Silicosis

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Silicosis is a fibrotic lung disease caused by inhalation of free crystalline silicon dioxide or silica. Occupational exposure to respirable crystalline silica dust particles occurs in many industries. Phagocytosis of crystalline silica in the lung causes lysosomal damage, activating the NALP3 inflammasome and triggering the inflammatory cascade with subsequent fibrosis. Impairment of lung function increases with disease progression, even after the patient is no longer exposed. Diagnosis of silicosis needs carefully documented records of occupational exposure and radiological features, with exclusion of other competing diagnoses. Mycobacterial diseases, airway obstruction, and lung cancer are associated with silica dust exposure. As yet, no curative treatment exists, but comprehensive management strategies help to improve quality of life and slow deterioration. Further efforts are needed for recognition and control of silica hazards, especially in developing countries.

Epidemiology

Silicosis is caused by the inhalation of crystalline silicon dioxide or silica[1] and is one of the most important occupational diseases worldwide.[2,3] Although prevention efforts have been made for many decades, silicosis is a problem worldwide.[2,3] The disorder occurs everywhere, but is especially prevalent in countries of low and middle income, where the burden is often under-reported because of poor surveillance. China has the most patients with silicosis, with more than 500 000 cases recorded between 1991 and 1995, and 6000 new cases and more than 24 000 deaths reported annually.[4] The problem is particularly acute for workers in small-scale mines, who often have an accelerated form of disease.[5] In the Brazilian gold-mining area in Minas Gerais alone, more than 4500 workers were reported to have had silicosis between 1978 and 1998.[6] Of gold miners in South Africa dying from external causes (eg, injuries, burns, poisoning, and drowning), proportions with silicosis identified at autopsy increased from 3% to 32% for black miners and from 18% to 22% for white miners between 1975 and 2007.[7]

Silicosis is also an occupational health concern in developed countries. About 600 000 workers in the UK and more than 3 million workers in Europe were exposed to crystalline silica from 1990 to 1993.[8] Mostly, less than 100 cases were reported every year in the UK between 1996 and 2009, and deaths from silicosis declined from 28 in 1993, to ten in 2008.[9] In the USA, more than 121 000 workers were exposed to concentrations of respirable crystalline silica of 0·05 mg/m³ or more in 1993,[10] and 3600–7300 silicosis cases occurred annually from 1987 to 1996.[11] Overall age-adjusted mortality rates in the USA declined from 8·9 per million in 1968, to 0·7 in 2004.[11,12] However, silicosis deaths in young adults (aged 15–44 years), which are probably a result of intense and recent exposures, have not fallen since 1995.[13] Protective measures (eg, dust control and respirators) have caused a steady decline in death rates due to silicosis in the past few decades in developed countries,[12,14] but new outbreaks still occur occasionally.[15]

Search strategy and selection criteria

We searched Medline, Embase, and the Cochrane databases for studies from between Jan 1, 1991, and July 31, 2011, with the search term "silicosis" alone, or with "silica" or "silicon dioxide" in combination with "tuberculosis" , "lung function", "airway obstruction", "carcinogen", or "cancer". We focused mainly on reports from between 2006 and 2011, but older publications were also included when they covered essential aspects of silicosis. We also searched the reference lists of selected reports and those from national and international agencies. Review articles and book chapters are also cited for further details about particular areas that might be of interest.

Causes

Worldwide, silicon dioxide or silica is the most abundant mineral and occurs in crystalline and amorphous forms.[16] The most common free crystalline forms of silica in workplaces are quartz, tridymite, and cristobalite. Quartz can occur naturally and at varying concentrations in rocks such as sandstone (67% silica) and granite (25–40% silica).[2] Cristobalite and tridymite occur naturally in lava and are formed when quartz or amorphous silica is subjected to very high temperatures. They can also be formed in the manufacture of silica bricks (refractory bricks) used in industrial furnaces.[1] Less common types include keatite, coesite, and stishovite. Opal, diatomaceous earth (tripolite), silica-rich fibreglass, fume silica, mineral wool, and silica glass (vitreous silica) are common amorphous forms of silica.[2]

Dusts composed of non-contaminated amorphous silica, with the exception of fibreglass, are not generally considered to be harmful to people.[17,18] Calcined diatomaceous earth and other calcined amorphous silica containing crystalline silica are fibrogenic. A few animal studies have shown associations between silica nanoparticles and lung inflammation, but not progressive fibrosis.[19] Exposure to both silica and non-fibrous silicates (silica combined with other minerals) has been linked to mixed dust pneumoconiosis.[20]

Occupational exposure to respirable crystalline silica (aerodynamic diameter <10 μm) occurs in many industries and occupations (table 1), whenever substances or materials containing free crystalline silica (eg, rocks and

stones) are mechanically broken down to form dust or when those containing fine particles of silica (eg, silica flour and sand) are handled or disturbed. Although cement does not contain much silica, substantial amounts of respirable quartz can be generated when concrete building materials containing sand and stone are cut, ground, or drilled. Drilling in confined spaces can cause excessive silica exposure, as reported in hand-dug caissons in Hong Kong.[22] Exposure to respirable silica dusts increases the risk of pneumoconiosis in young farmers.[16,23] Low environmental concentrations rarely pose any risk, but silicosis has been reported in Himalayan children exposed to frequent dust storms.[24]

The cumulative dose of silica (respirable dust concentration multiplied by crystalline silica content and exposure duration) is the most important factor in development of silicosis.[16,25–28] Nagelschmidt[28] summarised much of the historical data for the association between weight of silica retained in the lung and increasing pathological grades of silicosis. Positive correlations have also been reported between hydroxyproline (as an index of fibrosis), silica dust content, non-silica inorganic dust, radiographical category of pneumoconiosis, and pathological grade of silicosis in hard-rock miners in Ontario, Canada.[29] Animal data suggest that tridymite, cristobalite, and quartz are more fibrogenic than is amorphous silica, with tridymite having the greatest effect, then cristobalite, then quartz, in line with the ratios of surface areas (for equal crystal weights).[30] Freshly fractured quartz produces greater quantities of active oxygen species than does aged quartz.[31]

Trace metals also seem to modulate pulmonary toxicity of silica dusts in animal studies.[32] In gold miners or foundry workers exposed to fairly pure silica, total retained silica loads of 1–3 g are sufficient to cause silicosis.[28] In coal or hematite miners with concomitant exposure to other dusts, the same weight of silica causes few cases of silicosis.[28] In China, tin and tungsten workers have a higher risk of silicosis than do pottery workers for a specific exposure level.[33] Much higher alumino-silicate occlusion of silica dusts was reported in pottery work sites, suggesting a potential effect of crystal surface characteristics.[34]

Associated disorders

Silica exposure has been associated with several disorders (panel). Only tuberculosis, airway obstruction, and lung cancer will be discussed further in this Seminar.

	Industries or occupational activities
Breaking down substances or materials	
Drilling	Construction Quarrying and related milling Mining and related milling Tunnelling
Breaking and crushing	Construction Quarrying and related milling Mining and related milling Tunnelling
Cutting	Arts, crafts, and sculpture Jewellery Construction Quarrying and related milling Grindstone production
Abrasive blasting and sand blasting	Boiler scaling Production of dental material Metal products Automobile repair (removal of paint and rust) Arts, crafts, and sculpture Shipbuilding and repair Foundries Construction Quarrying and related milling Production of denim jeans Tombstone production
Grinding	Arts, crafts, and sculpture Jewellery Construction Quarrying and related milling
Sanding	Automobile repair (removal of paint and rust) Construction
Excavation and digging	Agriculture Construction Quarrying and related milling Mining and related milling Tunnelling
Hammering	Boiler scaling Construction
Casting and moulding	Jewellery Foundries Ceramics
Furnace installation and repair (refractory materials)	Iron and steel mills Foundries Glass, including fibreglass
(Continues in next column)	

	Industries or occupational activities
(Continued from previous column)	
Producing and handling materials	
Cleaning (dry sweeping and brushing, and pressurised air blowing)	Construction Arts, crafts, and sculpture Jewellery
Polishing and buffing	Production of dental material Arts, crafts, and sculpture Jewellery
Mixing of silica flour and clay	Arts, crafts, and sculpture Paint fillers Ceramics Potteries Production of rubber and plastics Concrete production
Handling raw materials containing silica flour and sand	Paint fillers Glass, including fibreglass Production of rubber and plastics Foundries Cement production Roofing asphalt felt Manufacturing or occupational use of abrasive soaps and scouring powders

Information taken from National Institute of Occupational Safety and Health[16] and Akgun et al.[21]

Table 1: **Common operations or tasks that involve exposure to free crystalline silica**

Panel: Conditions that have been associated with silica exposure

Silicosis
- Chronic silicosis[16,25–29]
- Accelerated silicosis[16]
- Silicoproteinosis[16]

Infections
- Tuberculosis (pulmonary and extrapulmonary)[16,35–39]
- Other mycobacterial, fungal, and bacterial lung infections (usually with silicosis)[16,35]

Airway disease
- Chronic obstructive pulmonary disease[16,40–44]

Malignant disease
- Lung cancer[16,45–55]
- Gastric, oesophageal, and several others (possible association)[16]

Autoimmune diseases
- Scleroderma[16,56]
- Rheumatoid arthritis[16,56]

Renal diseases
- Chronic renal disease[16]

See Online for appendix

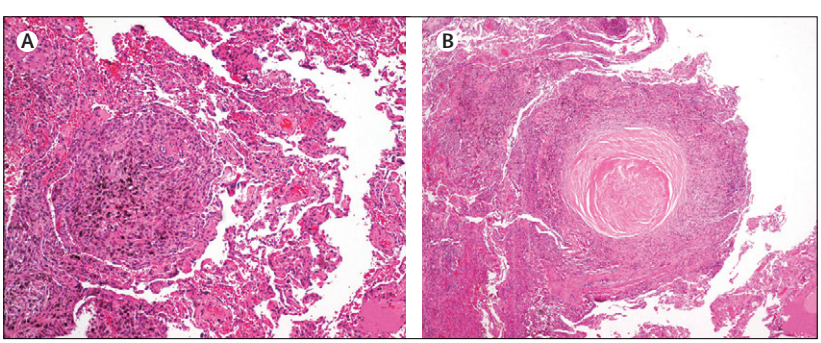

Figure 1: **Histological sections of lung with silicotic lesions**
Early silicotic lesion as cellular nodule of dust-laden macrophages (A; ×100). Chronic silicotic nodule with concentric fibrosis in the centre and peripheral dust-laden macrophages (B; ×40).

Tuberculosis risk increases with severity of silicosis, and in acute and accelerated silicosis.[37–39] Silica exposure increases tuberculosis risk even without silicosis.[37,38] In developing countries, mineral mining (particularly gold mining) might contribute to tuberculosis rates at a country level.[57] Tuberculosis risk remains high for gold miners in South Africa after they are no longer exposed.[58] Additionally, active tuberculosis at baseline predicts radiological progression of silicosis.[58] The effects of silicosis and HIV infection on tuberculosis are multiplicative.[59] Smoking is another aggravating factor.[60] Major morbidities and mortalities result when these epidemics of silicosis, tuberculosis, HIV, and smoking coexist in developing areas.[59,61]

Chronic obstructive pulmonary disease (COPD) has also been associated with silica exposure, independent of smoking.[16,40–42] In South African gold miners, an increase of 1 mg/year/m³ in cumulative respirable dust exposure is associated with a loss of 18·7 mL in forced vital capacity and 16·2 mL in forced expiratory volume in 1 s.[40] Longitudinal studies suggest that loss of lung function occurs with exposure to silica dust at concentrations of 0·1–0·2 mg/m³, but a disabling loss of lung function would not occur in the absence of silicosis until after 30–40 years of exposure.[41] Obstructive lung function patterns were noted in 17·3% of patients with silicosis who had never smoked in a US silicosis registry.[43] Age, cigarette pack-years, history of tuberculosis, size of lung nodules, and progressive massive fibrosis are independent predictors of airflow obstruction in patients with silicosis in Hong Kong.[44]

In 1997, the International Agency for Research on Cancer (IARC) classified crystalline silica inhaled in the form of quartz or cristobalite from occupational sources as a human (Group 1) carcinogen.[45] The US National Institute for Occupational Safety and Health and National Toxicology Program subsequently classified crystalline silica as a human carcinogen.[16,46] 60 reports of the relation between lung cancer and silica exposure or silicosis, or both, have since been published, including six meta-analyses[47–52] and one pooled exposure-response analysis[53] (appendix).

The meta-analyses generally showed significantly increased risks of lung cancer in patients with silicosis, but the effect of silica exposure on lung cancer is weak and variable in workers who do not have silicosis. Heterogeneity in exposure measures adopted across different cohorts meant meta-analysis was difficult, aside from concerns about inadequate adjustment for smoking and other confounding factors.[52,54] The pooled exposure-response analysis[53] used case-control comparison nested in ten cohorts to minimise the effect of potential confounders, which could differ between exposed workers and the general population. A monotonic increase in lung cancer risk was noted after a 15-year delay with the logarithm of cumulative exposure, and little heterogeneity was present across different industries. The low exposure-response slope of silica, as compared with other known carcinogens, might have partly accounted for the difficulty in detection of its carcinogenic effect in workers without the disorder in previous studies. Citing this important study, the Working Group for IARC Monographs[55] reaffirmed crystalline silica dust as a human carcinogen in March, 2009.

Pathophysiology

Pathological varieties of silicosis include simple (nodular) silicosis, progressive massive fibrosis, silicoproteinosis, and diffuse interstitial fibrosis.[1,62] Gross pathological examination of the lung identifies discrete hard nodules, usually with upper-lobe predominance. Hilar and peribronchial lymph nodes are frequently enlarged. Microscopically, the distinguishing silicotic nodules are in hilar lymph nodes and lung parenchyma (figure 1). Under polarised light microscopy, birefringent particles are

often seen in the centre of silicotic nodules, but most are silicates rather than silica (which is weakly birefringent). In progressive massive fibrosis, lung nodules become confluent, resulting in lesions of 1 cm or more in diameter. The histological features of silicoproteinosis resemble those of primary alveolar proteinosis, with granular periodic acid-Schiff-positive lipoproteinaceous material filling the alveolar spaces.[63] Minimal collagen deposition and fibrosis are present. Silicotic nodules, when present, are smaller than in other forms of silicosis.

Inhalation of respirable silica dusts leads to deposition in distal airways. Various in-vitro and animal experiments have focused on how alveolar macrophages interact with inhaled silica particles and the effects of silica-induced toxicity on cells.[64–66] Silica can produce reactive oxygen species either directly on freshly cleaved particle surfaces or indirectly through its effect on the phagocytic cells.[65] Scavenger receptors, especially the macrophage receptor with collagenous structure expressed in alveolar macrophages, seem to have a role in the recognition and uptake of silica.[66]

Three recent in-vitro and animal studies[67–69] have indicated the probable sequence of events after phagocytosis (figure 2). The source of lipopolysaccharide priming in vivo is unknown, but it could be a potential point for interaction with other environmental and genetic risk factors. The IL-1 signalling pathway and other inflammatory cytokines, such as tumour necrosis factor, have a crucial role in subsequent inflammation and fibrosis.[64,69,70] Additionally, caspase-1 modulates secretion of unconventional proteins, such as fibroblast growth factor-2, which may play a part in the pathogenesis.[71] With silica-induced apoptosis, ingested silica is released to trigger another cycle of phagocytosis and inflammation.[64]

In response to silica, dendritic cells have been shown to exhibit cellular activation and migrate from the alveoli into the lung parenchyma in mice.[72] In mice with lymphopenia, silica-induced fibrosis and inflammation can occur independently of T, B, natural killer T, and natural killer cells, but lymphocytes could participate in the regulation of silica-induced inflammation through modulation of the NALP3 inflammasome.[73] In the mouse model, regulatory T cells exert the modulating function both directly by expressing cytotoxic T-lymphocyte antigen 4 at the inflammatory stage and indirectly by secreting increasing amounts of IL-10 and transforming growth factor (TGF)-β during the fibrotic stage.[74] Data suggest a potential role of lung epithelial cells in pulmonary inflammation, with mechanisms of quartz-induced proinflammatory activation of lung epithelial cells in vivo and in vitro dependent and independent of nuclear factor-κB.[75] An in-vitro study also showed that TGF-β1 can induce epithelial to mesenchymal transition in human bronchial epithelial cells and such effect is enhanced by IL-1β.[76] However, the exact roles of TGF-β1 and IL-1β in silicosis remain unknown.

Diagnosis

History

Diagnosis of silicosis generally relies on a history of substantial exposure to silica dusts and compatible radiological features, together with exclusion of other

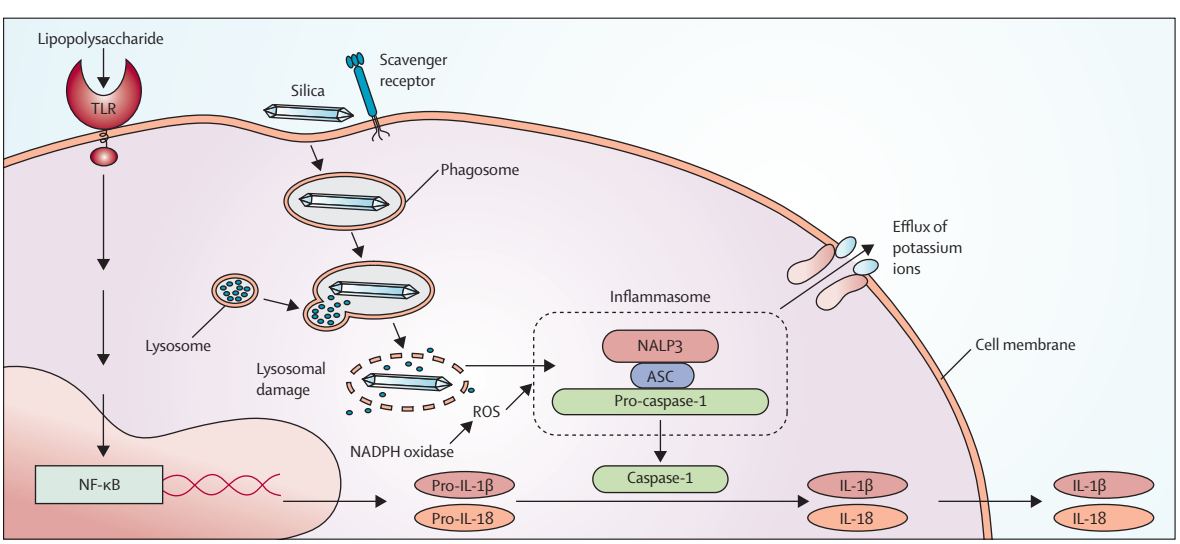

Figure 2: **Activation of the NALP3 inflammasome by a silica crystal after initial priming by a lipopolysaccharide**
Phagocytosis of crystalline silica leads to active swelling of phagosomes, followed by phagosomal destabilisation, releasing their contents into the cytosolic compartment.[69] Activation of the nucleotide-binding domain, leucine-rich repeat protein NALP3 leads to its association with the intracellular adapter protein ASC, which combines with and activates pro-caspase-1. The resulting active enzyme complex (NALP3 inflammasome) activates the potent proinflammatory molecules such as IL-1β and IL-18. Activation of the NALP3 inflammasome by silica also necessitates generation of ROS by an NADPH oxidase after particle phagocytosis and an efflux of intracellular potassium ions, suggesting a possible interaction of the silica with a membrane-associated protein.[67,68] TLRs or IL-1 receptors do not seem to be essential for activation of the inflammasome.[67,69] However, secretion of IL-1β by mouse or human macrophages in response to silica or asbestos in vitro seems to be a two-step process because priming by a lipopolysaccharide is necessary.[67–69] Scavenger receptors seem to have a role in the recognition and uptake of silica. TLR=toll-like receptor. ROS=reactive oxygen species. ASC=apoptosis-associated speck-like protein containing a caspase recruitment domain. NF-κB=nuclear factor-κB. IL=interleukin.

competing diagnoses, such as miliary tuberculosis, fungal infections, sarcoidosis, idiopathic pulmonary fibrosis, other interstitial lung diseases, and carcinomatosis. The diagnosis of an occupational lung disease depends on a thorough occupational history, without which the diagnosis of silicosis could easily be missed in the absence of typical nodular lesions. In one pathological series, the occupational aetiology was missed in as many as 25% of lung biopsies referred for idiopathic pulmonary fibrosis.[77] Unusual exposures should be considered, such as in denim sandblasting in Turkey[21] and work with rush mats in China.[78] With the long latency of silicosis, a chronological account of all jobs held is needed, with details of job processes and dust exposure estimates (including as bystanders).[79] Potential environmental or domestic exposures should also be taken into account when relevant occupational exposure cannot be identified.[24]

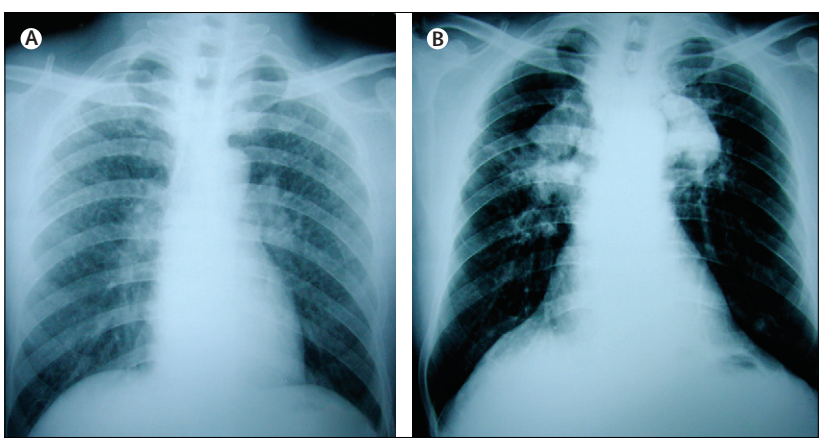

Figure 3: **Chest radiographs of a patient with silicosis**
Simple nodular silicosis (A) and progressive massive fibrosis (B).

	Notes and further scale divisions
Small opacities (<1 cm)	
Four-point major scale for profusion	
0	0/–, 0/0, 0/1
1	1/0, 1/1, 1/2
2	2/1, 2/2, 2/3
3	3/2, 3/3, 3/+
Round shape and size	
p	≤1·5 mm
q	1·5–3 mm
r	3–10 mm
Irregular shape and size	
s	≤1·5 mm
t	1·5–3 mm
u	3–10 mm
Large opacities (>1 cm)	
A	≤5 cm
B	5 cm to the size of the right upper zone
C	Bigger than the right upper zone

Grades given on the basis of comparison with standard films. Classifications from the International Labour Organization.[85]

Table 2: **Radiographical classification of silicosis**

Chronic silicosis—the most common form of the disease—usually develops after 10 years or more of exposure at low concentrations.[1,2,16] Some patients with simple silicosis could be asymptomatic and diagnosed incidentally after radiological examination. Individuals might have a cough, possibly because of nerve irritation caused by silicotic nodules or associated COPD. Shortness of breath is more common at later stages than it is initially, especially with progressive massive fibrosis. Other patients with chronic silicosis could present with associated conditions such as tuberculosis and lung cancer.

Accelerated silicosis develops 5–10 years after initial exposure.[16] It shares similar clinical features with chronic silicosis, but tends to progress rapidly.[1,2] Acute silicosis, in the form of silicoproteinosis, occurs rarely after exposure to high concentrations of respirable crystalline silica for a few weeks to 5 years. It most commonly affects sandblasters but has been reported in quartzite millers, tunnel workers, silica flour workers, and workers in the scouring powder industry.[63,80] Besides dyspnoea and dry cough, constitutional symptoms could be present, such as fever, fatigue, and weight loss. Respiratory failure and death often occur within a few months.

Imaging

With its wide availability, chest radiography is the primary method of diagnosis. In simple silicosis, chest radiography usually shows small round opacities, often symmetrically distributed with upper-zone predominance. Some patients have a diffuse interstitial pattern of fibrosis without the typical nodular opacities.[81–83] In progressive massive fibrosis, opacities larger than 1 cm develop. Over time, they increase in size and become confluent and the small opacities might disappear (figure 3). With contraction of these large fibrotic masses, hilar structures are pulled up, leaving hypertranslucent zones of lung in the periphery and lower-lung zones, often with several bullae. The hilar and mediastinal lymph nodes often enlarge and can also calcify, sometimes in a characteristic eggshell pattern. Similar calcification can, however, be reported in sarcoidosis, radiation-treated Hodgkin's disease, scleroderma, amyloidosis, histoplasmosis, and blastomycosis.[84] The International Labour Organization published guidelines in 2000 to enable classification of radiographs for pneumoconioses in epidemiological investigations (table 2).[85]

The sensitivity of chest radiography improves with increasing degree of silicosis, but a substantial proportion of patients with moderate or a severe degree of silicosis classified by histology might not be diagnosed radiologically.[86] In some centres, digital chest radiography is replacing conventional radiography, and in optimal conditions and with standard methods reader visualisation of small pneumoconiotic opacities does not seem to substantially differ.[87]

Studies suggest that high-resolution CT is more sensitive than is conventional radiography in detection of specific features: nodular changes in lung parenchyma; progressive massive fibrosis; bullae; emphysema; and pleural, mediastinal, and hilar changes in silicosis (figure 4).[88–90] Additionally, high-resolution CT often has higher inter-observer agreement and better correlation with lung function than does conventional radiography.[88,89] Qualitative and quantitative parameters on high-resolution CT could be used as indirect measures of functional impairment in silicosis,[91] and they have been correlated with clinical dyspnoea, airflow obstruction, and reduced lung volume and diffusing capacity.[90,91]

In a 2007 study,[82] 12% of patients with silicosis and mixed-dust pneumoconiosis showed chronic interstitial pneumonia on high-resolution CT. Three-quarters had the typical pattern of idiopathic pulmonary fibrosis, although they had less traction bronchiectasis, more subpleural homogeneous attenuation (pathologically corresponding with dense fibrosis, often with abundant silicotic nodules) and more randomly distributed fibrosis than did patients with idiopathic pulmonary fibrosis. In another study of serial high-resolution CT changes in chronic interstitial pneumonia related to silica exposure,[83] the earliest abnormalities included faint ground-glass opacity limited to lung bases or only coarse reticular opacity. The coarseness was the best representation of how far chronic interstitial pneumonia had progressed, a disease that eventually leads to honeycomb changes.

In acute silicosis, chest radiography typically shows bilateral patchy consolidation and ground-glass opacification like that of primary alveolar proteinosis.[92] Hilar lymph nodes might be prominently enlarged. With initiation of fibrosis, linear opacities might be noted in the lower lobes. High-resolution CT usually shows bilateral air-space disease with consolidation in the posterior portions of the lungs and many centrilobular nodules of either soft-tissue or ground-glass attenuation.[80] The centrilobular nodules are a result of the inhalational and bronchiolocentric cause of silicoproteinosis and are not a feature in alveolar proteinosis. Punctate calcification within areas of consolidation is another characteristic feature.

Multidetector CT has been applied to the study of denim-sandblasting-induced silicosis.[93] The use of low-dose, high-resolution CT for lung cancer screening in silicosis is complicated by the presence of silicotic nodules, which could increase false-positive results.[94] MRI helps to distinguish between progressive massive fibrosis and lung cancer,[95] and PET helps to differentiate active inflammation and lung cancer from chronic changes.[96]

Other methods

Spirometry can be normal in the early stages of silicosis.[44] However, both restrictive and obstructive patterns are reported in simple silicosis, with obstruction commonly, but not exclusively, recorded in smokers.[43,44,97] Diffusion capacity might be more sensitive in early fibrosis, even though it is not entirely specific.[90,91,97] Decreased total lung capacity and lung compliance are possibilities, especially in severe cases and those of progressive disease.[90,91] Forced oscillation techniques could help to detect increases in total respiratory resistance and airway resistance, as well as decreases in lung compliance.[98] Exercise tests are not more sensitive than are lung function tests in assessment of ventilatory impairment in early silicosis, but might correlate with exertional dyspnoea.[99] Although hypoxaemia is not common at early stages of silicosis, pulse oximetry might be useful for detection of hypoxaemia at rest and with exercise in silicosis at high altitudes.[100]

Invasive investigations, such as lung biopsy, are seldom needed for the diagnosis of silicosis, but could be done to exclude other potentially treatable conditions or in assessment of advanced disease for lung transplantation. Additionally, bronchoscopy and bronchoalveolar lavage might be useful for diagnosis of silicoproteinosis.

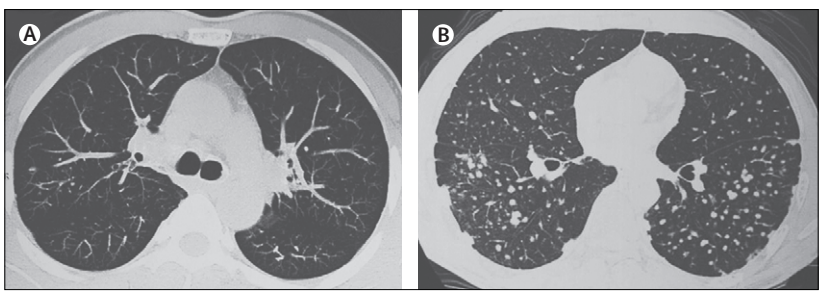

Figure 4: **Axial high-resolution CT sections of two patients with silicosis**
Early silicosis with sparse and small silicotic nodules (A) and silicosis with many nodules of varying sizes (B).

Management

No proven curative treatment for silicosis exists. An investigation[101] showed that particles coated with aluminium did not produce fibrosis in the lungs of rabbits, leading to the hypothesis that inhalation of aluminium powder might prevent or halt progression of silicosis in people. However, inhalation of aluminium dust did not have any definite effect on the symptoms or radiological progression in one trial.[102] No sustained benefits in objective parameters of disease status have been reported for surface-coating compounds (such as aluminium citrate and polyvinyl-pyridine-N-oxide) or herbal substances (eg, tetrandrine).[103] Whole lung lavage might remove large quantities of dust, cells, and soluble materials from the lungs and relieve symptoms in some patients,[104] but sustained improvement in lung function parameters has not been shown in a clinical trial.

There is no evidence that corticosteroid treatment confers long-term benefit for patients with chronic or accelerated silicosis, and such treatment could increase the risk of tuberculosis.[2] Anecdotal improvement in clinical status, chest x-ray, and pulmonary function has been reported after treatment with corticosteroids in acute silicosis.[105] Oral prednisolone every day also improved pulmonary function parameters and total cell count in

bronchoalveolar lavage in a small case series of chronic silicosis.[106] However, with persistence of the primary insult, steroids are not believed to alter the final outcome. Herbal qidan granules (a compound herbal preparation used for its vasoactive properties in traditional Chinese medicine),[107] suppressive oligodeoxynucleotides[108] and tetrapeptide N-acetyl-seryl-aspartyl-lysyl-proline[109] have possible beneficial effects in animal models, but no human data are available to support their clinical use.

Silicosis patients should generally be removed from further exposure. Job accommodation and personal protective measures are essential for individuals remaining in their jobs, even though these measures cannot fully protect those with proven disease from further damage. Smoking cessation, and influenza and pneumococcal vaccines are useful in reduction of complications.

Empirical treatment with bronchodilators should be considered for symptomatic patients with airflow obstruction. Cough suppressants and mucolytics could be useful for symptomatic relief. Antibiotics should be given as necessary for intercurrent chest infections. Pneumothorax, cor pulmonale, and respiratory failure should be managed accordingly.

Table 3 summarises recommendations for management of latent tuberculosis infection and silicotuberculosis.[36,110–113] Treatment of latent tuberculosis infection was beneficial in silicosis patients in Hong Kong,[111] but not in South Africa,[114] possibly because of a high risk of reinfection. In silica-exposed workers with a high prevalence of tuberculosis and HIV infection, innovative approaches are necessary for control of tuberculosis. Community-wide isoniazid preventive therapy is being investigated in South African gold miners.[115] Clinicians should be aware that pulmonary malignancies might be radiologically mimicked or masked by silicotic nodules or lymph nodes.[116] Sputum cytology followed by fluorescent bronchoscopy has had some encouraging results in detection of early-stage lung cancer in chronic smokers, but such an approach might not be useful for peripheral tumours.[117] Although PET could differentiate lung cancer from benign fibrotic nodules, its reliability might be confounded by tuberculosis.[118]

Long-term oxygen therapy improves survival in patients with severe hypoxaemia (<8·0 kPa) due to COPD, but its benefit has not been established in those with a lesser degree of hypoxaemia or with interstitial lung disease.[119] The role of ambulatory oxygen therapy during exercise has not been clearly assessed.[120] Physical training improves functional exercise capacity, dyspnoea, and quality of life in patients with interstitial lung disease and COPD.[121] Lung transplantation is a potential alternative for advanced disease, especially for young patients with acute silicosis. However, patients with silicosis had poorer outcomes than did patients with idiopathic pulmonary fibrosis in an unadjusted analysis from one centre.[122]

Compensation for silicosis is often crucial for financial support and medical care of the affected workers. Compensation arrangement varies in different jurisdictions and could involve claims for benefits in a statutory compensation system or civil claims for damages.[123–125] The source of funds might be governmental,[124] or a result of special levies on relevant industries,[125] the employers, or their insurers. A statutory compensation system avoids legal action against an employer years after the relevant exposure, and it also removes the burden to prove negligence.[124,125]

	Notes
LTBI periodic screening*	
Tuberculin skin test[36]	Cutoff of 10 mm Possible interference from BCG vaccination Booster effect on serial testing
Interferon-γ release assay (eg, T-SPOT.TB)[110]	T-SPOT.TB predicted tuberculosis more accurately than did the tuberculin skin test in patients with silicosis in one study[110]
LTBI treatment[111]	
Isoniazid for 6–12 months	Recommended regimen
Rifampicin for 3–4 months	Alternative regimen
Isoniazid and rifampicin for 3 months	Alternative regimen
Tuberculosis screening	
Periodic chest x-ray screening in areas with high prevalence[112]	Compare serial films and look for features such as cavity, effusion, consolidation, and rapid or focal deterioration
Bacteriology when clinically suspected	Smear not sensitive enough Culture takes time, but more sensitive than is smear Identification required to exclude other mycobacteria Drug susceptibility assays when drug resistance suspected
Rapid molecular testing	For rapid diagnosis and detection of rifampicin resistance
Tuberculosis treatment	
Usual anti-tuberculosis drugs with directly observed therapy	Extended duration of 8 months recommended (to reduce chance of relapse)[113]

LTBI=latent tuberculosis infection. *Frequency depends on risk of infection.

Table 3: **Recommended measures for detection and treatment of LTBI and tuberculosis in patients with silicosis**

Prevention

Silicosis is a major cause of morbidity and mortality in both developed and developing countries. Further efforts are therefore needed to recognise and control silica hazards worldwide. In 1995, the Global Program for the Elimination of Silicosis was established by a joint International Labour Organization and WHO committee. In the past decade, outbreaks of silicosis have been reported in some small-scale companies or mines in developing countries, mainly caused by poor hazard recognition and few protective measures.[5] The initiative is encouraging and supporting countries with silica hazards to establish national action programmes to control silicosis. Table 4 summarises the key control measures against silicosis.[126]

The potential of silica exposure should be assessed before a job begins, especially in industries that have previous reports of silicosis.[126] Periodic monitoring of respirable silica should be done in all industries with silica exposure. Respirable dust can be collected by cyclone or impact dust sampler.[127] Free silica content of respirable dust can be assessed by the Talvitie (phosphoric acid) method, infrared spectrophotometry, or x-ray diffraction method.[128] The limit of detection ranges from 5 μg to 10 μg

per sample, but accuracy is poor at low filter loadings (<30 μg) that are typically collected when airborne concentrations of crystalline silica are similar to regulatory standards.[16] Enforced or suggested permissible exposure limits for respirable silica were chosen according to the desired level of protection and available methods of dust control and monitoring technologies, and they vary between 0·025 mg/m³ and 0·35 mg/m³ in different countries.[16,129,130] However, these standards have not been confirmed as fully protective by epidemiology studies.

Quantitative risk assessments by the National Institute for Occupational Safety and Health predicted that 19 of every 1000 people exposed to silica dust at the US Occupational Safety and Health Authority standard for respirable cristobalite dust concentration (about 0·05 mg/m³) in a 45-year working life are at risk of lung cancer mortality, 54 of lung disease other than cancer, and 75 of radiographic silicosis with exposure.[131] The technical and economic feasibility of more restrictive exposure limits would need to be assessed to justify better protection.

Avoidance or control of silica exposure by various measures directed at the source, transmission, and workers is the primary method of silicosis prevention.[3,132] Source control can be banning of sandblasting, and substitution of metal grits for abrasive blasting, as implemented in most developed countries, such as those in Europe. Whenever source control is not feasible or sufficient, other measures should be implemented to isolate or capture dust and introduce clean air to prevent workers being exposed to hazardous silica. Engineering controls (table 4) are the most common methods.[3,132,133] Studies have shown that they are cost-effective in developed and developing countries.[14,134,135] Automating techniques—eg, automated palletisers, bagging machines, and equipment monitored with programmable logic controllers and computer software—are probably the best means to prevent exposure in the workplace.[132,136] Good housekeeping practices and regular maintenance are essential after implementation of these control technologies.[3,132,136]

For workplaces with high dust levels, administrative measures can be used, such as short working hours or job rotation. Personal protection equipment—eg, respirators—is useful for short duration tasks. However, it might not be fully effective in workplaces with high dust concentrations and should be the last resort for routine full-shift protection. The National Institute of Occupational Safety and Health recommends the use of so-called half-facepiece particulate respirators with good filters (N95 or better) for exposure to crystalline silica at concentrations of 0·5 mg/m³ or lower.[137]

Besides education about symptoms of silicosis, regular medical assessment might detect adverse health effects in exposed workers before disease reaches an advanced stage.[126] Assessment commonly includes respiratory questionnaires, physical examination, chest radiography, and spirometry. No universal standard exists for the frequency of such assessment because the decision may be affected by past and present respirable silica concentrations, dust particulate characteristics, and economic conditions. WHO recommends routine evaluation every 2–5 years, ideally for the rest of the lives of workers exposed to silica dust.[138] The American College of Occupational and Environmental Medicine suggests tests at baseline and after 1 year, then every 3 years for the first 10 years, and every 2 years thereafter when silicosis is a concern and respirable silica concentrations are lower than 0·05 mg/m³.[139] The Institute for Occupational Safety and Health of the German Social Accident Insurance recommends examination every 3 years.[140] Biomarkers of early disease could potentially aid prevention efforts and clinical diagnosis. Although several biomarkers have had promising results, none have been fully validated for clinical use.[141]

A new case of silicosis should prompt a thorough assessment of silica exposure and control measures in workplaces.[16,142] In addition to reports of new cases, occupational health doctors or hygienists should periodically analyse health records of all exposed workers in an industry or factory and assess the effects of prevention activities. Occupational hygiene and health records should also be properly maintained to enable calculation of disease rates and latency periods according to various exposure scenarios.

	Suggested measures
Primary prevention	
Silica exposure control at source	Substitution of materials; modification of processes and equipment; wet methods; silica warning sign; work practices
Control silica dust emission or transmission	Isolation of the source or workers; enclosed processes; air curtain; water spray; local exhaust ventilation; general ventilation system; enclosed cabs; air supply system
Control silica dust at worker level	Training and education about work practices; personal protection; personal hygiene; personal protective equipment; health promotion
Secondary prevention	
Surveillance of working environment	Establish concentration of silica dust; assess health risk for workers exposed to silica dust
Surveillance of worker health	Periodic health examination, such as chest radiography; early detection of the disease; research into biomarkers for early stages of silicosis
Tertiary prevention	Removal from environment; prevention of complications; modification of work processes; rehabilitation

Information taken from National Institute of Occupational Safety and Health.[126]

Table 4: **Suggested preventive measures**

Contributors
CCL drafted parts of the report about pathophysiology, and diagnosis and management; and had input into sections about epidemiology and prevention. ITSY drafted the parts about epidemiology and contributed to the other sections. WC drafted the section about prevention and contributed to the other sections. All authors reviewed and approved the final report.

Conflicts of interest
We declare that we have no conflicts of interest.

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