Silicosis and Asbestosis

Method of
Vinicius C. S. Antao, MD, MSc, PhD, and John E. Parker, MD

Pneumoconioses are lung diseases caused by the inhalation and deposition of mineral dust. Silica, coal mine dust, and asbestos can lead to pulmonary fibrosis and other types of respiratory diseases.

Silicosis

Silicosis is the oldest recognized form of pneumoconiosis. Crystalline silica in respirable dust (~0.5-5 μm diameter) can reach the alveolar regions of the lungs and cause fibrosis. The three most important forms of crystalline silica are quartz, tridymite, and cristobalite.

EPIDEMIOLOGY

Exposure to silica dust occurs in many occupations, such as mining, quarrying, drilling, and tunneling operations. It is also a hazard to stonecutters and to refractory brick, pottery, foundry, and sandblasting workers. Ground silica, which is used in porcelain, cosmetics, and soap, also represents a risk.

Exact information on the incidence and prevalence of silicosis worldwide is unknown, but it seems to be decreasing in industrialized countries due to improvements in working conditions and dust-control measures. Nevertheless, silicosis persists as a serious public health problem, especially in developing countries, where occupational diseases are commonly misclassified and underdiagnosed. In the United States, more than two million workers are exposed to silica and at potential risk of developing the disease.

PATHOGENESIS

In terms of pathology, the fundamental lesion is a concentric silicotic nodule. The pathogenesis is complex, and four basic mechanisms are involved: direct cytotoxicity, resulting in the local release of enzymes; activation of oxidant production by alveolar macrophages; activation of mediator release from alveolar macrophages and epithelial cells, causing recruitment of polymorphonuclear leukocytes and macrophages and also resulting in production of proinflammatory cytokines and reactive species; and secretion of growth factors from alveolar macrophages and epithelial cells, stimulating fibroblast proliferation. These different mechanisms can lead to eventual cell injury and lung scarring. Many studies have demonstrated that freshly fractured silica particles are more toxic to lung cells than aged silica particles, which can be explained by the presence of free radicals.

CLINICAL FEATURES

There are four forms of silicosis: chronic, complicated, accelerated, and acute. The form is generally related to the degree or intensity of silica exposure.

Patients with chronic silicosis may be asymptomatic. The radiograph shows small (<10 mm), rounded opacities, mainly in the upper zones, that appear more than 15 years after initial exposure. These parenchymal abnormalities can occur without significant changes in pulmonary function or can lead to mild restriction. An obstructive pattern may be observed on spirometry testing, due to smoking habits or the presence of dust-induced lesions in the small airways. Carbon monoxide diffusing capacity (DL_{CO}), which measures the transfer of a diffusion-limited gas (carbon monoxide) across the alveolocapillary membrane, may be decreased due to silicotic changes.

Accelerated silicosis occurs with high levels of exposure after a shorter latency (usually 5-10 years). The radiographic patterns are similar to chronic silicosis, but the progression of disease is more rapid. Patients present with symptoms early, and the lung function deteriorates very quickly, with a rapid decline in forced expiratory volume in one second (FEV_1).

Complicated silicosis, also known as progressive massive fibrosis, is a more advanced form of chronic or accelerated silicosis. The most common symptom is exertional dyspnea. Cough can occur due to superimposed infections or chronic obstructive pulmonary disease (COPD). The radiograph is characterized by the presence of large opacities greater than 1 cm in diameter. Spirometry often shows a restrictive pattern caused by fibrosis or a mixed pattern with associated obstruction due to emphysema and dust-related airflow limitation. Carbon monoxide diffusing capacity is reduced. Because of extensive areas of fibrosis and gas exchange abnormalities with hypoxemia, cor pulmonale and respiratory failure can occur in the final stage of the disease.

Acute silicosis can develop within 6 months to 2 years after massive silica exposure. The symptoms are severe dyspnea, weight loss, and weakness. The radiograph shows a pattern completely different from other types of silicosis, with bilateral airspace filling. Pathologically, this pattern is very similar to alveolar proteinosis. Pulmonary fibrosis is not a prominent finding in acute silicosis. The prognosis is guarded and the disease usually progresses, resulting in severe hypoxemia and respiratory failure.

Patients with silicosis are at risk for tuberculosis, nontuberculous mycobacterioses, and bacterial infections, as well as infection-associated bronchiectasis. *Nocardia* infections can occur in patients with acute silicosis.

DIAGNOSIS

Three important criteria are generally sufficient for a diagnosis of silicosis: a careful occupational history documenting silica exposure with an appropriate latency period; a chest radiograph classified as category 1/0 or greater in accordance with the International Labour Organization (ILO) International Classification of Radiographs of Pneumoconioses; and absence of diseases that can mimic silicosis, such as tuberculosis, sarcoidosis, or pulmonary fungal infections. Lung biopsy typically is not necessary. High-resolution computed tomography (CT) can be useful in achieving more accurate categorization of the parenchymal changes in all types of pneumoconiosis, but the descriptions of the findings are not standardized and the procedure is expensive for medical screening purposes.

CURRENT DIAGNOSIS

- Take a detailed medical and occupational history, including all past exposures, with special attention to latency between exposure and onset of disease.
- The chest radiograph shows small, rounded opacities, mainly in the upper zones for silicosis, and small, reticular opacities, mainly in the lower zones for asbestosis.
- Exclude other diseases that can mimic the radiographic appearance of pneumoconiosis.
- Assess severity of disease with lung function tests.

CURRENT THERAPY

- There is no specific treatment for pneumoconiosis.
- Primary prevention is the key to avoid disease.
- Complications such as infections, chronic bronchitis, and cor pulmonale should be recognized and treated promptly.
- A pulmonary rehabilitation program may improve quality of life.
- Lung transplantation is appropriate in select cases.

TREATMENT

Treatment of Silicosis

All forms of silicosis are irreversible, often progressive (even after the exposure has ceased), and potentially fatal, although they are completely preventable. Many experimental studies have been conducted to establish a treatment for this disease but, because of toxicity and lack of efficacy, they are not generally available for human use.

Tetrandrine,[2] an extract of the root of *Stephania tetranda*, a traditional Chinese medicine, was approved by the State Drugs Administration of China as a drug for the treatment of silicosis. It exhibits anti-inflammatory, antifibrogenetic, and antioxidant effects. Tetrandrine is not available in the United States, and additional research must be conducted to document safety and efficacy. More recently, it has been demonstrated that heme oxygenase-1 (HO-1), a rate-limiting enzyme in heme catabolism, with antioxidative, anti-apoptotic, and anti-inflammatory activities, is persistently expressed in the lung lesions of patients with silicosis. It has been suggested that up-regulation of HO-1 might offer a novel strategy for the treatment of silicosis because it suppresses silica-induced reactive oxygen species (ROS) activity. Nevertheless, this form of treatment is still experimental.

Acute silicosis has been treated with whole-lung lavage to remove the alveolar exudates. The benefits are uncertain, and serious bacterial infections can occur after this procedure. Some reports suggest using prednisone[1] to treat acute silicosis. The initial doses are 40 to 60 mg/day for 1 month. If benefits can be documented, the treatment can be maintained with lower doses (15-20 mg/day) for 6 months. Steroids are potentially dangerous and increase the risk and progression of coexistent tuberculosis or other infections.

After an initial evaluation, based on guidelines for recipient selection, single or bilateral lung or lung-heart transplantation should be considered for select patients with end-stage silicosis. Once a patient is selected as a potential candidate for lung transplantation, further studies, including pulmonary function tests, high-resolution CT scan, complete cardiac evaluation, serologic tests for hepatitis and HIV, and renal and liver function tests, are often required to be performed at the referring center.

Because there is no specific drug to control or reverse the fibrosis, the treatment of silicosis should be focused on alleviating symptoms and preventing and treating the complications of the disease.

Treatment of Complications

Tuberculosis

A common complication of silicosis is pulmonary tuberculosis. Tuberculosis can be present in up to 15% of silicosis patients in some countries. Workers with silicosis or silica exposure for 25 years or more should have tuberculin skin testing. Those who are asymptomatic but have an area of induration greater than 9 mm should receive chemoprophylaxis with isoniazid (INH [Nydrazid]) for 9 to 12 months.

Clinical symptoms compatible with tuberculosis should prompt rigorous efforts to obtain bacteriologic confirmation of the diagnosis. The current recommended treatment is a course of pyrazinamide (PZA), rifampin (Rifadin), ethambutol (Myambutol), and INH for 2 months, followed by 6 to 7 months of isoniazid and rifampin. Some authors suggest that the two-drug continuation phase of treatment should be prolonged up to 12 months. Long-term follow-up with bacteriologic culture and radiographs is mandatory.

Nontuberculous mycobacteria (NTM), such as *Mycobacterium kansasii* or *Mycobacterium avium-intracellulare*, account for an increasing percentage of mycobacterial diseases in those with silicosis in industrialized countries. Cultures should be done, because treatment needs to be modified according to the type of mycobacterium grown and its drug sensitivity. *Mycobacterium kansasii* usually responds well to a course of rifampin[1] and ethambutol[1] given for 9 months.

Connective Tissue Disorders

Silicosis is also associated with connective tissue disorders, mainly scleroderma and rheumatoid arthritis.

Treatment of sclerodermatous involvement of the skin and internal organs is a challenge. Immunosuppressive drugs such as prednisone,[1] azathioprine (Imuran),[1] chlorambucil (Leukeran),[1] cyclosporine (Neoral),[1] and many others have been used in attempts to treat this disease. Calcium channel blockers, mainly nifedipine (Procardia),[1] are indicated for treating Raynaud's phenomenon. Some physicians recommend α-adrenergic receptor blockers.

Many drugs are available to control and manage rheumatoid disease, such as corticosteroids, methotrexate (Rheumatrex), or other disease-modifying agents.

Lupus erythematosus has been described in sandblasters with silicosis; pleuritic pain and effusions can occur, and usually there is a significant response to corticosteroids and resolution of effusion within 2 weeks. Spontaneous resolution does not occur. The use of immunosuppressive agents can trigger infections and, although a negative skin test does not rule out infection, tuberculin skin testing must be assessed before treatment.

Chronic Obstructive Pulmonary Disease

Workers exposed to silica dust are at increased risk for development of COPD. Classification of severity of this obstructive disease can be used as the basis for treatment.

Use of an inhaled short-acting bronchodilator on demand is recommended for all patients with COPD. Long-acting bronchodilators such as formoterol (Foradil) or salmeterol (Serevent), given twice daily, may be used in stage II as continuous medication. Tiotropium bromide (Spiriva) is a long-acting anticholinergic bronchodilator that maintains bronchodilation for at least 24 hours, allowing once-daily administration.

Inhaled steroids (budesonide [Pulmicort], fluticasone [Flovent]) are indicated for severe disease. Systemic corticosteroids can be used

[2]Not available in the United States.
[1]Not FDA approved for this indication.

[1]Not FDA approved for this indication.

during exacerbations as short-course therapy. Theophylline (Slo-Phyllin) can achieve small improvements in FEV_1 with long-term use.

Pulmonary hypertension is the underlying cause of cor pulmonale. If hypoxemia is present, supplemental oxygen is necessary to improve pulmonary hypertension and cor pulmonale. Oxygen therapy should be prescribed when the arterial partial pressure of oxygen (Pao_2) is less than 55 mm Hg, arterial oxygen saturation (Sao_2) is less than 88%, or Pao_2 is 56 to 59 mm Hg with electrocardiographic evidence of P pulmonale, pedal edema, or secondary erythrocytosis. Patients using oxygen for at least 15 hours per day can achieve a decrease in their pulmonary artery pressures and enhanced cardiac output.

More recent advances in the treatment of pulmonary hypertension include phosphodiesterase-5 inhibitors (sildenafil [Revatio]) and endothelin receptor antagonists (bosentan [Tracleer]).

Noninvasive positive-pressure ventilation has a useful role in the treatment of severe COPD exacerbations. Mechanical ventilatory support for respiratory failure is indicated when it is caused by a treatable complication. Pulmonary rehabilitation programs can improve dyspnea and enhance quality-of-life scores.

Episodes of acute bronchitis can occur and are commonly caused by *Haemophilus influenzae, Streptococcus pneumoniae, Pseudomonas aeruginosa*, and *Moraxella catarrhalis*. Antibiotics should be prescribed for purulent exacerbations. Viral infections and *Mycoplasma pneumoniae* can also be investigated. After dust exposure is controlled, smoking cessation remains the most effective intervention to reduce the risk of COPD and to slow its progression.

Other Conditions

The International Agency for Research on Cancer (IARC) has classified crystalline silica in occupational exposures as a human lung carcinogen; however, the issue whether silicosis or silica exposure per se is associated with lung cancer remains controversial in the medical literature. Other conditions such as chronic renal disease have also been linked with occupational exposure to silica in a number of populations, although the overall levels of morbidity and mortality probably do not justify medical screening. Pneumothorax can occur spontaneously or may be ventilator related and generally requires urgent placement of a chest tube.

PREVENTION

In the absence of specific treatment for silicosis, primary prevention is the key to avoiding the disease. Dust controls and a professionally managed respiratory protection program are essential in preventing this disease, combined with specific programs to educate workers regarding the risks of silica dust exposure. Engineering controls such as dust suppression, local exhaust, appropriate general ventilation, and wet techniques have been proved to be effective in reducing exposures when vigorously implemented in workplaces.

Silicosis reporting is required in many states to ensure investigation of possible continuing workplace hazards. National surveillance is also essential to obtain knowledge of the extent and distribution of the disease, thereby facilitating elimination of this disease in the United States.

Asbestosis

Asbestosis is an interstitial pneumonitis and fibrosis caused by the inhalation of asbestos fibers. In the United States the number of asbestosis deaths increased from 77 (annual age-adjusted death rate: 0.54 per million population) in 1968 to 1493 deaths (6.88 per million) in 2000 as an historical legacy of asbestos exposure; during the same period, deaths for all other pneumoconioses decreased. The geographic distribution of mortality indicates that asbestosis increased particularly in the coastal states, where asbestos was often used in shipbuilding. Other activities with potential risk for asbestosis are mining, insulation application and removal, and use of asbestos-containing materials in construction and manufacturing of cement products.

Other nonmalignant respiratory health effects associated with asbestos are localized pleural plaques, acute pleuritis with effusion, diffuse pleural thickening, rounded atelectasis, and chronic airflow obstruction. Lung cancer and mesothelioma (a type of pleural cancer) are malignant diseases related to asbestos exposure. The type of fiber, its dimensions (length and diameter), and its biopersistence are important variables in determining the risk of disease, as are dose and latency period. All types of asbestos fibers are potentially fibrogenic and carcinogenic, including chrysotile (the most common type of asbestos) and amphiboles (crocidolite, amosite, and anthophyllite).

The latency period for the development of asbestosis is commonly between 15 to 20 years after initial exposure to this mineral. It usually occurs as an occupational disease related to the intensity of workplace exposure; nevertheless, environmental and nonoccupational exposures to this fiber can cause other types of asbestos-related diseases, such as mesothelioma.

DIAGNOSIS

The criteria recommended for the clinical diagnosis of asbestosis are a history of asbestos exposure, dyspnea, bibasilar crackles, and pulmonary function showing a restrictive or mixed pattern or reduced lung volumes, plus radiographic abnormalities consistent with small irregular opacities predominant in lower lung fields. In advanced phases of this disease, middle and upper lobes are often affected, and honeycombing can be noted. If findings on routine radiographs are not sufficient to support the diagnosis, high-resolution CT scanning should be performed. An open lung biopsy is occasionally required to establish the diagnosis but only if the history does not clearly document sufficient occupational exposure or the latency period is not compatible with the disease. The presence of asbestos bodies in sputum or bronchoalveolar lavage would be helpful in this differentiation.

MANAGEMENT

There is no effective treatment for asbestosis, and the disease often progresses after cessation of exposure. Pulmonary hypertension and cor pulmonale can develop, and supplemental oxygen should be provided when indicated (see earlier). Respiratory infections are treated with antibiotics based on the sensitivity of the organism. Mechanical ventilatory support for respiratory failure should be evaluated with careful consideration for the presence of reversible complications or comorbidities.

PREVENTION

Asbestosis is a preventable disease, and efforts to eliminate it should be vigorous and persistent. Reporting of asbestosis cases to public health authorities is mandatory in some states. According to the Environmental Protection Agency, there is no safe level for asbestos exposure to assure avoidance of asbestos-associated cancer. Engineering controls to eliminate dust in the workplace and material substitution are important preventive measures. Appropriate protective respirators should be selected by an industrial hygienist based on levels of exposure. Smoking cessation is also an important approach to reduce the risk of asbestos-related lung cancer among those with a history of exposure to asbestos, given the synergistic effects of smoking and asbestos on lung cancer.

REFERENCES

Akira M: High-resolution CT in the evaluation of occupational and environmental disease. Radiol Clin North Am 2002;40:43-59.

American Thoracic Society: Adverse effects of crystalline silica exposure. Am J Respir Crit Care Med 1997;155:761-768.

American Thoracic Society: Diagnosis and initial management of nonmalignant diseases related to asbestos. Am J Respir Crit Care Med 2004;170:691-715.

American Thoracic Society; CDC; Infectious Diseases Society of America: Treatment of tuberculosis. MMWR Recomm Rep 2003;52(RR-11):1-77.

Becklake MR: Occupational exposures: Evidence for a causal association with chronic obstructive pulmonary disease. Am Rev Respir Dis 1989;140: S85-S91.

Castranova V, Vallyathan V: Silicosis and coal workers' pneumoconiosis. Environ Health Perspect 2000;108(Suppl 4):675-684.

Centers for Disease Control and Prevention: Changing patterns of pneumoconiosis mortality—United States, 1968-2000. MMWR Morb Mortal Wkly Rep 2004;53:627-632.

Centers for Disease Control and Prevention: Silicosis screening in surface coal miners—Pennsylvania, 1996-1997. MMWR Morb Mortal Wkly Rep 2000;49:612-615.

Harkin TJ, McGuinness G, Goldring R, et al: Differentiation of the ILO boundary chest roentgenograph (0/1 to 1/0) in asbestosis by high-resolution computed tomography scan, alveolitis, and respiratory impairment. J Occup Environ Med 1996;38:46-52.

Huuskonen O, Kivisaari L, Zitting A, et al: Emphysema findings associated with heavy asbestos-exposure in high resolution computed tomography of Finnish construction workers. J Occup Health 2004;46:266-271.

International Agency for Research on Cancer: Silica and some silicates. IARC Monogr Eval Carcinog Risk Chem Hum 1987;42:1-239.

National Institute for Occupational Safety and Health (NIOSH): Work-Related Lung Disease Surveillance Report 2002. Morgantown, WV: NIOSH, 2003. PDFs available for download at http://www.cdc.gov/niosh/docs/2003-111/2003-111.html (accessed June 1, 2007).

Sato T, Takeno M, Honma K, et al: Heme oxygenase-1, a potential biomarker of chronic silicosis, attenuates silica-induced lung injury. Am J Respir Crit Care Med 2006;174:906-914.

Wagner GR: Screening and Surveillance of Workers Exposed to Mineral Dusts. Geneva: World Health Organization, 1996.

Wilt JL, Parker JE, Banks DE: The diagnosis of pneumoconiosis and novel therapies. In Banks DE, Parker JE (eds): Occupational lung disease. London: Chapman & Hall, 1998, pp 119-138.

Xie QM, Tang HF, Chen JQ, Bian RL: Pharmacologic actions of tetrandrine in inflammatory pulmonary diseases. Acta Pharmacol Sin 2002;23:1107-1113.

CONN'S Current Therapy 2008

Robert E. Rakel, MD
Professor, Department of Family and
Community Medicine
Baylor College of Medicine
Houston, Texas

Edward T. Bope, MD
Director, Riverside Family Practice Residency Program
Clinical Professor, Department of Family Medicine
The Ohio State University College of Medicine
Columbus, Ohio

LATEST APPROVED METHODS
OF TREATMENT FOR
THE PRACTICING PHYSICIAN

SAUNDERS

ELSEVIER