inhaled into the alveolar space. Macrophages are activated and stimulate production of neutrophils, mast cells, and T lymphocytes. Activated macrophages produce cytokines to stimulate fibroblast production. Ineffective phagocytosis of asbestos fibers results in release of reactive oxygen species (ROS). Direct epithelial injury leads to hypertrophy and hyperplasia of type II epithelial cells. Repeated epithelial injury and cytokine production leads to epithelial mesenchymal transition, fibrin deposition, and fibroblast proliferation.

bronchitis. Coal dust contributed to 25,000 deaths worldwide in 2013.[29] There has been a resurgence in the prevalence of CWP in the United States in the last few decades (1970s—6.5%, 1990s—2.1%, and 2000s—3.2%), specifically contributed by cases in Central Appalachia, and in this population there has also been an increase in the rate of PMF.[30] The factors for this increase are multifactorial, and may be explained by increased exposure to silica due to change in rock composition and more powerful mechanization, longer work hours, and reduced vigilance in dust control measures.

Diagnosis

Many countries have implemented screening programs for at-risk workers. Patients therefore may present with a wide spectrum of disease, from asymptomatic to advanced illness. Common signs and symptoms include cough productive of black

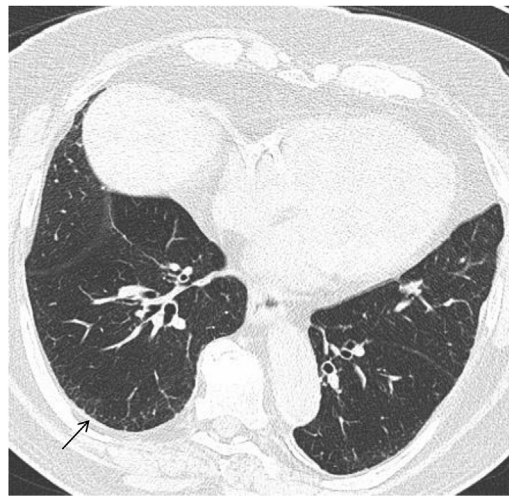

Fig. 5. Axial HRCT image of asbestosis, with a calcified pleural plaque in the left posterior thorax (*arrow*). Septal thickening is noted.

sputum, dyspnea, and air flow obstruction. Development of PMF may lead to respiratory failure and death.

Imaging. CXR is commonly used in screening programs to identify presence of disease. HRCT is more commonly used for diagnosis and to characterize disease progression. Imaging typically depicts small round reticular nodular opacities, in a diffuse perilymphatic upper zone predominant distribution. PMF with coalescence of nodules, surrounding parenchymal distortion, and mediastinal and hilar lymphadenopathy may also be present (see **Table 2**; **Fig. 6**).[31]

Histopathology. Lung biopsy is rarely required. If performed, the histopathology typically displays nodules containing dust-filled macrophages around a terminal bronchovascular bundle, with fibrosis and collagen surrounding it. A halo of emphysema surrounding the nodule may also be present. Evidence of PMF with coalescence of fibrotic masses, distortion of the surrounding parenchyma, and presence of other dust diseases such as silicosis may also be noted.[31,32]

Disease Behavior and Treatment

There are no specific therapies for CWP. Avoidance of further dust exposure may reduce progression. Although not specifically studied in these patients, those with PMF who meet criteria for progressive fibrosing-ILD (PF-ILD) could consider antifibrotic therapy. Disease progression is dependent on the level of exposure, profusion of nodules, presence of PMF, and concomitant risk factors including advancing age, smoking, and tuberculosis.[33]

Granulomatous Lung Diseases

Inhalation of metals can cause granulomatous lung disease, the most common of which is chronic beryllium disease. Occupations with heavy beryllium exposure include aerospace and defense industries, alloy, and automotive industries.

Patients with chronic beryllium disease may present with cough, fever, night sweats, and fatigue. Diagnosis is made on confirmatory occupational history, a positive serum

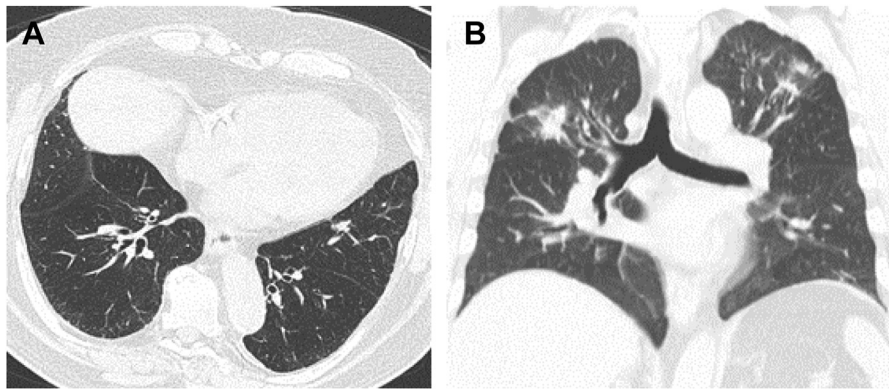

Fig. 6. Axial and coronal HRCT images of coal worker's pneumoconiosis, with upper lobe predominant peribronchovascular nodules and conglomerate masses.

or BAL beryllium lymphocyte proliferation test, and evidence of granulomatous inflammation on lung biopsy (either via transbronchial or VATS or open biopsy).[34] Chronic beryllium disease may have a similar radiological and histopathological appearance to sarcoidosis, although chronic beryllium disease may display less prominent lymphadenopathy, and lack extra-pulmonary features showed in sarcoidosis (**Fig. 7**). Differentiation between sarcoidosis and chronic beryllium disease is not only important to reduce ongoing exposure from occupational sources, but may also alter treatment regimens; chronic beryllium disease commonly requires ongoing immunosuppression whereas in a proportion of sarcoidosis patients, immunosuppression is not needed or required for a short term to induce remission.[35–37] Avoidance of exposure is important once the diagnosis of chronic beryllium disease is made. Treatment includes immunosuppression using corticosteroids and steroid sparing agents, though this is based on limited retrospective evidence.[38]

Hard Metal Lung Disease

Hard metal lung disease is derived from exposure to cobalt, tungsten, titanium, nickel, and chromium. These metals themselves are not "hard," rather their combination results in a strong and heat resistant composite material used in drilling, cutting, and mining.[39] These cases are rare, and limited to small case series.[40] Histopathology shows presence of "cannibalistic" giant cells (giant cell interstitial pneumonitis) with or without fibrosis. The altered appearance of these giant cells differentiates hard metal lung disease from other granulomatous diseases such as chronic beryllium disease, sarcoidosis, and hypersensitivity pneumonitis (HP).[39,40]

OCCUPATIONAL BURDEN OF OTHER INTERSTITIAL LUNG DISEASES

Although some ILDs are directly attributable to occupational and environmental exposures, there is a growing body of evidence to support the contributory pathogenic role of exposures in other ILDs. A large meta-analysis found that occupational exposures contributed to at least 26% of IPF, 19% of HP, and 30% of sarcoidosis cases.[41]

Idiopathic Pulmonary Fibrosis

IPF, the most common and prototypical ILD, is caused by a combination of intrinsic genetic factors in addition to external noxious stimuli and other contributory factors.

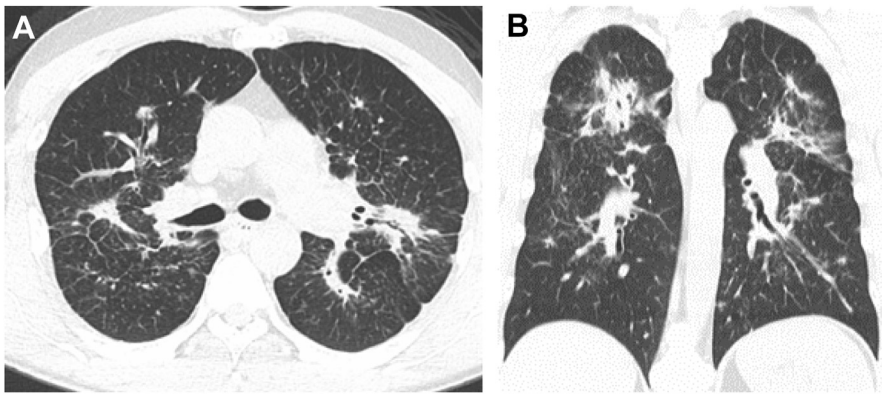

Fig. 7. Axial and coronal HRCT images of chronic beryllium disease, with upper lung predominant fine nodularity with septal thickening and peribronchovascular coalescent nodules.

Repeated microinjury of the alveolar epithelium is considered the initiating factor, leading to aberrant repair processes and ultimately the development of fibrosis.[42] Occupational exposures that are associated with IPF include vapors, gases, dusts, and fumes, wood dusts, agricultural dusts, and silica. In addition, smoking, microbial agents, and particulate matter from air pollution may play a role in the pathogenesis of IPF.[43,44]

Connective Tissue Disease-Associated Interstitial Lung Diseases

The link between occupational and environmental exposure and a subgroup of CTD-ILD cases has long been described.[45] Although complete mechanisms are yet to be fully elucidated, it is thought that ingestion of silica particles by alveolar macrophages stimulates pro-inflammatory cytokine production, activation of the adaptive immune system, loss of tolerance, and the production of autoantibodies.[46,47] Autoantibodies, in turn, exert direct effects on the epithelial endothelium, or form antigen-antibody complexes, which initiate further inflammation and fibrosis.[48]

Silica-associated scleroderma is more common in men, and associated with greater risk of ILD, as well as a diffuse phenotype, digital ulcers, cardiac dysfunction, and cancer, in addition to greater mortality. Positive anti-topoisomerase I antibodies are detected with greater frequency in silica-exposed patients. Cases of rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis, polymyositis, and ANCA-vasculitis in association with silica have been described.[49]

Other exposures associated with CTD-ILDs include organic solvents, typically aromatic compounds, trichloroethylene, and ketones, derived from petrochemical industries, motor vehicle production, and dry cleaning. Particulate matter from air pollution, welding fumes, pesticides, and heavy metals may also increase risk.[49]

Sarcoidosis

Sarcoidosis is a granulomatous disease that predominantly affects the lungs, but can also show extrapulmonary manifestations including cardiac, renal, dermatologic, and neurologic manifestations. Sarcoidosis is typically considered a diagnosis of exclusion, that is, attributable no other cause. However, occupational and environmental exposures as well as other noxious stimuli can play a role in initiation and perpetuation of inflammation and fibrosis. Clinical signs, symptoms, imaging, pathology, and

exposure may overlap with other parenchymal lung diseases including silicosis, HP, and rarer granulomatous diseases.

Commonly implicated exposures associated with sarcoidosis included organic dusts (agriculture, bakers, food makers), inorganic dusts (silica including miners, firefighting, World Trade Center first responders, and dental technicians), and solvents (machine operators, aerospace industry).[50]

Hypersensitivity Pneumonitis

HP is an immune-mediated ILD that arises as a result of occupational and environmental exposures to inhaled antigens, in susceptible individuals. The first cases of HP were described in farmers, attributable to moldy hay (*Saccharomyces spp.*).[51,52] Reports of HP associated with maple bark and sugar cane processing,[53] mushroom cultivation,[54] and cleaning pigeon excreta[55] soon followed. Prevalence of exposure varies with geography and seasonality, but common occupational sources include farming and manufacturing industries, bird breeding, and poor ventilation or contaminated water systems.[56] Additional risk factors including occupational exposure to pesticides,[57] and previous viral infections,[58] also increase risk. Unlike other workplaces exposures such as asbestosis and silicosis where the exposure is obvious, the exposures associated with the development of HP can be difficult to elicit. Furthermore, multiple exposures may be present, derived from the workplace or home. A detailed clinical history, serum precipitins testing, and in select cases specific inhalational challenge may aid in elicitation and differentiation of relevant exposures.[59] Workplace visits may be useful to identify exposures for the individual, and risk for others such as in the case of metal-working fluid contamination or swimming pool outbreaks. Similar to other ILDs, identification and remediation of the exposure significantly reduces the risk of progression of HP.[60]

LIMITATIONS OF THE EVIDENCE AND FUTURE RESEARCH DIRECTIONS

Occupational exposures remain an under-recognized risk factor in the development of ILDs. Drawing associations between occupation and the development of disease requires clinicians to take a detailed clinical history (**Box 1**) and requires systematic incorporation of such details into ILD registries. An occupational exposure history should include not only presence or absence of exposure, but also the nature of the tasks undertaken, frequency, duration, what type of reduction of exposure and personal protective equipment was used, and additional relevant risk factors. These details will allow us to better understand the pathologic link between exposure and disease, and the steps required to reduce disease occurrence.

The current literature reflects that there are few treatment options for many occupationally derived diseases. Although the pathogenesis of many occupational-related ILDs is predicated on the up-regulation of inflammatory pathways, the effect of immunosuppression has been disappointing. Availability of antifibrotic treatment for those who display a progressive-fibrosing phenotype may add possible options to the treatment arsenal but is unlikely to be a panacea. Further research into more effective treatment options is required in these ILDs.

In addition to addressing mortality and prevention of disease progression in these patients, focus should also be on assessment and improvement of quality of life. Work is good for our health, and in many cases our occupation forms part of our identity. Advising patients that work may have contributed to their disease, and advising work cessation, has considerable effects on quality of life, and this should also be considered in the overall care of the patients.

Box 1
Taking an occupational history

Respiratory Symptoms
- What are the relevant symptoms and signs? (eg, cough, wheeze, dyspnea, chest tightness, and reduced exercise tolerance)
- Do symptoms worsen when at work and improve when away from work?
- Are other workers experiencing similar symptoms?

Occupational details
- What is your current job?
- What industry is that in?
- What tasks do you do?
- What materials do you work with?
- Are there exposure protections in place? (eg, dust suppression, wet cutting, extraction, ventilation, personal protective equipment)
- How long have you been in this job?
- What job did you do before this? (for each previous job, ask about the industry, tasks, exposure protections, etc.).

Other environmental exposures
- Do you have frequent and prolonged exposure to birds, mold, wood dust, metals, gases, vapors, or fumes?
- Are there any hobbies or environmental exposures from which you experience respiratory symptoms?
- Is there anyone in the household who has prolonged exposure to occupational exposures of concern?

Relevant medical history
- Do you have a history of smoking, previous respiratory infections, symptoms, and signs of autoimmune disease?
- Do you have any medical conditions?
- Is there a family history of respiratory or autoimmune disease?

SUMMARY

Occupational exposures contribute to a significant burden of ILDs. Exposure may be partly or wholly contributory. A detailed clinical history paired with radiological and additional biological tests are required to confirm a diagnosis. Management includes reduction and avoidance of ongoing exposure; beyond that, treatment options are often limited. Further research into the systematic inclusion of occupational details in ILD registries, therapeutic options for these patients, and a focus on quality of life, is needed.

CLINICS CARE POINTS

- Clinicians should consider occupation as a potential contributing factor to those with interstitial lung diseases (ILDs).
- A detailed occupational history includes job details, tasks involved, and whether symptoms are associated with work.
- Diagnosis requires a detailed occupational history, compatible high-resolution computed tomography findings, and histopathology where indicated.
- Clinicians should assist patients in reduction or cessation of workplace exposures if causative of their ILD.

DISCLOSURES

H. Barnes and I. Glaspole do not have any disclosures relevant to this article.

AUTHOR CONTRIBUTIONS

H. Barnes and I. Glaspole conceived, drafted, and edited the article, and both approved the final version.

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