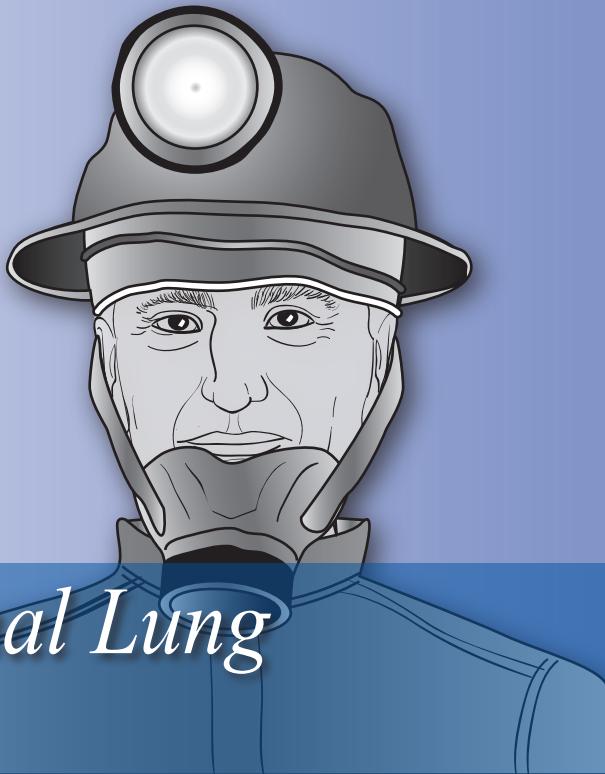


# 13



## *Occupational Lung Diseases*

Occupational lung diseases are a broad group of diagnoses caused by the inhalation of dusts, chemicals, or proteins. “Pneumoconiosis” is the term used for the diseases associated with inhaling mineral dusts. The severity of the disease is related to the material inhaled and the intensity and duration of the exposure. Even individuals who do not work in the industry can develop occupational disease through indirect exposure. Although these diseases have been documented as far back as ancient Greece and Rome, the incidence of the disease increased dramatically with the development of modern industry.

### **Whom does it affect?**

#### ***Epidemiology, prevalence, economic burden, vulnerable populations***

In most cases, these diseases are man-made, resulting from inorganic dust exposure during mining, processing, or manufacturing. In New York and New Jersey in the 1970s, asbestos could be diagnosed in over 70 percent of asbestos insulation workers with greater than 20 years of exposure (1). After the introduction of regulatory agencies and promulgation of dust regulations and their enforcement, these high prevalence rates and others dropped dramatically. For instance, the prevalence of coal workers' pneumoconiosis dropped to 5 percent among miners

with greater than 25 years' exposure (1). The pneumoconioses primarily affect those exposed at work, but environmental exposure can make others sick as well. Asbestos insulators expose their wives and children by bringing home their asbestos-covered clothing, and asbestos factories and mines expose residents of nearby neighborhoods.

Different exposures result in different diseases. With silica exposure, the classic and most common disease is chronic silicosis, which develops decades after exposure and is characterized by the silicotic nodule, predominantly in the upper lobes of the lungs, and "eggshell" calcification of the lymph nodes. These findings do not always have clinical symptoms. Higher intensity exposure can result in accelerated or acute silicosis, in which symptoms develop much earlier. Acute silicosis is the least frequent, but it also has the highest mortality rate. The accelerated and chronic forms of silicosis can become complicated silicosis or progressive massive fibrosis, in which the silicotic nodules coalesce into larger lesions in the upper lobes of the lung, and the patients develop increasing breathing difficulty.

Silicosis increases susceptibility to tuberculosis anywhere from 2- to 30-fold. There also is an association between silicosis and immune-mediated diseases, such as systemic sclerosis and rheumatoid arthritis, which may develop with silica exposure alone. Systemic lupus erythematosus has been linked to acute and accelerated silicosis. In 1996, the International Agency for Research on Cancer (IARC) classified silica as carcinogenic to humans. There is evidence to suggest that silicosis patients have an increased risk of lung cancer, but it remains uncertain whether silica exposure alone increases lung cancer risk. Finally, there is the issue of airflow obstruction. Many of these patients smoke and have concomitant occupational dust exposure, as well as chronic bronchitis, all of which can lead to increased airflow obstruction over time.

Due to poor reporting and uncertain numbers of exposed individuals, information on the exact number of persons with silicosis is limited. In the United States between 1979 and 1990, there were 4,313 deaths attributed to silicosis as the primary or a contributing cause (2). Underreporting of the disease makes it likely that it is much more common, although it is difficult to know the true prevalence.

Asbestos has been used by humans for centuries for its qualities of fire resistance, tensile strength, and malleability. Asbestos is an industrial term that describes a variety of minerals (hydrated magnesium silicates) that break into fibers when crushed. The type of asbestos minerals (chrysotile, amosite,

crocidolite, anthophyllite, tremolite, and actinolite) are important because they determine in part the disease potential. Industrialization increased the number of people exposed—although symptoms did not begin to develop until years after exposure. While it is well known to cause lung cancer and mesothelioma, asbestos also results in other diseases. Asbestosis is a scarring, or fibrotic lung, disease. The most common manifestation of asbestos-related disease is in the pleura. Pleural plaques are areas of thickened fibrous tissue, which often calcify. They cause no symptoms and may be found with other forms of asbestos-related disease. Fluid may collect in the pleural space (benign asbestos-related pleural effusion), which is believed to be a response to the pleural irritation by the asbestos fibers. The word “benign” is used to distinguish it from malignant mesothelioma, but the effusions can bring about chest discomfort and shortness of breath. These effusions may also be persistent and are a risk factor for pleural fibrosis.

Coal dust exposure can cause coal worker’s pneumoconiosis (CWP), also known as black lung, which was recognized as a distinct entity from other pneumoconioses in the 1940s. Simple CWP is largely only an abnormality on the chest radiograph; there are small spots in the upper lung zones that reflect inhalation of coal dust, but nothing more. However, it can develop into complicated CWP, which is also called progressive massive fibrosis, a term and process shared with silicosis in which the smaller shadows coalesce into large nodules, 1 to 2 centimeters in diameter. These lesions can distort and destroy normal lung architecture and result in shortness of breath and disability. Exposure to coal dust has been found to result in airflow obstruction and chronic bronchitis and is also associated with the development of rheumatoid arthritis, which when combined with CWP is known as Caplan syndrome. Finally, an association of stomach cancer has been described in coal miners, potentially related to ingestion of the coal dust.

Other exposure-related diseases are “farmer’s lung,” or hypersensitivity pneumonitis (HP). Hypersensitivity pneumonitis, which was originally recognized by Bernardino Ramazzini in wheat reapers in 1713, is an interstitial lung disease caused by an immune response to an inhaled antigen. The well-described at-risk populations are farmers and bird hobbyists, but many other exposures can cause HP. The most recent addition is popcorn workers’ lung, noted in workers and consumers with a history of heavy exposure to microwave popcorn butter flavoring. The true prevalence of HP is unknown because there

### CASE STUDY

A 62-year-old man originally from Bolivia saw a physician for increasing shortness of breath. He had smoked one or two cigarettes a day for 15 years but quit at age 26. He immigrated to the United States at age 42 and worked for 12 months at a dental bridge manufacturing company, where he wore a mask while grinding bridges. At age 42, he was treated for suspicion of tuberculosis. Based on persistent abnormal chest x-ray images, he was diagnosed with accelerated silicosis with progressive massive fibrosis. A lung biopsy was performed to rule out lung cancer and showed mixed dust pneumoconiosis and silicosis, but no evidence of cancer. He was also found to have significant airflow obstruction and required oxygen supplementation. Currently, he is undergoing a lung transplant evaluation.

### Comment

This case illustrates a number of points about silicosis. Many cases are arising from occupations not previously recognized as placing workers at risk. This lack of awareness means that these patients often are not diagnosed in a timely manner and continue to accrue exposure. Additionally, this case raises the issue of the elevated risk of tuberculosis and lung cancer in persons with silicosis. Because this patient came from a country with a high tuberculosis rate, it was likely he was exposed to the infection and at increased risk of developing active tuberculosis.

are many products that cause it; the illnesses have a great range of symptoms, and many people with mild disease do not seek medical attention. HP, however, has been reported to be present in as many as 12 percent of farmers and 20 percent of bird hobbyists (3).

Workers including sandblasters, miners, tunnelers, millers, and potters—among many others—are exposed to these inhaled particles and, therefore, are at risk of developing the disease. The true economic burden is difficult to estimate due to the uncertain number of at-risk individuals and likely underestimated prevalence numbers.

**table 1 exposure, disease process, and prevalence of occupational lung diseases (1)**

<b>Occupational exposure</b>	<b>disease</b>	<b>Prevalence in exposed population</b>	<b>time of exposure to onset of symptoms</b>
Silica	Acute Silicosis	Unknown	< 1 year
	Accelerated Silicosis	Unknown	3–10 years
	Chronic or Classic Silicosis	12.8 percent	Decades
Asbestos	Asbestosis	10–92 percent	Years
	Benign Asbestos Pleural Effusion	3 percent	< 20 years
	Pleural Plaques	6–70 percent	Years
Coal	Simple Coal Workers' Pneumoconiosis	5 percent	Years to decades
	Complicated Coal Workers' Pneumoconiosis (or Progressive Massive Fibrosis)	Unknown	Years to decades
Numerous (see Table 3)	Hypersensitivity Pneumonitis	12–20 percent	Day of exposure

**table 2 Occupational lung disease and its workforce exposure**

<b>Occupational lung disease</b>	<b>exposed workforces</b>
Silicosis	Sandblasters, miners, tunnelers, millers, potters, glassmakers, foundry and quarry workers, abrasive workers (including dental workers), silica flour mixers, and construction workers
Asbestos	<u>Primary:</u> Miners, millers <u>Secondary:</u> Asbestos insulators (laggers), ship building and repair, boilermakers, fireproofing, brake liners, ceramics workers <u>Indirect:</u> Electricians, plumbers, carpenters
Coal	Coal miners

## What are we learning about the diseases?

### ***Pathophysiology, causes: genetic, environment, microbes***

In silicosis, fine (less than 5 micrometers) airborne particles of crystalline silica are inhaled and deposited in the smallest bronchioles and their neighboring alveoli. The disease-causing forms of silica are quartz, cristobalite, tridymite,

**table 3** Most frequent causes of hypersensitivity pneumonitis

disease	source of antigens
<b>Plant products</b>	
Farmer's lung	Moldy hay
Bagassosis	Moldy pressed sugarcane (bagasse)
Mushroom-worker's disease	Moldy compost
Malt-worker's lung	Contaminated barley
Maple bark disease	Contaminated maple logs
Sequoiosis	Contaminated wood dust
Wood pulp-worker's disease	Contaminated wood pulp
Humidifier lung	Contaminated humidifiers, air conditioners
Familial HP	Contaminated wood dust in walls
Compost lung	Compost
Cheese-washer's disease	Cheese casings
Wood-trimmer's disease	Contaminated wood trimmings
Thatched roof disease	Dried grasses and leaves
Tea-grower's disease	Tea plants
Coffee-worker's lung	Green coffee beans
Streptomyces albus HP	Contaminated fertilizer
Cephalosporium HP	Contaminated basement (sewage)
Sauna-taker's disease	Sauna water
Detergent-worker's disease	Detergent
Paprika-splitter's lung	Paprika dust
Japanese summer house HP	House dust; possibly bird droppings
Dry rot lung	Infected wood
Office-worker's or home HP	Dust from ventilation or heating systems

(continued on next page)

disease	source of antigens
Car air conditioner HP	Dust from air conditioner
Potato-riddler's lung	Moldy straw around potatoes
Tobacco-worker's disease	Mold on tobacco
Hot tub lung	Mycobacteria
Tap water lung	Contaminated water
Wine-grower's lung	Mold on grapes
Suberosis	Cork dust
Woodman's disease	Mold on bark
Saxophone lung	Saxophone mouthpiece
Grain-worker's lung	Grain dust
Fish meal-worker's lung	Fish meal dust
Soy sauce worker's HP	Fermenting soybeans

**animal products**

Pigeon-breeder's disease	Pigeon droppings
Duck fever	Duck feathers
Turkey-handler's lung	Turkey products
Bird-fancier's lung	Bird products
Dove-pillow's lung	Bird feathers
Laboratory-worker's HP	Rat fur
Pituitary snuff-taker's disease	Pituitary powder
Mollusk shell HP	Mollusk shells

**Insect products**

Miller's lung	Wheat weevils
---------------	---------------

**Reactive simple chemicals**

TDI HP	Toluene diisocyanate
--------	----------------------

(continued on next page)

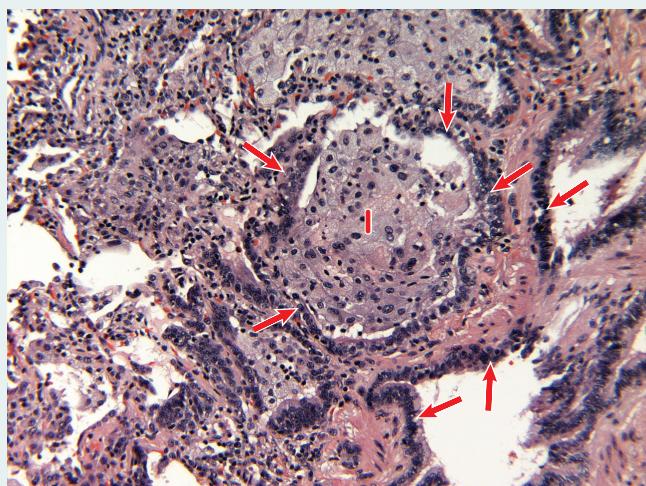
disease	source of antigens
TMA HP	Trimetallic anhydride
MDI HP	Diphenylmethane diisocyanate
Epoxy resin lung	Heated epoxy resin
Pauli's HP	Pauli's reagent
Popcorn worker's lung disease	Microwave popcorn flavoring

HP, hypersensitivity pneumonitis; IgA, immunoglobulin A; MDI, diphenylmethane diisocyanate; TDI, toluene diisocyanate; TMA, trimetallic anhydride.

and stishovite. Exactly how the damage occurs is not fully understood, but it is believed that freshly fractured particles of silica are the most dangerous, probably because the surface of the particles is more chemically active. These silica particles are taken up by the specialized cells (macrophages), which become activated and release oxidants, enzymes, growth factors, and other inflammatory mediators (cytokines). The macrophages eventually die and release the silica, which is indigestible. The silica particle is then taken up by other macrophages, and the process is perpetuated. As other inflammatory cells are recruited to the alveoli, the process continues to gather momentum, resulting in destruction of more cells and the tissue around them.

In the case of asbestos, the fibers are similarly inhaled, taken up by the macrophages and transported to the pleural space. The activated macrophages incite inflammation that can progress into fibrosis if the particles are not cleared. If the macrophages cannot eliminate the fibers, the needle-like particles are surrounded by an iron-containing protein ( hemosiderin), forming what is called an “asbestos body.” The extent of disease depends not only on the type of asbestos mineral but also on the intensity and duration of exposure.

In coal worker’s pneumoconiosis, the disease begins with the inhalation of coal dust. Coal dust also is taken up by macrophages, which generate inflammatory cytokines and damaging oxidants. The spot on the chest radiograph is called a coal macule and consists of a collection of dust-laden macrophages surrounded by focal emphysema. Other factors that play a role in the degree of lung destruction are related to the coal. Intrinsic qualities of the coal have an



Dean E. Schraufnagel

Inflammation in hypersensitivity pneumonitis is centered around the bronchi. The arrows in this microscopic view point to the bronchial lining cells. The small bronchioles are often plugged with inflammatory cells (!). Collections of cells called granulomas are often present but not shown here.

impact on disease—the higher the carbon content, the higher the risk of disease. With the exception of drillers, surface coal miners tend to have less CWP. The level of silica exposure during the mining process can dictate who develops silicosis; the lung disease caused by silica and coal exposure can be difficult to distinguish from each other clinically.

Hypersensitivity pneumonitis is an allergic reaction. The first step involves exposure to an antigen of organic material from bacterial, fungal, plant, or animal proteins. Initial exposure results in sensitization in which the body forms antibodies to these antigens. Repeated exposure results in inflammation. If the exposure is not halted, it can permanently damage the lung. Due to this, HP represents a continuum of disease sometimes categorized as acute, subacute, and chronic. It is likely that some individuals may have a genetic predisposition to HP. Interestingly, the damage that smoking causes may decrease the delivery of the antigen to the alveoli and decrease the antibody response, resulting in a lower risk of HP.

### **How are they prevented, treated, and managed?**

#### *Prevention, treatment, staying healthy, prognosis*

For asbestos, coal, and silica-related disease, there is no treatment other than optimizing the patient's current health and preventing further exposure. Prognosis varies depending on the severity of the disease. Persons with simple CWP or classic silicosis may never experience symptoms, whereas complicated CWP results in severe respiratory debilitation and death. Although these materials are present in nature, it is their mining and commercial use that generates the toxic exposure for humans.

Worldwide production of asbestos peaked in the 1970s, but there were still over 2 million tons of asbestos mined in 2000 (4). In 2005, the Collegium Ramazzini, an international organization of occupational and environmental scientists, called for a worldwide ban on commercial use of asbestos, but it is estimated that worldwide 125 million people still are exposed to asbestos in the workplace, and 90,000 people die each year from lung cancer, malignant mesothelioma, and asbestosis secondary to asbestos exposure. Moreover, since the use of asbestos has been banned in the United States only since the 1990s, the peak of disease incidence may lie ahead. The prognosis for mesothelioma and lung cancer is dismal, with less than 20 percent 5-year survival rates. For all individuals exposed to asbestos, there is the need for surveillance for development of malignancy.

Coal is only used as a fuel and, therefore, exposure is limited to miners. Aggressive regulations in the coal industry have resulted in reductions in the burden of disease. In 1969, the Federal Coal Mine Health and Safety Act was passed, which put in place standards designed to ensure that cumulative exposure over the typical career span of 25 years would not exceed levels known to cause respiratory impairment. Effective in 1980, the respirable coal mine dust standard was decreased from 3 to 2 milligrams per cubic meter ( $\text{mg}/\text{m}^3$ ). These regulations have served to decrease the prevalence rate of CWP among 25-year mine workers from 20 percent in 1987 to slightly more than 5 percent in 2002 (1). In conjunction with these standards, secondary prevention measures also require all coal miners to receive regular medical screening. Furthermore, if a worker shows signs of CWP, he or she has the option of transferring to a lower-dust area (less than  $1 \text{ mg}/\text{m}^3$ ) and receiving increased monitoring. All patients are encouraged to stop smoking, and other treatments are offered as clinically indicated.

Silica is the least regulated of the agents causing occupational lung diseases. Silicosis is an irreversible fibrotic process without a cure. Treatment rests on preventing further insult to the lungs. Reduction in risk of tuberculosis is also critically important, and all patients should be screened for latent or active tuberculosis infection and evaluated for other tuberculosis risk factors, such as HIV infection. As with any lung disease, smoking cessation is a must. In treatment trials thus far, no drug has been found to halt the progression of disease.

In the case of hypersensitivity pneumonitis, treatment consists of removing the source of the exposure and eradicating any residual antigens to prevent re-exposure—for example, drying hay to prevent molding or removing stagnant water to prevent bacterial or fungal overgrowth. Often, the most challenging part of care is convincing the patient that removal of the antigen is necessary or that he or she must leave the workplace. If the disease is severe at diagnosis, a short course of oral corticosteroids can help expedite recovery. The prognosis depends on the degree of continued exposure. Farmers are often exposed at the end of winter when using the remainder of the previous year's hay supply. Because this exposure is usually self-limited and occurs once a year, most individuals will recover completely. Conversely, the individual who has repeated or long-term exposure might suffer permanent damage to the lungs.

## **Are we making a difference?**

### ***Research past, present, and future***

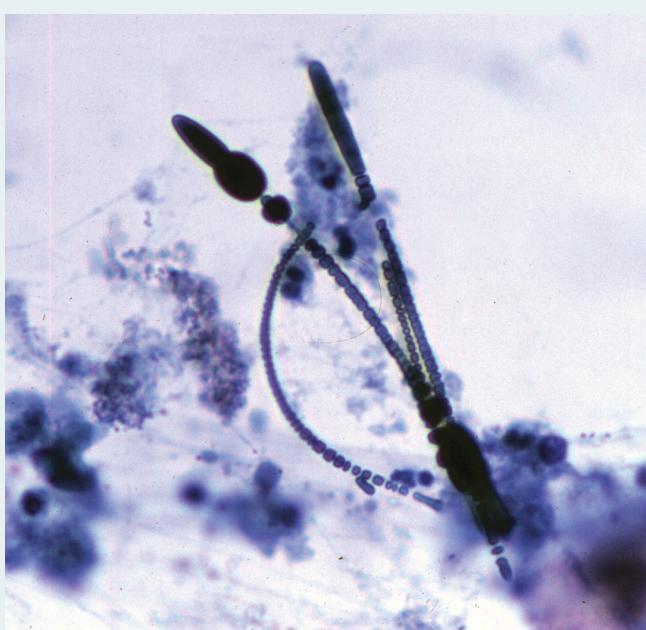
Each of the occupational diseases begins with the inhalation of disease-inducing particles. Therefore, the main goals have been to identify and regulate the industries that generate these particles on one hand and to determine ways to prevent or minimize their inhalation on the other. In dealing with silica, coal, and asbestos, the significant latency period between exposure and diagnosis makes it difficult to determine dose-response relationships.

There is no treatment for any of the occupational diseases that can reverse the damage already done. However, for those who were or continue to be exposed, the search for treatments must continue. Early reports of gene therapy resulting in anti-tumor responses may hold promise for those with mesothelioma. Research in pulmonary fibrosis may be applicable to asbestosis in the future. In the case of HP, early research was based on observation and the discovery of the causative antigens, the removal of which improved symptoms. Studying the

patient's serum allowed the discovery of antibodies that reacted with the specific antigen (precipitins). It is still not possible to predict who will develop HP, which antigens set up the inflammation, and how or in whom the disease will progress, but there are reasons to hope. Certain genetic predispositions have been discovered, and recent studies in the mouse have shown that certain cells and their signaling cytokines are important in the pathogenesis of HP.

### ***What we need to cure or eliminate occupational lung diseases***

In occupational lung diseases, the primary strategy must be prevention. Strong federal regulations and funding for CWP prevention in conjunction with scientific research have laid a foundation for a continuing reduction of the burden of disease in the United States. This approach should serve as a model for how to proceed in preventing other occupational lung diseases.



Dean E. Schraufnagel

*Needle-like asbestos particles penetrate the lung and cannot be dissolved or destroyed by the body. Instead, the body coats them with a protein associated with iron. The presence of asbestos bodies in the lungs only signifies exposure, not disease.*

When the underlying disease mechanism is understood, as it is with smallpox and polio, there is the potential to eliminate the disease. In the case of asbestos-related diseases, the etiology is known—without asbestos exposure there is no asbestos-related disease. A worldwide ban of asbestos would eventually virtually eliminate its associated diseases.

Increased monitoring of air concentrations of silica in the workplace, as well as duration of exposure for workers, is necessary. A registry that then follows populations of workers over time to determine the rate of silicosis would help to determine if there are safe levels of silica exposure in the workplace. Based on this, regulations could be enacted worldwide to decrease the burden of silicosis. For those who are unfortunate enough to develop silicosis, continued research on the pathogenesis of the disease and studies on whether or not there is a genetic component could help develop potential treatments.

In the case of HP, increased awareness in the community and in relevant industries will help to bring patients to medical attention earlier in their disease process. More organized follow-up will help to better characterize the natural history of the disease and cease exposure. An organized reporting system for new cases would serve to initiate the proper investigation in a timely fashion. Further research on signaling cytokines could lead to new treatment or preventative options.

### References

1. Rom WN, Markowitz S, eds. *Environmental and Occupational Medicine*. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007.
2. Adverse effects of crystalline silica exposure. American Thoracic Society Committee of the Scientific Assembly on Environmental and Occupational Health. *Am J Respir Crit Care Med* 1997;155:761–768.
3. Mason RJ, Murray JF, Nadel JA, Broaddus VC, eds. *Murray and Nadel's Textbook of Respiratory Medicine*. 4th ed. Philadelphia, PA: Elsevier Saunders; 2005.
4. World Health Organization. *Elimination of Asbestos-Related Diseases*. Geneva, Switzerland: World Health Organization; 2006.

### Web sites of interest

International Agency for Research on Cancer

[www.iarc.fr](http://www.iarc.fr)

World Health Organization

[www.who.int/en/](http://www.who.int/en/)