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Seminars in
ROENTGENOLOGY

Imaging Of Occupational Lung Diseases

Kiran Batra, MD,* Muhammad U. Aziz, MD,* Traci N. Adams, MD,† and J. David Godwin, MD‡

Introduction

Occupational lung diseases (OLDs) are a unique group of lung diseases specifically related to work environment following exposure to dust, chemicals, or proteins. Despite safety standards issued by the Occupational Safety and Health Administration, the National Institute of Occupational Safety and Health, and other organizations, OLD remains one of the most common work-related injuries, responsible for about 70% of all deaths from all occupational diseases.[1,2] Diagnosis of occupational lung disease requires documented exposure to an agent known to cause disease and a sufficient latency period between exposure and onset of that disease. Airway-related respiratory disease is the largest category of OLD, and occupational exposures contribute substantially to the development or worsening of respiratory diseases such as chronic obstructive pulmonary disease and lung cancer. Computed tomography (CT) has become essential in evaluating OLD, and high-resolution CT (HRCT) findings are significantly associated with outcomes such as impairment in pulmonary function and mortality.[3,4]

This article reviews the radiographic and CT findings of the classic mineral dust pneumoconioses caused by inhalation of silica, coal dust, asbestos, beryllium, talc, and hard metal. We include the organic dust pneumoconiosis caused by inhalation of cotton dust (byssinosis).

Silicosis

Silicosis is an ancient, uncurable lung disease caused by inhalation of crystalline silicon dioxide dust. Occupations exposing workers to silica dust include sandblasting, polishing, porcelain enameling, foundry and masonry work, and quarrying of sand, gravel, and limestone.[5,6] Recently, denim sand blasting and hydraulic fracking for extracting natural gas[7] have emerged as new sources of exposure, with many of the patients experiencing rapid progression and complications.[8] Occupational exposure to crystalline silica dust is also linked with systemic autoimmune diseases, such as systemic lupus erythematosus, systemic sclerosis, and rheumatoid arthritis.[9]

Because of its long latency period, silicosis affects mostly older workers. Silicosis developing in a younger adult (15-44 years of age) suggests acute or accelerated disease. Despite established and effective control strategies, new cases and epidemics still occur throughout the world.[10] In a recent report from the Occupational Safety and Health administration, air samples at 11 fracking sites in five states in the United States showed silica levels 47% greater than the permissible exposure limits.[11]

Mediastinal and hilar lymphadenopathy may be the earliest manifestation of lower levels of silica exposure; it develops in about 75% of cases. Egg-shell calcification is found in two-thirds of cases, but is not specific for silicosis; it also occurs in sarcoidosis, amyloidosis, chronic beryllium disease (CBD), and mycobacterial infection. Chronic ingestion of sharp silica particles can lead to chronic esophageal inflammation, ulceration, and even esophagobronchial fistula.

Silica exposure causes 4 types of lung disease: simple silicosis, complicated silicosis, accelerated silicosis, and acute silicoproteinosis.

Simple silicosis occurs after 10-20 years of low-to-moderate exposure and typically does not cause symptoms or respiratory impairment. It manifests as well-defined, solid nodules that are 2-5 mm in diameter and that concentrate in the apical and posterior upper lung zones. Sometimes the nodules calcify (Fig. 1). On CT, the nodules have a centrilobular or perilymphatic distribution. Small airway disease may be earliest manifestation of silicosis, manifesting as air-trapping on expiratory CT;[12] the extent of air-trapping correlates with the degree of obstruction on spirometry.[13] Coalescence of subpleural nodules results in pseudoplaques (Fig. 1). Actual pleural thickening or pleural effusion occurs occasionally.[14]

Complicated silicosis or progressive massive fibrosis (PMF) occurs more commonly with silicosis than with coal workers'

*Department of Radiology, University of Texas Southwestern Medical Center, Dallas, TX.
†Department of Pulmonary and Critical Care Medicine, University of Texas Southwestern Medical Center, Dallas, TX.
‡Department of Radiology, University of Washington Medical center, Seattle, WA.
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Address reprint requests to Kiran Batra, MD, Department of Radiology, University of Texas Southwestern Medical Center, Dallas, TX. E-mail: kiran.batra@utsouthwestern.edu

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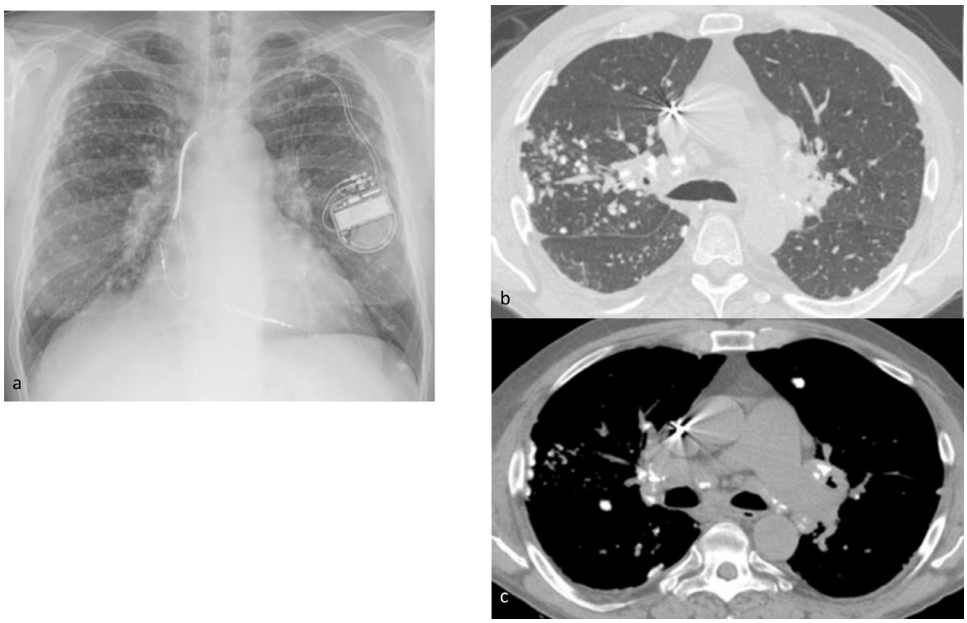


Figure 1 Simple silicosis in a 44-year-old former sandblaster. (a) Radiograph shows silicotic nodules with some concentration in the right upper lobe. The nodules are dense because of calcification. (b) CT with lung window shows the calcified and noncalcified small nodules. (c) CT with soft-tissue window shows subpleural coalescence of the calcified nodules near the right axilla, forming a pseudoplaque.

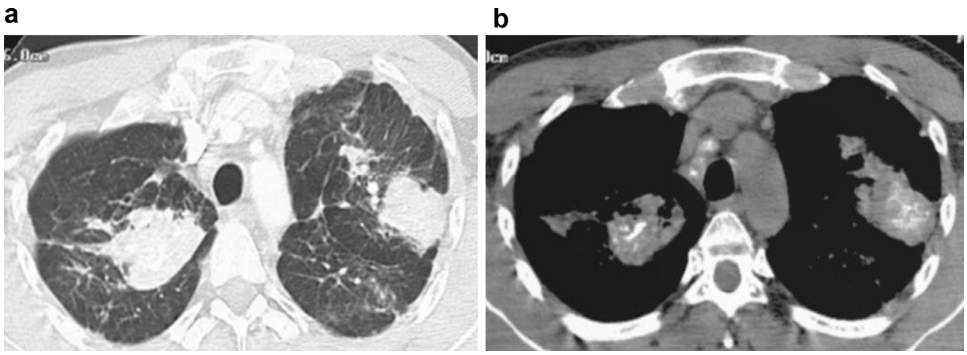


Figure 2 Complicated silicosis with PMF in a tile cutter. (a) CT shows conglomerate masses in both upper lobes with distortion of surrounding lung architecture and paracicitricial emphysema, particularly on the left. (b) CT with soft tissue window shows calcification in the conglomerate masses and in mediastinal lymph nodes.

pneumoconiosis, since silica is more fibrogenic than coal dust. PMF develops from coalescence of small silicotic nodules into conglomerate nodules and masses of greater than 1 cm in diameter (Figs. 2 and 3).

The masses are typically bilateral and symmetrical and located in apical and posterior segments of upper lobes on a background of small silicotic nodules. Their lateral margins are often smooth and parallel to the chest wall. Over time, they may migrate from the periphery centrally toward the hila, leading to a rim of paracicatricial emphysema laterally between the opacities and the pleura. The masses can calcify (Fig. 2) or cavitate (Fig. 3); cavitation results from ischemic necrosis or complications such as tuberculosis or lung cancer.[15,16]

Silicosis is a risk factor for development of lung cancer (Fig. 4), emphysema, and lung fibrosis[17] (Fig. 5). Large fibrotic masses secondary to PMF may mimic lung cancer on CT. MRI may be helpful in distinguishing these masses from lung cancer as fibrosis shows a low-signal intensity on T2-weighted imaging as compared to lung cancer, which shows high signal on T2-weighted imaging.[18,19]

Accelerated silicosis occurs with high-intensity exposure to silica dust; its latency is short, only about 4-10 years. Progressive fibrosis may continue even after exposure has ceased; signs and symptoms are similar to those of complicated silicosis.

Acute silicosis (silicoproteinosis) is rare, occurring mostly in sand blasters working with inadequate protection; it can develop within days of exposure and can lead to permanent intestitial scarring in as little as 1-3 years after high-intensity exposure. Histopathologic findings are similar to pulmonary alveolar proteinosis, since the high dust burden causes type II pneumocytes to proliferate and overproduce surfactant, which fills the airspaces. HRCT shows ground-glass opacity, crazy paving, centrilobular nodules, and consolidation (Fig. 6). Silicoproteinosis can lead to respiratory failure, cor pulmonale, and death.[20]

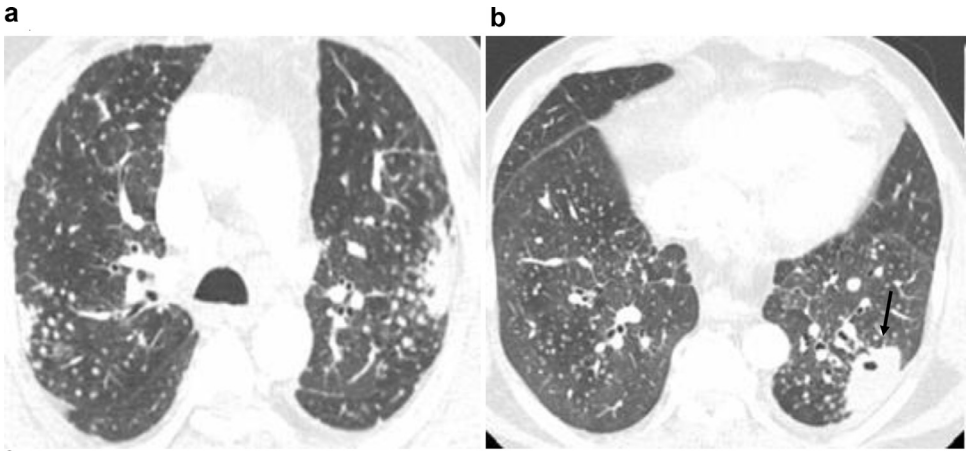


Figure 3 Complicated silicosis in a 54-year-old man with history of sandblasting. (a) CT with lung window shows small discrete centrilobular nodules and coalescence of subpleural nodules, forming pseudoplaques. (b) The 3.5 cm cavitary nodule (arrow) in the left lower lobe raises the question of tumor, tuberculosis, or lung cancer. After negative biopsy and culture, the lesion was considered to be a sterile cavitary conglomerate mass.

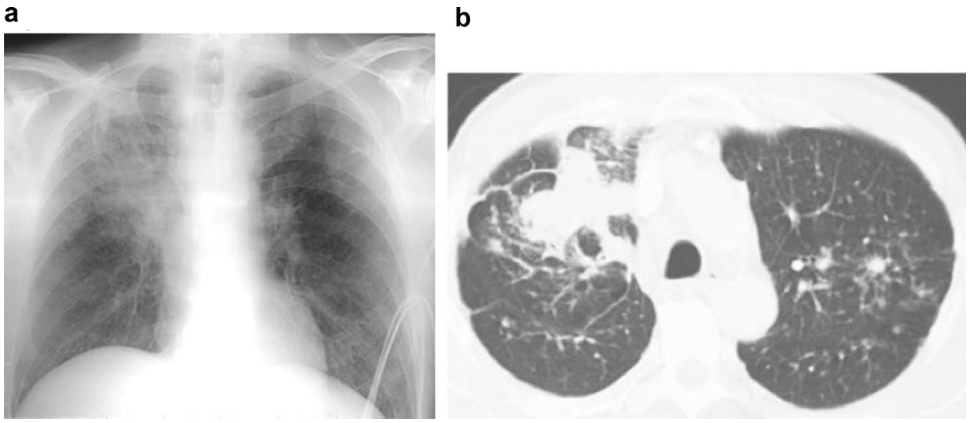


Figure 4 Lung cancer in a man with silicosis. (a) Radiograph shows ill-defined tumor above the right hilum. The amorphous shape of the tumor helps distinguish it from a large pneumoconiotic opacity. (b) CT shows the right upper lobe tumor and also small silicotic nodules in both upper lobes with some coalescence on the left.

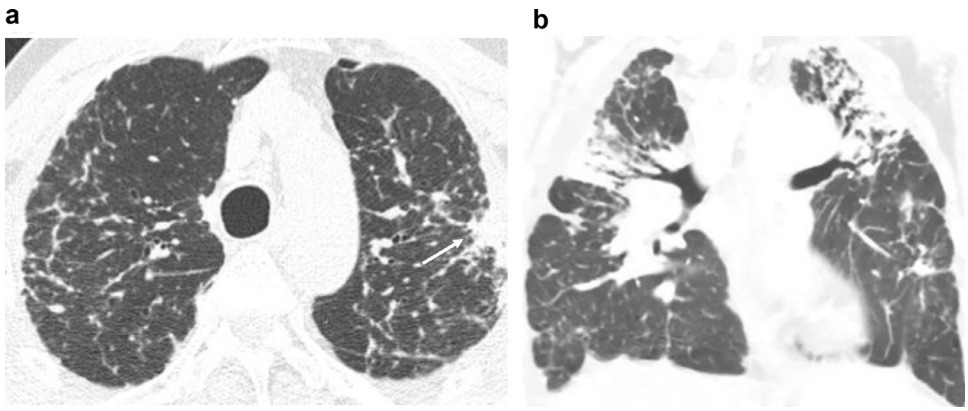
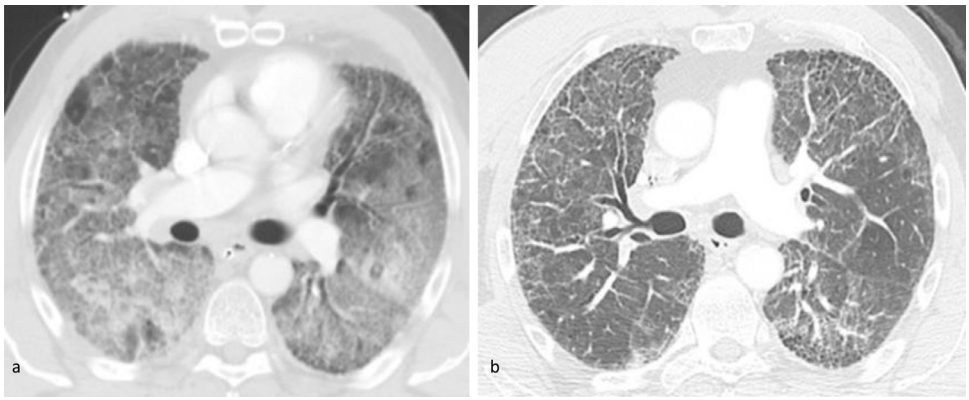


Figure 5 Silicosis progressing to PMF in a 74-year-old stone mason. (a) CT shows small nodules in peribronchial and subpleural distribution. Confluent subpleural nodules form a pseudoplaque (arrow) in the left upper lobe. (b) Four years later, conglomerate masses have developed with architectural distortion and traction bronchiectasis in the upper lobes.



Fugure 6 Acute silicosis (silicoproteinosis) in a 55-year-old man, who was sandblasting in a confined space. (a) CT shows diffuse ground-glass opacity with reticulation (crazy paving). (b) CT 2 weeks later shows some clearing.

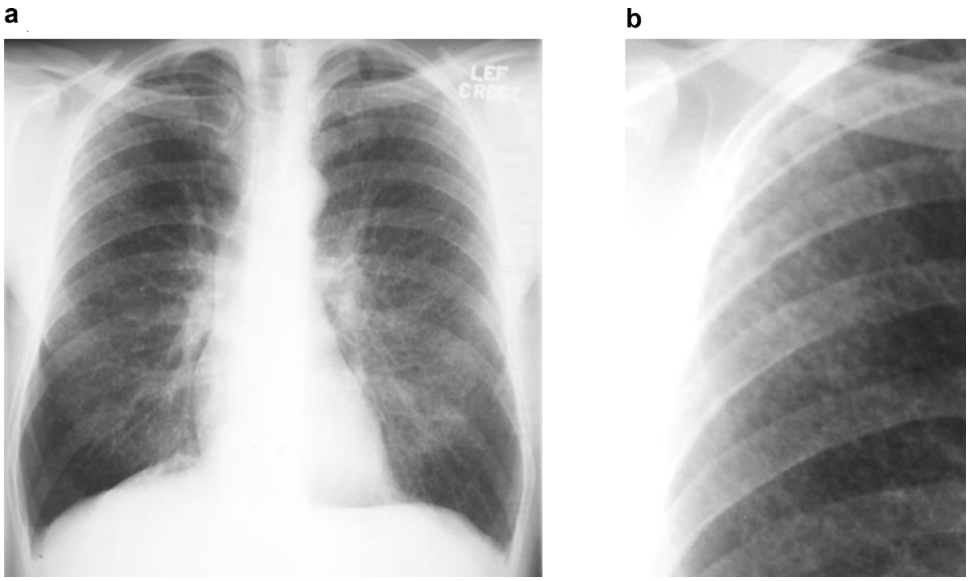


Figure 7 Simple coal workers' pneumoconiosis in a West Virginia miner. (a) Radiograph shows small nodules concentrated in upper lobes, particularly in the right upper lobe. (b) Close-up better shows the small nodules. The small nodules in coal workers' pneumoconiosis are often less distinct than those in silicosis.

Coal Mine Dust Lung Disease

Coal mine dust lung disease includes classical coal workers' pneumoconiosis (CWP) and its severe and potentially fatal form, complicated CWP or progressive massive fibrosis (PMF). Coal mine dust lung disease also includes mixed—dust pneumoconiosis from inhaled coal, silica, kaolin, and mica. Coal mine dust containing high concentrations of respirable silica and silicates can cause rapidly-progressive pneumoconiosis in miners.[21] Chronic bronchitis, emphysema, and dust—related diffuse fibrosis are additional lung diseases associated with exposure to coal mine dust.[22]

Coal Workers' Pneumoconiosis

Coal workers' pneumoconiosis (CWP) is another preventable but incurable lung disease that can lead to respiratory failure and death. The introduction of the Federal Coal Mine Health and Safety Act in 1969 decreased the prevalence of CWP among underground coal miners from 11.2% during 1970-1974 to 2.0% during 1995-1999, but prevalence has recently risen.[23] The rise has been attributed to modern mining technology that grinds rock faster and generates more dust; also the dust in modern mining may contain a greater proportion of crystalline silica than in the past because the coal seams are thinner; and the miners often work longer shifts at the face of the mine.[22]

The latency period for development of CWP ranges from 6 to 20 years. Development of CWP depends on the hardness of the coal, the method of mining, the amount exposure to coal and other mineral dusts, and the degree of protection used.[24] Coal dust accumulation in lung tissue can range from mild airways anthracosis to irreversible lung fibrosis and emphysema.[25]

Coal dust accumulating in distal bronchioles is engulfed by alveolar and interstitial macrophages (0.5-6 mm); dense collagen fibers are deposited in the walls of the respiratory

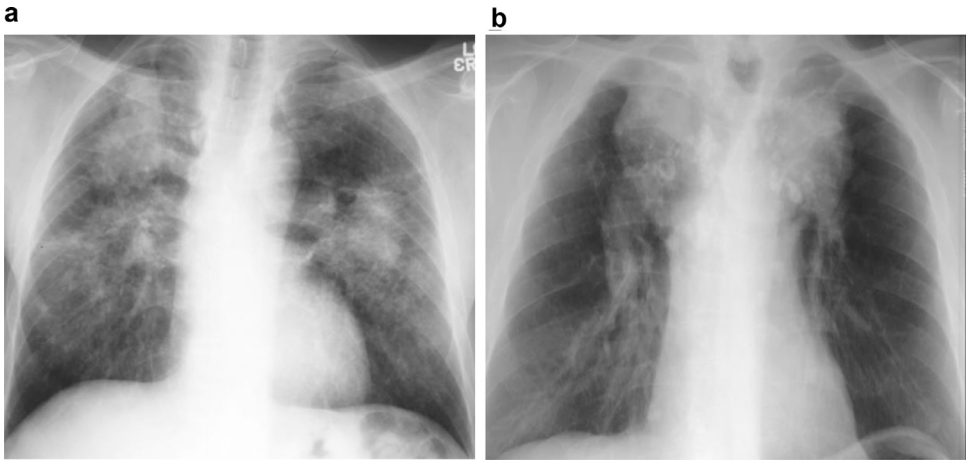


Figure 8 Complicated coal workers' pneumoconiosis in 2 West Virginia miners. (a) Radiograph shows bilateral conglomerate masses in upper and central lungs. There is a background of small pneumoconiotic nodules. (b) Radiograph shows progressive massive fibrosis (PMF) with distortion. The profusion of small nodules decreases as they are coalasced into the conglomerate masses. Note the calcification of mediastinal and hilar lymph nodes, in both solid and egg-shell patterns.

bronchioles and alveoli, forming coal macules and nodules with surrounding emphysema.[26]

Simple CWP. On radiographs, simple CWP manifests as well-defined round, diffuse nodules, and reticulonodular opacities with an upper and midlung predominance (Fig. 7). The right lung predominance has been attributed to differences in lymphatic clearance,[24] but alternatively could reflect greater deposition in the right lung because of the shorter airway. Compared to silicosis, the nodules are typically smaller and less well defined. The nodules tend to involve the apical and posterior segments of the upper lobes and superior segments of the lower lobes; they calcify in about one-third of the cases. Coalescence of peripheral nodules can lead subpleural pseudoplaques, as in silicosis. Mediastinal and hilar adenopathy is present in less than one-third of the cases.[9,10] Egg-shell calcification (Fig. 8) is less frequent than in silicosis.

Complicated CWP. PMF in the setting of CWP is less common than in silicosis, probably because coal dust is less fibrogenic than silica. The large opacities in CWP contain mineral dust, calcium salts, and proteinaceous material. On microscopy, they differ from those caused by silica by the presence of coal dust and absence of silicotic nodules.[27,28]

On CT, PMF is characterized by one or more large (>1 cm) masses that usually form peripherally and eventually migrate toward the hila (Fig. 9). The masses are round or lentiform, and their lateral borders parallel the chest wall. As in silicosis, small nodules decrease in number as the fibrotic masses enlarge, and paracicatrial emphysema develops lateral to the masses; the masses may calcify, and they can cavitate, reflecting ischemia or infection, especially tuberculosis.

As in complicated silicosis, MRI can help distinguish PMF from lung cancer, not only by different behavior on T1- and T2-weighted imaging, but also by the slower and more prolonged contrast enhancement of PMF masses (up to 15 minutes), compared to the more rapid enhancement of lung cancers.[20,29-32]

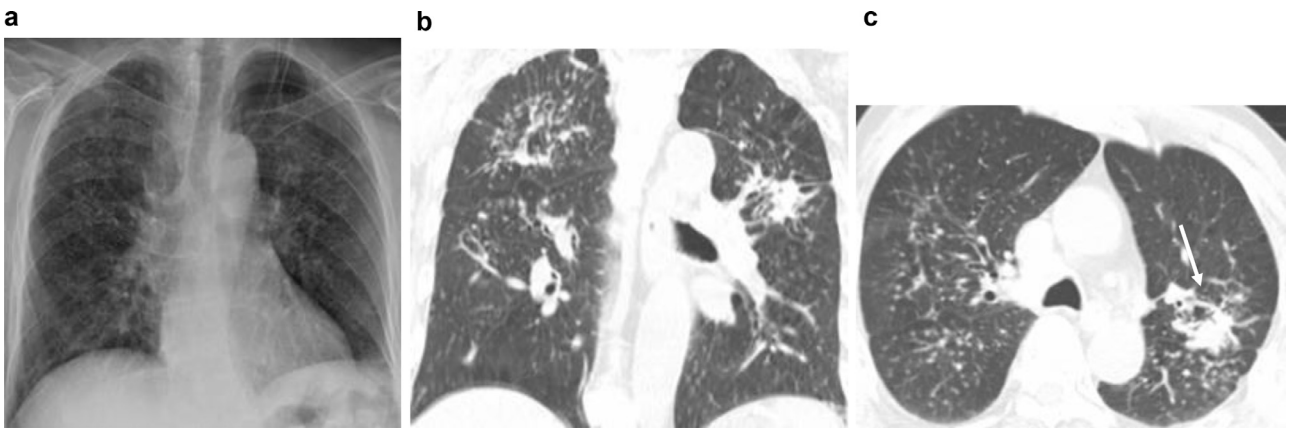


Figure 9 Complicated coal workers' pneumoconiosis in a miner. Radiograph (a) shows numerous small calcified and noncalcified nodules in the upper and midlungs. Coronal (b) and axial (c) CT images show small nodules and a conglomerate mass (arrow) in the superior segment of the left lower lobe.

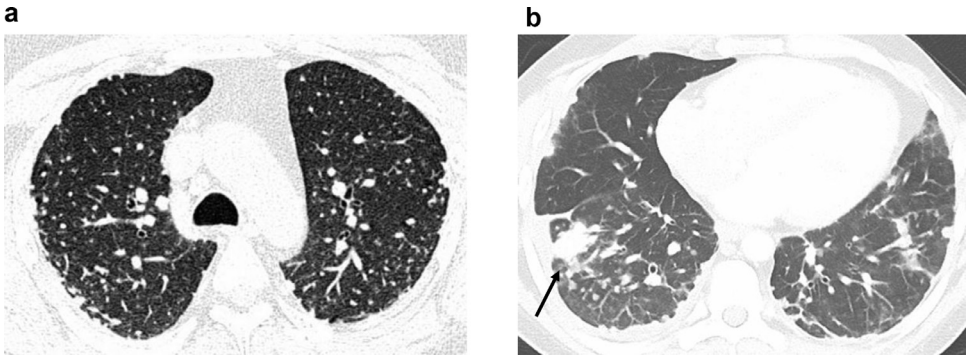


Figure 10 Caplan syndrome in a 33-year-old man with rheumatoid arthritis and silicosis. CT through upper (a) and lower (b) lungs shows small nodules in centrilobular and subpleural distribution and a basal rheumatoid nodule (arrow), confirmed by biopsy.

Exposure to coal dust or to silica predisposes to rheumatoid arthritis. Caplan syndrome (rheumatoid pneumoconiosis) is the presence of 1 or more rheumatoid lung nodules in the setting of coal workers' pneumoconiosis or silicosis (Fig. 10). The nodules range in diameter from 0.5 cm to several centimeters; they have a peripheral preponderance, they may cluster, and they may progress or regress over time.[24] Histologically, rheumatoid nodules consist of central necrosis surrounded by collagen, polymorphonuclear cells, and a few macrophages. Similar nodules can follow exposure to asbestos, carbon, and dolomite.

Dust-related Diffuse Fibrosis (DDF). DDF has been described recently in 15%-20% of autopsies of coal workers.[33] The finding of intra-alveolar silica or silicate particles and anthracotic pigment-laden macrophages combined with interstitial fibrosis constituted a newly recognized disease: coal mine dust desquamative chronic interstitial pneumonia, which can lead to both fibrosis and emphysema.[29,33] DDF can resemble idiopathic pulmonary fibrosis (IPF) but has a better prognosis.[27] HRCT findings are diffuse interlobular septal thickening; histologic findings are anthracotic nodules with pigment, inflammation and bridging fibrosis connecting macules.[33]

Mixed-dust Pneumoconiosis (MDP). Mixed−dust pneumoconiosis occurs secondary to concurrent exposure to silica and less fibrogenic dusts, such as coal or iron.[30,31] A proposed MDP definition is pneumoconiosis with mixed-dust macules and fibrotic nodules with or without silicotic nodules in a worker with exposure history to mixed dust.[28] MDP can develop in quarry workers, metal miners, and foundry workers, among others. Unlike silicosis, the imaging findings are basal-predominant fibrosis that resembles IPF.

Asbestosis

Asbestos is a naturally occurring mineral composed of fibrous silicates. Its durability, tensile strength, and resistance to high temperature make it useful in mining, milling, construction, shipping, friction products (such as brakes), and in talc products.[33] Paraoccupational exposure occurs, for instance to family members when a worker brings home dust in hair or clothing.[34] Nonoccupational exposure during home renovation or car maintenance also occurs. Environmental exposure results when natural deposits become airborne and dust is inhaled.[35]

In the United States, asbestos use has been limited since the 1970s, but asbestos is still allowed in automotive brake pads and gaskets, roofing products, and fireproof clothing. Because of its long biopersistence, asbestos continues to be responsible for benign and malignant diseases. Despite the decline in the use of amphiboles, the peak in incidence of asbestos−related disease is not expected until the decade after 2020.[36]

The 6 types of regulated asbestos fibers include chrysotile and 5 types of amphibole minerals: amosite, crocidolite, actinolite, anthophyllite, and tremolite. There is some controversy about the definition of asbestos, given that some other minerals, such as erionite (used in home construction in Turkey) are associated with the same diseases as asbestos, including mesothelioma.[37]

Chrysotile (known as white asbestos), whose fibers have a serpentine shape, accounts for 90% of the asbestos used in the United States. Amphiboles, whose fibers have a long, rigid, rod-like shape, are considered more fibrogenic and carcinogenic. Crocidolite (known as blue asbestos) and amosite are the most common amphibole asbestos fibers in use. Mined minerals such as vermiculite can also contain significant amounts of amphiboles.[38]

Inhaled asbestos fibers initially accumulate in alveoli and respiratory bronchioles and then penetrate into the interstitium and pleura. Compared to serpentine fibers, amphibole fibers clear more slowly from the lungs, and possibly because of their rigidity and needle-like shape, the fibers can reach the pleural surface more easily.[39]

Asbestos exposure has been linked to malignancies, particularly pleural mesothelioma.[40] The latency period for mesothelioma may be as short as 10 years, but is typically longer than 30 years. Asbestos exposure increases the risk of lung cancer and some other cancers.[40] If the worker is also a cigarette smoker, the risk of lung cancer is more than additive.[41] Low-dose CT is appropriate to screen for early-stage lung cancers in asbestos-exposed workers.[41]

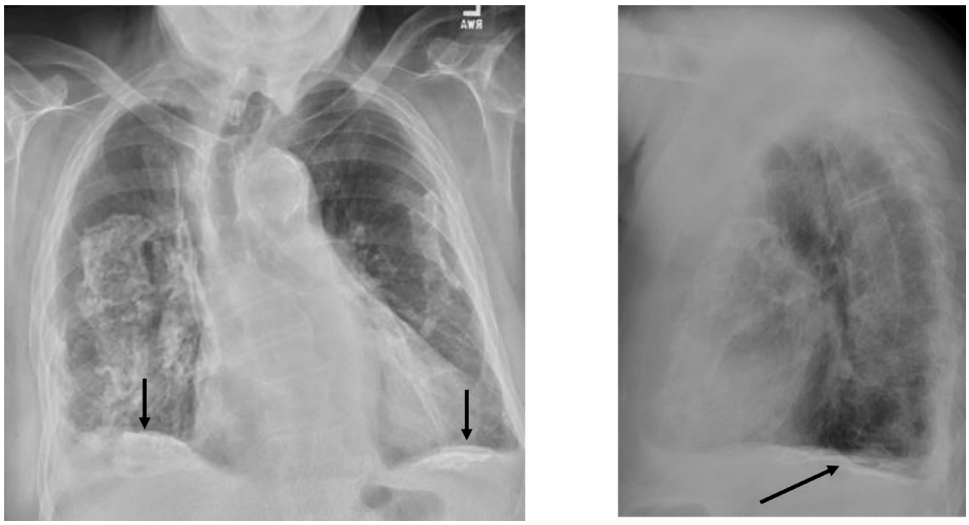


Figure 11 Asbestos pleural plaque in a 90-year-old man who worked cutting asbestos boards 40 years earlier. PA and lateral radiographs show extensive en face and diaphragmatic (arrows) calcified plaque. The lateral view shows that most of the calcified plaque is anterior. The white border of en face plaque has been called the "rolled edge" sign. There is also diffuse pleural thickening on the right with blunting of the costophrenic angle.

Three requirements have been set by the American Thoracic Society for the clinical diagnosis of benign asbestos-related thoracic disorders.[42,43] First is histologic or imaging evidence of asbestos exposure, such as pleural plaques, thickening or effusion on imaging or asbestos bodies or fibers on microscopy. Second is documentation of occupational or environmental exposure. Third is exclusion of alternative explanations for the pleural or pulmonary abnormalities.

Asbestos-Related Pleural Abnormalities

Benign asbestos-related pleural abnormalities include pleural plaque, pleural thickening, and pleural effusion.

Pleural Plaques are discrete, well-demarcated patches of hyaline fibrosis, composed of acellular collagen. They develop predominantly on the parietal pleura, but occasionally on the visceral pleura, including the fissures. Plaque usually develops from 10 to 30 years from initial exposure, and plaque formation increases with exposure. The exposure dose required to produce plaque is lower than that required to produce lung fibrosis (asbestosis), and the latency for plaque is shorter.[44] Plaques are usually bilateral, but can be unilateral in 30% of cases. They are usually less than 1 cm thick and are located most commonly along the lateral chest wall between the sixth and ninth ribs, along the posterolateral chest wall between the 7th and the 10th ribs, and along the dome of the diaphragm, with sparing of the costophrenic angles and the apices.[45,46] Plaques calcify in about 10%-15% of cases,[24] and calcification increases over time. Most studies have shown no decrement in lung function from pleural plaques.[46,47] The presence of pleural plaque suggests that lung fibrosis that is basal-predominant and peripheral may be asbestosis.[48]

On radiographs, calcified en face plaque may resemble a holly leaf or may have a white edge called the "rolled-edge" sign (Figs. 11 and 12). CT is more sensitive and specific than radiography for identifying plaque. Calcified plaques along the chest wall are easily identified (Fig. 13), but noncalcified plaques are sometime hard to distinguish form innermost intercostal muscle. Helpful differences are that plaques are usually located along the inner surface of ribs and vertebral bodies, whereas the innermost intercostal muscle spans the spaces between the ribs; also, plaques are thicker than intercostal muscle and higher in attenuation. Prone images can help distinguish transient dependent pleural thickening from pleural plaque. Coronal and sagittal CT reformatting is useful in identification of diaphragmatic plaque if findings are not clear on transaxial images.

Plaque may cause indentation atelectasis in the adjacent lung. Since plaque does not fuse the visceral and parietal pleura together, lung mobility is not restricted during breath-

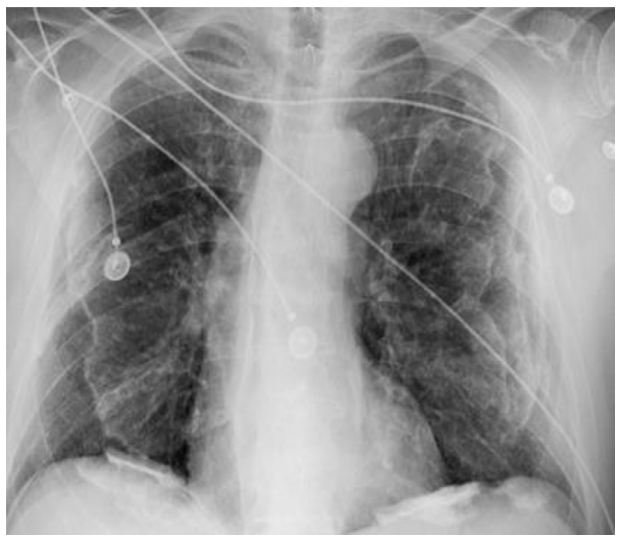


Figure 12 Asbestos pleural plaque. PA radiograph shows calcified pleural plaque along the hemidiaphragms and en face, with rolled edge sign. En face plaque can also have a "holly leaf" shape.

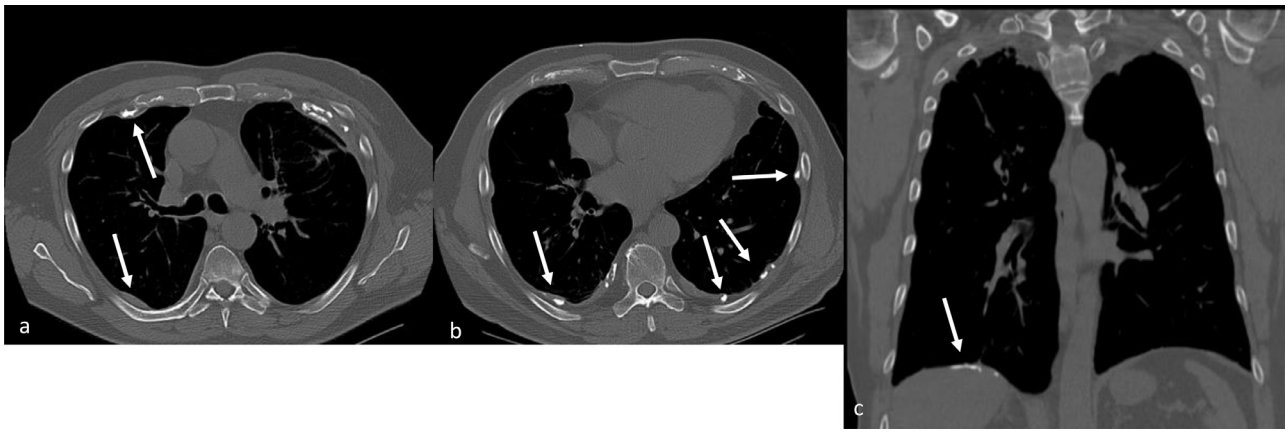


Figure 13 Calcified and noncalcified asbestos pleural plaques (arrows) in a 75-year-old man. In (b) there are also patches of diffuse pleural thickening posteriorly near the spine on both sides.

ing, so round atelectasis and parenchymal bands do not form as with diffuse pleural thickening. Prominent extrapleural fat may mimic plaque on radiographs, but fat's smooth, symmetric, and tapering contour, its extension into fissures and over the lung apices, in addition to its low attenuation on CT are distinguishing features.[24]

Diffuse pleural thickening (DPT) is said to occur in up to a quarter of workers exposed to asbestos,[49] but is not so common in our experience. It usually develops as pleural effusion resolves in the setting of benign asbestos pleural effusion (below). Unlike plaque, DPT fuses the visceral and parietal pleural layers together, causing functional impairment by restricting lung motion. Unlike plaque, DPT causes blunting of the costophrenic angle.

Both pleural effusion and diffuse pleural thickening have many more common causes than asbestos exposure, but asbestos etiology should be considered when effusion or thickening develops in a patient who also has pleural plaque.

DPT has been defined by Lynch et al as having thickness of 3 mm or more and extent of 5 cm or more in the transverse dimension and 8 cm or more in the craniocaudal dimension.[49] Other proposed CT definitions of DPT include uninterrupted pleural thickening of 3 mm or greater thickness, involving up to 25% of the chest wall, and blunting the costophrenic angle.[24] DPT is usually less than 1 cm in thickness, and usually does not calcify (Figs. 14 and 15).

By contracting the surface of the adjacent lung, DPT causes parenchymal bands and round atelectasis to form, which may resolve after decortication. Round atelectasis is the most common cause of a mass-like opacity in patients with asbestos exposure.[49] It occurs adjacent to pleural thickening and manifests as a peripheral mass with curvature of lung vessels and bronchi toward the mass (the "comet tail" sign; Fig. 14). This morphology is usually sufficient to distinguish round atelectasis from tumor. Another helpful finding on CT is that after contrast injection, round atelectasis enhances more strongly than most tumors. On PET-CT, round atelectasis is usually not FDG-avid.[46]

The differential diagnosis of asbestos-related DPT includes hemothorax from trauma or surgery, pleural infection (including tuberculosis), drug reaction, autoimmune disease (such as rheumatoid arthritis), and uremia.[50]

Benign pleural effusion can occur early as early as 5 years, but as late as 20 years, after exposure. Effusion develops in 3% to 7% of exposed persons, but may go unrecognized if symptoms are minimal. Asbestos bodies or fibers are sometimes detected by light microscopy, and chrysolite fibers can be occasionally detected by electron microscopy of a pleural

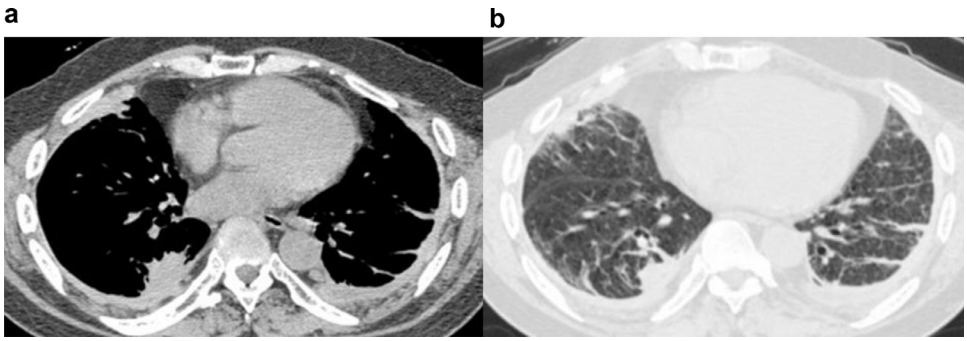


Figure 14 Diffuse pleural thickening from asbestos exposure. (a) CT with soft tissue window shows bilateral diffuse pleural thickening. (b) CT with lung window better shows the parenchymal bands on both sides and the round atelectasis with comet tail sign of curved vessels on the right. Lung bands and round atelectasis form when pleural thickening contracts the surface of the lung; they may resolve after decortication.

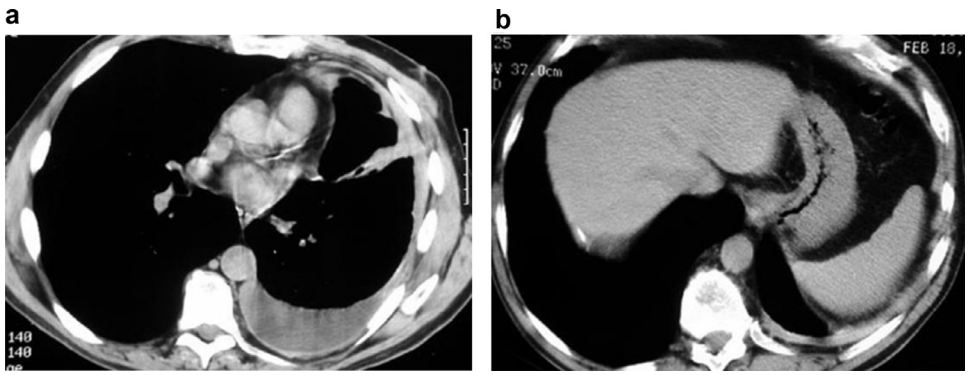


Figure 15 Asbestos pleural effusion leading to diffuse pleural thickening in a 78-year-old man. (a) CT shows left pleural effusion with mild parietal pleural thickening. (b) CT a few months later shows resolution of effusion, but development of diffuse left pleural thickening. There is a small calcified pleural plaque along the right hemidiaphragm.

biopsy. The effusion is exudative and often hemorrhagic. It can be unilateral (Fig. 15) or bilateral, and it typically resolves without treatment within 3-4 months.[41,47] Persistent or recurrent pleural effusion, especially if accompanied by chest pain, raises the concern for mesothelioma.

Lung Fibrosis (Asbestosis)

The term asbestosis should be reserved for the lung fibrosis caused by asbestos exposure; it should not be applied to pleural plaque, thickening, or effusion. Asbestosis usually develops 15-20 years or more after initial exposure. The degree of fibrosis is linked to duration and intensity of exposure to dust.[51] Asbestosis is basal-predominant on radiographs. On HRCT, it has a similar pattern to usual interstitial pneumonia, but subpleural dots and branching opacities and parenchymal bands are more common than with IPF, and honeycombing is less common[52] (Fig. 16). As with IPF, prone imaging helps distinguish fibrosis from dependent atelectasis.

Although the presence of pleural plaques suggests that fibrosis may be asbestosis, it is possible for a patient with asbestos plaque to also develop IPF or another kind of lung fibrosis, such as chronic hypersensitivity pneumonitis.

CT-pathologic correlation has shown that interlobular lines correspond to septal thickening and edema, intralobular lines to peribronchial fibrosis, and subpleural dots and lines to fibrosis.[48] Parenchymal bands reflect fibrosis and atelectasis along peribronchovascular bundle sheaths or tandem interlobular septal thickening, and subpleural curvilinear lines suggest peribronchial fibrosis and collapse of the alveoli, but in our experience they sometimes reflect atelectasis, as shown by their resolution when the patient is repositioned prone.

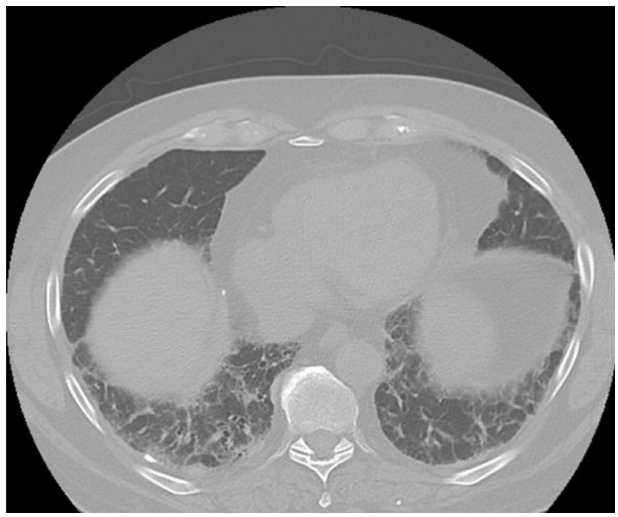


Figure 16 Asbestos pleural plaque, pleural thickening, and lung fibrosis (asbestosis) in a 73-year-old man. CT shows small calcified pleural plaques posteriorly at the right base and along the right hemidiaphragm. There is also diffuse pleural thickening on the right. The subpleural fibrosis, worse on the right than the left, causes mild traction bronchiectasis and, in the presence of asbestos plaque, is consistent with asbestosis.

Mesothelioma

Mesothelioma is a rare, aggressive malignancy, most commonly arising in the pleura, less commonly in the peritoneum, and least commonly in the pericardium. CT findings (Figs. 17 and 18) of nodular and circumferential pleural thickening measuring more than 1 cm, fissural involvement, contraction of the ipsilateral hemithorax, and invasion of mediastinal structures, chest wall, or diaphragm are all common findings with mesothelioma, but none is specific, since they also occur with metastatic carcinoma, which is much more common.[47,53] Unilateral pleural effusion is a common presentation, with tumor becoming visible only weeks or months later. As tumor becomes more extensive, pleural effusion often decreases.

Berylliosis

Beryllium is a light-weight metal used in nuclear, defense, and aerospace industries, in recreational and dental equipment, and in fluorescent lamps and neon lights.[54] More than

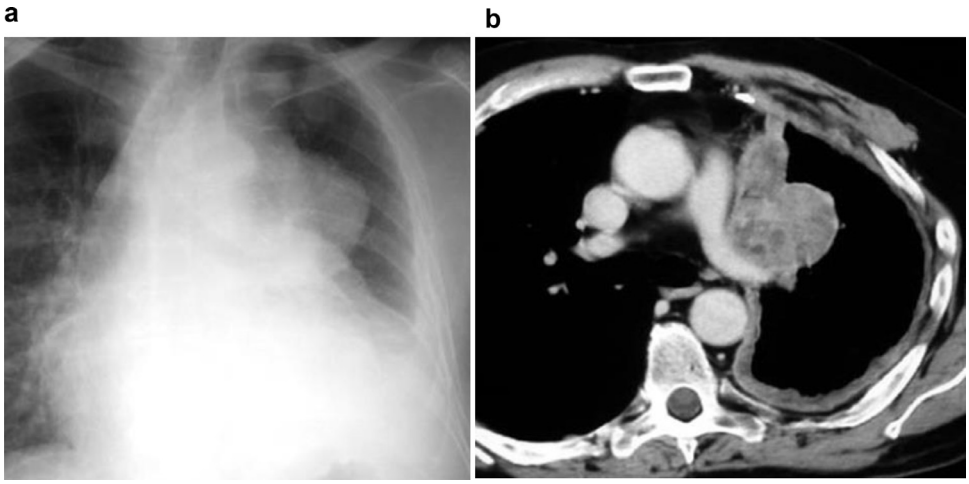


Figure 17 Mesothelioma. (a) Radiograph shows left pleural effusion and a large pleural mass along the mediastinum. (b) CT shows diffuse left pleural tumor with the large mass along the left mediastinal border. Lower levels showed left pleural effusion and right paraspinal pleural plaque from asbestos exposure.

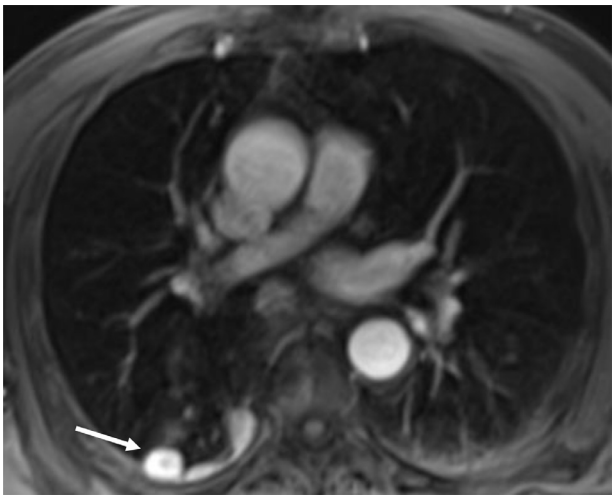


Figure 18 Mesothelioma. MRI shows enhancing pleural nodule (arrow) and paraspinal pleural tumor on postcontrast T1-weighted post contrast gradient echo image.

100,000 cases of beryllium exposure were thought to occur in the USA in the 1990s.[55]

Acute beryllium exposure leads to pneumonitis about 1-3 weeks after exposure that can be self-limited, but can progress to acute respiratory failure. Because of controls on exposure, acute berylliosis is now rare.

CBD is an immune-mediated lung condition in which activated CD4 T lymphocytes combine with macrophages to form noncaseating epithelioid granulomas. CBD develops in up a quarter of exposed subjects, months to year after initial exposure.[56] Duration of exposure to beryllium has not been shown to be linked to the onset or severity of disease.[57] Workers can be exposed not just by inhalation, but also by skin contact.[58]

CBD shares many histologic, clinical, and radiological features with sarcoidosis, and it has been suggested that as many as 6% of sarcoidosis cases actually represent CBD.[59] About 6%-8% cases of beryllium sensitization advance to CBD annually, depending on genetic susceptibility.[60,61] Symptoms of CBD include shortness of breath, chest pain, and dyspnea. Extrapulmonary involvement includes granulomatous hepatitis, hypercalcemia, skin lesions, and kidney stones. Lung function abnormalities include obstruction, restriction, and impaired gas exchange.[61]

Although the definitive diagnosis of CBD is established by the beryllium lymphocyte proliferation test on blood or on bronchoalveolar lavage fluid or by the in vivo patch test (BeS) used in distinguishing beryllium from sarcoidosis, a medically probable diagnosis is often made when a beryllium-exposed patients has consistent clinical and imaging findings.[62]

Radiographic features of CBD range from absence of findings to sarcoidosis-like findings of small nodules in mid and upper lungs, septal thickening, and hilar and mediastinal lymphadenopathy[63,64] (Figs. 19 and 20). Conglomerate masses may develop, caused by aggregation of small nodules. Hilar and mediastinal adenopathy occurs in about 40% of cases, less often than in sarcoidosis,[51] and nodes can calcify in egg-shell or amorphous patterns, as in sarcoidosis or silicosis. Advanced cases may show honeycombing, pleural irregularity, interlobular septal thickening, and scarring with architectural distortion, upward retraction of the hila, and bullae[63,64] (Fig. 21). No significant association has been seen between the degree and spectrum of radiological findings and the time interval from initial exposure and diagnosis.[65]

CT findings range from small nodules (Fig. 20) in a perilymphatic distribution along bronchovascular bundles and pleural surfaces that are concentrated in upper and mid-lungs, to septal lines, conglomerate masses, and pseudoplaques (subpleural aggregates of small lung nodules, resembling localized pleural thickening), in addition to emphysema, and bullae.[51,63] Ground-glass opacities and bronchial wall thickening reflect granulomatous infiltration. In advanced cases, fibrosis leads to traction bronchiectasis and honeycombing.[51,63]

Restriction on pulmonary function testing results from fibrosis and pleural thickening.[63] Other sequelae of CBD

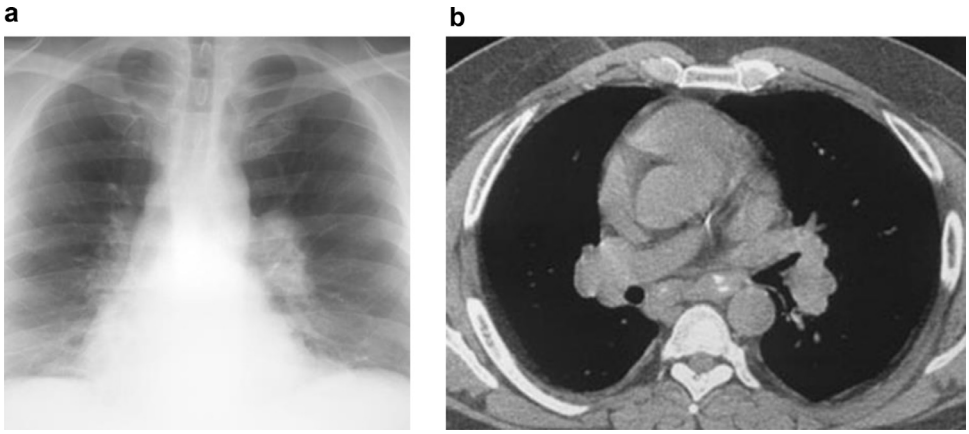


Figure 19 Berylliosis with mediastinal and hilar lymphadenopathy in a man with beryllium sensitization. (a) Radiograph shows left hilar lymphadenopathy. (b) CT shows mediastinal and bilateral hilar lymphadenopathy with some calcification.

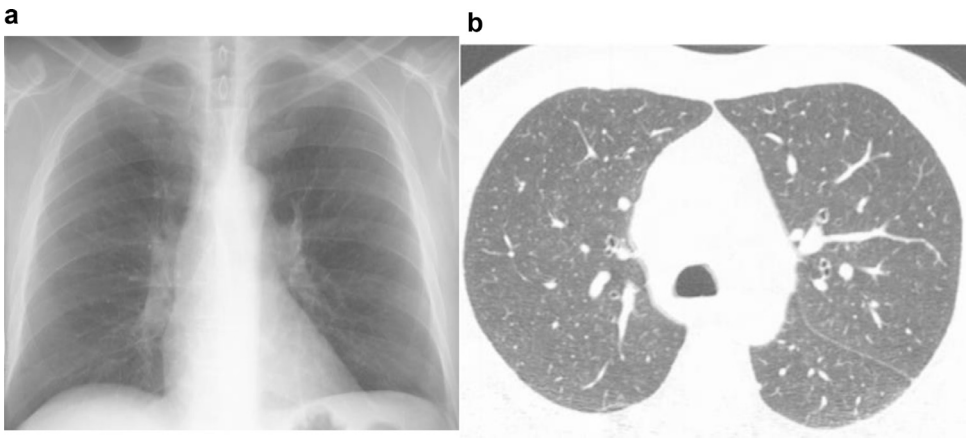


Figure 20 Berylliosis in a machinist with dyspnea and beryllium sensitization. (a) Radiograph shows clear lungs. (b) CT shows faint centrilobular nodules, suggesting bronchiolitis.

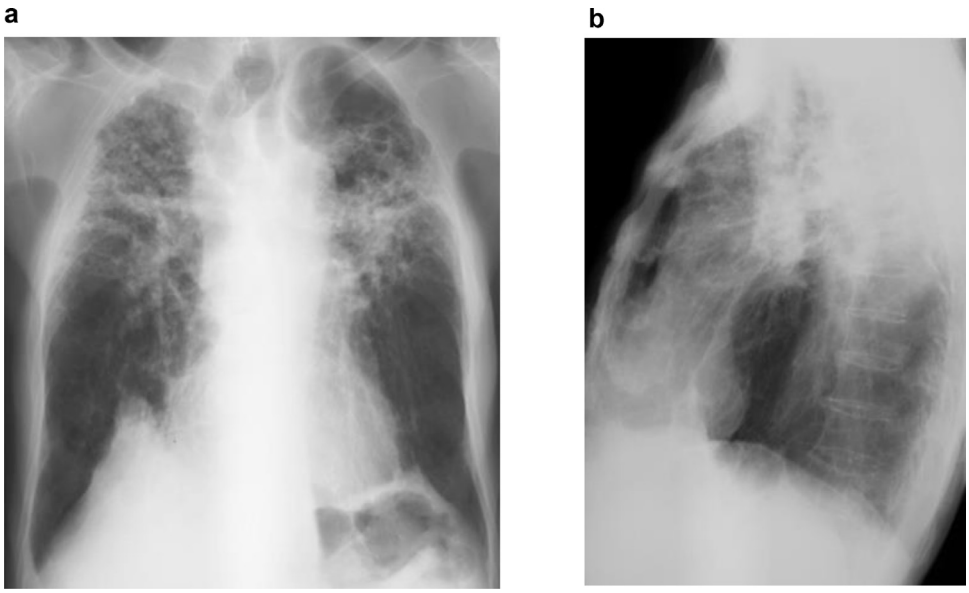


Figure 21 Chronic berylliosis in a man who worked on the Manhattan Project. (a) PA and (b) lateral radiographs show bilateral, sarcoidosis-like perihilar scarring and distortion, with tracheal buckling and juxtaphrenic peaks along both hemidiaphragms.

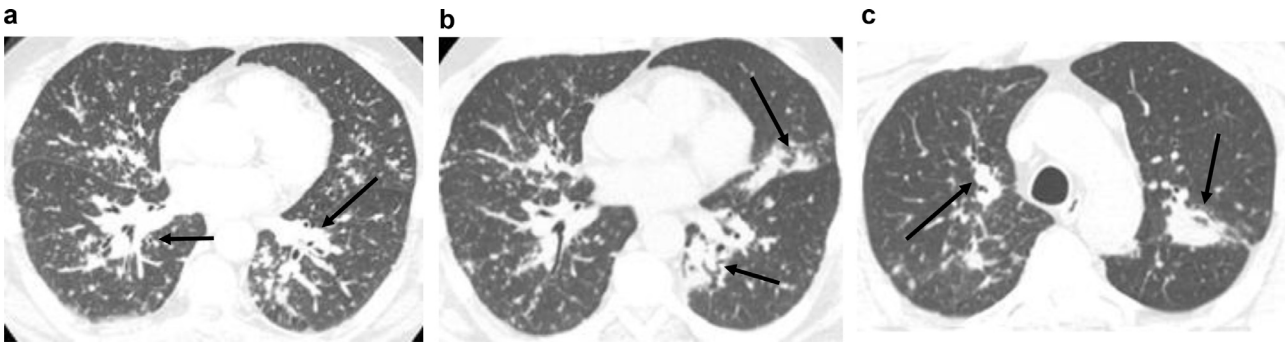


Figure 22 Inhalational talcosis in a 53-year-old man who used talcum powder every day after exercise. (a) CT shows central peribronchial thickening small peribronchial and subpleural nodules, and central conglomerate masses (arrows). (b and c) CT 3 years later shows fewer small nodules, many of which have aggregated into central conglomerate masses (arrows).

include pneumothorax, cavitary lesions, and pulmonary infection[66] CBD is also associated with lung carcinoma.[67]

Berylliosis can be self-limited, but if it progresses to fibrosis, it can be fatal, especially when complicated by cor pulmonale.[67] Corticosteroid treatment has been used to try to slow the progression of CBD.[46]

Talcosis

Talc silicates are used in industries involving rubber, leather, textiles, plastics, ceramics, and soap.[51,68] Talc can be inhaled by itself (pure talcosis) or in combination with other dusts, for instance with silica (talcosilicosis) or asbestos (talcoasbestosis) in mining.[68] Excessive use of cosmetic talcum powder can also lead to pulmonary talcosis.[69]

Talc can also reach the lungs if it is injected intravenously, for instance, when injected heroin has been cut with talc. Some drug users inject ground-up tablets intended for oral ingestion, and some tablets contain talc as the filler.[70-72]

Talc causes a non-necrotizing granulomatous reaction that may evolve into pulmonary fibrosis.[71] Injected talc leads to perivascular and intravascular granulomas, identified as a characteristic finding in intravenous talc abuse patients.[72]

Radiographic findings of inhalational talcosis include small nodules and septal thickening on radiography. The small nodules are concentrated in the upper and mid zones with sparing of the apices and costophrenic angles.[71] Nodules may coalesce into larger masses, mimicking progressive massive fibrosis.[71] If larger opacities are already visible on the initial examination, they can be expected to enlarge with follow-up.[73] Hilar adenopathy can occur.

CT findings in inhalational talcosis include small nodules (1-2 mm in diameter) in centrilobular and subpleural distributions[51] (Fig. 22). These nodules may show high attenuation, resembling calcification, because of their talc content. Confluent small nodules can create ground-glass appearance on CT. Small nodules can also coalesce into large masses with high attenuation due to talc. Emphysema, septal thickening, honeycombing (in a few cases), calcified and noncalcified pleural plaques may be present.[73]

CT findings in intravenous talcosis include large patches of consolidation and opacities in upper lobes and in perihilar regions. Hilar lymphadenopathy is uncommon.[73] Basal

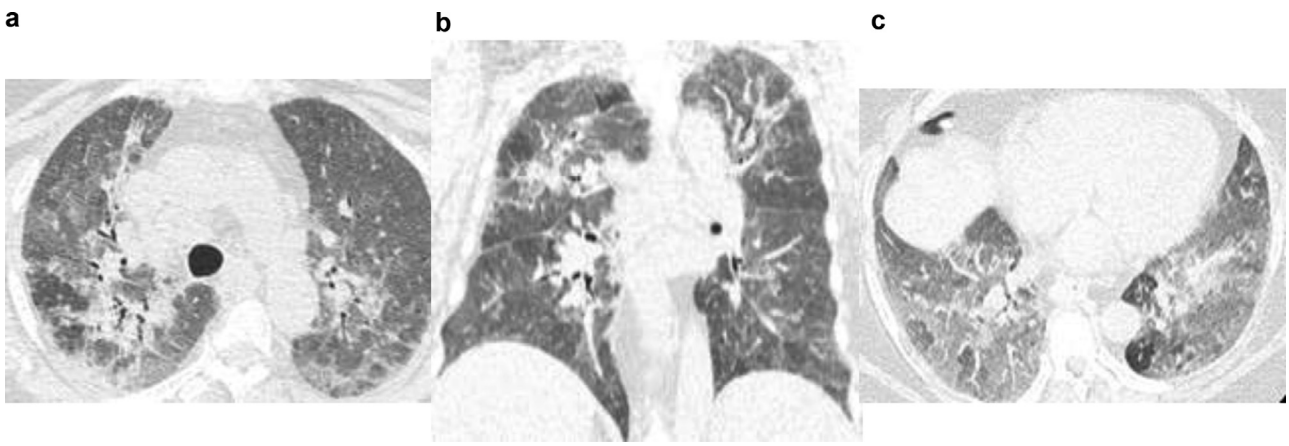


Figure 23 Hard metal pneumoconiosis from cobalt exposure. (a) Axial CT shows peribronchial fibrosis mild traction bronchiectasis with ground glass opacity and mosaic attenuation. (b) Coronal image shows the upper lobe concentration of the peribronchial fibrosis. (c) Expiratory CT shows ground-glass opacity and mosaic attenuation, reflecting lobular air-trapping.

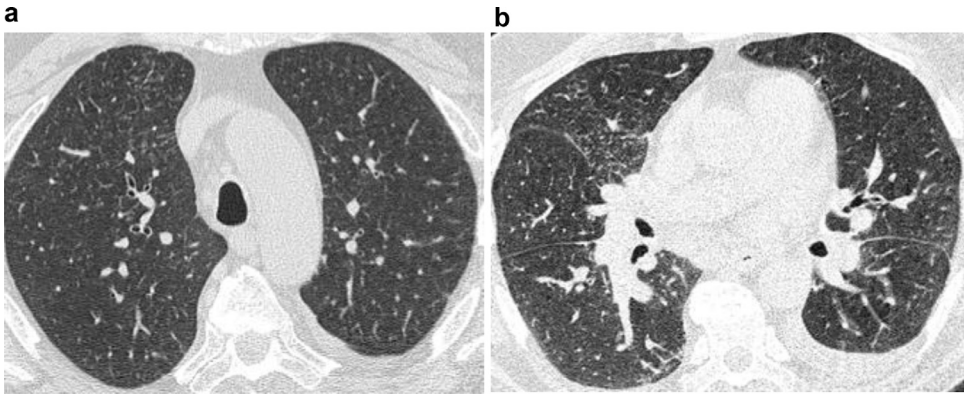


Figure 24 Byssinosis (cotton dust lung disease) in a 70-year-old cotton farmer with heavy exposure from plowing cotton fields. (a) CT shows multiple solid and ground-glass centrilobular micronodules, particularly anteriorly, and some bronchial wall thickening. (b) Expiratory CT shows lobular air-trapping in right middle lobe and left lower lobe.

panlobular emphysema similar to that of alpha-1 antitrypsin as well as paracicatrial emphysema can develop.[73]

Hard Metal Pneumoconiosis

Hard metal pneumoconiosis is caused by inhalation of hard metals, which are alloys composed primarily of cobalt and tungsten carbide. Hard metal is 90%-95% as hard as diamond, so it is used in tools for machining, grinding, cutting metal, or drilling.[74] Cobalt is considered to be the main contributor to the pulmonary damage; it is also a recognized cause of occupational asthma, constrictive bronchiolitis, hypersensitivity pneumonitis, and interstitial lung disease.[51,75,76]

Cobalt-related lung disease classically manifests histologically as giant cell interstitial pneumonia, characterized by bronchiolocentric inflammation and fibrosis containing cannabilistic multinucleated giant cells.[51,77,78] Sometimes paucicellular interstitial granulomas and well-formed sarcoid-like granulomas are found. Cobalt or tungsten detection by scanning electron microcopy is useful in making the diagnosis. Biopsy can be avoided if BAL fluid contains multinucleated giant cells and cannabilistic macrophages.

Constrictive bronchiolitis, characterized by mosaic attenuation and expiratory air-trapping on CT (Fig. 23), is the earliest imaging manifestation of cobalt related ILD.[51] CT findings are nonspecific, most commonly comprise of centrilobular nodules, ground-glass attenuation, and consolidation. In advanced fibrosis, basal and peripheral reticulation with traction bronchiectasis occur. Honeycombing is rare. Subpleural cysts may develop, corresponding histologically to hyperaerated lobules.[79]

Byssinosis

Byssinosis occurs in textile workers exposed to raw nonsynthetic textiles including cotton, jute, flax, and hemp fibers during manufacture.[80] Cigarette smoking adds to the risk that the worker will develop byssinosis. Release of endotoxins from the cell walls of gram-negative bacteria on textile fibers contributes to symptoms, as do host variations in expression of the gene for tumor necrosis. Also, inhalation of lipopolysaccharides contaminating cotton dust may influence development of lung fibrosis.[81] Although, there has been a significant decline in the number of reported deaths from byssinosis in the United States, prevalence is still high in major cotton producing countries, such as India, Pakistan, and Turkey.[82]

Byssinosis is a cause of "Monday fever," in which symptoms of chest tightness, cough, wheezing, and sputum production recur most severely on Mondays, when the patient returns to work after the weekend off.[82] Symptoms then decrease during the week to chronic low-grade baseline from continuing exposure. This pattern is different from occupational asthma, in which symptoms get worse toward the end of the week. The severity of symptoms and functional impairment are related not only to duration of exposure, but also to differing sites of deposition of cotton dust in the bronchial tree, and to differing composition of the cotton dust.

Chest radiographs show small interstitial opacities. CT shows centrilobular nodules (Fig. 24), thickened airway walls, air trapping (reflecting small airways dysfunction), and fibrosis in advanced cases. Histology shows peribronchial thickening, granulomas, and string-like foreign bodies (cotton fibers), with cellulose detectable by infrared spectrophotometry.[83] The clinical diagnosis is often difficult because symptoms are similar in asthma and other pneumoconiosis. The disease can be prevented by following strict adherence to the workplace regulations and avoidance of exposures to cotton and fabrics.

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