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# 34

# The Pneumoconioses: Coal Worker's Pneumoconiosis

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Historical accounts of carbonaceous pigment in the lungs date back to 1813, when Pearson noted that, with age, black pigment collects in the lungs.[1] Using simple analytical techniques, he concluded that the pigment was carbonaceous and had come from the atmosphere by inhalation. Gregory, in 1831, first reported the association between coal mining and black lungs.[2] In 1838, Stratton introduced the term anthracotic, which is now used to describe coal and other black pigments of which carbon is a major constituent.[3]

Investigations of coal worker's pneumoconiosis (CWP) in the modern era started in 1928, when Collis and Gilchrist made observations on the effects of coal dust on the lungs of coal trimmers.[4] They reviewed the death certificates of these workers and discovered that bronchitis often contributed to death. A review of x-ray films revealed that the trimmers had radiographic findings in their lungs that resembled silicosis.

Public concern about lung disease in coal workers first received public notice in 1932, when the governor of Pennsylvania asked the United States Public Health Service to investigate the "nature and prevalence of chronic incapacitating miners 'asthma.'"[5] Four years later, a study of 2711 working anthracite miners disclosed that 23% of them had evidence of a pneumoconiosis.[5]

## *ANTHRACOTIC PARTICLES*

Anthracotic pigment in the lungs is derived from many sources; the most frequent are combusted fossil fuels, incinerators, and coal mine dust. The carbon from all of these sources is in an amorphous, nonfibrogenic form.[6] Unfortunately, this otherwise innocuous carbon is often accompanied by other organic compounds, gases, metals, and minerals, some of which are toxic.

The size of the carbon particles usually determines the distance they travel into the respiratory tract. Most particles less than 0.1 μm in diameter remain suspended in the air after they enter the respiratory tract and therefore do not have to be removed by the defense mechanisms of the lungs. Those that are more than 10 μm in diameter are usually filtered and trapped in the mucus of the nasal passages, which leads to their being swallowed or expectorated.

Particles between 2 and 10 μm in diameter land on the lining of the trachea and airways proximal to the respiratory bronchioles, where they are picked up by the mucociliary escalator, promptly moved to the pharynx, and then swallowed or expectorated. A few 2- to 10-μm particles penetrate the bronchial and bronchiolar epithelium, which promptly leads to the appearance of acute inflammatory cells in the mucosa.[7] This inflammatory reaction is presumably a manifestation of the processes that eventually lead to chronic bronchitis and bronchiolitis in coal miners.

Particles less than 2.0 μm in diameter are responsible for most of the lung damage in the carbonaceous pneumoconioses. The handling of these small particles is complex. They initially deposit on the walls of the respiratory bronchioles and alveoli, where they are engulfed by macrophages (Fig. 34-1). Alveolar clearance begins within minutes.[8] When large numbers of particles are present, many macrophages are drawn into the alveoli, where they pick up a load of the particles and then move on to the mucociliary escalator or to lymphatic channels.

Even large particle loads do not interfere with the motility of the macrophages.[8] Toxic particles are the least dangerous when they quickly reach the mucociliary escalator and are thereby removed from the alveoli and vulnerable respiratory bronchioles. The consistent absence of bacteria from the lower airways in healthy individuals is witness to the efficiency of this macrophage and mucociliary clearance mechanism.

The path the macrophages take to the mucociliary escalator is assumed to be by way of a layer of fluid lining the alveoli, but routes outside of the alveoli may also be used. The vigor and coordination of the cilia that move the mucus in the mucociliary escalator, the viscosity of the mucus, the duration and size of

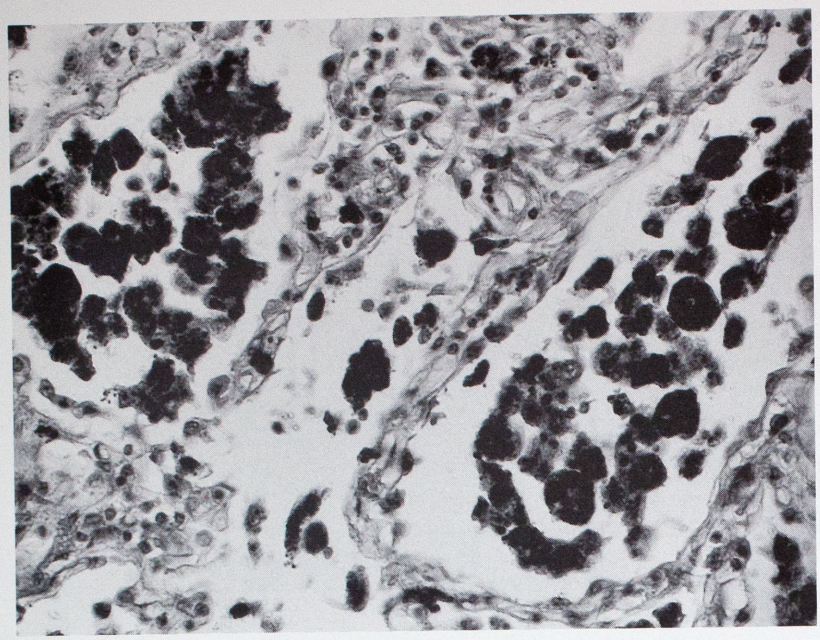

**FIGURE 34-1.** Coal mine dust particles are present within alveolar macrophages in this patient. The individual particles range in size from about 0.4 to 0.9 μm. (H & E stain; intermediate magnification.)

particle loads, and the time intervals between particle loads influence the amount or pigment that is retained in the alveoli or in nearby sites for prolonged periods of time.

Some of the macrophages that engulf small carbonaceous particles transport the particles through lymphatic channels to sites adjacent to the respiratory bronchioles. Whether or not this process leads to tissue damage depends on the number of the carbonaceous particles that are present and the toxicity of noncarbon substances that are mixed with the carbon or are absorbed on the surface of the carbon particle. These noncarbonaceous substances are most often minerals derived from mine dust, metals and organic compounds from combustion engines, and gases that are the products of the burning of fossil fuels.

Because of the many variables that influence the movement of carbonaceous particles, the time that it takes to clear them from sites around the respiratory bronchiole can vary from hours to years. Anthracosis, which is the deposition of anthracotic pigment around the respiratory bronchioles without accompanying tissue damage, develops when the removal of nontoxic carbonaceous particles is slower than the deposition of new such particles.[9]

The efficiency of the pulmonary clearance mechanisms that move dust from the lungs to the lymph nodes varies considerably from one individual to another.[10] This presumably is one of the reasons why coal miners working side by side for many years often develop different degrees of anthracosis. In all of the carbonaceous pneumoconioses, there is usually abundant pigment in local and regional lymph nodes. Carbonaceous dusts are transported in and out of these lymph nodes, but firm data on the rates at which this movement takes place are not available. In some patients, the dusts remain in local and regional lymph nodes for many years. As a result, evidence of old tissue damage in the form of hyalinized fibrous tissue is sometimes more conspicuous in hilar lymph nodes than in the lungs themselves.

Spencer has postulated that the deposition of carbonaceous dusts in periseptal, perivascular, and subpleural areas alters lymph drainage, which in turn slows the movement of subsequently deposited dust out of the lungs.[11] Some carbonaceous particles can remain within macrophages for years without damaging nearby tissues, whereas those particles that carry toxic minerals or organic compounds often destroy the macrophages in which they reside. Einbrodt has postulated that the amount of dust in the lungs as compared with that in lymph nodes is a marker of a dust's cytotoxicity.[12] If the ratio is greater than 1:1, the material is cytotoxic; for instance, the lung-lymph node ratio for free silica (*i.e.*, quartz) is about 1.4:1.0.

## ANTHRACOTIC DEPOSITS IN THE LUNGS OF URBAN RESIDENTS

Analyses of lung pigments from urban residents often show more silicon, iron, aluminum, and titanium than carbon.[13] Calcium, sulfur, magnesium, phosphorus, and phenolic compounds are also frequently present.[14] Sulfur dioxide, nitrogen dioxide, hydrocarbons, and other gases are commonly present on the surface of carbonaceous particles that are inhaled in urban environments. In experimental animals, the presence of these absorbed gases potentiates lung damage caused by the particles to which the gas is attached.[15] The solubility of the substances absorbed on the surface of the particles also influences their toxicity.

## ETIOLOGY AND DIAGNOSIS

Identifying the nature and causes of CWP has been a long and difficult process. The first difficulty is that CWP is not a single disease process. A number of disorders are involved, and each has an individual pathogenesis. These disorders include the following:

- primary dust macule
- anthracotic micronodules and macronodules
- silicosis
- progressive massive fibrosis
- chronic bronchitis and bronchiolitis
- focal emphysema
- Caplan syndrome

- centrilobular or proximal acinar emphysema, in some geographic locations.

There is considerable variability in the development of these individual disorders in miners working side by side in the same mine. There are even greater variations in the prevalence and severity of the disorders that constitute CWP in a single geographic region, within a single type of coal, with different dust concentrations in a single mine, and from one type of job to another within a given mine. Most of this variation is due to the mix and concentrations of various toxic materials in the mine atmosphere and to the variations in the way individual miners handle these toxic materials.

## *Constituents of Coal Mine Dust*

Coal forms when organic materials from forests and swamps are compressed in sedimentary layers. There is no single substance in coal or in the underground atmosphere of coal mines that can explain all of the constituent disorders of CWP. The lungs of coal miners contain more than 20 different metals and minerals in addition to carbon and a large number of organic compounds.[16,17] The percentage of free carbon in dust at the coal face, where coal is removed from the coal seam, is usually above 60% and often greater than 80%, whereas free silica in the dust at the coal face seldom exceeds 3%.

The operators of the trains that move coal out of the mines sometimes inhale high concentrations of small silica particles that have been produced by sand that has been pulverized under the wheels of their trains. Men who are roof bolters sometimes encounter high levels of free silica particles that are less than 2 μm in diameter when they drill into silica-bearing rock located over the coal seams. Miners who construct communicating shafts between adjacent coal seams and who remove hard rock can also inhale high concentrations of silica in small particles.

Other potentially toxic substances in the coal mine atmosphere include the following:

- toxic noncarbon components of the coal
- compounds released from the machines used to mine coal
- fumes that arise when electrical cables break and set their insulation coverings on fire
- fumes from diesel engines
- polluted above-ground air pumped underground to ventilate the mines.[18]

## *Intrinsic Toxicity of Coal*

Many years ago, Collis and Gilchrist[4] and Gough[19] discovered that exposure to coal dust can lead to CWP without exposure to any of the other components of mine dust. This raises the possibility that something in coal itself can damage the lungs. The specific toxic substances could not be identified until the 1980s, when researchers found new categories of toxic compounds in coal and became aware of new cellular and biochemical mechanisms involved in the genesis of inflammation, tissue damage, and fibrogenesis. Dalal and colleagues found that the reactive free radicals released by the crushing and grinding of coal are a possible cause of some of the tissue damage that constitutes CWP.[20] Tissue levels of these free radicals are increased in the lungs of bituminous miners with simple CWP; still higher levels are present in the lungs of anthracite miners and workers who have silicosis. These free radicals are at their peak in freshly crushed coal. Their activity decreases thereafter but does not completely disappear for months or years.

Tissue damage produced by free radicals could explain why acute-phase proteins like fibrinogen and C-reactive protein are elevated in the blood of some coal workers.[21] The damaging activity of free radicals could also be the reason why gallium uptake studies often show evidence of an acute inflammatory process in miners with CWP.[22,23] Gallium uptake reflects the inflammatory activity of effector cells in the lungs, particularly the number and activation state of macrophages.

Macrophages from miners with CWP reportedly are in an activated state.[24–26] These activated macrophages produce oxidants, fibronectin, and other fibroblast growth factors such as the cytokine known as tumor necrosis factor (TNF), which indirectly stimulate the growth of fibroblasts.[24–26] TNF also enhances the production of reactive oxidants from polymorphonuclear leukocytes. All the above new findings suggest that at least part of the tissue features of CWP are initiated by inflammation, which in turn starts a cascade that recruits inflammatory cells and leads to the release of multiple mediators of inflammation and fibrosis.

## *Silica*

Free silica (*i.e.*, quartz) is a well-known fibrogenic agent. It is a more effective recruiter of neutrophils and macrophages into the bronchioles and alveoli than is coal dust.[27] The resulting release of cytokines and growth factors by macrophages is postulated to be responsible for the development of the well-known tissue damage and fibrosis that is associated with free silica.[28]

For many years, free silica was considered to be the principal if not the sole toxic agent in coal mine dust. As previously mentioned, Collis and Gilchrist found evidence that coal itself could be toxic apart from the presence of silica.[4] They found x-ray evidence of CWP in 426 workers who shoveled coal that had been washed relatively free of silica. Workers in the carbon electrode and graphite industries who are exposed to carbonaceous dusts that are free of silica can also develop pulmonary lesions indistinguishable from CWP.[29,30] In subsequent studies it has been determined that quartz (*i.e.*, silica) rarely increases the risk of developing simple CWP when it constitutes less than 7% of the respirable dust in the workplace.[31] All forms of CWP can develop and progress in the absence of silica.[19,31,32]

None of this information should be taken as an indication that silica has no role in CWP. Fibrosis has been reported to progress more rapidly when the quartz (*i.e.*, silica) levels in mine dust are exceptionally high.[32–34] As previously noted, silicotic lesions are quite often present in coal workers whose jobs expose them to high levels of free silica, particularly roof bolters who drill through rock overburden, workers who construct tunnels through hard rock, and motormen who are exposed to finely ground silica dust from the sand thrown under the wheels of trains to improve traction.[32,35] These workers sometimes develop a progressive form of CWP that is indistinguishable from silicosis.[33,36] In such patients, lesions are composed of irregular, layered whorls of collagen that are typical of silicosis (Fig. 34-2).

More frequently, silica plays a role in the development of mixed-dust pneumoconiosis, a condition in which some silicotic nodules are present along with many lesions that are characteristic of CWP. I have found such mixed-dust pneumoconiosis in 35 (5%) of the 709 lungs of Appalachian bituminous miners exam-

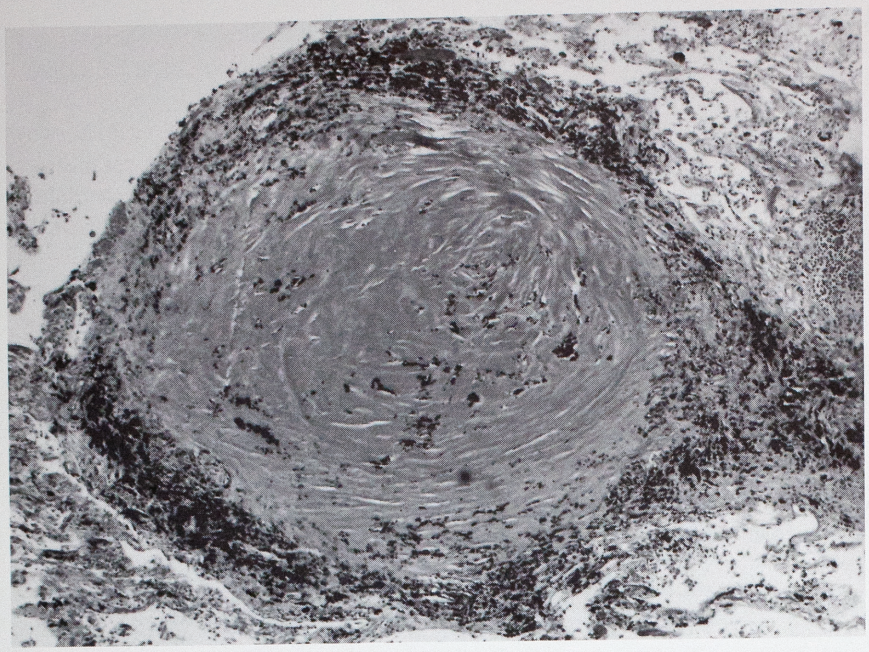

**FIGURE 34-2.** A silicotic nodule is present in the lung of a coal miner. Note the concentric arrangement of the hyalinized collagen fibers. Coal dust pigment is present both within and on the periphery of the nodule. (H & E stain; low magnification.)

ined at postmortem. Most of the affected 35 miners had a history of roof bolting or some other job that exposed them to rock or to sand dust that presumably contained high levels of free silica.

Free silica has long been postulated to be a cause of complicated CWP, otherwise known as progressive massive fibrosis (PMF). This postulate has been based on the fact that silica can remain in the lungs for many years and can cause progressive damage that resembles PMF.[33] A major role for silica in causing PMF was not disproved until it was shown that silica levels are usually no higher in PMF lesions than in the anthracotic micronodules and macronodules of simple CWP.

There is some evidence that the well-known variations in susceptibility to silicotic lesions from one coal miner to another are in part due to differences in the deposition and clearance of free silica and other harmful constituents of mine dust. Because of these variations, some miners progressively increase the concentrations of these harmful substances in their lungs until they reach levels that damage lung tissues.[37]

It has long been puzzling why high levels of silica in bituminous mine dust produce fewer silicotic lesions than similar levels of silica in the mine dust of high-rank anthracite coals. It has been postulated that illite and kaolinite—constituents of the clay that is mixed with carbon in bituminous coals—afford some protection against the fibrogenic properties of silica.[38–40]

### *Identification of Silicosis*

Grossly silicotic lesions that occur in the mixed-dust lesions of coal workers are firmer, are more uniform in size, and have paler centers and smoother borders than the anthracotic micronodules and macronodules of simple CWP in the same lungs.[41] Free silica is not easily seen in lung tissues. The birefringent crystals of many different sizes and shapes that are readily seen in the anthracotic deposits of coal workers by light microscopy with polarized light are not free silica but mainly silicates that do not injure the lungs. The roughly triangular crystals of free silica that damage the lungs are difficult to see because they are very tiny and have a refractive index that is close to that of the glass on which the tissue is mounted (see Chap. 35).

To visualize free silica crystals under the microscope, the tissue in which the crystals are embedded must be removed by microincineration or by digestion, and the residual material must be examined in air or in a mounting fluid that has a refractive index different from that of glass and silica.[42] Even when free silica cannot be seen, there is value in observing the number and size of the large birefringent silicate crystals in the lungs of coal workers, because where silicates are present, free silica is often present as well.

### *Fumes From Cable Fires*

A cable fire starts in coal mines when a high-voltage cable breaks and an arc of electricity crosses the break and ignites the insulation that covers the cable. The resulting dense, acrid smoke often contains the combustion products of cotton, jute, hemp, neoprene, copper, zinc, and polyvinyl chloride.[43] The principal combustion product of polyvinyl chloride is hydrochloric acid. A preliminary study found that miners who had been exposed to underground cable fires had a higher incidence of chronic bronchitis than did miners who had not been exposed to such fires.[43]

## *PATHOLOGY CLASSIFICATION*

CWP is categorized as simple or complicated. Simple CWP is diagnosed when anthracotic pulmonary lesions are less than 2.0 cm in diameter by direct tissue measurement or less than 1.0 cm in diameter on an x-ray film. Different diagnostic size is used because the x-ray images of CWP lesions are always smaller than the lesions assessed by direct measurement in lung tissue.

### *The Primary Macule*

During the first one half of this century, the prevailing opinion was that the disabling pulmonary disease in coal workers was diffuse in nature. It was Gough[19] and Heppleston,[44] in the 1940s, who first determined that the primary disorder was a focal collection of dust-filled macrophages that surrounded the respiratory bron-

chioles. Grossly, this primary lesion, termed the anthracotic macule, is black and round.[42] These macules are present in all lobes but are usually most numerous and largest in the subapical areas of the lungs. A committee appointed by the American College of Pathologists defined the coal dust macule as "a focal collection of coal dust–laden macrophages at the division of respiratory bronchioles that may exist within alveoli and extend into the peribronchiolar interstitium with associated reticulum deposits and focal emphysema."[42]

This committee set the upper diameter for an anthracotic macule at less than 7 mm.[42] If this latter criterion is used, the definition for an anthracotic macule will overlap the definition for an anthracotic micronodule, which the committee defined as a black deposit up to 7 mm in diameter. To avoid this overlap, I define anthracotic micronodules as black deposits that are between 1.0 and 6.9 mm in diameter and anthracotic macules as black deposits less than 1 mm in diameter.

The anthracotic macule first forms as an accumulation of macrophages filled with black pigment adjacent to a respiratory bronchiole (Fig. 34-3). As this accumulation grows, more and more nearby alveoli become filled with the pigment, most of it within macrophages. CWP never evolves beyond this primary dust macule, even after several decades of exposure to coal mine dust, in at least one half of U.S. bituminous coal miners. As previously mentioned, anthracotic macules without associated fibrosis or focal emphysema are also often formed as the result of exposures to burned fossil fuels and to other carbonaceous particles.

When the process of coal dust accumulation continues, bronchiole walls are damaged and the bronchiole dilates because the elastic tissue and muscle in its wall are destroyed.[45] The walls of immediately adjacent alveoli are often destroyed. This destruction produces a halo of open space both within and around the black deposits. This halo is termed focal dust emphysema (Figs. 34-4 and 34-5).[9,42,46] Because respiratory bronchioles are destroyed, focal dust emphysema in some respects fits the description of centrilobular emphysema.[47] However, because it rarely extends beyond a narrow zone immediately surrounding the dust macule, it does not correspond to the more advanced stages of centrilobular emphysema in which individual focal zones of emphysema coalesce to form much larger confluent areas.

Because focal dust emphysema usually affects only a small area around individual respiratory bronchioles, it rarely causes more than minimal impairments in lung function.[47–49] All forms of centrilobular emphysema, including the focal emphysema of CWP, are presumably caused by the activity of proteolytic enzymes. Coal mine dust, tobacco smoke, the combustion products of fossil fuels, and infections all appear capable of initiating an inflammatory process that activates macrophages to release these damaging enzymes.[50] Cigarette smoke, repeat episodes of bronchitis, bronchiolitis, and urban air pollution are the usual underlying causes of the confluent forms of centrilobular emphysema (see Chap. 26).

Whether or not working in the underground atmosphere of coal mines leads to the development of inflammation severe enough to produce disabling centrilobular emphysema is a subject of dispute both among scientific investigators and among litigants seeking compensation for lung injury caused by CWP. This issue will be discussed at greater length later in this chapter.

The individual black particles in some anthracotic macules are tightly packed with a few barely visible, admixed inflammatory cells, reticulum fibers, and strands of collagen. At the other end of the spectrum, the dust particles are widely separated and interspersed with easily visible macrophages, fibroblasts, reticulum, and collagen. Special stains enhance the visibility of the collagen; the reticulum fibers can be seen only with special stains.

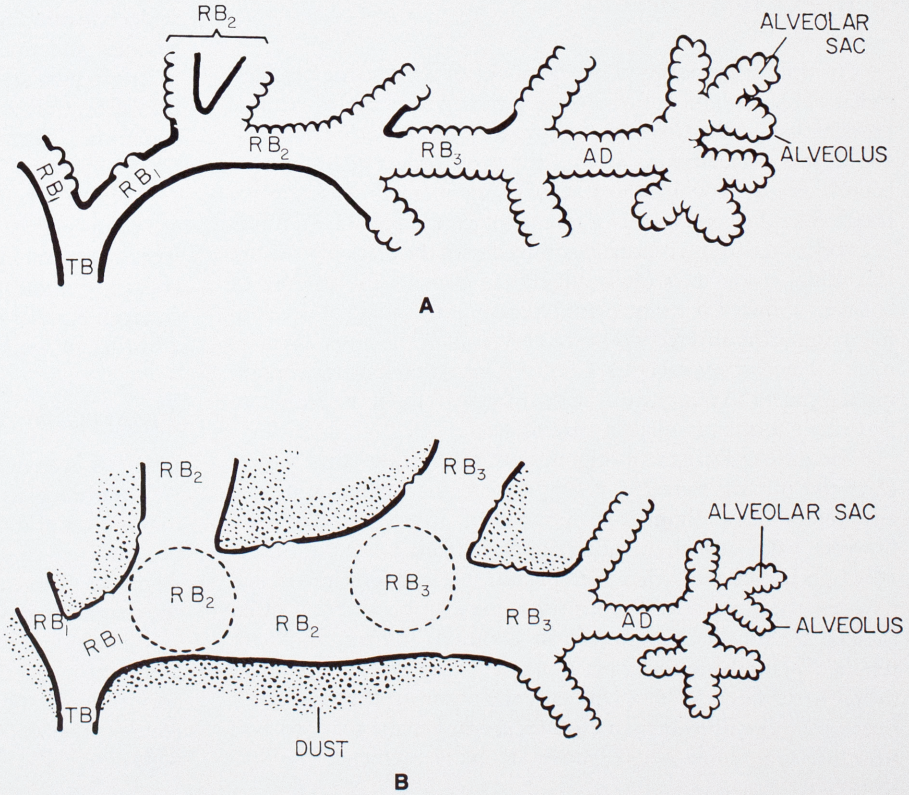


**FIGURE 34-3.** Diagrams of the microanatomy of (**A**) normal distal airways and (**B**) distal airways that have been damaged and are now dilated by deposited coal mine dust. (AD, alveolar duct; RB1, RB2, RB3, first-, second-, and third- order respiratory bronchioles; TB, terminal bronchiole; from Wolman M, ed. Pigments of pathology. New York: Academic Press, 1969.)

**FIGURE 34-4.** Focal emphysema is seen within and surrounding collections of dust macules and micronodules in this whole-mount of a coal worker's lung (see Fig. 5-6). (Gough section; courtesy of Lorin Kerr, M.D., Atobicoke, Ontario, Canada).

In the earliest stage of development of anthracotic macules, sheets of black pigment first appear at the division of the terminal bronchiole and the first-order respiratory bronchiole. The maximal dust accumulation is around the three orders of respiratory bronchioles, after which the mass of pigment tapers off and leaves the alveolar duct and the distal alveoli intact (see Fig. 34-3). A fine network of reticulum is usually admixed with the black pigment in this initial lesion. It is often difficult to evaluate the amount of collagen admixed with the black pigment at this stage of development unless the affected worker has been out of the dusty environment for at least several years, because it takes that long for enough black pigment to migrate out of the macule to make the reticulum and other forms of collagen easy to see.

Because coal pigment migrates out of the lungs after miners leave the mining industry, it might seem that quantitating the amount of black pigment in lungs is of little value. There is, however, value in such quantitation, particularly when pigment is very tightly packed. In these latter cases, special efforts are needed to assess the amount of fibrous tissue present, because it is often masked by the black pigment. In addition, miners who have retained a large amount of black pigment may also have retained the toxic substances that accompany the pigment; therefore, they may have more fibrous tissue and focal emphysema than workers from the same mine who retained less black pigment.

## *Nodular Lesions*

Anthracotic lesions 7.0 mm to 19.9 mm in diameter have been designated by the previously mentioned committee[42] as anthracotic macronodules. Unlike anthracotic macules, anthracotic micronodules and macronodules are not confined to the area immediately adjacent to respiratory bronchioles. They often extend to encompass more proximal bronchioles, wider zones of alveolar ducts and alveoli, and tissue at other sites, particularly in the subpleural and periseptal regions.

Anthracotic micronodules and macronodules are more apt to be firmer than anthracotic macules because they often contain more collagen (Fig. 34-6). The majority of U.S. Appalachian bituminous coal miners who have anthracotic micronodules do not have anthracotic macronodules. Their pneumoconiosis is most accurately described as simple, micronodular CWP. Anthracotic micronodules in currently working or recently retired miners are almost always black. If the worker has been away from mine dust for many years, the lesions are sometimes gray because much of the original coal dust migrated out of them during the intervening years.

As lesions become larger than 1 mm in diameter, their edges usually become irregular and often stellate, and the zones of focal emphysema around them widen. Coalesced alveolar walls and other residual tissues that contain earlier deposited anthracotic pigment sometimes give the appearance of interstitial fibrosis (Fig. 34-7).[47] When individual anthracotic micronodules expand or fuse with adjacent micronodules to form nodules 7 mm to 19.9 mm in diameter, the lesions are termed anthracotic macronodules. The resulting disorder is most accurately described as simple, macronodular CWP.

In an analysis I conducted, anthracotic macronodules were present in 13 (6%) of the lungs of 223 recently deceased U.S. Appalachian bituminous miners. Anthracotic macronodules often have more fibrous tissue, more small birefringent crystals, and wider surrounding halos of focal emphysema than do anthracotic macules and micronodules. Even when simple CWP is at the macronodular stage, it rarely progresses to a more severe disorder if a worker quits exposure to coal mine dust.[51,52] By contrast, PMF sometimes continues to expand and damage more and more lung tissue even after cessation of exposure to coal mine dust.[53,54]

Histologically, anthracotic micronodules and macronodules are composed of collagen and dust-filled macrophages in a network of reticulum. If there is very little free silica in the lesion, the collagen bundles will be interlacing and lack orientation. If the collagen bundles have a layered appearance, there is almost always a history of work exposure to silica.

## *Progressive Massive Fibrosis*

PMF has been defined by the previously mentioned committee of U.S. pathologists as a massive black pulmonary mass or nodule that is 2 cm or more in diameter (Fig. 34-8).[42] The opacity has to be only 1 cm or greater in diameter on an x-ray film to make the diagnosis. Three centimeters in diameter is the standard used for the diagnosis in Great Britain.

The lesions of PMF are most often located in either the upper lobes or the apical segments of the lower lobes of the lungs. They are more apt to be located posteriorly than anteriorly in a lobe. The younger the worker, the more likely are PMF lesions to enlarge with time.[53] PMF is almost always asymmetrical in the two lungs,

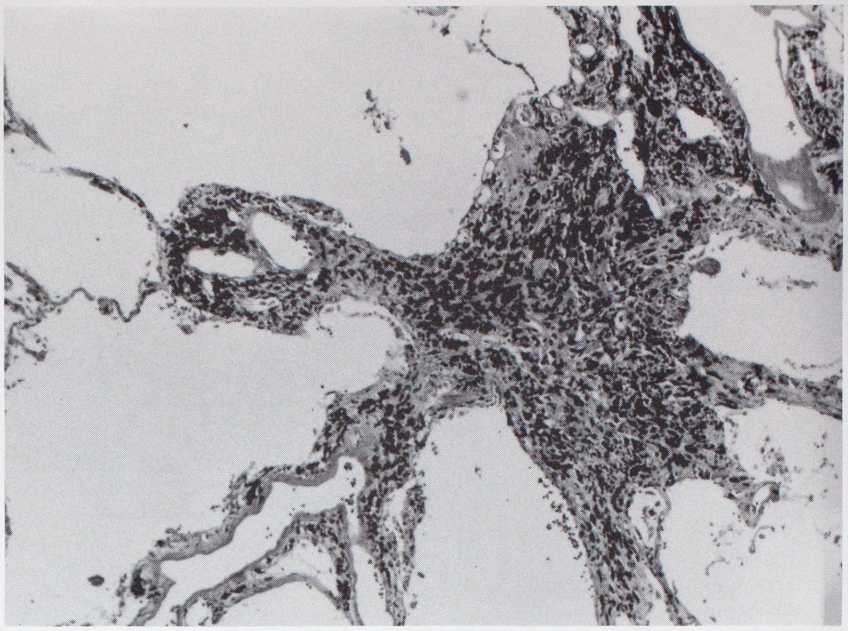

**FIGURE 34-5.** A halo of focal emphysema surrounds an anthracotic macule. (H & E stain; low magnification.)

and the lesions can cross interlobular fissures. They can replace a whole lung, but this is rare. On cut surface, PMF is homogeneously black and has a rubbery consistency. Variably sized fluid-filled cavities are usually present in the central areas of PMF lesions. The halo of emphysema that surrounds most PMF lesions can vary from very narrow to wide.

The histology of a PMF lesion varies from its edge to its center. At the periphery there is usually an admixture of reticulum, haphazardly arranged collagen, and anthracotic pigment. The collagen is quite often hyalinized. Anthracotic pigment near the periphery is usually within macrophages, whereas in the center of PMF lesions such pigment is often free in the tissues. As one moves toward the center of PMF lesions, the collagen often disappears, and only a mixture of fibronectin, other amorphous proteins, and black pigment is present in a zone of necrosis (Fig. 34-9).

Giant cells are sometimes visible at the edge of the necrotic areas, and cholesterol crystals are sometimes present. Thrombosis, sclerosis, and obliterative lesions are often evident in arteries near or within PMF lesions (Fig. 34-10). These arterial lesions are presumably responsible for some of the necrosis by making central areas of the PMF lesions ischemic.

The possible presence of silicosis, Caplan syndrome, tuberculosis, or histoplasmosis should always be considered when making the diagnosis of PMF. PMF is distinguished from a silicotic nodule by the greater amount of black pigment in the PMF lesion and by the absence of the layered collagen characteristic of a silicotic nodule. Special stains are often used to search for mycotic and mycobacterial organisms because tuberculosis and fungal infections can produce lesions that in some respects resemble PMF (Fig. 34-11).

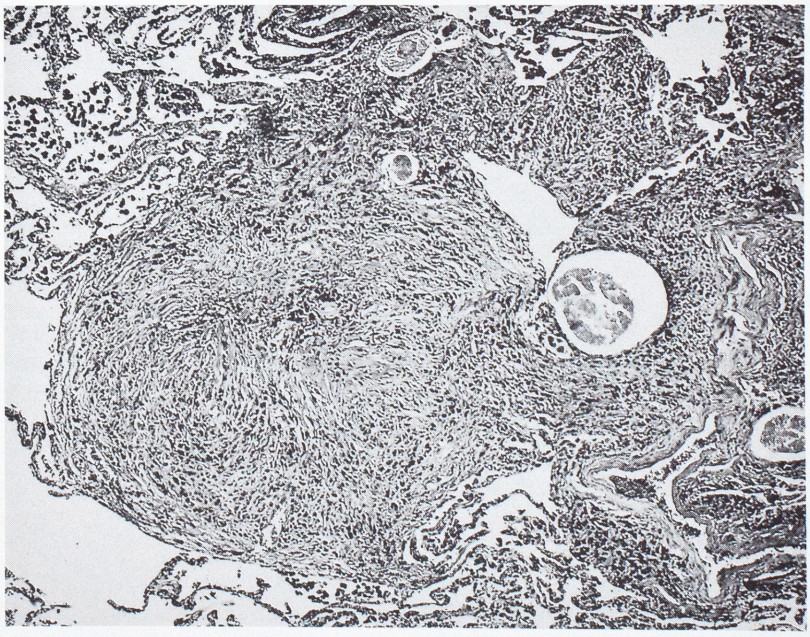

**FIGURE 34-6.** Most of the black pigment has migrated out of this anthracotic macronodule in the lung of a retired coal miner. Note the arrangement of the collagen fibers, which run in all directions. (Trichrome stain; low magnification.)

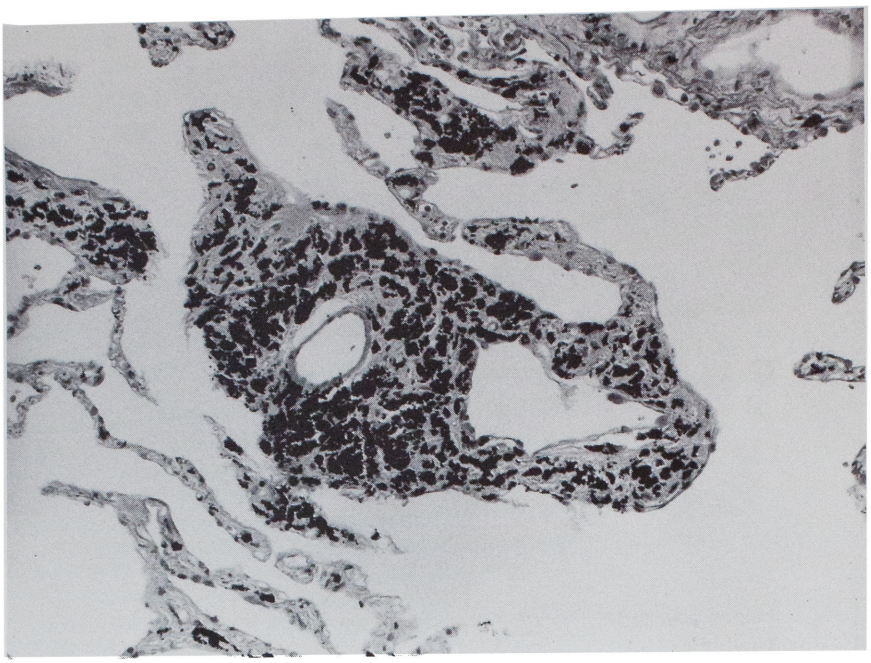

**FIGURE 34-7.** Section from the lung of a 55-year-old Appalachian miner shows black pigment around a small muscular artery. This man had been a heavy cigarette smoker for many years, and there is already a zone of centrilobular emphysema contiguous with a thin halo of focal emphysema around the black deposit. (H & E stain; intermediate magnification.)

**FIGURE 34-8.** Progressive massive fibrosis is present in the lung of a 40-year-old coal miner (see Fig. 5-7). (Gough section; courtesy of Lorin Kerr, M.D., Atobicoke, Ontario, Canada.)

The pathogenesis of PMF has eluded every generation of investigators since the lesion was first described. Identified risk factors include advanced age of the worker, many years of exposure to coal dust, and a presumed inefficiency of the mechanisms that remove coal dust from the lungs.[37,55] PMF is most likely to develop in those who already have simple CWP, particularly when there is a large dust accumulation.[55,56]

PMF is more common in miners of high-rank coal than in miners of low-rank coal. PMF in a miner of high-rank coal often develops by the enlargement of single nodules, whereas PMF in a miner of low-rank coal usually forms by the expansion and fusion of several smaller nodules.[37] The frequent presence of the immune globulins IgG and IgA in PMF lesions along with fibronectin and fibrinogen suggests the presence of exudation.[57] This is supported by the observation that superoxide anion released by alveolar inflammatory cells is many times greater when PMF is present than when a worker has only simple CWP.[26]

Tubercle bacilli have been recovered in 1% to 35% of PMF lesions, so an infectious origin must always be considered. In a famous study, Zaidi and colleagues showed that the joint administration of coal dust and tubercle bacilli of low virulence to guinea pigs produced massive pulmonary fibrosis, whereas neither agent by itself produced such fibrosis.[58] The significance of this animal study for coal miners is now in doubt, because antituberculous chemotherapy has not prevented early-developing PMF from expanding, and a decreasing rate of tuberculosis has not resulted in a decrease in the occurrence of PMF.[53,59]

PMF is usually associated with dyspnea, impaired lung function, and increased mortality.[60] Occasionally, it occurs as a solitary lesion, and the affected miner has near-normal lung function.[60] When PMF involves a large volume of lung tissue, workers usually have marked reductions in ventilatory capacity and diffusing capacity, poor gas exchange, and cor pulmonale.[61,62]

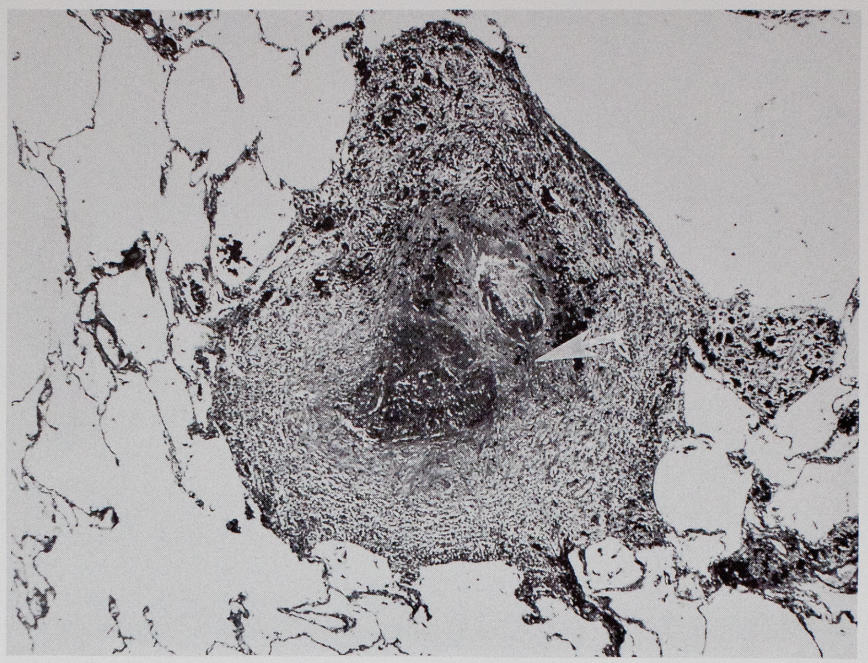

**FIGURE 34-9.** In a developing lesion of progressive massive fibrosis, the center of the nodule (*arrow*) is necrotic. (H & E stain; low magnification.)

## *Rheumatoid Pneumoconiosis or Caplan Syndrome*

In 1953, Caplan described an unusual form of CWP in Welsh coal miners with rheumatoid arthritis.[63] Subsequently, the lesions have been reported in miners who have elevated serum titers of rheumatoid factor but little or no clinical evidence of arthritis.[64] It has also been reported that coal workers with rheumatoid arthritis have an increased incidence of PMF.[65,66] Some of this latter increase has been postulated to be the result of rheumatoid nodules developing in the lung in batches and then fusing.[66]

Rheumatoid pneumoconiosis can run a rapid, fatal course. The lesions are characteristically pale yellow, rounded, well-defined nodular masses ranging from 0.5 cm to 5.0 cm in diameter located in the periphery of the lung. Radiographically, the lesions often enlarge rapidly. They characteristically have internal laminations of darker and lighter layers (Fig. 34-12).[67] These laminations are the result of alternating zones of coal dust and necrosis with clefts and calcium deposits in the lighter areas. There is usually a zone of acute inflammation and vasculitis at the periphery of the lesions. Only occasionally are histiocytic pallisading and necrobiosis, so characteristic of an ordinary rheumatoid nodule, present in the rheumatoid lesions of coal workers.[42,67]

The central areas of the rheumatoid lesions in coal workers are often composed of necrotic, eosinophilic debris. This necrotic debris is usually sharply demarcated from the surrounding tissues by a layer of collagen and fibroblasts with varying numbers of chronic inflammatory cells. As in patients with PMF, sclerosis and

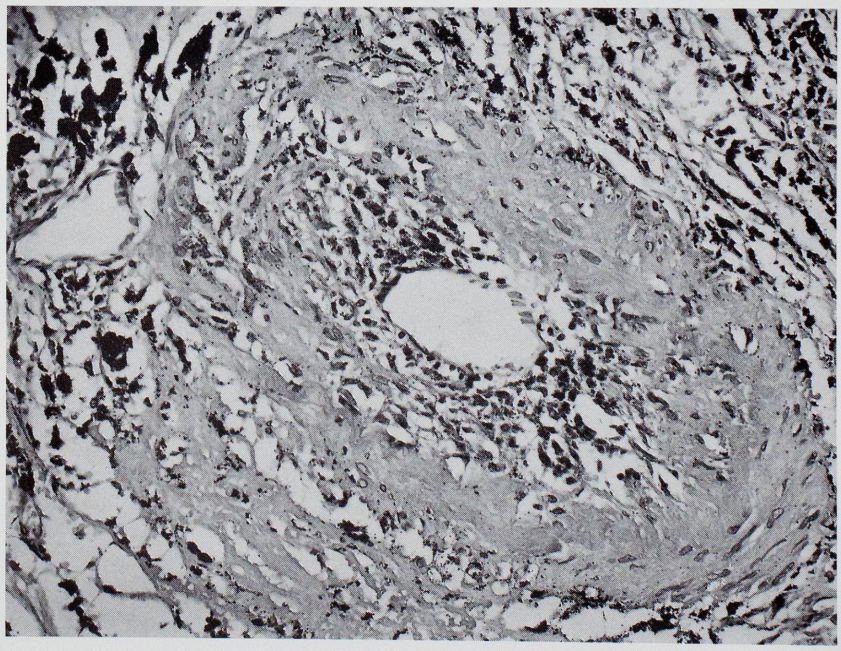

**FIGURE 34-10.** Partial destruction of a pulmonary muscular artery on the edge of a progressive massive fibrosis lesion has taken place in a coal miner. The wall of the vessel is fibrotic and is infiltrated by lymphocytes and macrophages containing anthracotic pigment. (H & E stain; intermediate magnification.)

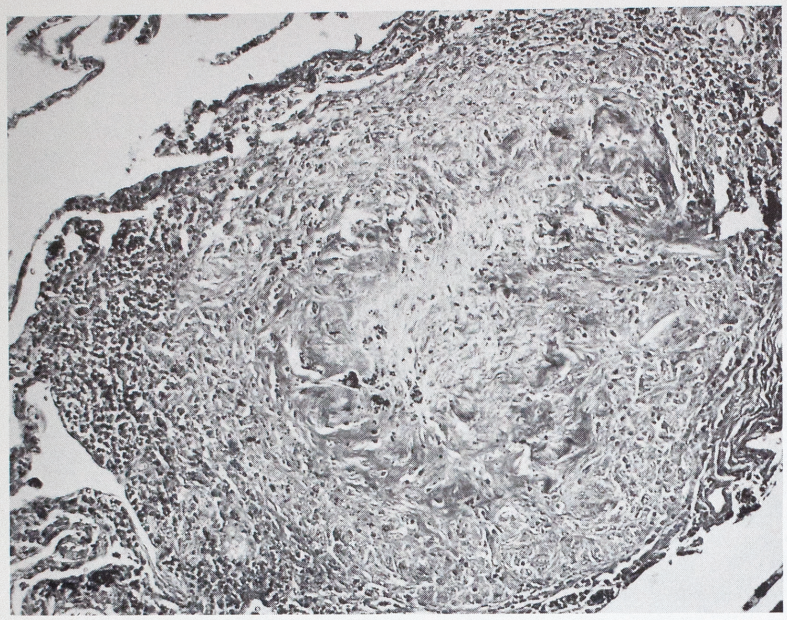

**FIGURE 34-11.** Tuberculosis is seen in the lung of an elderly Appalachian coal miner. Caseous necrosis occupies the center of the nodule, whereas coal dust is seen on the periphery. (H & E stain; low magnification.)

endarteritic obliterations are often prominent in blood vessels adjacent to and within the rheumatoid lesions. These vascular abnormalities likely contribute to the necrosis in the lesions.

## *Bronchitis*

Chronic bronchitis and bronchiolitis are characterized by persistent cough, excessive sputum production, breathlessness, wheezing, and a slowing of airflow in the airways. Structurally, chronic bronchitis is evidenced by hypertrophy and hyperplasia of mucous glands in bronchial walls. Chronic bronchiolitis is recognized by a hyperplasia of goblet cells in the epithelial lining of bronchioles. In patients with chronic bronchitis, the lumen of airways is often narrowed by mucus. The occlusion of small airways by mucus with resultant pulmonary atelectasis is the final event that leads to death in many individuals with chronic bronchitis, particularly when another debilitating chronic disorder is also present. The mucociliary escalator is often slow in individuals with chronic bronchitis because their mucus has a high viscosity (see Chap. 27).[68]

Cigarette smoking and underground exposure to coal mine dust are the two major factors that predispose to the development of chronic bronchitis in coal miners.[69,70] Several studies have shown that exposure to coal mine dust causes the signs, symptoms, and airflow reduction characteristic of chronic bronchitis.[70–74] Several of the studies show that both exposure to mine dust and smoking have a dose-related effect on the frequency and severity of bronchitis independent of any radiographic evidence of CWP.[75] In mines where diesel engines are used, emissions from the engines may increase the frequency of bronchitis.[76] A number of toxic products that may cause bronchitis have been identified in diesel

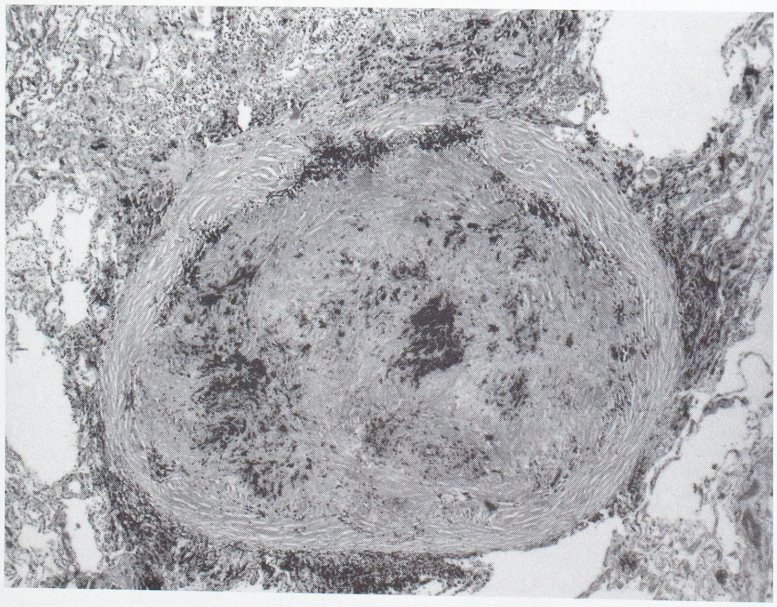

**FIGURE 34-12.** Rheumatoid pneumoconiosis is present in this 59-year-old coal miner with rheumatoid arthritis who had worked underground for 38 years. Rings of black pigment with accompanying fibrous tissue and chronic inflammatory cells are immediately adjacent to zones of necrosis. There is only a small amount of black pigment in the surrounding lung. This is a rare lesion in coal miners in the United States. (H & E stain; low magnification.)

exhaust, including sulfur dioxide.[77] No long-term studies are available in miners, but the results of animal studies suggest that diesel exhaust may be more toxic to the lungs than coal dust.[78]

Coal miners who develop chronic bronchitis tend to acquire their symptoms within the first year of employment and retain them thereafter.[74] Their principal physiologic abnormality is a slowing of airflow in the lungs at large lung volumes.[71,72] When cigarette smoking is the principal cause of bronchitis, airflow tends to be slow at low as well as large lung volumes, indicating that small as well as larger airways are obstructed.[71,72]

Studies from the United Kingdom and Australia have found that bronchial mucus-secreting glands increase in number and size with emphysema in coal workers but not necessarily with the number of years miners work at the coal face.[79] This suggests that mucus hypersecretion is an important feature of the bronchitis that develops in British and Australian coal miners.[79]

The relative frequency, severity, and outcome of chronic bronchitis in coal workers appears to vary from one mining area to another. One can speculate that these differences relate to the differing compositions of coal, the differing mixes of other constituents in mine dust, the toxicity of above-ground air that is pumped to ventilate the mines, and perhaps the tendency of miners to change jobs.[73,74,79] In interviews with U.S. Appalachian coal miners, I was struck by the number of young miners recently employed in the industry who had developed signs and symptoms of chronic bronchitis after starting work and were ready to quit soon. Many of these symptomatic workers probably had very reactive airways.[72,73,79,80]

Changing jobs is common in the United States, so if miners who develop chronic bronchitis quit the industry at an early age, not many career miners would be inherently highly vulnerable to bronchitis. It may be more difficult to change jobs in some other countries, which could result in work forces with a higher proportion of individuals vulnerable to chronic bronchitis and disabling emphysema.

## *Emphysema*

Emphysema is defined as the enlargement of air spaces in the lung distal to the terminal bronchiole. The enlargement of air spaces is accomplished in large part by the destruction of alveolar walls and other lung structures. Exposure to coal and coal mine dust has been claimed to have a role in the development of both focal and centrilobular (*i.e.*, proximal acinar) emphysema.[81,82] The nature of these two types of emphysema is described in Chapter 26.

Focal dust emphysema rarely constitutes more than 1% to 2% of the total emphysema in the lungs of coal miners. In 1991, I reviewed the gross descriptions and microscopic slides from the lungs of 223 recently deceased U.S. Appalachian coal miners. All had been sent for my review because their widows were applying for a pension to which they were entitled if their husbands had CWP that was severe enough to have disabled them or contributed to their deaths. Focal emphysema constituted less than 1% of the total emphysema in the lung sections of 81% (180 patients) of these miners. In 17% (39 patients), focal emphysema accounted for 1% to 5% of the total emphysema present, and in only 2% (four patients) did focal emphysema constitute more than 5% of the total emphysema in the lung sections. Therefore, only in rare patients did focal emphysema constitute a significant portion of the total emphysema that was present in these miners' lungs.

Most of the emphysema in the 223 miners' lungs was centrilobular in type, and its severity often correlated with the results of pulmonary function studies that had been conducted prior to death (Fig. 34-13). In the United Kingdom and in some other European nations, functionally significant pulmonary emphysema appears to be more frequent and more severe in coal miners than in the general population.[79,83–85] In the United States, disabling pulmonary emphysema is reportedly no more frequent in coal miners than in the general population when cigarette smoking is taken into consideration.[86–90] Therefore, disabling centrilobular emphysema can hardly be attributed to occupational exposures to coal and coal mine dust in U.S. miners.

One group of U.S. investigators has recently come to a different conclusion based on their claimed finding that an inverse correlation exists between coal mine dust exposure and lung function as measured by forced expiratory volume in 1 second ($FEV_1$) and forced vital capacity (FVC).[81,82] These latter correlations cannot be given serious consideration because they are based on dust data whose validity has been thoroughly discredited.[91]

A higher proportion of coal with toxic properties may explain the apparently higher frequency of disabling emphysema in British than in U.S. miners. In Britain there is reportedly a much lower frequency of centrilobular emphysema associated with the mining of low-rank than of high-rank coal, and significant emphysema is usually present only when CWP lesions are fibrotic.[83] In British miners of low-rank coal, there appears to be no correlation be-

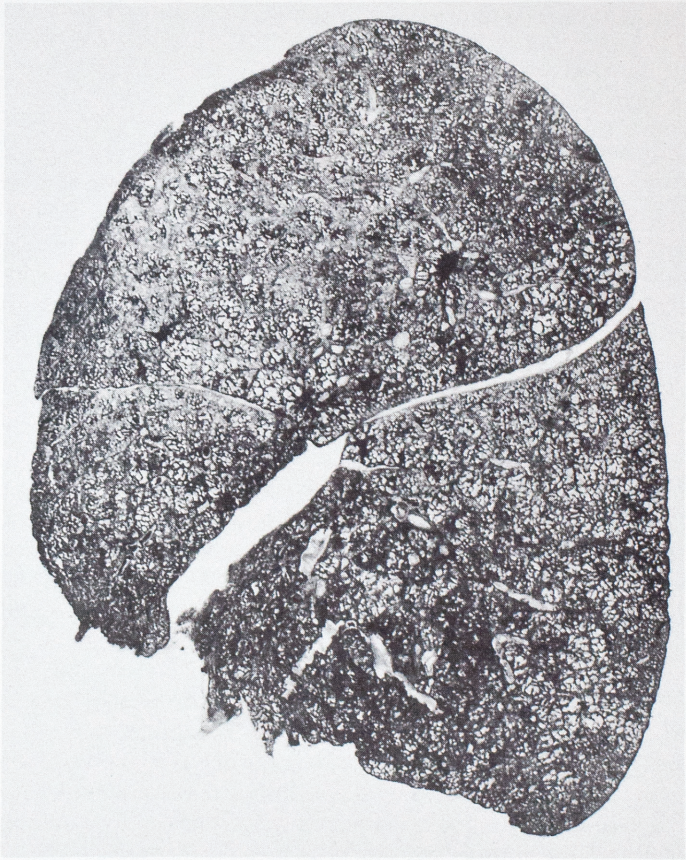

**FIGURE 34-13.** A mixture of severe confluent centrilobular emphysema and focal emphysema is present in a 55-year-old coal miner. This patient had a history of smoking one pack of cigarettes a day for 38 years. (Gough section; courtesy of Lorin Kerr, M.D., Atobicoke, Ontario, Canada.)

tween the severity and extent of emphysema and the amount of dust retained in the lungs.[83] Almost all of the coal mined in the United States in recent years is of low rank. As a result, large dust accumulations with accompanying severe fibrosis are now rare in U.S. miners.

In the previously mentioned 223 coal workers whose lungs I reviewed in 1991, 41% (92 patients) had no CWP and 51% (113 patients) had anthracotic deposits that were usually less than 1 mm in diameter, a few reaching 1 to 6 mm in diameter. Six percent (14 patients) had one or more anthracotic deposits that reached or exceeded 7 mm in diameter, and 2% (4 patients) had PMF. Even when large anthracotic deposits were present, there was often very little fibrosis admixed with the black pigment, and usually only mild centrilobular emphysema if the miner had never smoked cigarettes.

In a study by Morgan and colleagues, no relationship was found between ventilatory capacities in U.S. miners and the radiographic category of simple CWP.[90] The situation was quite different before 1950; large numbers of miners in the United States had mined high- or medium-rank coal with the result that they often had fibrosis and severe focal emphysema associated with their anthracotic pigment. Since 1950, the underground mining of high- and medium-rank coal has nearly ceased in the United States, and the dust levels in still-operating low-rank coal mines have been markedly reduced. The concentrations of respirable dust in U.S. mines are usually less than 2 mg/m$^3$, whereas 40 years ago the values were commonly five to six times higher. All of this is an indication that, in recent years, most coal miners in the United States have been mining coal of low toxicity.

## *Coal Rank*

In general, the development of CWP relates to the cumulative exposure to dust, but there are other factors as well. One of these other factors is the rank of coal. Coal is ranked by a classification system that is based on percents of fixed carbon, volatile matter, and moisture, as well as agglomeration indices and caloric content.[92] The rank of coal increases from lignite through bituminous to anthracite and reflects an increasing content of fixed carbon and a diminishing content of volatile matter and ash.[92]

The ash in coal comes from inorganic matter in vegetation that was transformed into coal, and from sand and clay that were washed into swamps and mixed with the decayed organic material. Radioisotopes of uranium and thorium are also present in trace amounts in coal deposits.[93] There are also some highly toxic organic compounds in coal that are carcinogenic when released by heating or other processing. These include benzene, phenol, naphthalene, phenanthrene, cyclohexane, polymethylene, and dihydroaromatics.[94]

One might expect that the prevalence and severity of CWP would decrease with increasing coal rank because the silica content of coal dust decreases with coal rank. Just the opposite is true. It is well known that the frequency and severity of CWP increase in the United States with the rank of coal mined underground. I have found that both the number of birefringent crystals and the amount of fibrous tissue associated with black pigment increase in Appalachian coal miners as the rank of coal mined increases.

In the United Kingdom, workers mining low-rank coal have been able to tolerate much higher levels of silica in mine dust without developing CWP than have the miners of high-rank coal.[38–40] This has been attributed in part to the protective effects of high levels of illite, which is a mica, and kaolin in the dust of low-rank coal mines. Within the Appalachian region there are bituminous coal seams whose miners have a high frequency of severe CWP and silicotic lesions.[95] The miners of other Appalachian bituminous coal seams almost never develop severe CWP unless they have jobs that place them, over a long period of time, in contact with hard rock dust that contains high levels of free silica. A similar situation prevails in the United Kingdom, where there are considerable variations in the prevalence and severity of CWP within coal fields that have the same rank of coal.[34]

In the United States, some of the increase in the prevalence and severity of CWP with increasing coal rank appears to be due to the amount of small particulate silica that has been generated under the wheels of trains that transport coal out of the mines. In Appalachia, the slope of coal seams increases with the rank of coal, so that the highest ranked coal (*i.e.*, anthracite) often requires sand beneath train wheels to provide the traction needed to prevent the wheels from slipping off the tracks. The sand has a high content of free silica, and in past years the train wheels ground the sand into particles so small that when inhaled they deposited in alveoli and necessitated macrophages for their removal.

Toxic particles that must be removed by macrophages have the potential for damaging the lungs. Most bituminous coal seams in Appalachia have a near horizontal slope, so much less sand is needed under train wheels for traction than is the case in anthracite mines. In general, silicotic lesions in the lungs of U.S. coal miners are confined to workers exposed to mine dust with high concentrations of silica particles less than 5 μm in diameter, namely roof bolters who drill into hard rock and workers who tunnel through hard rock and remove hard rock overburden (see Chap. 35).

## *Role of Cigarette Smoking*

British investigators have made systematic investigations of the role of cigarette smoking in the development of emphysema in coal workers. Marine and colleagues found that cigarette smoking increased the severity of obstructive airway disease in coal workers.[96] Other British investigators have stated that the centrilobular emphysema that is so often present in coal workers is usually the result of cigarette smoking.[97] Others recognize the important role of smoking but claim that exposures to coal mine dust have at least a small role in the genesis of centrilobular emphysema.[83,96] There is no evidence that cigarette smoking affects the attack rate or the overall severity of CWP.[74,98,99] Histologically, it is easy to differentiate between the black pigment that is derived from coal mine dust and the tan, finely granular pigment that comes from tobacco smoke.

## *Pulmonary Vascular Abnormalities*

A variety of pulmonary vascular abnormalities are present in CWP. Blood vessels are frequently destroyed in anthracotic macules and nodules when fibrosis develops. This vessel destruction is probably the major mechanism by which pulmonary vascular resistance increases and chronic cor pulmonale develops in individuals with severe simple CWP. This destructive process is particularly notable in PMF.[100]

Emphysema is probably the other major factor responsible for chronic cor pulmonale in CWP.[101] When emphysema is severe,

levels of oxygen are low in many alveoli, which in turn reduces the level of oxygen in the walls of nearby arteries. This hypoxia causes the arteries to constrict, which in turn leads to hyperplasia and hypertrophy of muscle fibers in their walls.[102]

Another abnormality that may increase pulmonary vascular resistance in coal miners is the hypertrophy that takes place in smooth muscle cells in small pulmonary arteries as they pass through the mantle of coal dust in a dust macule.[101,103] This abnormality is usually not associated with chronic cor pulmonale, so it presumably does not increase pulmonary vascular resistance to a significant level in the absence of clinically important emphysema or fibrosis.[103] The presence of chronic cor pulmonale is a poor prognostic sign for long-term survival in miners and ex-miners with CWP.

## Tuberculosis and Other Infectious Processes

There is no convincing evidence that individuals with CWP are at an increased risk for contracting tuberculosis. However, several studies have shown that antituberculosis chemotherapy is less effective in the treatment of tuberculosis when CWP is present.[104] This raises the possibility that CWP can increase the pathogenicity of tuberculosis once the infection is in progress.

There is strong evidence that silicosis predisposes to the development of tuberculosis, and it must be kept in mind that some coal workers have silicotic lesions. As discussed earlier, tuberculosis only rarely plays a role in the development of PMF in coal workers.

## Pulmonary Neoplasms

Carbon in its common forms appears to be noncarcinogenic, but individuals with some types of anthracotic pneumoconioses have an increased frequency of malignant neoplasms because of other constituents of mine dust or noncarbon substances in coal that are released by heating. Neither U.S. nor European coal miners have an increased frequency of carcinoma of the lung when cigarette smoking is taken into consideration.[105,106] In fact, U.S. coal miners reportedly have a lower frequency of lung cancer than that found in the general population.[107] The distribution of cancer cell types in coal workers is similar to that in the general population.[108] Several studies have found that stomach cancer is more frequent in coal workers than in other workers, both in the United States and in Europe.[106,109]

Several studies have shown no overall increase in mortality for miners with simple CWP.[110,111] Coke oven operators, particularly those who work on the sides and on the tops of the coke ovens, have an increased frequency of squamous cell carcinoma of the lung.[112] Selikoff and Hammond, who studied the disorder in coke oven workers, postulate that the neoplasms may be the result of exposure to benzopyrene and other well-known carcinogens in coke oven gas, or to asbestos, which is used as insulation in the ovens.[113]

## Surface Mining

Surface miners of coal rarely develop CWP because concentrations of respirable dust are low.[114,115] A few such workers have developed x-ray evidence of CWP and associated pulmonary ventilatory impairments.[36] Almost all of these workers had engaged in drilling operations, which suggests that they had been exposed to significant levels of small particulate silica through their contact with pulverized silica-bearing rock.

## Graphite Workers

Graphite is widely used in industry in the manufacture of pencils, dry-cell batteries, crucibles, and crucible steels and alloys, as a rust-proofing and acid-proofing agent, and as a lubricant. Two forms are in use, a natural form known as plumbago, which can contain 4% to 10% of free silica, and synthetic graphite, which contains little or no silica. The natural form is mined on several continents from siliceous sediments.[116] Dunner, in 1945, first described x-ray changes in the lungs of five men exposed to graphite dust.[117] Exposure during mining to the natural product can produce significant lung disease, both from the high levels of free silica that are admixed with the graphite and from silica derived from drilling hard rock in which the seams of graphite are often embedded.

Graphite miners in Sri Lanka have developed a disorder that closely resembles CWP. In 1972, 63 (18%) of 344 miners in one mine had radiographic evidence of CWP.[118] In subsequent years, measures were taken to reduce dust levels in all of the Sri Lanka mines. In 1987, an x-ray study found evidence of pneumoconiosis in only 3.4% of miners.[119]

Most synthetic graphite contains only traces of free silica, and therefore it is less of a threat for lung disease. The one exception is pyrolite graphite, which can contain a significant amount of quartz (*i.e.*, free silica) and cristobalite.[120] It is estimated that more than 2 million U.S. workers are exposed to natural and synthetic graphite each year.[54] The prevalence of CWP in this population is not known, but it is presumed to be low. Grossly, the lesions closely resemble CWP. Microscopically, there are some differences. In graphite miners, giant cells are often present within the alveoli, and crystalline particles are often visible (Fig. 34-14). Ferruginous bodies with black cores are also sometimes present (see Chaps. 36 and 37).[121]

## Carbon Black

Carbon black consists of elemental carbon in the form of near-spherical colloidal particles and coalesced particle aggregates of colloidal size, obtained from the partial combustion or thermal decomposition of hydrocarbons. Most of this product is used for pigmenting and reinforcing rubber. Smaller amounts are used in inks, paints, the manufacture of paper, plastics, foods, ceramics, and chemicals. With such widespread use, there are many opportunities for workers to be exposed to carbon black.[122] It has been estimated that 35,000 U.S. workers are exposed to it each year.[41] Chronic bronchitis, emphysema, and pneumoconiosis have all been reported in carbon black workers. Epidemiologic data are sparse, but there is one report of exposed workers experiencing a progressive decline in lung function as measured by $FEV_1$ and FVC.[123] Most studies have shown no such abnormalities, and the general consensus is that carbon black is a nuisance dust without specific damaging effects on the lungs.[124,125] Extensive studies in Eastern Europe have found no evidence that carbon black is carcinogenic, and these studies have shown that it has little or no effect on the lungs and hearts of experimental animals.

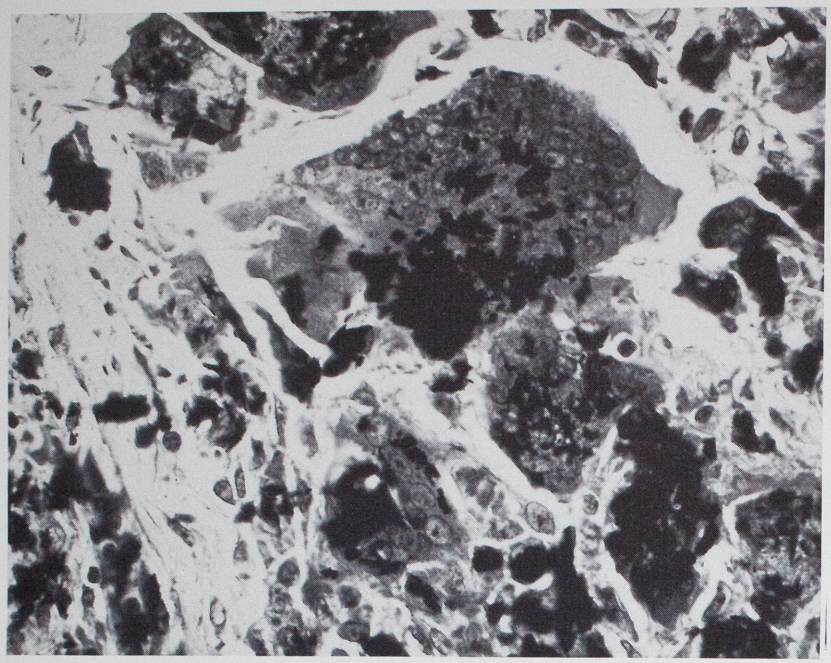

**FIGURE 34-14.** This lung section from a graphite worker shows giant cells with as many as several hundred nuclei and enclosed graphite crystals in cytoplasm. (H & E stain; high magnification; courtesy of F.A. Jaffe, M.D., U.S. Public Health Services, Chevy Chase, MD.)

## *Coke Oven Operators*

Coke is mainly used as fuel for blast furnaces to extract iron from iron ore. Coal is converted into coke by heating. Coke oven gas, one of the products of this process, is inhaled by those who work on the sides and on the tops of the ovens. The carbon that is inhaled from the emissions frequently forms anthracotic macules in the workers' lungs. A variety of gases and organic compounds, including benzopyrene and other aromatic hydrocarbons, are admixed with the carbon.

Some of the workers exposed to coke oven gas develop chronic bronchitis and, when the exposure is protracted, progressive signs and symptoms of centrilobular emphysema. Overall, their loss of pulmonary function as measured by $FEV_1$ may be as great as the losses produced by cigarette smoking.[126] Just as with cigarette smoking, constitutional factors play a role, because one worker may become disabled at a young age, whereas a peer, working under similar conditions, can continue until normal retirement age without signs or symptoms of pulmonary impairment.

Cytologic examinations of sputum conducted over a period of years in coke oven operators have shown correlations between the presence of inflammatory cells, reactive bronchial epithelial cells, metaplastic changes in bronchial lining cells, and decreases in $FEV_1$.[126] These findings suggest that an inflammatory process contributes to the development of the bronchitis and emphysema that are responsible for the progressive decrease in pulmonary function. The gaseous emissions from coke ovens contain many carcinogenic chemicals in addition to carbon. Studies in the United States have found that coke oven operators have an increased mortality due to carcinoma of the lung.[112] This risk has been much lower in Europe, perhaps because the exposures to benzene and other carcinogens are lower around European coke ovens.[127]

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