CHAPTER 59

COAL WORKERS' LUNG DISEASES AND SILICOSIS

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COAL WORKERS' LUNG DISEASES

Introduction and History

Coal miners are at risk for developing several distinct clinical illnesses in relation to their occupational exposures. Historically, some names applied to these disorders were miners' asthma, phthisis, anthracosis, and, in Scotland, miners' black lung. It was recognized early that these afflictions were related to the occupation of mining. However, it wasn't until the development of specialized techniques such as chest radiography and pulmonary function testing, the discovery of the tubercle bacillus, and the sophisticated histologic examination of tissue that respiratory diseases affecting miners could be differentiated and defined.

Coal workers' pneumoconiosis (CWP) is the parenchymal lung disease that results from the inhalation and deposition of coal mine dust and the tissue's reaction to its presence. This occupational lung disease was first defined in the early 1800s. In addition to CWP, coal mine dust exposure increases a miner's risk of developing chronic bronchitis and pathologic emphysema and accelerates loss of ventilatory lung function.

For a long time, the pneumoconiosis that affected coal miners was thought to be silicosis. In the 1930s, however, it was argued for the first time that silicosis, CWP, and bronchitis were distinct clinically and pathologically. Unfortunately, it was also suggested that coal dust was not harmful, despite reports of the adverse effects from coal dust among coal trimmers. It was not until washed coal that was free of silica was shown to produce a dust disease in the lungs of stevedores leveling coal in the holds of ships that CWP was widely accepted as a distinct pathologic entity.

In the United States, little attention was given to coal miners' respiratory diseases until the Public Health Service (USPHS) conducted a pilot prevalence study of CWP in the early 1900s. Since then, a large number of studies, performed by the National Institute for Occupational Safety and Health, have greatly increased our knowledge of the lung diseases associated with coal mining in the United States.[1]

Coal and Coal Mining

Coal is not a pure mineral. It is a conglomeration of carbonaceous rocks derived from the accumulation of vegetation sedimented under swampy conditions and subjected to extreme pressure over long periods. Coals are characterized by rank (which relates to geologic age), hardness, carbon content, and the amount of heat released (BTUs) when burned. Peat is the lowest-rank (softest) and geologically newest type of coal, while anthracite is the highest-rank (hardest) and oldest coal.

Since coal may be found in outcroppings and in seams that are only a few feet below the surface, it can often be readily obtained by simply scraping off the surface, or overburden, and mined with large earth-moving equipment. This type of mining, called strip mining, currently accounts for most U.S. coal production. Occasionally, surface mining is also performed by boring into coal outcrops with an auger. Dust levels in the air at surface mines are generally considerably lower than in underground mines, with a few notable exceptions (see below).

When coal seams are buried deep within the earth's crust, it is not economically feasible to strip away the overburden. The only practical way of mining the coal is to sink shafts from the surface to the coal seam and then follow the seam with a series of more or less horizontal tunnels. In the past, shaft mines of this sort were the most common type of coal mine in the world. They still represent an important source of coal and produce slightly less than half of the coal mined in the United States.

Not all coal-mining jobs are equally exposed to respiratory hazards. In underground mines, airborne dust concentrations are highest at the coal cutting face, where coal is removed from the intact seams. Face jobs include the loading of coal into transportation vehicles or train cars and, depending on the techniques used in the mine, operation of continuous or long wall mining machines. Exposure to crystalline silica and thus the risk of silicosis also occur in underground mines, particularly in miners engaged in roof support, called roof bolting (Fig. 59-1), or drilling operations, and in motormen who operate underground coal trains and use sand for traction on the rails. Workers in some exclusively aboveground coal-mining operations also may have important exposure to dusts. These include workers at tipples and preparation plants, where crushing, sizing, washing, and blending of coal are done and coal is stored and loaded into ships, railroad cars, or river barges. Workers at surface coal mines who operate the drilling rigs (drillers), to make holes in which explosives are placed, are exposed to silica and are at risk for the development of silicosis rather than CWP.[1,6]

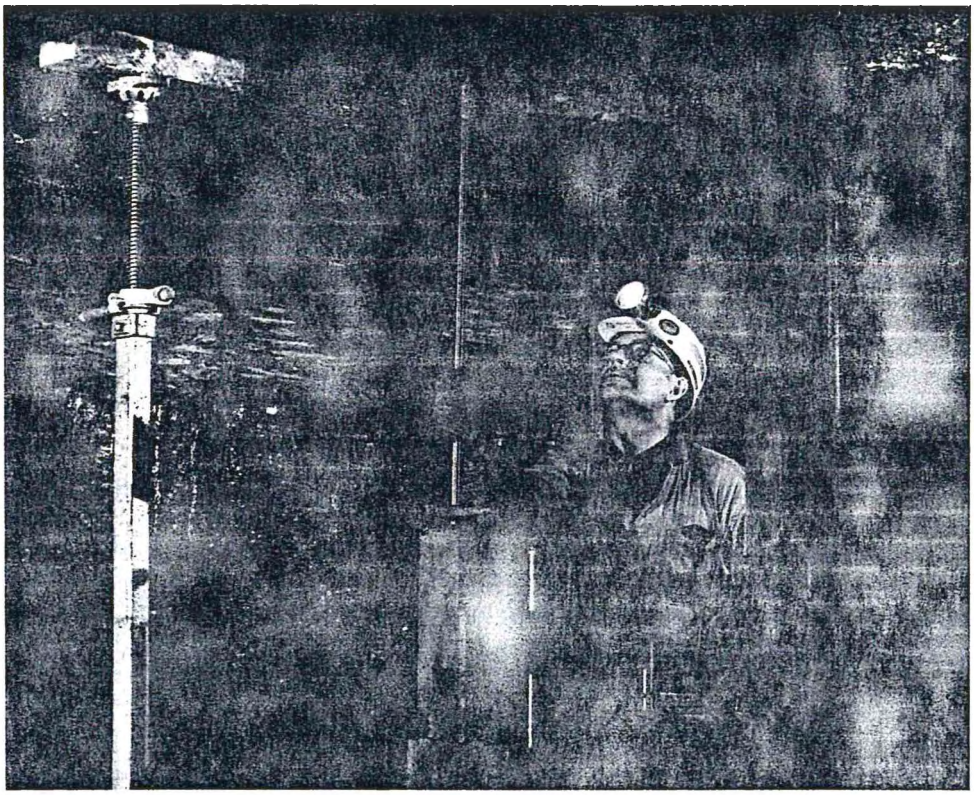

FIGURE 59-1 Roof bolting in underground coal mine. A potentially high-risk operation for respiratory exposures to airborne silica. *(Photo courtesy of U.S. Bureau of Mines.)*

Epidemiology of Lung Diseases in U.S. Coal Miners

The first major survey of the health of American coal workers was conducted by the USPHS from 1969 to 1971, evaluating symptoms, lung function, and chest radiographic findings.[3,4] This study included more than 9000 miners at two anthracite and 29 bituminous mines. Participation in the survey was over 90 percent. The mines were chosen to represent different geographic areas, coal seams, and mining methods. Since this initial study, subsequent surveys have studied miners at these and other U.S. mines.

RADIOGRAPHIC FINDINGS

Radiographic data from the initial survey showed an overall prevalence of simple and complicated CWP of nearly 30 percent. There was variation by region of the country and the type (rank) of coal mined. Among eastern Pennsylvania anthracite (high-rank) coal miners, 46 percent had simple and 14 percent had complicated CWP. In contrast, among miners in the western plateau of Colorado and Utah mining a lower-rank coal, only 5 percent had simple CWP and none had the complicated form.[3,4] Among underground miners, those working at the coal face and exposed to higher concentrations of coal mine dust had higher prevalences of CWP than surface workers or those whose jobs caused them to enter the face area intermittently.

After this initial survey, many miners with CWP became eligible to retire, and follow-up studies have demonstrated a decline in the prevalence of CWP in active US miners.[11] Enforcement of and compliance with dust control measures, adopted in 1969 and introduced about the time of the initial survey, also resulted in a reduced attack rate of CWP. This was confirmed in the periodic chest radiograph surveillance program in U.S. miners. In 1970–73, CWP was found in 28 percent of participants with 25 years or more underground. By 1992–95, fewer than 10 percent showed radiographic evidence of CWP (Fig. 59-2).[11] Compliance with lower exposure standards probably also reduced the risk of disease progression among miners with CWP who continued to work in mines that were in compliance with mandated dust standards.

Data from the U.S. studies noted above clearly demonstrated that the prevalence of radiographic changes of simple CWP is related to the duration and intensity of dust exposure, even at current dust levels.[5] Data from studies of British miners also demonstrated that the attack rate (incidence of new cases) and

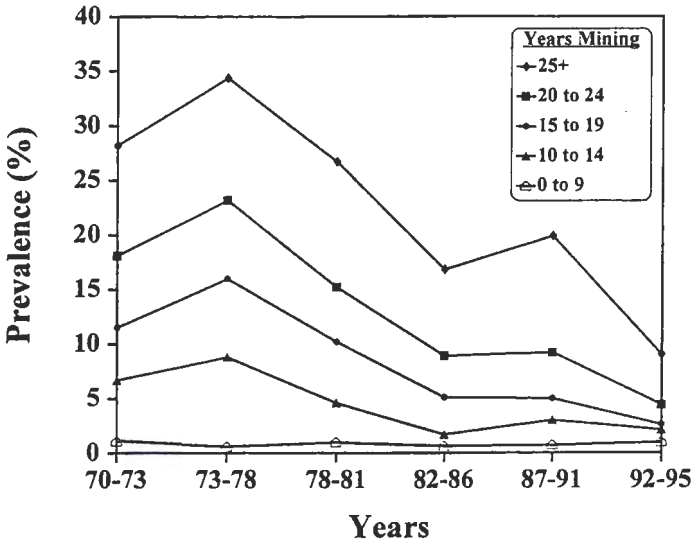

FIGURE 59-2 Percentage of miners with chest radiograph of ILO category 1/0 or greater, by tenure in mining, 1970–95, examined in the NIOSH Coal Workers' Radiograph Surveillance Program. Criteria for a recommended standard: Occupational exposure to respirable coal mine dust.[10] *(Courtesy of Rochelle Althouse, National Institute for Occupational Safety and Health, Morgantown, WV.)*

the probability of disease progression in simple CWP were related to the mass of respirable dust to which the miner was exposed during his or her lifetime.[24] The same cannot be said for the complicated form of CWP—progressive massive fibrosis (PMF). Once a person has inhaled sufficient coal mine dust into the lungs for the chest radiograph to be classified with at least ILO category 2 pneumoconiosis (see below), the probability of its progressing to the complicated form appears to be independent of any further dust exposure. The rate of progression to PMF appears to be influenced chiefly by the age at which the miner begins to show radiographic changes of CWP. Progression may also be influenced by the presence of a rheumatoid diathesis (see below).[30]

VENTILATORY LUNG FUNCTION

Ventilatory function was also evaluated in the large studies of U.S. miners mentioned above. Initial reports examined miners' lung function in comparison to their *radiographic findings.* Miners with complicated CWP were found to consistently show an important defect in lung function. This defect could be restrictive or obstructive, depending on the contributions of fibrosis and bronchitis, respectively. In contrast to the ventilatory findings associated with progressive massive fibrosis, mild obstructive abnormalities were often noted in miners with simple pneumoconiosis. However, the findings were not consistent, and with increasing category of simple CWP, the average functional decrement was small and quite variable.[33] Subsequent studies in the United States and Great Britain helped to clarify the adverse effects of dust on coal miners' lung function by evaluating lung function with respect to the miners' *cumulative dust exposure.*[29] They noted that miners manifest a progressively greater risk of lung function loss with increasing cumulative dust exposure and that this deterioration was independent of the chest radiographic findings of CWP.[3] The FEV_1 loss was most severe in those who worked for many years at the dustiest jobs. Among smoking miners, the effects of tobacco smoke appeared to be additive to the dust effect.[4] The studies also noted that miners experience a more rapid loss of lung function over their first few years of mining, with slower dust-related declines after that time.[41]

In summary, epidemiologic data have shown that coal miners experience ventilatory lung function loss with increasing exposure to dust, either in the presence or in the absence of CWP. Among smoking miners, the effects of tobacco and dust appear to be additive. Although, on average, functional losses associated with dust are small, it is estimated that 35 years of work at the current dust limit will cause a clinically important FEV_1 loss in eight of 100 nonsmoking coal miners.[36] When complicated CWP is present, an additional restrictive or obstructive ventilatory deficit is often noted.

MORTALITY

Studies of mortality in coal miners have been reported from the United States and Britain. The findings from both nations have been generally consistent, revealing that miners experience increased mortality attributable to pneumoconiosis, emphysema, and chronic bronchitis. Radiographic findings of advanced CWP (i.e., PMF) are consistently associated with mortality, especially in categories B and C (see below). Among miners with simple CWP, decreases in survival were significantly smaller.[26,31] Of interest is that miners' risks of dying from emphysema and chronic bronchitis exhibited a geographic pattern different from that associated with their mortality from CWP, suggesting that these dust effects may be mediated by different mechanisms.[13]

Pathology of Coal Miners' Lung Diseases

The coal macule is the primary lesion of simple CWP and is essential for the pathologic diagnosis of the disorder.[25] The lesion consists of a focal collection of coal dust in pigment-laden macrophages around respiratory bronchioles, tapering off toward the alveolar duct (Fig. 59-3). A fine network of reticulin is present in the early lesion. Macules may also contain a small amount of collagen, depending on the character of the initiating dust. Centriacinar emphysema, the dilation and injury of lung gas exchange units, is also observed with increased prevalence in the lungs of coal miners. The severity of this lesion is proportional to the miner's cumulative dust exposure and retention. Focal emphysema is the form of centriacinar emphysema that is seen as an integral part of the lesion of simple CWP. It is characterized by enlargement of the airspaces immediately adjacent to the dust macule (Fig. 59-3). Muscular thickening of pulmonary arteries can be observed in both simple and complicated CWP. In severe cases, especially when CWP is complicated or associated with other disorders, cor pulmonale with hypertrophy of the right ventricle is noted. Pathologic changes in the airways consistent with chronic bronchitis, including enlargement of mucous glands, have also been noted in miners' lungs.

With increasing dust exposure, owing to the overwhelming of the normal clearance mechanisms of the lung, coal-induced le-

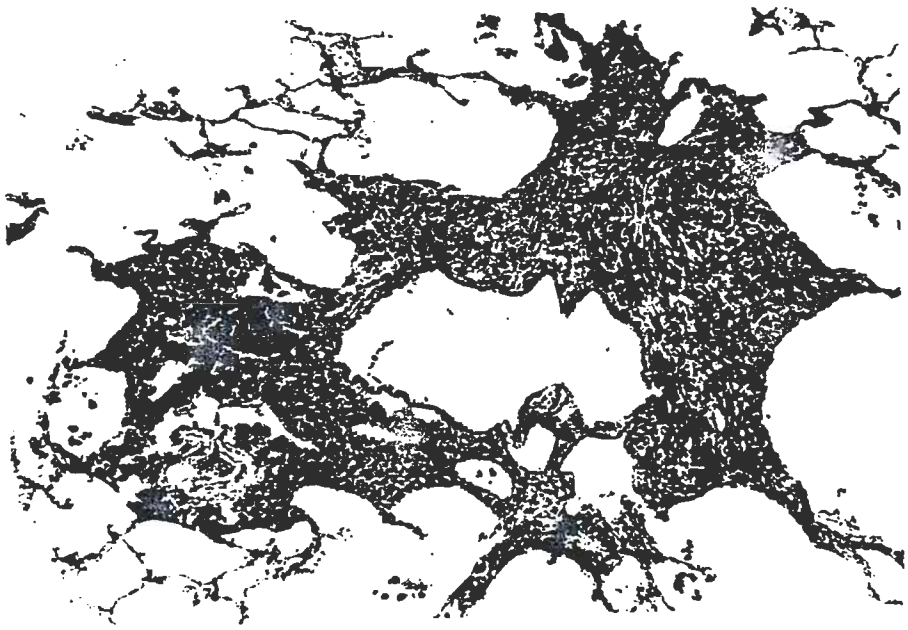

FIGURE 59-3 A coal macule, microscopic section. *(Courtesy of Dr. Val Vallyathan, National Institute for Occupational Safety and Health, Morgantown, WV.)*

sions increase in size and number. These larger fibrotic lesions are called *coal nodules* and are palpable in lung specimens. Palpable coal nodules are classified as micronodular up to 7 mm in diameter and macronodular if they are 7 mm or larger (Fig. 59-4).[25]

Complicated CWP or PMF is diagnosed when one or more nodules in a lung specimen are noted to attain a size of 2 cm or greater in diameter. The 2 cm cutoff is an arbitrary choice of a minimal diameter that permits better correlation with clinical and radiographic measurements.[25] Radiographically, PMF is said to be present when coal-induced radiographic shadows are at least 1 cm in diameter. These lesions are solid, heavily pigmented, and rubbery to hard, and they occur most commonly in the apical posterior portions of upper lobes or the superior segments of lower lobes (Fig. 59-5). They tend to occur symmetrically, but they may be asymmetric and cavitate. Airways and vessels adjacent to the lesions may be distorted, and within the lesions, they are destroyed. PMF generally occurs in association with background pathologic changes of simple CWP.

Clinical Features of Coal Workers' Lung Diseases

Some coal-exposed workers, even those with simple pneumoconiosis, do not manifest respiratory signs or symptoms. Others experience a variety of respiratory problems, with chronic cough and sputum production being the most common. These symptoms are more common with increasing dust exposure and can be seen in the presence or absence of simple pneumoconiosis. The symptoms are probably related to bronchitic changes in the large airways, including thickening of the airway wall and mucous gland enlargement and hypersecretion. These findings result from continued inhalation of dust particles, presenting a chronic burden to the mucociliary escalator. With more severe airflow obstruction or advanced pneumoconiosis, dyspnea can be noted, cough and sputum production are more frequent, and edema of the lower extremities and cor pulmonale may occur. Melanoptysis (expectoration of black sputum) has also been reported; it is due to the excavation of progressive massive fibrosis lesions.

Clubbing is not a feature of coal miners' lung diseases; if noted, it should prompt further studies. In contrast to silicosis, CWP has not been associated with an increased risk for the development of coexisting mycobacterial infection. It should be kept in mind, however, that in autopsy studies, the lungs of 12 percent of miners show classic silicotic nodules.[18] Thus, the appearance of a cavity in PMF should prompt examination of the sputum for typical and atypical mycobacteria.

RADIOLOGY AND DIAGNOSIS OF CWP

The diagnosis of CWP can be made with confidence, without histologic confirmation, in the presence of an adequate history (at least five to ten years) of coal mine dust exposure and a characteristic chest radiograph. The radiograph in simple pneumoconiosis shows small opacities, ranging in size from a pinhead up to 1 cm in diameter. Rounded nodules predominate and tend to appear first in the upper zones and invaded middle and lower zones as the number of opacities increase. Progressive massive fibrosis is characterized by one or more large opacities greater than 1 cm in diameter. An upper-lobe predominance is typical of this complicated pneumoconiosis. Lower-lobe emphysema is also commonly noted, and atelectisis and consolidation can be appreciated. High-resolution computed tomographic scanning appears to be the most sensitive radiologic technique in coal workers, since it can reveal parenchymal nodules and emphysema when standard radiographs are normal.[14]

Several schemes have been used to classify the radiographic shadows of pneumoconiosis in epidemiologic studies. Currently, the 1980 classification of the International Labour Office (ILO) is the most widely accepted.[23] When the ILO system is used, simple pneumoconiosis is divided into major categories 1, 2, and 3, according to the profusion of small opacities in the lung fields. Category 0 represents a normal radiograph. Each major category, including 0, is subdivided into 3 minor categories, providing a range of 12 categories for simple CWP. A reading of category 1/0 indicates the definite presence of opacities consistent with pneumoconiosis (see Chapter 56). Complicated CWP (PMF) is divided into categories A, B, and C, based on the size of the large opacities.

The clinician may be presented with the diagnostic dilemma of distinguishing a primary or metastatic neoplasm from an unusual presentation of progressive massive fibrosis or Caplan's syndrome. When typical large opacities of PMF occur symmetrically and bilaterally on a background of simple CWP, one can be confident that the lesions are unlikely to represent neoplastic disease. Prior radiographs from medical screening pro-

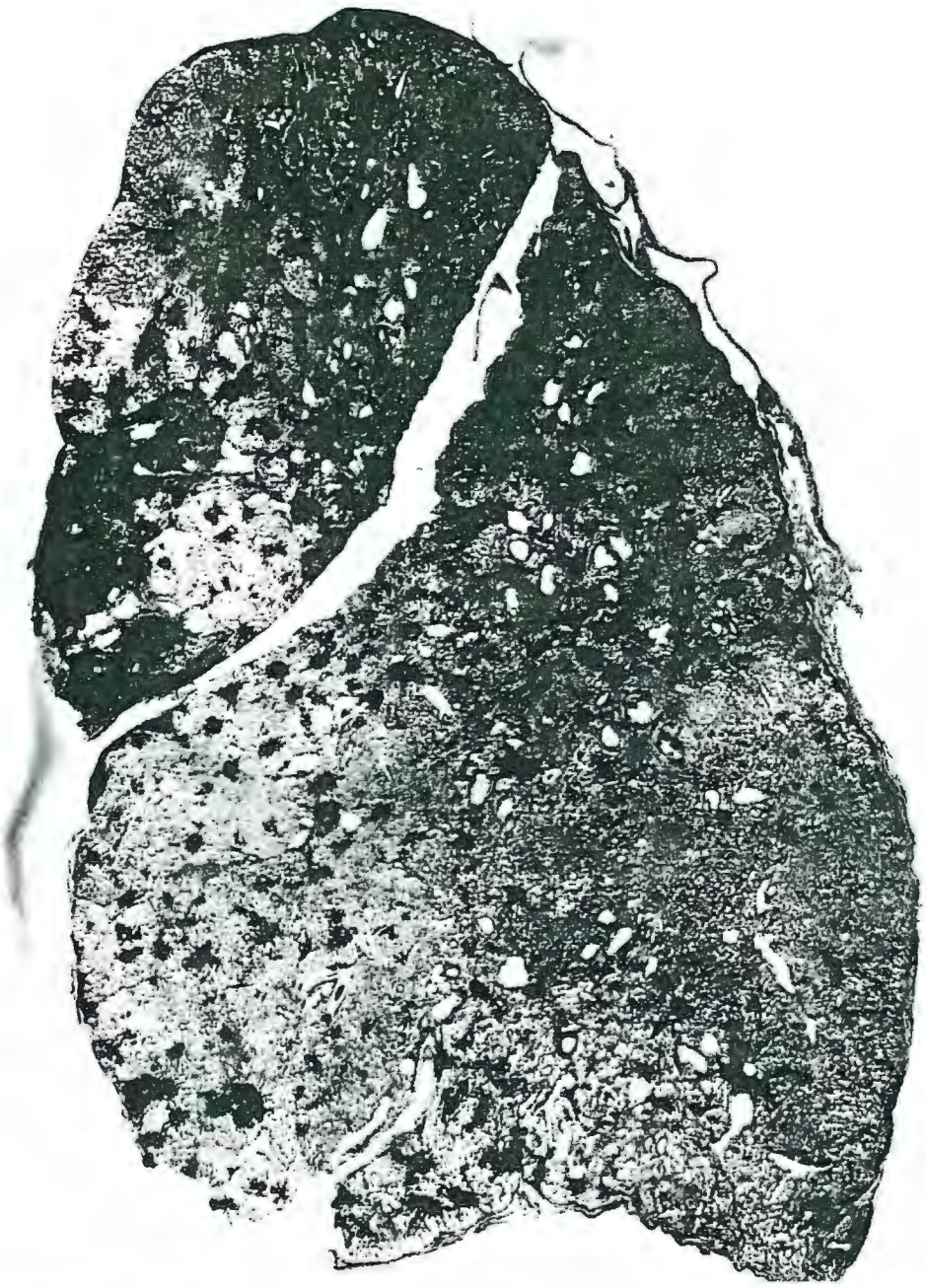

FIGURE 59-4 Simple coal workers' pneumoconiosis. sagittal section. *(Courtesy of Prof. J. Gough.)*

grams are often obtainable, and they can help confirm stability or progression over a long time. If the background of simple CWP is sparse or absent, the lesion is unilateral. or there are multiple peripherally situated nodules (Caplan's syndrome). the differentiation from a neoplasm may indeed be impossible without a biopsy.

Lung Function and Respiratory Impairment in Coal Miners

Coal mine exposures may result in several pathologic processes. including simple and complicated CWP, chronic bronchitis. emphysema, and dust-related airflow limitation. Each of these may have adverse physiological consequences. In an individual miner, the pattern and severity of impairment will be related to such recognized factors as the intensity and duration of respirable dust exposure, geologic factors (e.g., coal rank, silica content), residence time of dust in the lung, and exposure to other respiratory hazards (e.g., tobacco smoke). In miners with airway hyperresponsiveness, greater functional deficits and an increased risk of symptoms may be expected.[37] Other factors that are also hypothesized to affect the lung function of coal workers, but have not been adequately investigated, are childhood respiratory diseases, home heating fuels, and variations in the subject's immunologic, biochemical (e.g., antiprotease), and inflammatory responses to dust inhalation.

VENTILATORY FUNCTION

A variety of studies have focused on the lung function abnormalities in patients with CWP. They have characterized the abnormalities in simple and complicated CWP and investigated the natural history of these disorders. In keeping with the bronchitic and fibrotic features of PMF, prominent obstructive and restrictive abnormalities have been noted in this disorder. Similarly, the mild obstructive abnormalities seen in nonsmokers with simple CWP[20] are frequently the result of small-airway dysfunction—a finding that correlates nicely with the pathologic features of dust deposition in this disorder.[50]

The epidemiologic studies, as discussed above, have extensively documented the occurrence of exposure-related decreases in FEV_1 and FVC in coal miners. The magnitude of the average dust effect has varied between studies. Over a working lifetime, average predicted losses in FEV_1 under current U.S. dust standards ranged from 124 ml[3] to 610 ml,[40] with 6 to 8 percent of miners being expected to develop clinically significant airflow limitation.[36] Subgroups of miners may, however, experience a more severe effect. For example, a much more severe effect of dust on loss of lung function was observed in a group 199 men who had chosen to leave coal mine work.[21] The magnitude of the effects coal dust has on pulmonary function can be appreciated when they are compared to those caused by cigarette smoking. In one study evaluating the lung function of 1072 miners over an 11-year period, work at coal face jobs resulted in lung function losses essentially similar to those due to smoking. When tenure in less dusty work

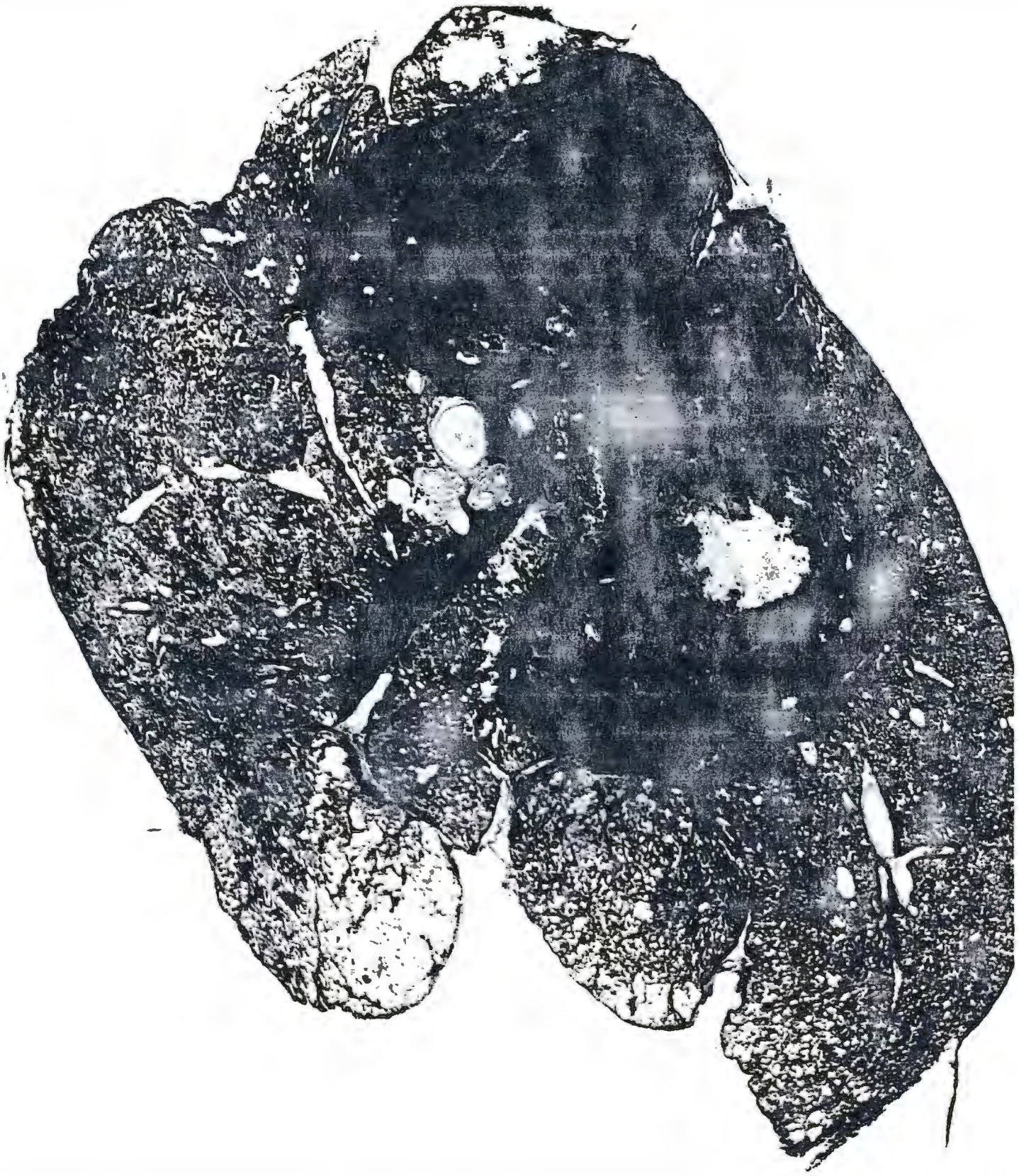

FIGURE 59-5 Complicated coal workers' pneumoconiosis or progressive massive fibrosis. Sagittal section. *(Courtesy of Prof. J. Gough.)*

was included in the analysis, mine dust exposure resulted in lung function losses about 38 percent of that attributable to smoking (average 13 cigarettes per day).[2]

GAS EXCHANGE

Diffusing capacity has been studied in relation to the radiographic changes of CWP. In general, the small rounded opacities seen in miners with simple CWP have not been associated with measurable reductions in DLCO. However, subgroups of miners do have abnormal diffusing capacities that correlate with radiographic alterations. Gas transfer is often low when the large opacities of complicated CWP are present, and it may also be reduced in miners who show either predominantly pinpoint opacities ("p" type by the ILO classification) or small irregular opacities on their chest radiographs.[12,39]

Gas exchange on exercise has also been used in studying coal miners. Many of the reports have been based on patients referred for disability evaluations, and thus suffer from ill-defined selection biases. Exposure-response relationships are also unclear with respect to findings in these series. Exertional hypoxia, pulmonary arterial hypertension, and excess ventilation have frequently been observed in miners, particularly those with complicated CWP or airflow obstruction.[27,35] However, the proportion of miners who show exertional gas exchange abnormalities in the absence of either PMF or clinically important airflow obstruction is still a topic of investigation.[17]

Caplan's Syndrome

In 1953, Anthony Caplan described an association between distinctive nodular opacities in the lungs of Welsh coal miners and rheumatoid arthritis.[9] The pulmonary nodules were 0.5 to 5 cm in diameter, bilateral, and located peripherally. They often developed rapidly (over weeks) in the presence of a mild pneumoconiosis and could cavitate or calcify. In many cases, the pulmonary opacities preceded the onset of the arthritis by months to years. In others, the pulmonary nodules and arthritis appeared coincidentally or the pulmonary lesions appeared only after the arthritis was full-blown. In its early stages, the opacities of Caplan's syndrome and progressive massive fibrosis are readily distinguishable. They are not mutually exclusive, however: Caplan's lesions and PMF lesions have been found in the same subjects. Although Caplan's syndrome was originally seen in coal miners, its definition has since been broadened to include patients with rheumatoid arthritis, similar radiographic abnormalities, and a variety of other pneumoconioses, including silicosis and asbestosis.

Immunology of CWP

The potential role of immunologic factors in the pathogenesis of mineral dust pneumoconioses was first noted with the description of Caplan's syndrome. A number of lines of evidence have provided additional support for this concept. First, a Caplan's-like syndrome has been noted in miners without arthritis but with circulating rheumatoid factor (RF), and coal workers with rheumatoid arthritis have been noted to have an increased prevalence of progressive massive fibrosis. In addition, patients with CWP have a high prevalence of autoantibodies, with RF and antinuclear antibody (ANA) evaluations being positive in 9 to 10 percent and 17 to 34 percent of patients, respectively.[28,43] It is interesting to note that the prevalence of these autoantibodies varies with the stage of CWP, with a positive ANA or RF being detected in 13 percent of patients with simple CWP and 45 percent of patients with stage C CWP.[28,43,47]

To further understand the mechanisms of injury and repair in CWP, a variety of serum parameters have been examined in patients with simple and complicated CWP and Caplan's syndrome.[19] These studies noted significantly higher serum concentrations of C3, α_1-antitrypsin, IgA, and IgG in anthracite miners than in bituminous miners with PMF. Compared to normal controls, the miners' C3, α_1-antitrypsin, IgG, and IgA values were also elevated. The significance of these findings is not clear, since the authors did not find any association between the elevated immunoglobulins and FEV_1. The IgA antibodies may play a role, however, since IgA autoantibodies against collagen and reticulin have been detected in the sera of patients with CWP.[8]

A reproducible feature of CWP is the variability in the responses manifested by different persons with similar levels of dust exposure. As a result, it has been suggested that constitutional differences contribute, in a major way, to important facets of this response, such as attack rates and rates of disease progression. To date, however, no definite associations between personal or genetic factors and CWP have been noted.

Bronchoalveolar Lavage Evaluations

The development of bronchoalveolar lavage (BAL) has provided a means for sampling lung cells and fluids in a variety of pulmonary disorders. When it is applied to the pulmonary reactions in CWP, somewhat divergent results have been noted. Early studies of symptomatic, nonsmoking coal miners with simple CWP found no significant difference between miners with CWP and controls in the number or differential of cells recovered by BAL or their release of superoxide anion or hydrogen peroxide. They did, however, note elevated levels of production of fibronectin and alveolar macrophage–derived growth factor, providing insight into potential mechanisms that could contribute to fibrogenesis in this disorder.[38] In contrast, others have noted that BAL in miners with simple and complicated CWP yields increased numbers of lung cells, alveolar macrophages, lymphocytes, and neutrophils, and alveolar cells that produce significantly more superoxide than controls.[48]

Management of Coal Workers' Lung Diseases

There is no specific therapy for CWP. Thus, management is best directed at prevention, early recognition, and treatment of complications. The primary prevention of lung disease in miners must include continuing efforts at reducing exposure to coal mine dust. The major clinical challenges are the recognition and management of airflow obstruction, respiratory infection, hypoxemia, respiratory failure, cor pulmonale, arrhythmias, and pneumothorax.

Improved mining methods and lower dust levels appear to be reducing exposure and the number of new cases of both simple and complicated pneumoconiosis. Medical surveillance programs, using chest radiographs, allow early recognition of workers with simple pneumoconiosis. Workers with simple pneumoconiosis should be encouraged to exercise transfer rights to low-dust jobs. Any worker with the unexpected finding of PMF should be carefully advised about the hazards of further dust exposures.

Workers presenting with respiratory symptoms should have a careful evaluation. The history and physical examination should be supplemented by chest radiography, spirometry with lung volume and diffusing capacity assessments, an evaluation of bronchodilator responsiveness (if the patient has airway obstruction), and resting arterial blood gas measurement as indicated. A thorough initial database allows accurate assessment of the worker's respiratory health and serves as a starting point for observing the response to therapy or progression of disease.

Symptomatic reversible airflow obstruction may benefit from treatment with inhaled and oral bronchodilators. Patients with severe obstruction and inadequate improvement from the usual measures should be considered for a monitored trial of corticosteroids. If improvement is objectively documented, continuation of inhaled and, rarely, oral steroids may be of benefit. When it is an issue, smoking cessation needs to be strongly encouraged.

Hypoxemia can be a serious complication in advanced, complicated pneumoconiosis, categories B and C. It may be present at rest, with exercise, or during sleep. Chronic hypoxemia can lead to additional complications, including polycythemia, pulmonary hypertension, cor pulmonale, and cerebral dysfunction. Therapy with low-flow oxygen is indicated when arterial oxygen tension is less than 55 mmHg. Oxygen therapy in this setting may improve exercise tolerance, reduce dyspnea, and prevent arrhythmias, polycythemia, and heart failure.

Patients with significant airflow obstruction or PMF should receive appropriate immunization with influenza and pneumococcal vaccines. Bacterial and viral episodes of bronchitis or pneumonia should be promptly recognized and appropriately treated.

Patients with complicated CWP, especially those who have been exposed to silica as well as coal mine dust, deserve special attention with regard to mycobacterial infection. Patients with a history of weight loss, fever, sweats, or malaise should be promptly investigated with chest radiographs and their sputum examined for AFB with stains and cultures. Occasionally, fiberoptic bronchoscopy with brushings and washings is required to establish the diagnosis. Active tuberculosis in patients with CWP can usually be successfully treated with the usual drug regimens, provided rifampin is one of the drugs employed.[16] In coal miners with a significant history of concurrent silica exposure (such as motormen, roof bolters, and shaft development workers), some authorities suggest that the treatment for tuberculosis should be more aggressive (see silicosis section below). Long-term follow-up is also indicated in view of several reports of recurrent pulmonary tuberculosis in patients with PMF after completion of apparently adequate therapy.[32]

Respiratory failure may complicate advanced disease in coal miners, as it does in other chronic obstructive respiratory disorders. Ventilatory support measures are indicated when the failure is precipitated by a treatable complication. The application of ventilatory support measures should be discussed with the patient before the need arises.

Clinicians may need to assess the contribution of coal dust exposure to the ventilatory impairments of their patients. Factors that can assist in this evaluation include a careful work history, with documentation of the mining region, duration and categories of coal mine employment, as well as the duration and intensity of any tobacco smoking. Factors associated with an increased risk of a clinically significant dust effect are a history of prolonged exposures in dusty jobs, exposures to higher-rank coals, a younger age at first employment, and the finding of radiographic changes of CWP.

SILICOSIS

Introduction and High-Risk Occupations

Silicosis is a fibrotic disease of the lungs caused by the inhalation, retention, and pulmonary reaction to crystalline silica. Despite knowledge of the cause of this disorder—respiratory exposures to silica-containing dusts—this serious and potentially fatal occupational lung disease remains prevalent throughout the world. Silica, or silicon dioxide, is the predominant component of the earth's crust. It is particularly important in sandstone, granite, and slate, as it makes up 20 to 100 percent of these rock formations. When the earth's crust is disturbed or silica-containing rock is used or processed, there are potential respiratory risks for workers. Occupational exposure to silica particles of respirable size (aerodynamic diameter of 0.5 to 5 μ) is associated with mining, quarrying, drilling, tunneling, and abrasive blasting with quartz-containing materials (sandblasting). Silica exposure also poses a hazard to stonecutters (Fig. 59-6) and pottery, foundry, ground silica, and refractory workers. The silicon dioxide that is inhaled is usually crystalline and most often quartz. Cristobalite and tridymite are other crystalline forms of silica. These three crystalline forms are also called "free silica" to distinguish them from silicates, such as asbestos and talc.

The development and progression of silicosis frequently occur after exposure has ceased. Because of this latency, the true prevalence of the disease is unknown. However, crystalline silica exposure is so widespread, and silica sand is such an inexpensive and versatile component of so many manufacturing processes, that millions of workers throughout the world are at risk of the disease. This is reflected in the fatal cases of silicosis, multiple cases of silicosis from the same work site, and epidemics of silicosis that continue to be recognized, even in developed countries.[6,10,46]

Forms of Silicosis

EXPOSURE HISTORY AND CLINICOPATHOLOGIC DESCRIPTIONS

Chronic, accelerated, and acute forms of silicosis have been well characterized. These clinical and pathologic expressions of the disease reflect differing exposure intensities, latency periods, and natural histories. The chronic or classic form usually follows one or more decades of exposure to respirable dust containing quartz. The accelerated form results from heavier exposures, often with a du-

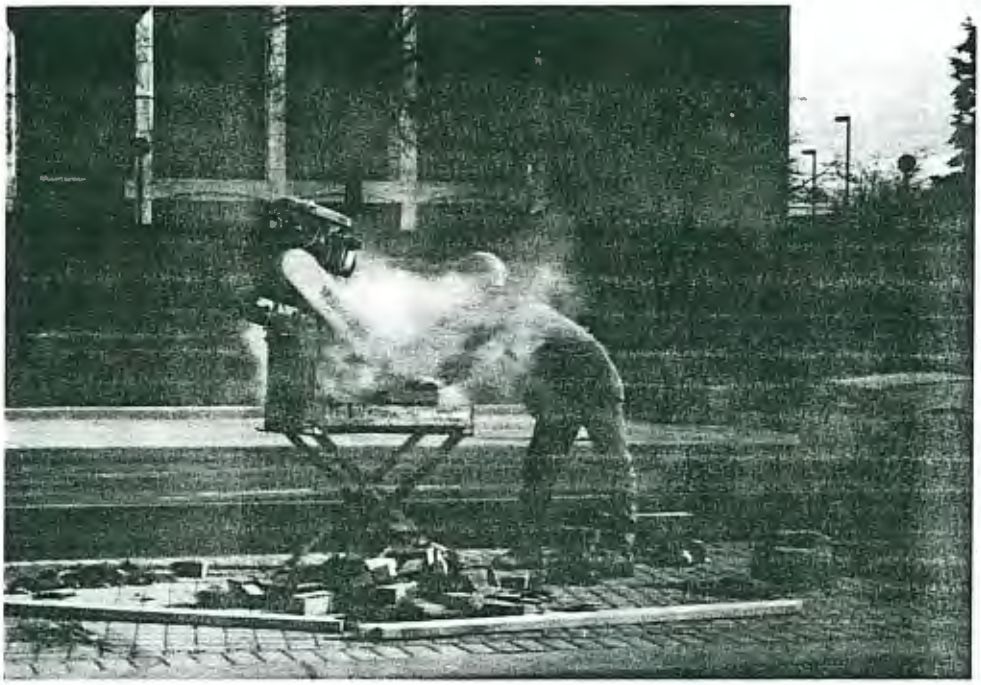

FIGURE 59-6 Masonary cutting. Note the potential for respiratory exposure to excessive silica-containing dusts. *(Courtesy of Kenneth Linch, National Institute for Occupational Safety and Health, Morgantown, WV.)*

ration of 5 to 10 years. Accelerated silicosis develops more rapidly than the chronic form and in general progresses inexorably even after silica exposure is interrupted. The acute form of silicosis is a consequence of intense exposures to high levels of respirable dust that contain a significant proportion of silica. The reported exposure period is usually from several months up to about 5 years, and the clinical course is usually one of rapid progression.

Chronic (or Classic) Silicosis Chronic silicosis may be asymptomatic or result in insidiously progressive exertional dyspnea or cough. A latency of 15 years or more since onset of exposure is common. Radiographically, it presents with small (less than 10 mm) rounded opacities, predominantly in the upper lung zones (Fig. 59-7). The pathologic hallmark in the lungs of patients with the chronic form is the silicotic nodule (Fig. 59-8). The lesion is characterized by a cell-free central area of concentrically arranged whorled, hyalinized collagen fibers, surrounded by cellular connective tissue with reticulin fibers. When it is examined under polarized light, birefringent particles are typically seen most prominently in the periphery of the silicotic nodule. Electron microscopy utilizing specialized techniques can help to identify the specific mineral content of the nodules, but it is rarely needed for routine diagnostic purposes. Silicotic nodules in the visceral pleura, in regional lymph nodes, and occasionally in other organs may also result from silica exposure.

Progressive Massive Fibrosis Progressive massive fibrosis (PMF) or conglomerate silicosis occurs when one or more groups of the small nodules in the lungs of a patient with chronic silicosis coalesce to form larger (over 10 mm) shadows on the chest radiograph (Fig. 59-9). The chest radiograph often contains multiple nodules that are bilateral, located in upper lung zones, and associated with basilar emphysema. This progressive illness may occur even after exposure to silica-containing dust has ceased. The result is a clinically significant compromise of lung structure and function and, as a consequence, symptoms of exertional dyspnea and reduced functional status. Common laboratory findings include a diminished carbon monoxide–diffusing capacity, reduced arterial oxygen tension at rest or with exercise, and a demonstrable restrictive pattern on pulmonary function evaluation. Concomitant dust-induced bronchitis or distortion of the bronchial tree may also result in productive cough or airflow obstruction. Recurrent bacterial infections, not unlike those seen in bronchiectasis, may occur. Weight loss and cavitation of the large opacities should prompt concern for tuberculosis or other mycobacterial infections. Pneumothorax may be a life-threatening complication, since the fibrotic lung may be difficult to reexpand. Hypoxemic respiratory failure with cor pulmonale and congestive heart failure can be terminal findings.

Accelerated Silicosis Accelerated silicosis results from exposures that are more intense and of shorter (5 to 10 years) dura-

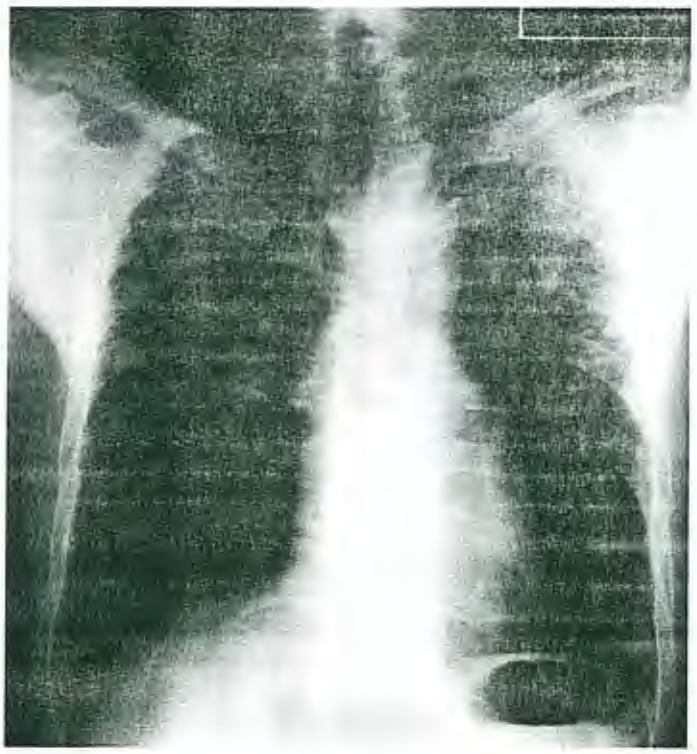

FIGURE 59-7 Chronic silicosis, ILO profusion category 2/3 with typical "r" size rounded opacities.

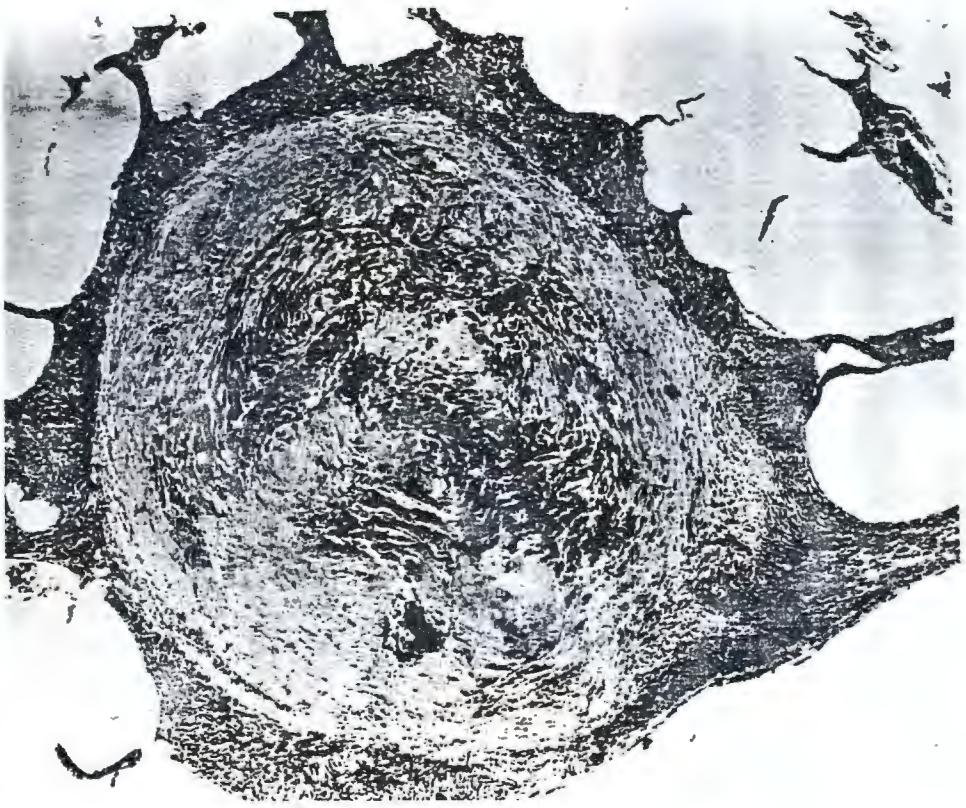

FIGURE 59-8 A silicotic nodule, microscopic section. *(Courtesy of Dr. Val Vallyathan, National Institute for Occupational Safety and Health, Morgantown, WV.)*

tion than in the chronic form. The symptoms, radiographic findings, physiological measurements, and lung pathology of chronic and accelerated silicosis are quite similar. However, rate of disease progression is more rapid for accelerated silicosis, and workers with accelerated disease may develop superimposed mycobacterial infection. Findings consistent with autoimmune diseases such as scleroderma are also more frequent in the accelerated form of silicosis. When these autoimmune findings are present, the progression of radiographic abnormalities and functional impairment can be quite striking.

Acute Silicosis Acute silicosis develops within a few months up to about 5 years after a massive inhalation of silica.[6] Dramatic dyspnea, weakness, and weight loss are often presenting symptoms. The radiographic findings differ from those in the more chronic forms of silicosis, and are dominated by a diffuse alveolar filling pattern with a lower lung zone predominance (Fig. 59-10). Air bronchograms may be present. Histologic findings similar to those of pulmonary alveolar proteinosis have been described, and extrapulmonary (renal and hepatic) abnormalities are occasionally reported. The usual clinical course of this rare form of silicosis is rapid progression to severe hypoxemic ventilatory failure and death.

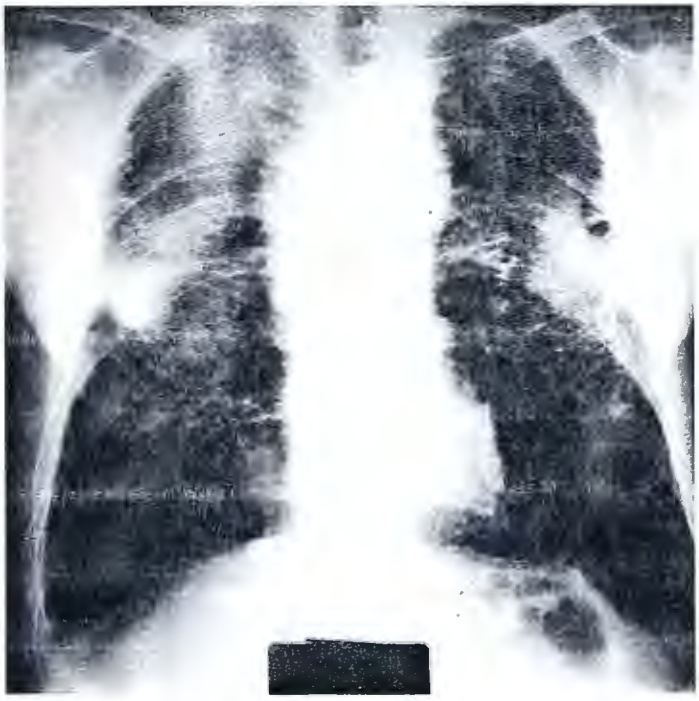

FIGURE 59-9 Complicated silicosis demonstrating progressive massive fibrosis.

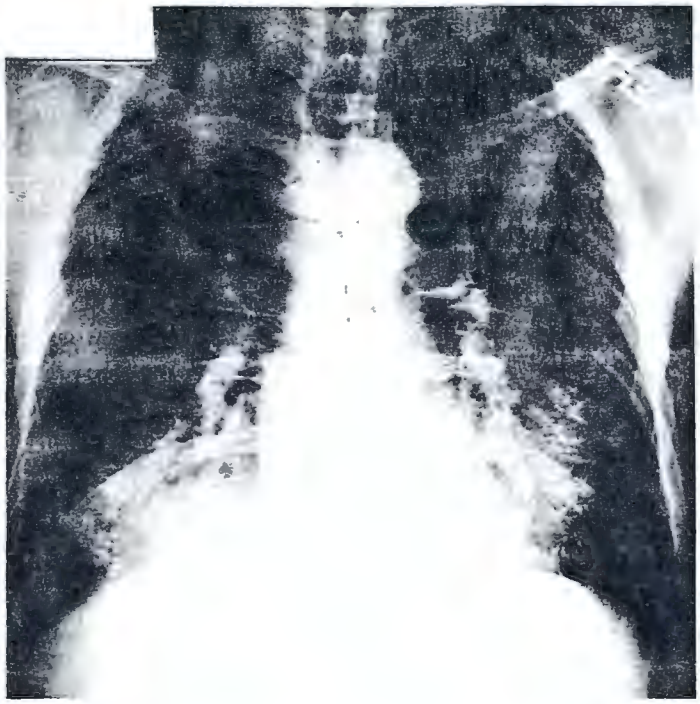

FIGURE 59-10 Acute silicosis, silicoproteinosis pattern, in a surface coal miner. *(Courtesy of Drs. Daniel E. Banks and N. LeRoy Lapp, University of West Virginia, Morgantown, WV.)*

Other Disorders Even in the absence of radiographic silicosis, silica-exposed workers may develop chronic bronchitis and emphysema from their occupational dust exposure. Progressive declines in lung function have also been documented in workers exposed to silica and other occupational mineral dusts.

Pathogenesis

The precise pathogenesis of silicosis is uncertain. An abundance of evidence, however, suggests that interactions between pulmonary alveolar macrophages and silica particles play a major role in the pathogenesis of this disorder. Surface properties of the silica particle appear to promote macrophage activation. These cells then release chemotactic factors and inflammatory mediators that elicit cellular responses by polymorphonuclear leukocytes, lymphocytes, and additional macrophages. Fibroblast-stimulating factors are also released; they promote hyalinization and collagen deposition. The resulting pathologic lesion is the hyaline nodule, which contains a central acellular zone, with free silica surrounded by whorls of collagen and fibroblasts, and an active peripheral zone composed of macrophages, fibroblasts, plasma cells, and additional free silica.[15]

The precise properties of the silica particles that evoke the pulmonary response described above are not known. The nature and the extent of the biologic response are, in general, related to the intensity of the exposure. The surface characteristics of the dust also appear to be important. For example, there is growing evidence that freshly fractured silica may be more toxic than aged silica-containing dusts, perhaps because of reactive radical groups on the cleavage planes of the freshly fractured moiety.[45] This may offer a pathogenic explanation for the more frequent observation of cases of advanced disease in both sandblasters and rock drillers, in whom exposures to recently fractured silica are particularly intense.

The initiating toxic insult in silicosis may occur with minimal immunologic reaction. However, a sustained immunologic response to the insult may be important in the generation of some of the chronic manifestations of the disease. For example, the antinuclear antibodies that are noted in the accelerated form of silicosis associated with scleroderma and other collagen vascular disorders may contribute to the pathogenesis of this syndrome. Indeed progressive systemic sclerosis and other autoimmune phenomena have been noted in patients with silicosis.[44]

Association with Tuberculosis

The propensity for people with silicosis to get tuberculosis has been recognized for nearly a century.[42] Tuberculosis can complicate all forms of silicosis. Patients with the acute and accelerated forms of the disease appear to be at the highest risk of infection. Silica exposure alone, even without silicosis, may predispose to this infection. *Mycobacterium tuberculosis* is the usual organism, but atypical mycobacteria (and, less often, *Nocardia asteroides*) can also be seen. The mechanism of this susceptibility is poorly understood. It may, however, be related to the toxic effects of silica on alveolar macrophages.

Clinical Manifestations of Silicosis

Patients with silicosis can be asymptomatic and present with abnormal chest radiographs. They can also be minimally symptomatic in spite of advanced radiographic abnormalities. When silicosis is symptomatic, the primary symptom is usually dyspnea. It is first noted with activity or exercise and later, as the pulmonary reserve of the lung is lost, also reported at rest. The appearance or progression of dyspnea may herald the development of complications, including tuberculosis, airway obstruction, or PMF. Productive cough is often present, secondary to chronic bronchitis from occupational dust exposure, tobacco use, or both. Cough may, at times, also be attributed to pressure from large masses of silicotic lymph nodes on the trachea or main-stem bronchi.

Other chest symptoms are less common than dyspnea and cough. Hemoptysis is rare and should raise concern for complicating disorders, such as pulmonary neoplasms or mycobacterial infection. Wheeze and chest tightness may occur in the presence of silicosis, but they occur more commonly as part of associated obstructive airway disease or bronchitis. Chest pain and finger clubbing are not features of silicosis. Systemic symptoms, such as fever and weight loss, suggest complicating infection or neoplastic disease. Advanced forms of silicosis are associated with progressive respiratory failure with or without cor pulmonale. Few physical signs may be noted unless complications are present.

Radiographic Patterns in Silicosis

The earliest radiographic signs of uncomplicated silicosis are generally small rounded opacities. These can be categorized using the ILO International Classification of Radiographs of Pneumoconioses by size, shape, and profusion category.[23] In silicosis, rounded opacities of the "q" and "r" type dominate (Fig. 59-7). Other patterns have also been described, including linear or irregular shadows. The opacities seen on the radiograph represent the summation of pathologic silicotic nodules. They are usually found to predominate initially in the upper lung zones and may progress to invade other zones. Hilar lymphadenopathy is also noted, sometimes in advance of nodular parenchymal shadows. Eggshell calcification of the lymph nodes is strongly suggestive of silicosis, although this feature is seldom seen (Fig. 59-11).

PMF is characterized by the formation of large opacities. These are generally categorized by size, using the ILO classification, as category A, B, or C. The large fibrotic lesions of PMF tend to contract to the upper lung zones, leaving areas of compensatory emphysema at their margins and in the lung bases (Fig. 59-9). As a result of this process, small rounded opacities that previously were evident on the radiograph may become less visible or at times disappear. Pleural abnormalities are not a frequent radiographic feature with silicosis but do occur, particularly in association with conglomerate lesions. Large opacities also frequently pose a concern regarding neoplasm. The radiographic distinction between PMF lesions and lung malignancies may be difficult, particularly if previous chest films are unavailable for comparison. Although ischemic necrosis may occur

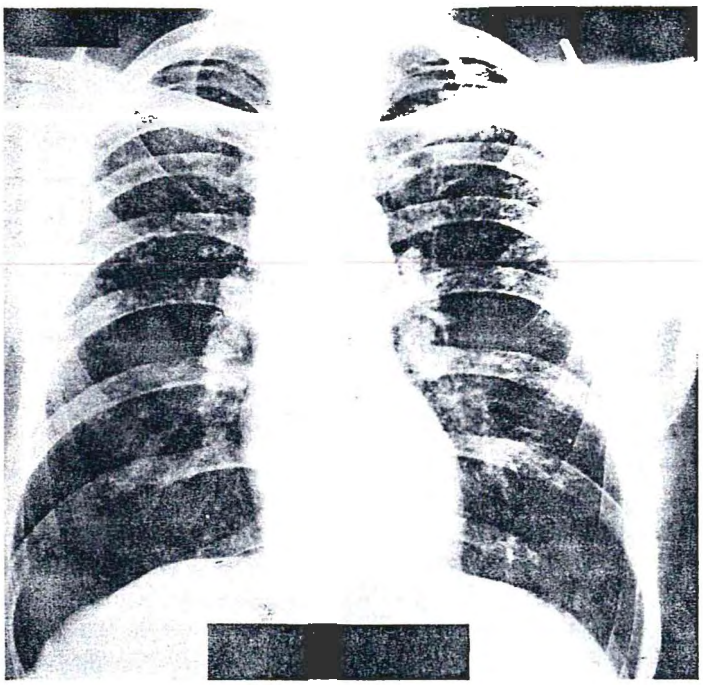

FIGURE 59-11 Eggshell calcification of hilar lymph nodes in silicosis.

in large silicotic lesions, the onset of cavitation or a rapid change in the radiographic appearance should prompt a search for active mycobacterial disease. Acute silicosis may present with a radiologic alveolar filling pattern (Fig. 59-10) and progress rapidly to PMF or complicated mass lesions.

Lung Function Abnormalities in Silicosis

Pulmonary function tests, such as spirometry and diffusing capacity, are helpful for the clinical evaluation of people with suspected silicosis. Spirometry may also be of value in the early recognition of the health effects from occupational dust exposures, as it can detect physiological abnormalities that may precede radiographic changes. No specific or characteristic pattern of ventilatory impairment is present in silicosis. Spirometry may be normal; when it is abnormal, the tracings may show obstruction, restriction, or a mixed pattern. Obstruction may indeed be the more common finding. Silica and mixed dust exposures[7] may lead to clinically significant airflow limitation independent of radiographic abnormality.[36]

In general, workers experience lung function loss proportionate to the duration and intensity of silica dust exposure. In addition, functional changes tend to be more marked with advanced radiologic categories. However, no good correlation exists between radiographic abnormalities and ventilatory impairment. Diffusing impairment may also occur in the absence of ventilatory impairment. In acute and accelerated silicosis, functional changes generally occur earlier, are more marked, and progress more rapidly than in the chronic form of the disease. In acute silicosis, radiographic progression is accompanied by increasing ventilatory impairment and gas exchange abnormalities, which lead to respiratory failure and eventually to death from intractable hypoxemia.

Complications and Special Diagnostic Issues in Silicosis

With a history of exposure and a characteristic radiograph, the diagnosis of silicosis is generally not difficult to establish. Challenges arise only when the radiologic features are unusual or the history of exposure is not recognized. Lung biopsy is rarely required to establish the diagnosis. However, tissue samples are helpful in some clinical settings when complications are present or the differential diagnosis includes tuberculosis, neoplasm, or PMF. Biopsy material should be sent for culture, and in research settings, dust analysis may be a useful additional measure. When tissue is required, open or thoracoscopic lung biopsies are generally necessary for adequate material for examination.

Vigilance for infectious complications, especially tuberculosis and other mycobacteria, cannot be overemphasized. New onset or a change in cough, hemoptysis, fever, or weight loss should trigger a workup to exclude this treatable problem. Nocardial and fungal infections are also reported in association with acute silicosis.

Lung Cancer and Silicosis

Substantial concern and interest about the relationship between silica exposure, silicosis, and cancer of the lung continue to stimulate debate. The International Agency for Research on Cancer[22] has classified crystalline silica as a 2A carcinogen on the basis of "sufficient" evidence of carcinogenicity in experimental animals and "limited" evidence of carcinogenicity in humans. Uncertainty over the pathogenic mechanisms for the development of lung cancer in silica-exposed populations exists, and the possible relationship between silicosis (or lung fibrosis) and cancer in exposed workers continues to be studied.

Prevention of Silicosis

Prevention remains the principal goal in dealing with this occupational lung disease. Exposures can be reduced through the use of improved ventilation and local exhaust, process enclosure, wet abrasive techniques, personal protection (including the proper selection of respirators), and, when possible, substitution of industrial agents less hazardous than silica. The education of workers and employers regarding the hazards of silica dust exposure and measures to control exposure are also important.

If silicosis is recognized in a worker, termination of exposure is advisable. Unfortunately, the disease can progress even without further silica exposure. Additionally, the finding of a case of silicosis, especially in the acute or accelerated form, should prompt a thorough evaluation of workplace exposures and industrial hygiene measures, with the goal of recognizing the hazardous operation and protecting other workers who may be at risk.

Medical Screening and Surveillance in Silicosis

Workers exposed to silica and other mineral dusts should undergo periodic screening for adverse health effects as a supplement to, but not a substitute for, dust exposure control. Such

screening commonly includes evaluations for respiratory symptoms, spirometric abnormalities, radiographic changes, and neoplastic disease. Evaluation for tuberculosis infection with intradermal skin testing should also be performed. In addition to the reporting of results to the individual workers, screening health data from all workers in a plant or operation should be periodically assembled and evaluated for surveillance and prevention activities.

Therapy, Management of Complications, and Control of Silicosis

Over the years, a variety of treatments for silicosis have been attempted. However, aerosolized aluminum did not prove successful in the treatment of the disorder, and polyvinyl pyridine-*N*-oxide, a polymer that has protective effects in experimental animals, is not available for use in humans. In addition, tetranidine, an agent that diminishes fibrosis in silica-exposed animals, has not been shown to be effective in humans and is highly teratogenic. As a result of this unsuccessful search, therapy for silicosis is directed largely at complications of the disease. Therapeutic measures are similar to those commonly used in the management of airflow obstruction, infection, pneumothorax, hypoxemia, and respiratory failure complicating other pulmonary disorders. For workers with a diagnosis of silicosis, further exposure to silica-containing dusts is undesirable. If the disease is advanced, or has occurred after a relatively short exposure (less than 15 years), further dust exposure should be assiduously avoided. Advice on job reassignment should be considered in the context of the worker's age, symptoms, and functional status and the current working conditions and measured silica exposures.

In the medical management of silicosis, vigilance for complicating infection, especially tuberculosis, is critical. This entails yearly chest radiographs and PPD evaluations. The use of prophylactic isoniazid for tuberculin-positive silicotic subjects is recommended. The use of bacillus Calmette-Guérin in the tuberculin-negative silicotic patient is not recommended.

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 with infection may be subtle and atypical. Enlargement and cavitation in conglomerate lesions or nodular opacities are of particular concern. Bacteriologic studies on expectorated sputum may not always be reliable in silicotuberculosis. Fiberoptic bronchoscopy for additional specimens for culture and study may be helpful in establishing a diagnosis of active disease. The use of multidrug therapy for suspected active disease in patients with silicosis is justified at a lower level of suspicion than in the nonsilicotic subject, owing to the difficulty in firmly establishing evidence for active infection. To obtain satisfactory results in the presence of silicosis, antituberculous treatment must be more prolonged, with regimens lasting at least 8 months.

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

Acute silicosis may rapidly progress to respiratory failure. When this disease resembles pulmonary alveolar proteinosis and severe hypoxemia is present, aggressive therapy has included massive 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 has not been established.[49] Glucocorticoid therapy has also been used for acute silicosis. However, it is still of unproven benefit.

The rare young patient with end-stage silicosis may be considered candidates for lung or heart-lung transplantation in centers experienced with this expensive and high-risk procedure. Early referral and evaluation for this intervention may be offered to selected subjects.

The discussion above underscores the serious and potentially fatal nature of silicosis. The lack of a specific therapy for silicosis further emphasizes the crucial role of primary prevention in our therapeutic approach to this disorder. The control of silicosis ultimately depends on the control of workplace dust exposures. This is accomplished by rigorous and conscientious application of fundamental occupational hygiene and engineering principles, with a commitment to the preservation of worker health.

REFERENCES

1. Amandus HE, Petersen MR, Richards TB: Health status of anthracite surface coal miners. *Arch Environ Health* 44:75–81, 1989.
2. Attfield MD: Longitudinal decline in FEV_1 in United States coalminers. *Thorax* 40:132–137, 1985.
3. Attfield MD, Hodous TK: Pulmonary function of U.S. coal miners related to dust exposure estimates. *Am Rev Respir Dis* 145:605–609, 1992.
4. Attfield MD, Hodous TK: Does regression analysis of lung function data obtained from occupational epidemiologic studies lead to misleading inferences regarding the true effect of smoking? *Am J Ind Med* 27:281–291, 1995.
5. Attfield MD, Seixas NS: Prevalence of pneumoconiosis and its relationship to dust exposure in a cohort of U.S. bituminous coal miners and ex-miners. *Am J Ind Med* 27:137–151, 1995.
6. Banks DE, Bauer MA, Castellan RM, Lapp NL: Silicosis in surface coalmine drillers. *Thorax* 38:275–278, 1983.
7. Becklake MR: Chronic airflow limitation: Its relationship to work in dusty occupations. *Chest* 88:608–617, 1985.
8. Burrell R: Immunological aspects of coal workers' pneumoconiosis. *Ann NY Acad Sci* 200:94–105, 1972.
9. Caplan A: Certain unusual radiological appearances in the chest of coal miners suffering from rheumatoid arthritis. *Thorax* 8:29–37, 1953.
10. CDC: Silicosis: Cluster in sandblasters—Texas, and Occupational Surveillance for Silicosis. *MMWR* 39:433–437, 1990.
11. CDC/NIOSH: *Criteria for a Recommended Standard, Occupational Exposure to Respirable Coal Mine Dust.* DHHS (NIOSH) Publication No. 95-106, September 1995.
12. Cockcroft A, Berry G, Cotes JE, Lyons JP: Shape of small opacities and lung function in coalworkers. *Thorax* 37:765–769, 1982.
13. Coggon D, Inskip H, Winter P, Pannett B: Contrasting geographical distribution of mortality from pneumoconiosis and chronic bronchitis and emphysema in British coal miners. *Occup Envir Med* 52:554–555, 1995.

14. Collins LC, Willing S, Bretz R, et al: High-resolution CT in simple coal workers' pneumoconiosis: Lack of correlation with pulmonary function tests and arterial blood gas values. *Chest* 104:1156–1162, 1993.
15. Craighead JE, Kleinerman J, Abraham JL, et al: Diseases associated with exposure to silica and nonfibrous silicate minerals: Silicosis and Silicate Disease Committee. *Arch Pathol Lab Med* 112:673–720, 1988.
16. Dubois P, Gyselen A, Prignot J: Rifampicin-combined chemotherapy in coal worker's pneumoconio-tuberculosis. *Am Rev Respir Dis* 115:221–228, 1977.
17. Fields CL, Roy TM, Dow FT, Anderson WH: Impact of arterial blood gas analysis in disability evaluation of the bituminous coal miner with simple pneumoconiosis. *J Occup Med* 34:410–413, 1992.
18. Green FHY, Althouse R, Weber KC: Prevalence of silicosis at death in underground coal miners. *Am J Ind Med* 16:605–615, 1989.
19. Hahon N, Morgan WKC, Petersen M: Serum immunoglobulin levels in coal workers' pneumoconiosis. *Ann Occup Hyg* 23:165–174, 1980.
20. Hall DR, Lapp NL, Reger R, Seaton A: Small airways disease in coal miners: A longitudinal study. *Bull Physiopathol Respir (Nancy)* 11:863–877, 1975.
21. Hurley JF, Soutar CA: Can exposure to coal mine dust cause a severe impairment of lung function? *Br J Ind Med* 43:150–157, 1986.
22. International Agency for Research on Cancer: IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans: *Silica and Some Silicates,* vol 42. Lyon, France, World Health Organization, International Agency for Research on Cancer, pp 49, 51, 73–111, 1987.
23. International Labour Office: *Guidelines for the Use of ILO International Classification of Radiographs of Pneumoconiosis,* revised ed. Geneva, International Labour Office, 1980.
24. Jacobsen M, Rae S, Walton WH, Rogan JM: The relation between pneumoconiosis and dust-exposure in British coal mines, in Walton WH (ed), *Inhaled Particles,* vol III. Woking, Surrey, Unwin Brothers, 1971, pp 903–917.
25. Kleinerman J, Green F, Lacquer W, et al: Pathology standards for coal workers' pneumoconiosis. *Arch Path Lab Med* 103:374–432, 1979.
26. Kuempel ED, Stayner LT, Attfield MD, Buncher CR: Exposure-response analysis of mortality among coal miners in the United States. *Am J Ind Med* 28:167–184, 1995.
27. Lapp NL, Seaton A, Kaplan KC, et al: Pulmonary hemodynamics in symptomatic coal miners. *Am Rev Respir Dis* 104:418–426, 1971.
28. Lippmann M, Eckert HL, Hahon N, Morgan WKC: Circulating antinuclear and rheumatoid factors in United States coal miners. *Ann Intern Med* 79:807–811, 1973.
29. Marine WM, Gurr D, Jacobsen M: Clinically important respiratory effects of dust exposure and smoking in British coal miners. *Am Rev Respir Dis* 137:106–112, 1988.
30. McLintock JS, Rae S, Jacobsen M: The attack rate of progressive massive fibrosis in British coal miners, in Walton WH (ed), *Inhaled Particles,* vol III. Woking, Surrey, Unwin Brothers, 1971, pp 933–950.
31. Miller BG, Jacobsen M: Dust exposure, pneumoconiosis, and mortality of coalminers. *Br J Ind Med* 42:723–733, 1985.
32. Morgan EJ: Silicosis and tuberculosis. *Chest* 75:202–203, 1979.
33. Morgan W, Handelsman L, Kibelstis J, et al: Ventilatory capacity and lung volumes of U.S. coal miners. *Arch Environ Health* 28:182–189, 1974.
34. Morgan WKC, Burgess DB, Jacobsen G, et al: The prevalence of coal workers' pneumoconiosis in U.S. coal miners. *Arch Environ Health* 27:221–226, 1973.
35. Nemery B, Veriter C, Brasseur L, Frans A: Impairment of ventilatory function and pulmonary gas exchange in non-smoking coalminers. *Lancet* 2:1427–1430, 1987.
36. Oxman AD, Muir DC, Shannon HS, et al: Occupational dust exposure and chronic obstructive pulmonary disease. A systematic overview of the evidence (see comments). *Am Rev Respir Dis* 148:38–48, 1993.
37. Petsonk EL, Daniloff EM, Mannino DM, et al: Airway responsiveness and job selection: A study in coal miners and non-mining controls. *Occup Environ Med* 52:745–749, 1995.
38. Rom WN, Bitterman PB, Rennard SI, et al: Characterization of the lower respiratory tract inflammation of nonsmoking individuals with interstitial lung disease associated with chronic inhalation of inorganic dust. *Am Rev Respir Dis* 136:1429–1434, 1987.
39. Seaton A, Lapp NL, Morgan WK: Relationship of pulmonary impairment in simple coal workers' pneumoconiosis to type of radiographic opacity. *Br J Ind Med* 29:50–55, 1972.
40. Seixas NS, Robins TG, Attfield MD, Moulton LH: Exposure-response relationships for coal mine dust and obstructive lung disease following enactment of the Federal Coal Mine Health and Safety Act of 1969. *Am J Ind Med* 21:715–734, 1992.
41. Seixas NS, Robins TG, Attfield MD, Moulton LH: Longitudinal and cross sectional analyses of exposure to coal mine dust and pulmonary function in new miners. *Br J Ind Med* 50:929–937, 1993.
42. Snider DE: The relationship between tuberculosis and silicosis. *Am Rev Respir Dis* 118:455–460, 1978.
43. Soutar CA, Turner-Warwick M, Parkes WR: Circulating antinuclear antibody and rheumatoid factor in coal pneumoconiosis. *Br Med J* 3:145–147, 1974.
44. Steenland K, Goldsmith DF: Silica exposure and auto-immune diseases. *Am J Ind Med* 28:603–608, 1995.
45. Vallyathan V, Shi X, Dalal NS, et al: Generation of free radicals from freshly fractured silica dust. *Am Rev Respir Dis* 138:1213–1219, 1988.
46. Wagner GR: The inexcusable persistence of silicosis (editorial). *Am J Public Health* 85:1346–1347, 1995.
47. Wagner JC, McCormick JN: Immunological investigations of coalworkers' disease. *J R Coll Physicians Lond* 2:49–56, 1967.
48. Wallaert B, Lassalle P, Fortin F, et al: Superoxide anion generation by alveolar inflammatory cells in simple pneumoconiosis and in progressive massive fibrosis of non-smoking coal workers. *Am Rev Respir Dis* 141:129–133, 1990.
49. Wilt JL, Banks DE, Weissman DN, et al: Reduction of lung dust burden in pneumoconiosis by whole lung lavage. *J Occup Environ Med* 38:619–624, 1996.
50. Wright JL, Cagle P, Churg A, et al: State of the art: Diseases of the small airways. *Am Rev Respir Dis* 146:240–262, 1992.