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Silicosis and Asbestosis

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

Silicosis

Silicosis is the oldest pneumoconiosis known in the world. Only respirable dust (0.5 to 5 μm) containing crystalline silica is able to reach the lungs and cause fibrosis. The three most important crystalline forms of silica are quartz, tridymite, and cristobalite. Quartz is the most common and commercially available form of this mineral, but tridymite and cristobalite are more fibrogenic. Exposure to silica dust occurs in many occupations such as mining, quarrying, drilling, and tunneling operations. It is also a hazard to stonecutters and refractory brick, pottery, foundry, and sandblasting workers. Silica flour added to porcelain, cosmetics, and soap also represents a risk.

Precise information on the incidence and prevalence of silicosis worldwide is unknown, but it seems to be decreasing in industrialized countries because of 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 frequently misclassified and underdiagnosed. In the United States, there are more than two million workers exposed to silica at a potential risk of developing the disease.

In terms of pathology, the fundamental lesion is a concentric silicotic nodule. The pathogenesis is complex, with four basic mechanisms involved:

1. Direct cytotoxicity that can release enzymes
2. Activation of oxidant production by pulmonary phagocytes
3. 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
4. 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 is more toxic to the lungs, which can be explained by the presence of free radicals.

Three important criteria are generally sufficient for a diagnosis of silicosis:

1. A careful occupational history documenting silica exposure with an appropriate latency period
2. A chest radiograph interpreted as 1/0 or greater in accordance with International Labour Organization (ILO) classification of radiographs of pneumoconioses
3. The absence of diseases that can mimic silicosis such as tuberculosis, sarcoidosis, or pulmonary fungal infections

Pulmonary biopsy typically is not necessary. High-resolution computed tomography (CT) can be useful in achieving more accurate categorization of the parenchymal changes in each type of pneumoconiosis, but these findings are not standardized and the procedure is expensive for medical screening purposes.

CLINICAL FEATURES

All four forms of this pneumoconiosis—chronic, complicated, accelerated, and acute—are related to the degree or intensity of silica exposure.

Patients with chronic silicosis are often asymptomatic. The chest radiograph presents with small (less than 10 mm), rounded opacities mainly in the upper zones that appear more than 15 years after onset exposure. These parenchymal abnormalities may occur without significant changes in pulmonary function or may lead to mild restriction. Because of smoking habits or the presence of dust, an obstructive pattern may be observed in the spirometry. Carbon monoxide diffusing capacity (DLCO) measures the transfer of a diffusion-limited gas (carbon monoxide [CO]) across the alveolocapillary membrane. The carbon monoxide diffusing capacity also may be decreased because of silicotic changes.

Progressive massive fibrosis also is known as complicated silicosis. The most common symptom is exertional dyspnea. Cough can occur as a result of superimposed infections or chronic obstructive pulmonary disease (COPD). The radiograph is characterized by the presence of large opacities greater than 1 cm in diameter. The spirometry usually presents a restrictive pattern

caused by fibrosis or mixed pattern with associated obstruction, because of emphysema causing hyperinflation of the lungs. Carbon monoxide diffusing capacity is reduced. These patients are at risk for tuberculosis, nontuberculous mycobacterioses, and bacterial infections, and may present with bronchiectasis. Because of extensive areas of fibrosis and gas exchange abnormalities, with hypoxemia, cor pulmonale and respiratory failure may be present in the final stage of the disease.

Accelerated silicosis occurs with high levels of exposure of shorter duration (usually 5 to 10 years). The radiographic patterns are similar to chronic silicosis, but the progression of disease is more rapid. Patients present symptoms early, and the lung function deteriorates very quickly with a rapid decline in forced expiratory volume in 1 second (FEV_1).

Acute silicosis may develop within 6 months to 2 years after massive silica exposure. The symptoms are severe dyspnea, weight loss, and weakness. The chest radiograph shows a completely different pattern from other types of silicosis with alveolar spaces flooded with exudates. 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, respiratory failure, and death. Superimposed bacterial infections, tuberculosis, and nocardia infections may be present.

MANAGEMENT

All forms of the disease are irreversible, often progressive (even after the exposure has ceased), and potentially fatal, although completely preventable. Many experimental studies have been conducted to establish a treatment for this disease, but, because of their toxicity, they are not available for humans. Tetrandrine, an extract of the root of *Stephania tetranda,* used in traditional Chinese medicine, was approved by 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 before it is considered safe and effective. Because there is no specific drug to reverse the fibrosis, the treatment of silicosis should be focused on alleviating symptoms and remediating the complications of the disease. A common complication is the association between silicosis and pulmonary tuberculosis. Tuberculosis can be present in up to 15% of the cases in some countries. Clinical symptoms compatible with tuberculosis should prompt bacteriologic confirmation of the diagnosis. The current recommended treatment is a course of pyrazinamide, rifampin (Rifadin), ethambutol (Myambutol), and isoniazid (INH) for 2 months, followed by 6 to 7 months of isoniazid and rifampin. Some authors suggest that the treatment with at least two drugs should be prolonged for 12 months. Long-term-follow-up with bacteriologic culture and radiographs is mandatory. Nontuberculous mycobacteria account for an increased proportion of the mycobacterial diseases in those with silicosis in the industrialized countries. *Mycobacterium kansasii* or *Mycobacterium avium-intracellulare* can occur, and cultures should be performed. The treatment will need to be modified according to the type of mycobacterium grown. *M. kansasii* usually responds well to therapy. Rifampin and ethambutol should be given for a period of 9 months. Silicosis also is 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, azathioprine (Imuran),[1] chlorambucil (Leukeran),[1] cyclosporine (Neoral),[1] and many others have been used as an attempt 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 steroids, 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 steroids and resolution of effusion within 2 weeks. Spontaneous resolution does not occur. The use of immunosuppressives can trigger infections, and purified protein derivative must be checked before treatment, although a negative skin test will not rule out infection.

COPD occurs more frequently in workers exposed to silica than in the general population. Classification of severity of this obstructive disease is the basis for treatment. Use of an inhaled short-acting bronchodilator on demand is useful in all stages. Long-acting bronchodilators such as formoterol (Foradil) or salmeterol (Serevent), given twice daily, may be used from 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 in severe stages. Systemic steroids should be used during exacerbations as short-course therapy. Theophylline (Slo-Phyllin) achieves small changes in FEV_1 with long-term use. Pulmonary hypertension is the underlying cause of cor pulmonale. Supplemental oxygen is necessary to prevent pulmonary hypertension and cor pulmonale if hypoxemia is present. Oxygen therapy should be prescribed when the arterial partial pressure of oxygen (PaO_2) is less than 55 mm Hg or arterial oxygen saturation (SaO_2) is less than 88% and partial pressure of oxygen 56 to 59 mm Hg with electrocardiogram (ECG) evidence of P pulmonale, pedal edema, and/or secondary erythrocytosis. Patients using oxygen for at least 15 hours per day had an important decrease in their pulmonary artery pressures and enhanced cardiac output. Noninvasive positive pressure ventilation has a significant role in the treatment of severe COPD exacerbations. Mechanical ventilatory support for respiratory failure is indicated when it is caused by a treatable complication. A pulmonary rehabilitation program has a role to improve dyspnea and enhance quality-of-life scores.

[1]Not FDA approved for this indication.

Episodes of acute bronchitis can occur and are usually caused by *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, and *Moraxella catarrhalis*. Antibiotics should be prescribed for purulent exacerbations. Viral infections and *Mycoplasma pneumoniae* also can 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.

The International Agency for Research on Cancer (IARC) has classified crystalline silica as a potential human lung carcinogen; however, the issue remains controversial in the medical literature. Other conditions such as chronic renal disease also have been linked with silica exposure in some populations, although the overall levels of morbidity and mortality are too low to justify medical screening for this health outcome. Pneumothorax may occur spontaneously or may be ventilator related, and a chest tube generally is required urgently.

Acute silicosis has been treated with whole-lung lavage to remove the inflammatory exudates and reduce the lung dust burden. The benefits are uncertain, and serious bacterial infections can occur after this procedure. Some reports suggest using prednisone[1] as an attempt to treat acute silicosis. The initial doses can vary from 40 to 60 mg per day for 1 month, and if benefits can be documented, the treatment can be maintained with lower doses (15 to 20 mg per day) for 6 months. Steroids are potentially dangerous if coexistent tuberculosis (TB) or other infectious agents are not recognized.

After an initial evaluation, based on guidelines for recipient selection, single or bilateral lung or lung-heart transplantation should be considered for selected 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, are often required to be performed at the referring center.

PREVENTION

In the absence of specific treatment for silicosis, primary prevention is the key to avoid the disease. Dust control and use of efficient respirators for brief periods when exposure might occur 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 and appropriate general ventilation, and wet techniques are effective when vigorously implemented in workplaces.

Although silicosis reporting is required in many states to assure investigation of continuing workplace hazards, a national surveillance is essential to obtaining 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 frequently used in shipbuilding. Other occupations with potential risk for asbestosis are mining, insulation application and removal, and use of asbestos-containing material in construction, and manufacturing of cement products.

Other nonmalignant outcomes associated with asbestos are pleural plaques, acute pleural effusion, pleural thickening, rounded atelectasis, and chronic airway obstruction. Lung cancer and mesothelioma (a type of pleural cancer) are malignant diseases related to asbestos exposure. The type of fiber (length and dimension) and its biopersistence are very important variables in determining the development of disease, as well as the dose-response and latency period. The most common type of asbestos is chrysotile, although amphiboles (crocidolite, amosite, and anthophyllite) are more fibrogenic and carcinogenic.

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

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, and radiographic abnormalities consistent with irregular opacities 1/1 predominant in lower fields. In advanced phases of this disease, middle and upper lobes can be affected, and the presence of honeycombing can be noted. If there are doubts about the diagnosis, a high-resolution CT should be performed. An open lung biopsy is required only in special cases to establish the differential

CURRENT DIAGNOSIS

- Obtain a detailed medical and working history, including all past exposures.
- Obtain a chest radiograph.
- Exclude other diseases that may mimic radiographic appearance of pneumoconiosis.
- Perform lung function tests to assess severity of disease.

[1]Not FDA approved for this indication.

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 treated.
- A pulmonary rehabilitation program may help the patient.
- Lung transplantation is appropriate in selected cases.

diagnosis with other interstitial diseases 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 (BAL) would be helpful in this differentiation. The disease often remains or progresses after cessation of exposure.

MANAGEMENT

There is no effective treatment for this disease. Some patients can develop pulmonary hypertension or cor pulmonale, and oxygen should be provided. Respiratory infections may occur and antibiotics should be given. Mechanical ventilatory support for respiratory failure should be evaluated with careful consideration for the presence of reversible complications or co-morbidities.

PREVENTION

Asbestosis is a preventable disease, and efforts to eliminate it should be constant. According to the Environmental Protection Agency, there is no safe level for asbestos exposure to avoid cancer. Engineering controls to eliminate dust in the workplace, material replacement, and selection of an appropriate respirator for different levels of exposure are important measures. Smoking cessation is also an important approach to reduce the risk for asbestos-related lung cancer.

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Hypersensitivity Pneumonitis

Method of

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Hypersensitivity pneumonitis (HP) is a respiratory disease caused by a hyperimmune response to a variety of inhaled antigens. These antigens include animal proteins, bacterial or fungal particles, and nonorganic compounds that act as haptens with human albumin. The clinical manifestations vary from an acute form characterized by fever, shortness of breath, and chest tightness, which start 3 to 8 hours after exposure, to a more insidious presentation in which the patient will develop progressive shortness of breath with cough and weight loss. Physical examination is unremarkable with inspiratory crackles, sometimes a fever, and, in some chronic cases, digital clubbing. Early in the disease, the physiologic abnormalities are restrictive and a marked reduction in lung diffusion capacity with a decrease in lung volumes. In acute cases or after a lengthy subacute presentation, hypoxemia is usually present. Lung functions can revert to normal when the disease is diagnosed early and prevented from progressing. If, however, the disease is allowed to continue for repeated bouts of acute reactions or for a prolonged period of time, irreversible lung damage can occur. The long-term outcome can be either in the form of lung fibrosis with restrictive lung functions or present as emphysema with associated irreversible airflow obstruction and hyperinflation.

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