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# SILICOSIS

method of
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Silicosis is a fibrotic disease of the lungs caused by the inhalation of, retention of, and pulmonary reaction to crystalline silica. Despite extensive knowledge about the cause of this pneumoconiosis (respiratory exposures to silica-containing dusts), this serious and potentially fatal occupational lung disease is tragically still seen even today, in the last part of this century in the United States and throughout the world. Silica, or silicon dioxide, is the predominant component of the earth's crust. The three important crystalline forms of silica are quartz, tridymite, and cristobalite. These forms are also called free silica to distinguish them from the silicates. The silica content in different rock formations, such as sandstone, granite, and slate, varies from 20% to nearly 100%. Occupational exposure to silica particles of respirable size (0.5 to 5 μm) is associated with mining, quarrying, drilling, and tunneling operations. Silica exposure is also a potential hazard to sandblasters, stonecutters, and pottery, foundry, ground silica, and refractory workers. The national or worldwide prevalence of silicosis is unknown, but more than 2 million workers in the United States alone are employed in trades at risk for the development of silicosis; in the developing world, cumulative estimates exceed 1 million cases of the disease.

The precise pathogenic mechanism for the development of silicosis remains uncertain. Abundant evidence implicates the interaction between pulmonary alveolar macrophages and silica particles deposited in the lung. It is proposed that surface properties of the silica particle activate macrophages. These cells then release chemotactic factors and inflammatory mediators that result in a further cellular response by polymorphonuclear leukocytes, lymphocytes, and additional macrophages. Fibroblast-stimulating factors are released that promote hyalinization and collagen deposition. The resulting pathologic silicotic lesion is the hyaline nodule, which contains a central acellular zone with extracellular silica surrounded by whorls of collagen and fibroblasts and an active peripheral zone composed of macrophages, fibroblasts, plasma cells, and additional extracellular silica. Impaired macrophage function also plays a role in susceptibility to infectious organisms such as *Mycobacterium tuberculosis* and *Nocardia asteroides*.

There is mounting evidence that freshly fractured silica may be more toxic than aged silica, perhaps related to reactive radical groups on the cleavage planes of freshly fractured silica. This may offer a pathogenic explanation for the observation of cases of advanced disease in both sandblasters and rock drillers where exposures to recently fractured silica are particularly intense.

## FORMS OF DISEASE: CLINICAL PICTURE

Chronic silicosis is often asymptomatic and presents as a radiographic abnormality with small (<10 mm), rounded opacities predominantly in the upper lobes. A history of 15 years or more since onset of exposure is common. Results of pulmonary function testing may be normal or may show mild restriction. Less commonly, mild obstruction to airflow or reduced diffusing capacity may be present. Chronic nodular silicosis not infrequently progresses to more advanced disease or progressive massive fibrosis.

Complicated silicosis, also called progressive massive fibrosis, is more likely to present with exertional dyspnea. Progressive massive fibrosis is characterized by nodular opacities greater than 1 cm on the chest radiograph and commonly involves reduced carbon monoxide diffusing capacity, reduced arterial oxygen tension at rest or with exercise, and marked combined obstruction and restriction on spirometry or lung volume measurement. Distortion of the bronchial tree may also lead to airways obstruction and productive cough. Recurrent bacterial infection not unlike that seen in bronchiectasis may occur. Weight loss and cavitation of the large opacities should prompt concern for tuberculosis or other mycobacterial infection. Pneumothorax may be a life-threatening complication, because the fibrotic lung may be difficult to re-expand. Hypoxemic respiratory failure with cor pulmonale is a common terminal event.

Accelerated silicosis may appear after more intense exposures of shorter (5 to 10 years) duration. Symptoms, radiographic findings, and physiologic measurements are similar to those seen in the complicated form. Deterioration in lung function is more rapid, and in some countries, as many as 25% of patients with accelerated disease may develop mycobacterial infection. Autoimmune diseases, including scleroderma and rheumatoid arthritis, are seen with silicosis, often of the accelerated type. The progression of radiographic abnormalities and functional impairment can be rapid when autoimmune disease is associated with silicosis.

Acute silicosis may develop within 6 months to 2 years of massive silica exposure. Dramatic dyspnea, weakness, and weight loss are often presenting symptoms. The radiographic findings of diffuse alveolar filling differ from those in the more chronic forms of silicosis. Histologic findings similar to pulmonary alveolar proteinosis have been described, and extrapulmonary (renal and hepatic) abnormalities are reported. Rapid progression to severe hypoxemic ventilatory failure is the usual course. The potential for mycobacterial infection in acute silicosis requires constant vigilance.

## PREVENTION

There is no specific therapy for silicosis. Prevention remains the cornerstone of eliminating this occupational lung disease. The education of workers and employers regarding the hazards of silica dust exposure and measures to control exposure is important. Improved ventilation and local exhaust, process enclosure, wet techniques, personal protection including the proper selection of respirators, and, where possible, industrial substitution of agents less hazardous than silica reduce exposure.

Silicosis is a reportable disease in many states. Even in the absence of legal reporting requirements, cases of silicosis should be viewed as sentinel health events and should initiate work site evaluations to reduce exposures that may be surprisingly excessive even for current workers. Medical examinations of coworkers may also identify additional cases of early or, at times, advanced disease. If silicosis is recognized in a worker, limiting future significant exposure is advisable. Unfortunately, the disease may progress even

without further silica exposure. In the United States, finding a case of silicosis, especially the acute or accelerated form, should prompt notification of state or federal agencies, such as the Occupational Safety and Health Administration, the Mine Safety and Health Administration, or the National Institute for Occupational Safety and Health (NIOSH) to obtain work place evaluations to protect other workers also at risk. NIOSH maintains a toll-free number, 1-800-35-NIOSH, for occupational safety and health information and assistance with work place "health hazard evaluations." In other nations, cases should also be reported by physicians to relevant public health authorities to address primary prevention efforts.

## TREATMENT

When prevention has been unsuccessful and silicosis has developed, therapy is directed largely at complications of the disease. Therapeutic measures are similar to those commonly used in the management of airway obstruction, infection, pneumothorax, hypoxemia, and respiratory failure complicating other pulmonary disease. Historically, the inhalation of aerosolized aluminum has been unsuccessful as a specific therapy for silicosis. Polyvinyl pyridine *N*-oxide, a polymer that has protected laboratory animals, is not available for use in humans. Laboratory work with tetrandrine has shown in vivo reduction in fibrosis and collagen synthesis in silica-exposed animals treated with this drug. However, strong evidence of human efficacy is currently lacking, and this drug is not available in the United States. The search for a specific therapy for silicosis to date has been unrewarding.

If obstructive airway disease with bronchospasm develops, bronchodilator therapy is indicated. Inhaled selective beta$_2$-adrenergic agents, such as albuterol (Ventolin, Proventil), 2 inhalations every 4 to 6 hours, may be helpful. Oral long-acting theophylline preparations, given twice daily, to achieve a blood level of 10 to 20 μg per mL may be beneficial in some patients in combination with inhaled beta agonists.

Episodes of acute bronchitis, commonly caused by *Streptococcus pneumoniae* or *Haemophilus influenzae*, can be treated with ampicillin 250 to 500 mg every 6 hours for a 10-day course. Erythromycin, trimethoprim-sulfamethoxazole (Bactrim, Septra), ciprofloxacin (Cipro), and other antibiotics are also useful for treatment of initial or recurrent episodes of infectious bronchitis. If infection does not improve on empirical therapy, re-evaluation of sputum with Gram's stain, culture, and sensitivity tests should be performed. Pneumococcal and influenza vaccinations are recommended.

Airway secretions causing copious, tenacious sputum production and occasionally disabling cough should be managed with time-honored methods of adequate hydration, humidification, and postural drainage. Cessation of smoking is clearly important and must be strongly encouraged.

Tuberculosis is a common and serious complication, especially in complicated, accelerated, and acute silicosis. Patients with silicosis who have a significant tuberculin skin reaction but no clinical, bacteriologic, or radiographic evidence of active disease should be treated with isoniazid (INH) or rifampin (Rimactane, Rifadin) preventive therapy. These antimicrobials should be given for a minimum of 6 months to 1 year. Some physicians recommend lifelong preventive therapy for tuberculin skin test–positive patients with silicosis. Silicotic patients receiving glucocorticoids should also be considered for INH or rifampin preventive therapy.

The diagnosis of active tuberculosis infection in patients with silicosis can be difficult. Clinical symptoms of weight loss, fever, sweats, and malaise should prompt radiographic evaluation and sputum acid-fast bacilli stains and cultures. Radiographic changes, including enlargement or cavitation of progressive massive fibrosis lesions or nodular opacities, are of particular concern. Bacteriologic studies on expectorated sputum may not always be reliable in silicotuberculosis. Fiberoptic bronchoscopy to obtain additional specimens for culture and study may often be helpful in establishing a diagnosis of active disease.

Proven active tuberculosis and clinically suspected disease should be treated with appropriate antimicrobials (see the article on tuberculosis), now commonly including three or four drugs such as INH, rifampin, pyrazinamide, and ethambutol for a minimum of 6 to 9 months. Because of the difficulties in treating tuberculosis in the setting of silicosis, many authorities have recommended more prolonged courses. Antituberculous therapy, of course, should always be guided by laboratory studies of sensitivity, especially with the increasing recognition of multidrug-resistant organisms. Initiation of therapy before bacteriologic confirmation is prudent in silicotic patients with clinical signs compatible with active tuberculosis. Careful long-term follow-up with chest radiographs, bacteriologic cultures, and monitoring of clinical symptoms is imperative in view of numerous reports of recurrent pulmonary tuberculosis in silicotic patients after the completion of conventional therapeutic courses of antimicrobials.

Hypoxemia should be treated with supplemental oxygen to prevent the development of polycythemia, to delay or prevent development of pulmonary hypertension and cor pulmonale, and to improve exercise tolerance. The goal of oxygen therapy should be to elevate the $Po_2$ above 60 mm Hg. Two to 4 liters per minute of oxygen by nasal cannula often achieves this level of arterial oxygenation. Measurement of arterial blood gases should guide the selection of inspired oxygen concentrations. Portable and home oxygen systems are widely available for managing these patients.

Ventilatory support for respiratory failure is indicated when it is precipitated by a treatable complication. Pneumothorax, spontaneous and ventilator related, is usually treated by chest tube insertion. Bronchopleural fistula may develop, and surgical consultation and management should be considered.

Acute silicosis may rapidly progress to respiratory failure. When this disease resembles pulmonary alveolar proteinosis and severe hypoxemia is present, aggressive therapy has included selective whole-lung lavage with the patient under general anesthesia in an attempt to improve gas exchange and remove alveolar debris. Although it is appealing in concept, the efficacy of whole-lung lavage remains to be established. Glucocorticoid therapy has also been used for acute silicosis; however, it is still of unproven benefit. Prednisone has been used at dosages of 40 to 60 mg per day for 1 to 2 months and, if accompanied by evidence of clinical improvement, has been tapered to 15 to 20 mg per day and continued for 6 months to 1 year. Early, rigorous initial evaluation for tuberculosis and other mycobacterial infection cannot be overemphasized. INH or rifampin should be given while steroids are administered. Empirical therapy with three or four antituberculous drugs pending results of cultures for 6 weeks may be appropriate in the life-threatening acute form of disease.

Some young patients with end-stage silicosis may be considered candidates for lung or heart-lung transplantation by centers experienced with this procedure. Early referral and evaluation for this intervention may be offered to selected patients.

The discussion of an aggressive and high-technology therapeutic intervention such as whole-lung lavage and transplantation serves to dramatically underscore the serious and potentially fatal nature of silicosis as well as emphasize the crucial role for primary prevention.