OXFORD

INTERNATIONAL EDITION

Oxford Textbook of Medicine

SIXTH EDITION
VOLUME 3

EDITED BY
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Volume 3: Sections 16–21

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UNIVERSITY PRESS

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Great Clarendon Street, Oxford, OX2 6DP,
United Kingdom

Oxford University Press is a department of the University of Oxford.
It furthers the University's objective of excellence in research, scholarship,
and education by publishing worldwide. Oxford is a registered trade mark of
Oxford University Press in the UK and in certain other countries

First Edition published in 1983
Second Edition published in 1987
Third Edition published in 1996
Fourth Edition published in 2003
Fifth Edition published in 2010
Sixth Edition published in 2020

Impression: 1

Published in the United States of America by Oxford University Press
198 Madison Avenue, New York, NY 10016, United States of America

British Library Cataloguing in Publication Data

Data available

Library of Congress Control Number: 2018933144

Set ISBN: 978–0–19–874669–0
Volume 1: 978–0–19–881533–4
Volume 2: 978–0–19–881535–8
Volume 3: 978–0–19–881537–2
Volume 4: 978–0–19–884741–0

Only available as part of a set

Printed in Malaysia by Vivar Printing

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Pneumoconioses

P.T. Reid

ESSENTIALS

Pneumoconiosis describes the pathological reaction of the lung to inhaled dust, most often, but not exclusively, related to exposures occurring at work. It may be defined as a permanent alteration of lung structure due to the inhalation of mineral dust and the tissue reactions of the lung to its presence, excluding bronchitis and emphysema.

The causes of pneumoconiosis are many and varied, but coal worker's pneumoconiosis, asbestosis, and silicosis are most common. Many epidemiological studies have shown an exposure–response relationship between the total mass of respirable dust to which workers have been exposed and their risk of developing disease. These form the basis of regulations specifying limits to permitted levels of exposure. Workers who develop pneumoconiosis as a consequence of their employment may be entitled to compensation in some countries.

Coal worker's pneumoconiosis

Caused by inhalation of coal-mine dust. Now uncommon in the United Kingdom and other Western countries, but in China the disease is widespread, and in India it affects about 1–2% of the coal industry workforce. Simple coal worker's pneumoconiosis causes no respiratory symptoms or physical signs and is recognized by the detection of coal macules on chest radiography. Complicated pneumoconiosis is characterized by the appearance of progressive massive fibrosis, which may be diagnosed when any radiographic lesion exceeds 1 cm in diameter. This condition often progresses, causing mixed airflow obstruction and restriction, and—when severe—leads to respiratory failure, cor pulmonale, and death.

Asbestosis

Exposure to asbestos fibres can cause a range of respiratory conditions, including benign pleural plaques, acute effusion, diffuse fibrosis of the visceral pleura, asbestosis, and mesothelioma. Asbestosis occurs only in people working regularly with asbestos over several years and not in those with occasional or incidental exposure. Disease is usually progressive, with radiological appearance identical to idiopathic pulmonary fibrosis (i.e. predominantly basal and peripheral irregular linear shadowing, progressing to honeycombing). The risk of lung carcinoma is related to asbestos exposure, interacting multiplicatively with smoking.

Silicosis

Caused by inhalation of crystalline silicon dioxide, usually in the form of quartz. Crystalline silica is highly fibrogenic, causing fibrous pleural adhesions, enlarged lymph nodes that contain fibrotic nodules and often calcify, and grey nodules throughout the lung with a typical whorled appearance when cut across. The clinical presentation ranges from acute silicosis, which is very rare, but leads to death within months, to slowly progressive lung fibrosis, to asymptomatic radiological abnormalities. The progression of silicosis may be complicated by tuberculosis, lung cancer, chronic obstructive pulmonary disease, and rarely by connective tissue disease and renal damage.

Introduction

The inhalation and clearance of inhaled particles and fibres

Respiration involves the inhalation of a variety of airborne dusts and fibres, which may be in the environment. Airborne dusts may be defined as small, solid particles, conventionally taken as those particles below 75 microns in diameter, which settle out under their own weight, but which may remain suspended for some time. Particle behaviour also depends on the aerodynamic properties (size, shape, and density), and the anatomical, clearance, and immune mechanisms of the lung into which they are inhaled.

Most inhaled particles with a diameter greater than 7 microns are trapped by the nose and expelled forcibly by sneezing or more gently by the nasal mucociliary escalator. However, physical activity, as often occurs during manual work, increases mouth breathing. Particles inhaled by the oral route impact on the vocal cords and may be expelled by coughing or pass into the

trachea and major bronchi, where they are trapped by airway mucous and transported caudally by the cilia to the upper airway, to be either expectorated or swallowed. Mucociliary clearance operates from the trachea to the terminal bronchioles. Cilia beat with a synchronous motion causing the mucous layer to have a continued upward movement of 5–10 mm/min. Ciliary clearance may be significant impaired by cigarette smoke and 'dust overload'.

Particles that escape entrapment by airway mucus may be engulfed and digested by macrophages and neutrophils. Soluble particles may enter the body by dissolution. Very small particles, usually taken to be between 0.5 and 7 microns may travel as far as the alveolar regions and these are termed respirable particles.

In common with larger particles, the aerodynamic characteristics of fibres are also affected by their size and shape. Short thick fibres are deposited in the upper respiratory tract and cleared by mucociliary action to the pharynx where they are expectorated, whereas longer and thinner fibres may transit to the alveolar regions.

On reaching the alveolar units, most inhaled particles are cleared by alveolar macrophages either by the airways to the pharynx or via the lymphatic system to the regional lymph nodes. Macrophages are avidly phagocytic and engulf, among other things, bacteria, surfactant, cell debris, and respirable particles. Increased numbers of alveolar macrophages, derived from peripheral blood monocytes, are recruited to the lungs of individuals exposed to dust and become resident in both the pulmonary interstitium and the alveolae. Ultrafine dust particles may directly traverse the epithelium entering the pulmonary interstitium. Free particles that are not ingested by macrophages enter the perivascular lymphatic channels to be translocated to the draining mediastinal lymph nodes as free particles or within macrophages. Ciliary clearance operates rapidly; for example, around 12 hours, but clearance by macrophages takes place over days to months. Longer fibres (over 100 μm in length) are cleared at a much slower rate, thereby being retained in the lung for longer periods.

For any individual, there is an important relationship between the cumulative amount of dust inhaled and the ability of the lung to clear this dust. Lung damage occurs when respirable dusts reach the acinus in sufficient quantity to overwhelm the normal phagocytic and clearance mechanisms.

The pathophysiology of pneumoconioses

Most dust accumulates in the upper lobes and hence, with the notable exception of asbestosis, pneumoconiosis has a predilection for these. Slightly more dust is deposited in the right than the left lung, although this is seldom clinically apparent.

Some dusts, such as carbon or tin, are relatively inert, but most others initiate the recruitment and activation of inflammatory cells and the release of pro-inflammatory and pro-fibrotic mediators. Commonly described tissue reactions include the formation of macules, nodules, interstitial fibrosis, granulomata, and emphysema.

The tissue reaction may be confined to the lung, or—as is the case with asbestos—involve the pleura. Silica-exposed workers may develop autoantibodies which, in some cases, precede the development of connective tissue disease. Systemic toxicity may follow the inhalation of lead, cadmium, beryllium, and manganese.

Several inhaled particles and fibres, notably asbestos, silica, hexavalent chromium, certain chromates, arsenic (elemental and organic compounds), particles containing polycyclic aromatic hydrocarbons and certain nickel-bearing dusts, act in a synergistic manner with tobacco to trigger carcinogenesis.

Most inhaled particles known to cause pneumoconiosis do so through altering macrophage function. The inability of macrophages to effectively phagocytose crystalline silica and amphibole asbestos is invariably accompanied by necrosis and disintegration of the cell, accompanied by the liberation of the ingested silica, which may be re-ingested and cause death of other macrophages. The biopersistence of silica and asbestos in the lung leads to a self-perpetuating inflammatory response and the progressive deposition of collagen.

Beryllium acts via a CD4 + T cell-mediated inflammatory mechanism. The positively charged metal is internalized by major histocompatibility (MHC) class II peptides, resulting in a conformational change on the surface of the cell. Beryllium specific toll-like receptors do not recognize beryllium itself, but the change in the surface of the complex induced by internalization of the metal. Thus, the mechanisms underpinning chronic beryllium disease are believed to lie on the border between allergic hypersensitivity and autoimmunity.

The radiology of pneumoconioses

The presence of pneumoconiosis is usually heralded by a profusion of rounded and irregular opacities, most often, but not always, predominating in the upper lobes. Complications such as emphysema, tuberculosis, and malignancy may also be observed on plain chest radiographs.

Chest radiograph

In 1950, the International Labour Office (ILO) issued guidance on how best to describe the radiographic abnormalities produced by the inhalation of dust. The system has undergone several iterations and was most recently updated in 2011, with the current edition providing advice on the acquisition, display, and storage of digital chest images.

The reporting of films is undertaken by certified readers who compare the image they are reporting with a standard set of films. Following a comment on the technical quality, readers record their opinion on the presence of any abnormalities in the parenchyma and pleura.

Each lung field is divided into three zones (upper, middle, lower) by horizontal lines drawn at approximately one-third and two-thirds of the vertical distance between the lung apices and the domes of the diaphragm. The profusion of small opacities, which refers to the concentration of opacities per unit area of lung, is determined by considering the profusion as a whole over the affected zones. Should the reader encounter marked (three subcategories or more) difference in profusion between different zones, then the zone or zones showing the least degree of profusion is/are ignored for the purpose of classifying the overall profusion.

Parenchymal abnormalities may be classified according to their size and shape. Opacities up to 1.5 mm, 1.5–3 mm, and 3–10 mm,

are called 'p', 'q' and 'r' respectively if rounded in appearance and 's', 't' and 'u' respectively if irregular in appearance. A large opacity is defined as an opacity having the longest dimension exceeding 10 mm and may be further categorized as A B or C. Category A refers to one large opacity having the longest dimension up to about 50 mm, or several large opacities with the sum of their longest dimensions not exceeding about 50 mm. Category B refers to one large opacity having the longest dimension exceeding 50 mm, but not exceeding the equivalent area of the right upper zone, or several large opacities with the sum of their longest dimensions exceeding 50 mm but not exceeding the equivalent area of the right upper zone. Finally, category C refers to one large opacity which exceeds the equivalent area of the right upper zone, or several large opacities which, when combined, exceed the equivalent area of the right upper lobe. Finally, the reader comments on pleural abnormalities such as pleural plaques, costophrenic angle obliteration, and diffuse pleural thickening.

The category which best describes the radiographic appearances under consideration is recorded as the first choice. In cases where a reader gives serious consideration to an alternative, then the first and second choices are separated by a slash. For example, if the first choice was category 1, but category 2 was seriously considered, the reading 1/2 is recorded. If no other category was given serious consideration, the number is listed twice (e.g. 1/1).

The application of the ILO classification represents an attempt to standardize descriptions and facilitate international comparisons of data on pneumoconioses, providing a tool for epidemiological investigation and research reports. It is not intended as a diagnostic tool and limited inference may be made as to the causative agent. It should not be used when forming an opinion on working capacity, and the system is not intended for compensation purposes.

High-resolution computed tomography

The greater sensitivity and specificity of high-resolution computed tomography (HRCT) overcomes many of the limitations of the chest X-ray. Its significantly greater sensitivity allows the presence of pneumoconiosis to be detected at a much earlier stage, even when the chest X-ray is normal, and the ability to observe both the extent and the pattern of distribution affords the radiologist a greater opportunity to comment on the likely differential diagnosis. For example, diseases causing nodules such as pulmonary tuberculosis (which may complicate silicosis), sarcoidosis, hypersensitivity pneumonitis, and respiratory bronchiolitis–interstitial lung disease may be more readily discriminated from a pneumoconiotic reaction by HRCT. Furthermore, the extent of radiological abnormality shown on HRCT correlates with the physiological or functional outcome, which is particularly helpful when the interpretation of lung function testing is confounded by a combination of pulmonary and pleural pathologies.

Positron emission tomography

Positron emission tomography (PET) exploits the avid ability of malignant tissue to absorb and metabolize glucose and have become central to staging malignant disease. In patients with pneumoconioses, the use of PET/CT may assist in the differentiation between the appearance of benign lesions such as progressive massive fibrosis (PMF) and lung cancer, and benign and malignant pleural lesions in asbestos-exposed workers.

Coal worker's pneumoconiosis

Coal worker's pneumoconiosis (CWP) describes the reaction of the lung to the inhalation of coal and coal dust. It may be classified as simple or complicated.

Coal is a complex chemical structure derived from peat. The principal constituent is carbon, which is present in varying proportions depending on the grade or rank of the coal. Lignite, the lowest rank coal contains the least carbon, whereas anthracite contains the highest rank; bituminous coal is intermediate rank. Higher rank coals have a greater calorific value. Coal also contains minerals originating from the rock in which it was formed, the most important of these being silica.

Coal worker's pneumoconiosis rose to prominence in the United Kingdom shortly after the Second World War, when around 3000 men per annum were identified with the condition. Cooperation between the Medical Research Council and the National Coal Board led to an increased understanding of the condition, which in turn led to improvements in occupational hygiene controls. This, together with the decline of the mining industry, has resulted in the condition becoming of largely historical interest in the United Kingdom. By contrast, in China the disease is widespread and in India it affects about 1–2% of the current coal industry workforce of 800 000. The strategic importance of coal as a long-term source of fuel supply and as a chemical feedstock means that it will continue to be needed, and any relaxation of dust control in mines for any reason will be followed by the reappearance of pneumoconiosis, such as has been described in young coal miners from West Virginia, United States.

Aetiology and pathology

The incidence and clinical manifestations following the inhalation of coal dust vary from mine to mine reflecting the influence of both the rank of coal and the constituency of the respirable dust. As a general rule, the higher the rank, the more likely the dust will cause pneumoconiosis (Fig. 18.13.1). In addition, the presence of

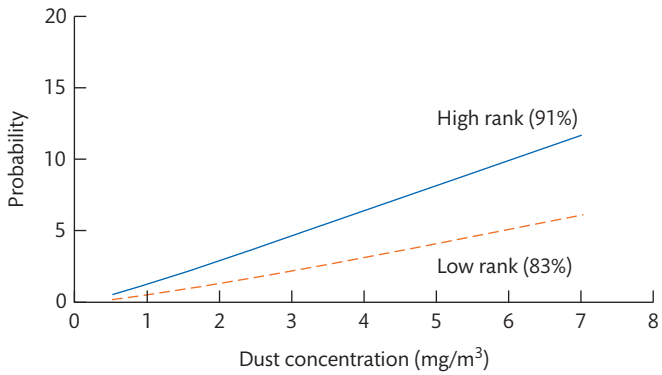

Fig. 18.13.1 Relationship between risk of category 2 or 3 radiological simple pneumoconiosis and daily exposure over a working lifetime to different concentrations of coal dust. The greater risk in association with exposure to dust from coals of higher combustibility (rank) should be noted.

different minerals in coal dust may modify the biological potency; for example, mining in areas with siliceous rock leads to the development of a condition more closely resembling silicosis. Some forms of clay may reduce the overall toxicity, probably by blocking the surface activity of the toxic fraction. An increased susceptibility to coal worker's pneumoconiosis is conferred by polymorphisms in genes regulating the inflammatory response such as glucocorticoid-induced tumour necrosis factor receptor-related protein (GITR), NOD-like receptor family, pyrin domain-containing 3 (NLRP3), and mucin 5B gene (*MUC5B*).

The earliest manifestation of coal worker's pneumoconiosis is the formation of the coal macule, an aggregation of dust-laden macrophages and free dust in a centriacinar distribution (Fig. 18.13.2). Macules are loosely bound by a reticulin framework and assume a stellate appearance. The absence of collagen renders them soft and impalpable to the pathologist and their presence does not equate to a formal diagnosis of CWP. However, if the response involves greater deposition of collagen, the more easily palpable nodule may develop. If these are less than 10 mm in dimension then this is pathologically regarded as CWP.

Macules have no effect on lung function and simple CWP only a limited effect. The coal macule is often surrounded by enlarged air spaces referred to as focal emphysema, which differs only from classical centriacinar emphysema by virtue of the presence of retained dust.

Complicated CWP includes cases were the fibrous nodules exceed 10 mm size, up to an including the presence of PMF. PMF consists of irregular masses of fibrous tissue that, by definition, exceed 1 cm in diameter (Fig. 18.13.3). It most often occurs against a background of simple pneumoconiosis and is most common in the upper lobes. The condition occurs either by aggregation of several, usually collagenous, smaller nodules, or through a more diffuse accumulation of dust associated with dead cells and ischaemic necrosis of lung tissue. The former mechanism is less common and occurs particularly in relation to relatively high quartz exposures, while the latter seems more frequent with exposure to high-carbon dusts. With either type there is a tendency for the lesions to grow and become associated with surrounding bullous emphysema. Central necrosis is common, and when cut the lesions may contain black fluid and cholesterol crystals. High-carbon or high-quartz dusts are particularly liable to cause the condition, and the higher the dust exposure the greater is the risk (Fig. 18.13.4).

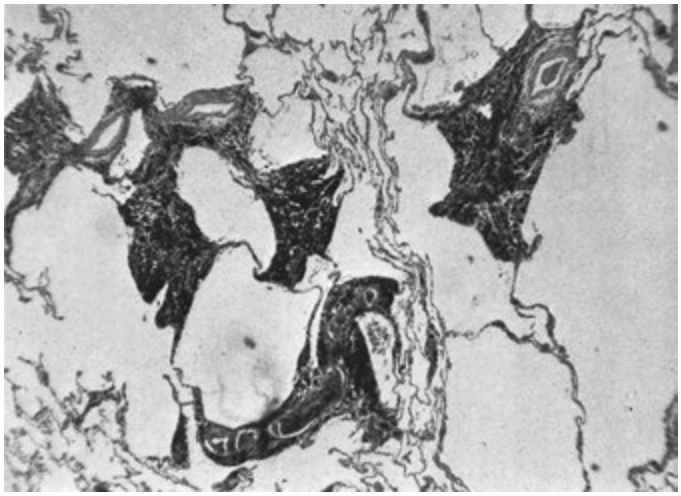

Fig. 18.13.2 Simple coal macules, showing accumulations of dust within macrophages but without fibrosis arranged around the centre of the acinus with associated emphysema.

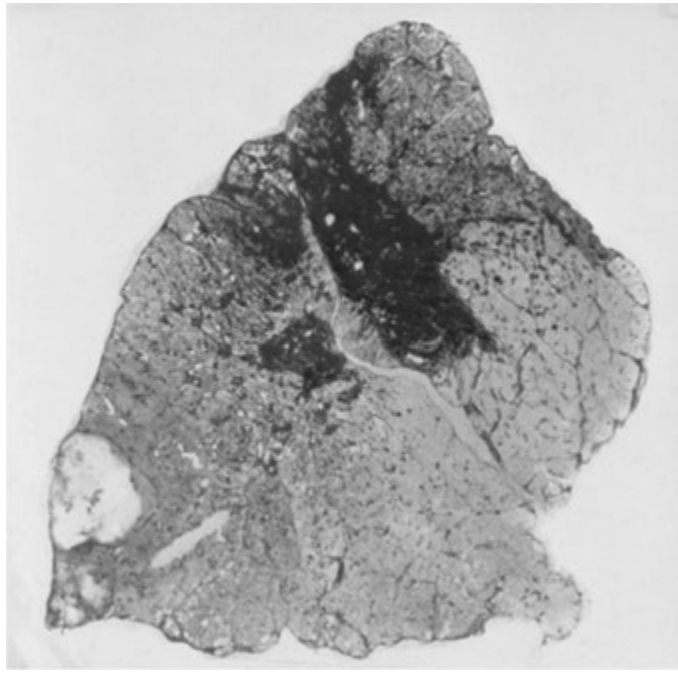

Fig. 18.13.3 Whole-lung section of a coal miner's lung showing progressive massive fibrosis.

Clinical features

CWP is most often described in underground coalminers, but anyone who inhales sufficient quantities ought to be considered at risk and the condition has been described in surface workers.

Simple coal worker's pneumoconiosis

Simple CWP is asymptomatic and usually detected by chest radiograph performed for the purposes of surveillance or the investigation of unrelated respiratory symptoms. Typical appearances include a profusion of small, discrete rounded opacities with an upper and middle zone predominance. It has been proposed that 'p' type opacities represent macules, 'q' type opacities represent stellate nodules, and 'r' type opacities represent rounded nodules.

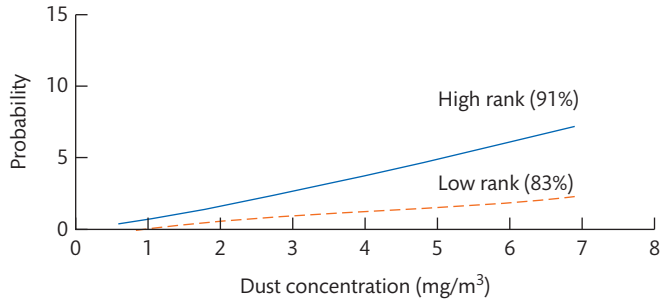

Fig. 18.13.4 Relationship between risk of progressive massive fibrosis and exposure to dust over a working lifetime. Greater risk in association with exposure to dust from coals of higher combustibility (rank) should be noted.

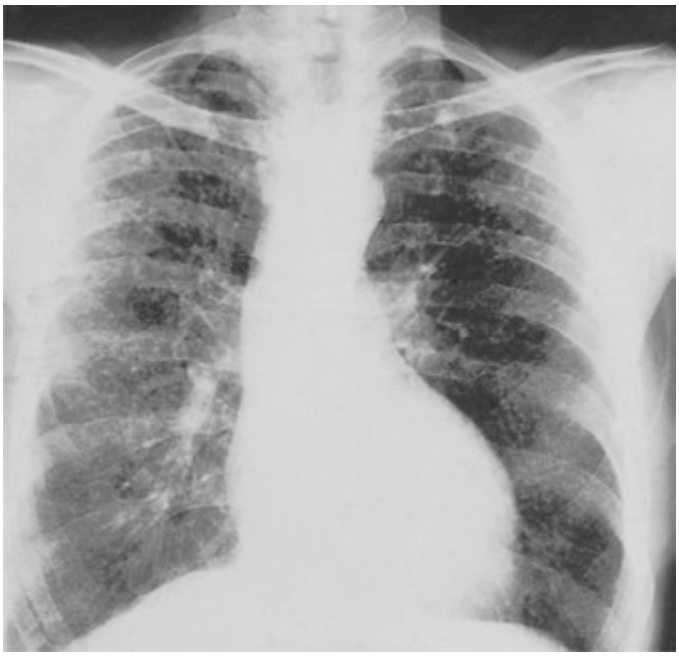

Fig. 18.13.5 Radiograph of a coal miner showing small round lesions of simple pneumoconiosis. Some irregular shadows are also present in the lower zones.

In addition, the accumulation of dust in the alveolar septae and pleural lymphatics is reflected by the presence of small irregular and linear opacities and Kerley B lines, which are more frequently present in the lower zones (Fig. 18.13.5).

As simple CWP is asymptomatic, should a miner report respiratory symptoms or develop physical signs, some other cause should be sought, such as chronic obstructive pulmonary disease, heart failure, or asthma.

Progressive massive fibrosis

The development of PMF is often accompanied by the development of symptoms, including cough, sputum, and shortness of breath. Melanoptysis, the expectoration of black contents from a cavitated lesion, may be reported. PMF usually occurs during working life, but it may appear for the first time many years after dust exposure has ceased. Simple CWP is usually present, typically ILO category 2/3.

The pattern and rate of change of PMF lesions is variable but almost always starts in the upper zone, gradually increasing in size until they may occupy up to one-third of the lung. Such lesions are frequently multiple, often shaped like short fat sausages, with their outer border curved with the chest wall and separated from the pleura by bullous emphysema (Fig. 18.13.6). Enlarged mediastinal and hilar nodes often accompany them.

Chronic obstructive pulmonary disease

Detailed research undertaken by the Pneumoconiosis Field Research programme and others have consistently demonstrated that coalminers are at increased risk of reporting chronic bronchitis, developing airflow obstruction, and experiencing an accelerated decline in lung function, that are all broadly related to their cumulative dust exposure. Pathological studies demonstrate a relation between exposure to coal-mine dust and emphysema, and mortality studies confirm increased deaths from chronic bronchitis and emphysema

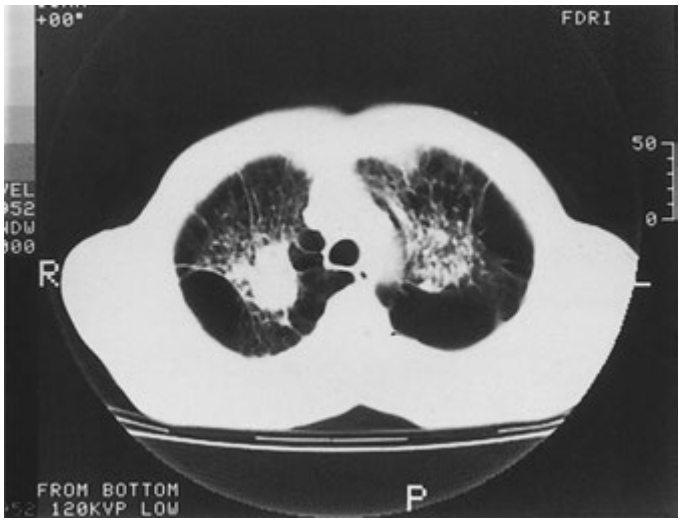

Fig. 18.13.6 CT scan of miner, showing central progressive massive fibrosis and surrounding bullous emphysema.

in miners. Most studies suggest that the effects of dust exposure and smoking in causing loss of lung function are additive.

Caplan's syndrome

In 1953, Anthony Caplan described the high prevalence of multiple, well-defined, round opacities, 0.5–5 cm. in diameter, distributed throughout both lung fields, but particularly at the periphery, in coal miners who suffered from rheumatoid arthritis. In contrast to PMF, background simple pneumoconiosis was often slight or absent (e.g. ILO category 1 or 0).

The opacities of Caplan's syndrome typically appear rapidly, within months, and while they may progress, more often than not remain stable. There is rarely any associated significant pulmonary impairment. Cavitation and calcification are frequent and in many instances the lesions become confluent and may be radiographically indistinguishable from PMF. The differential diagnosis includes malignancy, silicosis, pulmonary tuberculosis, and granulomatosis with polyangiitis (Fig. 18.13.7).

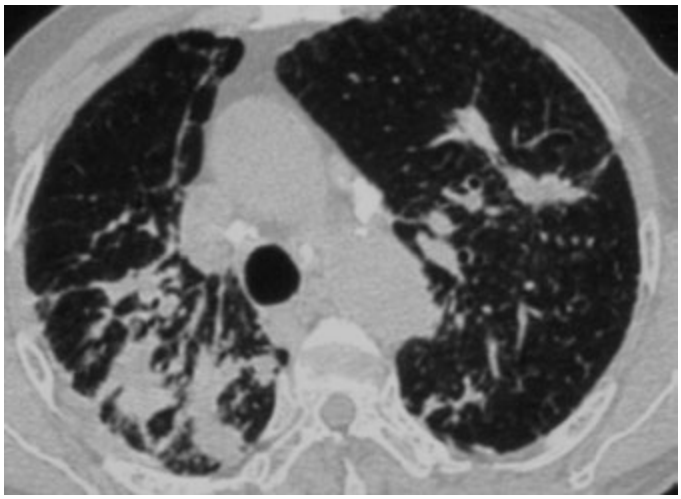

Fig. 18.13.7 CT scan appearances in a patient with Caplan's syndrome.
Image kindly provided by Dr Arnie Debaraj, Royal Brompton and Harefield NHS Trust.

Independent immunological studies showed that many miners with these radiographic appearances, or the classical chest radiographic changes of the rheumatoid pneumoconiosis syndrome, had positive rheumatoid factor tests, despite their having no history, symptoms, or signs of rheumatoid arthritis.

Pathological inspection of Caplan's lesions typically reveals large necrobiotic nodules with palisaded histocytes similar to that observed in rheumatoid nodules. Dust may be observed in circular bands or arcs within the necrotic centres of the lesions. The appearance bears no relationship with the severity of extrapulmonary disease activity or serological activity and, as inferred from the mild degree of background pneumoconiosis, no particular relationship with dust burden.

Prognosis

It is unusual for simple CWP to progress once a miner has ceased dust exposure. The exceptions to this include those in whom a silicotic element is present, and those in whom PMF develops. If PMF is present, the condition usually progresses and causes a mixture of restrictive and, owing to associated emphysema, obstructive ventilatory patterns. The rate of progression is variable. In general, the earlier PMF develops in a person's life, the more rapidly progressive the condition, and thus the worse the prognosis. In severe cases, PMF may progress to cause respiratory failure, cor pulmonale, and death.

Coal worker's pneumoconiosis is not associated with an increased risk of tuberculosis or lung cancer, although obviously these diseases can occur in coal miners and should be suspected, dependent on risk (e.g. living in an endemic area or smoking), if there is unusual progression of radiological changes.

Prevention and management

The exposure–response relationship between the total mass of respirable coal dust and the risk of developing coal worker's pneumoconiosis has allowed standards to be set for coal-mine dust levels that have resulted in a reduced prevalence of the disease in coal mines in developed countries. This success is dependent on adherence to control measures, such as regular monitoring of the respirable dust, constant attention to dust suppression by ventilation, and the use of water at points of dust production, combined with regular radiography of the workforce to detect early signs of dust retention. Preventing miners from contracting simple pneumoconiosis, by controlling the level of dust exposure, largely controls the incidence of PMF. The present United Kingdom standard is 7 mg/m^3, measured in the air returning from the coalface.

If a miner develops simple pneumoconiosis late in his career, no action is normally required, apart from (in the United Kingdom) advising him to apply to the Respiratory Diseases Board via the Benefits Agency for assessment of disablement and possible benefit payments. A younger man, with several years of potential dust exposure ahead, should be advised to work in an area of approved low dust conditions. In the United Kingdom the employer's occupational health provider would usually give this advice. Men with more than the earliest stages of radiological change are entitled to disablement benefits from the Benefits Agency, the value of these depending on the extent of disability. Since simple pneumoconiosis per se does not disable, these benefits are often small. Payment of benefits for airflow obstruction as an associated effect of coal dust exposure are also made in the United Kingdom if the miner has worked underground for a minimum of 20 years and his FEV_1 is 1 litre below that predicted. The presence of associated radiological change is not necessary. Following a legal judgement in the United Kingdom, civil compensation through the government is now available for individuals with symptoms of chronic bronchitis or with airflow obstruction, and such workers should be referred to their trade union for advice.

Asbestosis

Asbestos is a generic term for a group of fibrous silicates, the most important being chrysotile (white), crocidolite (blue), and amosite (brown). Chrysotile has a serpentine configuration and breaks up into microfibrils, while the other types (amphiboles) are straight and less liable to longitudinal fracture (Fig. 18.13.8). All types are resistant to physical and chemical destruction, which gives them their commercial value in fireproofing, insulation, reinforcement of

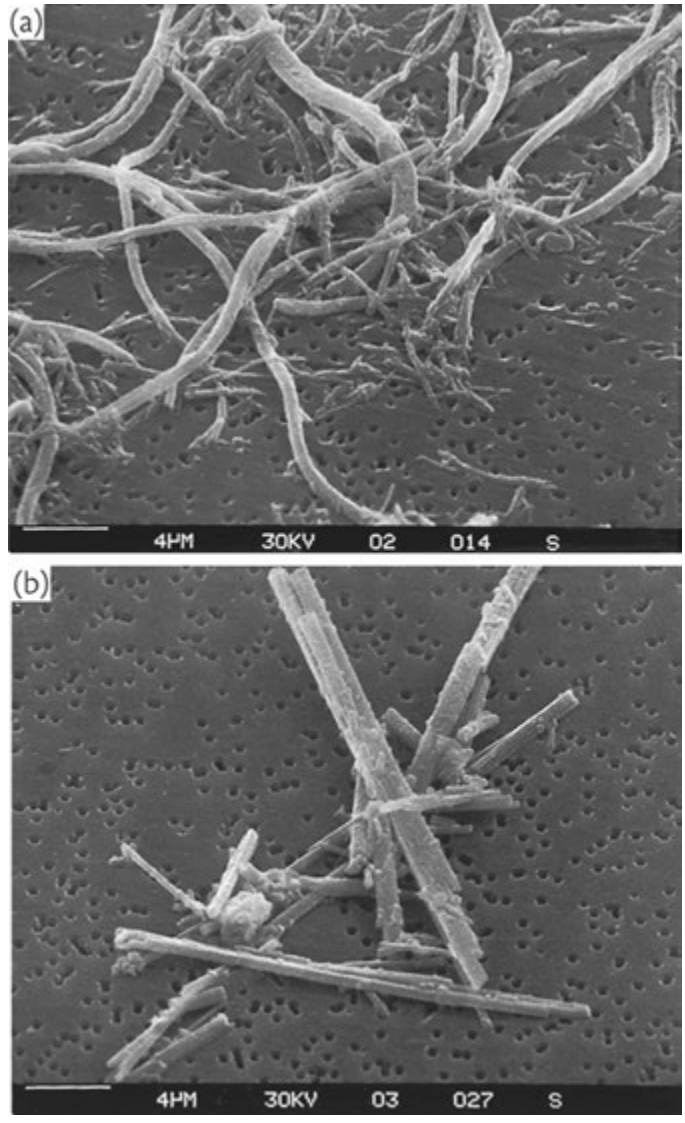

Fig. 18.13.8 Scanning electron micrographs of (a) chrysotile and (b) amosite on Millipore filters. The curly configuration and microfibrils of chrysotile should be noted. Scale bar, 4 μm.

cement, weaving into cloth, bonding in brake linings and plastics, and so on. Asbestos is mined principally in Canada, South Africa, and the former Soviet Union.

The inhalation of asbestos fibres causes several separate pleuropulmonary lesions including pleural plaques, acute benign asbestos pleurisy, diffuse (visceral) pleural thickening, lung cancer, and mesothelioma (discussed in Chapter 18.19.3). Asbestosis refers to the development of diffuse pulmonary fibrosis following inhalation of excessive amounts of asbestos fibres.

Aetiology and pathology

The toxicity of asbestos fibres may be related both to their dimensions and their persistence in lung tissue. The amphiboles crocidolite (blue asbestos) and amosite (white asbestos), and anthophyllite appear to be more fibrogenic than chrysotile (white asbestos). However, all types of asbestos increase the risk of asbestosis if a sufficient dose is inhaled.

It has widely been accepted that clinical asbestosis can be induced by cumulative asbestos exposure amounting to an estimated 25 fibres/ml–yrs. However, assuming the diagnosis is correct, this depends to some extent on how the diagnosis of asbestosis is ascertained and the fibres involved. Subclinical asbestosis, which may be detected incidentally by HRCT, can result from much lower cumulative doses.

The macroscopic appearances of asbestosis reflect the severity of the disease. The typical change is of grey fibrosis, more marked peripherally and in the lower zones (Fig. 18.13.9). In advanced disease, the lungs are shrunken and display honeycomb change. The airways are generally unremarkable, although traction bronchiectasis may be observed if fibrosis is severe. Lymph nodes may be enlarged but show no significant abnormalities on their cut surface. Pleural plaques or pleural thickening may be present.

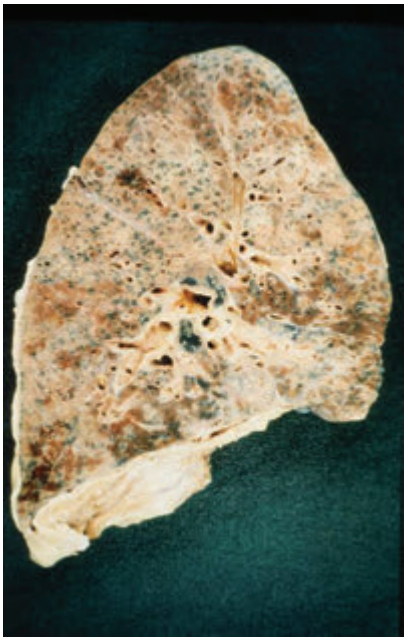

Fig. 18.13.9 Macroscopic picture of the lung from an individual with asbestosis.
Photograph kindly provided by Dr Richard Attanoos, Llandough Hospital, Vale of Glamorgan.

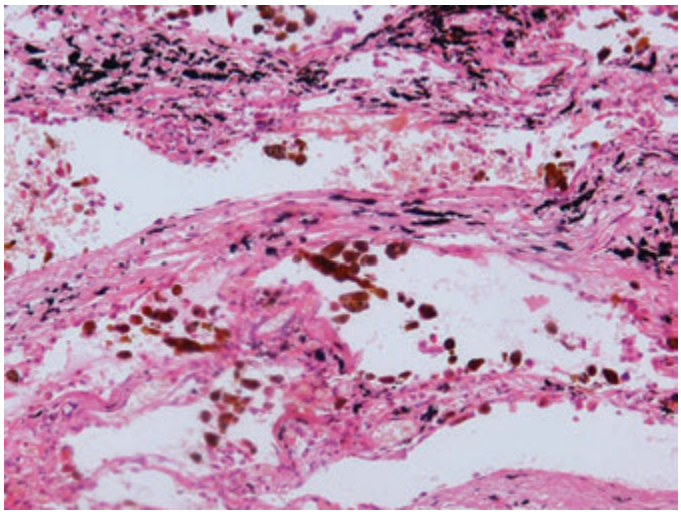

Fig. 18.13.10 Histological appearance of asbestosis, with interstitial fibrosis and asbestos bodies from a case of asbestosis.
Photograph kindly provided by Dr Richard Attanoos, Llandough Hospital, Vale of Glamorgan.

The microscopic features comprise both an appropriate pattern of interstitial fibrosis and the finding of asbestos bodies (Fig. 18.13.10). Fibrosis in asbestosis is always paucicellular, lacking any significant degree of inflammation, and is collagenous rather than fibroblastic. The distribution is similar to usual interstitial pneumonia, being predominantly lower lobe and peripheral, but with the temporal and spatial homogeneity of the fibrotic variant of nonspecific interstitial pneumonitis (NSIP). Fibroblastic foci may be observed but are uncommon. Honeycombing may be seen in advanced cases (Fig. 18.13.11).

Asbestos bodies are formed when asbestos fibres are coated with a protein–ferritin complex. They are usually readily identified in

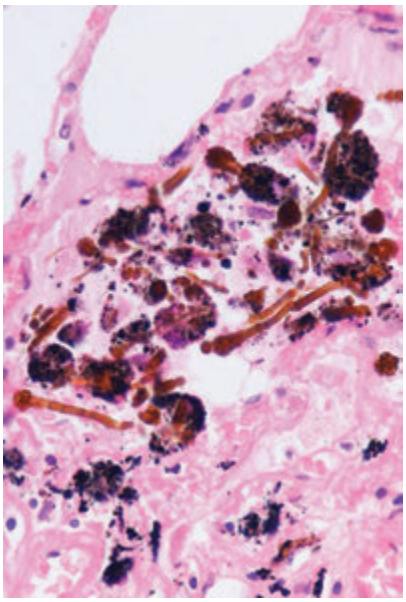

Fig. 18.13.11 Histological appearance of asbestos bodies.
Photograph kindly provided by Dr Richard Attanoos, Llandough Hospital, Vale of Glamorgan.

haematoxylin and eosin-stained or Perls-stained sections as dumbbell like structures. It is important to recognize that the pathologist may only detect ferruginous bodies, that is, asbestos bodies coated with, as described earlier, iron-containing compounds, and uncoated fibres may be more frequent. The finding of asbestos bodies alone is insufficient for a histologic diagnosis of asbestosis and indicates only asbestos exposure. In most cases of asbestosis at least two asbestos bodies should be observed per cm^2 of lung. In rare cases, fewer bodies are seen and the heavy fibre burden necessary for the diagnosis of asbestosis is only demonstrated by more sophisticated techniques involving tissue digestion.

Clinical features

The appearance of asbestosis follows a latent period, which is typically at least 20 years from initial exposure. Shorter latent periods have been described in those with much higher exposures but are uncommon nowadays, and the typical latent period is becoming longer as the pattern of disease changes with less severe forms of asbestosis being recognized by HRCT.

The symptoms of asbestosis are similar to those of other fibrosing lung diseases, with shortness of breath, initially on exertion, and dry cough. Repetitive end-inspiratory basal crackles may precede symptoms, and finger clubbing may be observed, but this is usually a late feature.

The typical chest radiographic changes are shown in Fig. 18.13.12. The classical lung function abnormalities include a restrictive ventilatory defect in the presence of reduced volumes and transfer factor, but these may not be present in those with early or limited asbestosis.

The greater sensitivity and specificity of HRCT provides greater delineation of parenchymal and pleural changes and is particularly useful if the chest radiograph is normal or only minimally abnormal, as may be the case in early disease. HRCT asbestosis (Fig. 18.13.13) evolves from isolated dot-like structures in the periphery of the lower lung, which correlate with peribronchiolar fibrosis found on histology, to pleural-based intralobular and interlobular lines, ground-glass attenuation, and finally honeycombing. HRCT scanning is also useful when emphysema or other respiratory pathology is present as it allows quantification of the relative contributions of different pathologies.

The severity of asbestosis present in an individual may be classified according to four grades. Grade 1 or Grade 2 asbestosis is not accompanied by clinical or radiological signs of disease and can be made only by histological examination of tissue obtained by biopsy in life or at post-mortem. Grade 3 and Grade 4 cases have radiological changes and symptomatic clinical signs of the disease. There is a broad correlation between the severity of disease and the level of asbestos exposure. However, there are wide variations within that spectrum, reflecting differing individual susceptibilities.

Differential diagnosis

In most cases the diagnosis of asbestosis can be confidently established on the basis of the history, clinical presentation, and radiological features. However, the differentiation of asbestosis from other causes of pulmonary fibrosis, particularly, idiopathic pulmonary fibrosis or the fibrotic form of NSIP, is important from the point of view of prognosis and of management, including giving advice on compensation issues. In such cases it can be helpful to focus on the

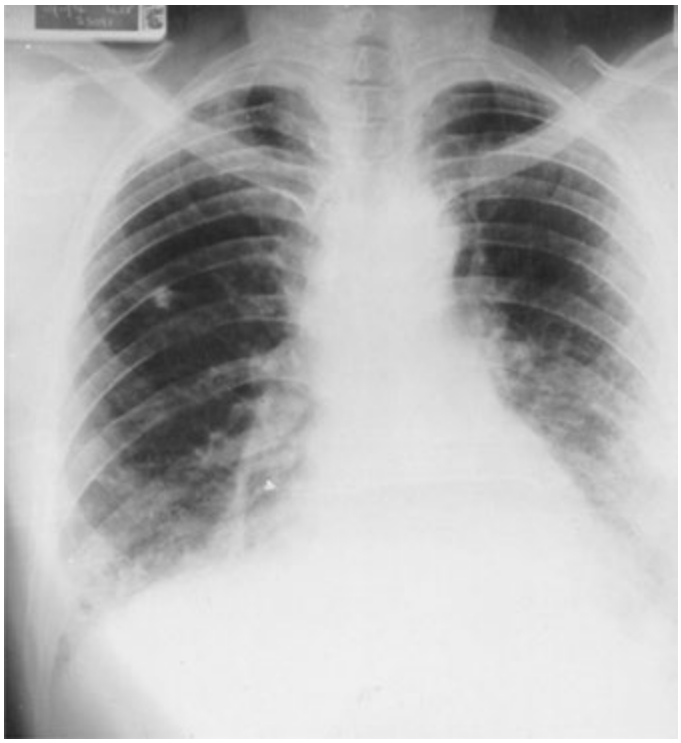

Fig. 18.13.12 Radiograph of a thermal insulator (lagger) with asbestosis. The typical chest radiographic changes are those of small irregular opacities, becoming increasingly coarse as the disease progresses and eventually coalescing to form a honeycomb pattern. In advanced asbestosis the fibrosis obscures the cardiac border, giving a shaggy appearance. In this case, a calcified TB focus is present in the right upper zone.

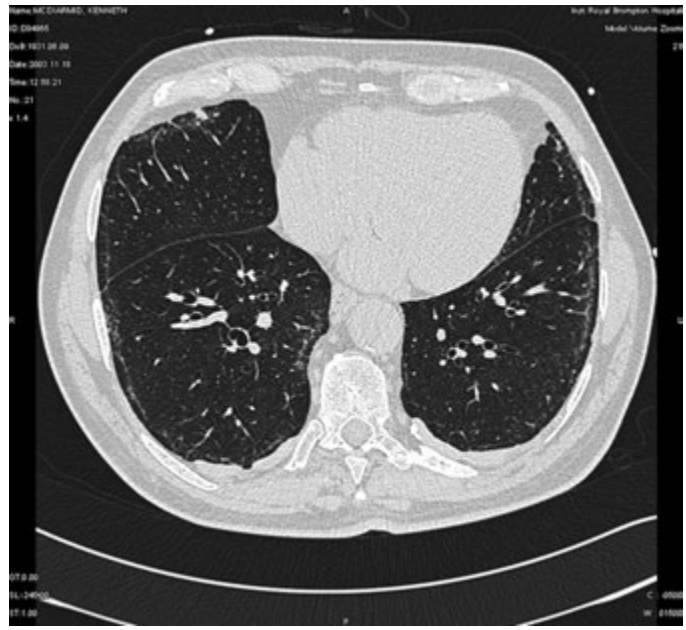

Fig. 18.13.13 CT from a patient with mild asbestosis showing a fine reticular pattern and subpleural lines. Bilateral pleural plaques are present.

Image kindly provided by Dr Michael Rubens, Royal Brompton and Harefield NHS Trust.

history of asbestos exposure, the presence of pleural disease, and if follow-up has occurred over a sufficient interval, the natural history of the condition.

The development of asbestosis requires substantial exposure to asbestos, in terms of both intensity and duration and the presence of a history of substantial asbestos exposure. The diagnosis should rarely be entertained in an individual with light or occasional exposure. If the individual has been under observation for a sufficient period, the rate of progress of the disease may be helpful. While rare cases of asbestosis with rapid progression are recognized, the clinical picture is typically one of slow change, contrasting with the more rapid progression of idiopathic pulmonary fibrosis.

The presence of pleural plaques (Fig. 18.13.14) is consistent with prior asbestos exposure, but pleural plaques may develop following lower levels of asbestos exposure than those necessary to cause asbestosis, hence on their own they are insufficient to confidently establish the diagnosis of asbestosis.

Investigation

If the diagnosis remains uncertain on clinical and radiological grounds, tissue biopsy may be contemplated. Given the uneven distribution of asbestosis, tissue samples should be taken from more than one site. If tissue is being obtained during resection of tumour, then, in the case of pneumonectomy, peripheral and central blocks should be taken from each lobe, and in the case of lobectomy, at least one peripheral and one central section should be examined. Areas immediately adjacent to tumour should be avoided. In post-mortem cases minimal sampling should include blocks from the peripheral and central portions of each lobe of both lungs.

As just stated, the histological criteria required include both a conventional pattern of alveolar septal fibrosis and an average of at least two asbestos bodies per square centimetre of lung tissue. In most cases asbestos bodies are readily identified in haematoxylin and eosin-stained sections, but they may be more easily identified and counted with Perl's stain. Fibroblastic foci may be occasionally observed in cases of asbestosis, but their presence is more typical of idiopathic pulmonary fibrosis, especially when numerous. In exceptional cases, where continuing diagnostic doubt exists, a more detailed fibre analysis may be undertaken by transmission electron microscopy or scanning electron microscopy. Energy-dispersive X-ray analysis may be used with both techniques, facilitating identification of the chemical composition of individual particles confirming fibre type.

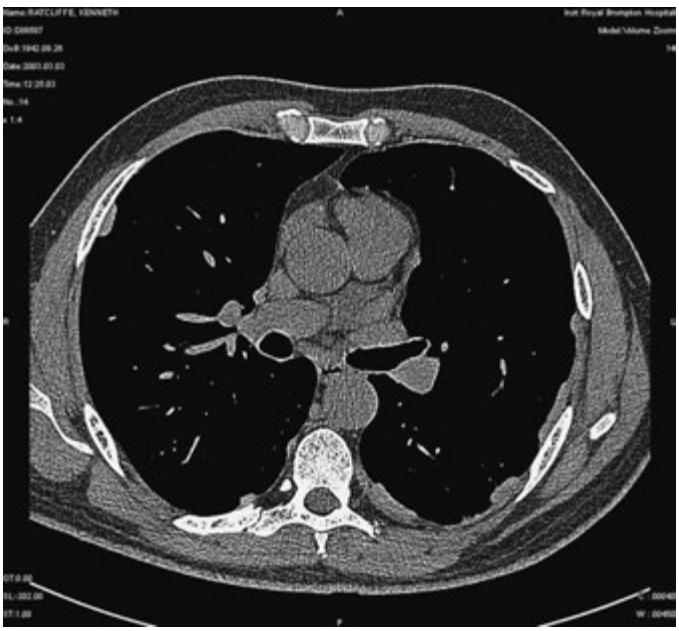

Fig. 18.13.14 CT scan showing extensive bilateral pleural plaques.
Image kindly provided by Dr Michael Rubens Royal Brompton and Harefield NHS Trust.

Prognosis

Cases of rapidly accelerated asbestosis associated with high levels of asbestos exposure have been described, but are rare nowadays in the United Kingdom. In most individuals late onset asbestosis reflects relatively low dose asbestos exposure over a very prolonged period of time; progression is typically slow and sometimes imperceptible. As asbestos and tobacco act as synergistic carcinogens, it is particularly important to advise individuals with asbestosis who smoke tobacco to stop smoking as they are at very high risk of lung cancer. The risk of lung cancer is greatest following exposure to amphiboles such as crocidolite and amosite, but is also present, albeit to a much lesser extent, following exposure to chrysotile.

Prevention and management

The prevention of asbestosis, as of other pneumoconioses, depends on reducing the exposure of individuals to levels that have been shown to be insufficient to cause the disease in a lifetime of exposure. Unfortunately, the difficulties of making valid measurements of airborne fibres and the uncertainties attached to the early diagnosis of asbestosis have prevented the formulation of reliable evidence on which to base a standard. The present British standard for chrysotile of 0.3 respirable fibres/ml has been based on work that suggests such levels would, when breathed over a working lifetime, result in asbestosis in less than 1% of those exposed. The corresponding standard for amphiboles is 0.2 fibres/ml. However, it should be noted that these concentrations do not take account of the much more serious risk of mesothelioma (see Chapter 18.19.3), and for this reason use of the mineral is now banned in the United Kingdom. It should also be noted that a concentration of 0.1 fibres/ml sounds small until it is realized that it represents 100 fibres/litre, or many hundreds of thousands of fibres inhaled over a working day.

The need for a material with the properties of asbestos has meant that many industries have now introduced other fibrous or crystalline minerals in its place. The potential of such new materials to cause similar diseases depends on their fibre dimensions, solubility in tissue, and the concentrations achieved in the workplace air. It is important that they should be handled with appropriate care by industry.

Regular medical and radiological examination of asbestos workers is essential for the early detection of asbestosis, and there is some evidence that removal of the worker from exposure at this stage is associated with slower progression. If asbestosis is suspected, workers in the United Kingdom should apply to the Benefits Agency for assessment for industrial injuries benefit.

Silicosis

Silicosis is caused by the inhalation of crystalline silica, which exists in several forms including quartz, cristobalite, and tridymite. In industry, quartz is the most commonly encountered form, being found in substantial quantities in sand, sandstone, granite, clay, shale, slate, and some concretes and mortar. The content of quartz found in different types of stone varies considerably, from some sandstones which are 100% quartz to shale and slate which may contain less than 10%. Cristobalite and tridymite may be encountered in the ceramic, refractory, and diatomaceous earth industries (which use furnaces, kilns, incinerators, and reactors). Considerable levels of respirable silica may be generated by natural phenomena such as volcanic explosions and sandstorms.

Silicosis has been described in metal miners and masons since ancient times, but assumed particular importance in the cutlery and pottery trades to the United Kingdom in the nineteenth century. Today, the condition may affect anyone involved in quarrying, carving, mining, tunnelling, grinding, or sandblasting. Activities in the work place such as cutting, grinding, and polishing stone produce fine dust that contains respirable crystalline silica. Working with hammers and chisels tends to produce a greater proportion of coarse dust and chippings, whereas dry cutting, grinding, and polishing produces a greater proportion of fine dust. However, both processes produce respirable dust. Power tools such as angle grinders generate far greater concentrations of airborne dusts than those produced from hand tools. Recently, colleagues in Italy, Spain, Israel, the USA and Australia have drawn attention to the occurrence of silicosis following exposures cutting artificial stone in the construction of kitchen and bathroom finishings.

Very high rates of silicosis continue to be reported from South Africa, China, Vietnam, India, Brazil, Columbia, and even the United States and Canada. Recent reports indicate that more than 23 million workers are exposed to crystalline silica in China and over 10 million in India alone. In the United States and Europe, the respective figures are 1.7 million and over 3 million. High rates of silicosis continue to be reported from South Africa, China, Vietnam, India, Brazil, Columbia, and even the United States and Canada. Outbreaks of silicosis have been reported in Spanish quartz conglomerate workers and in agate-grinding workers in Iran and India. In fact, recent estimates from India suggest that over 3 million workers are exposed to silica dust.

Aetiology and pathology

The inability of macrophages to effectively phagocytose crystalline silica is accompanied by necrosis and disintegration of the cell, followed by the liberation of the ingested silica, which may be re-ingested by other macrophages fuelling a complex self-perpetuating inflammatory response accompanied by the progressive accumulation of collagen and an influx of other inflammatory cells.

The earliest effects of this inflammatory and fibrotic response occur in the lymph nodes. It is important, however, to recognize that the finding of an inflammatory or fibrotic response in the lymph nodes is insufficient to establish a diagnosis of silicosis. However, as these nodes become progressively blocked, impairing the normal clearance mechanisms and promoting further retention of silica in the lung. Some silica is also transported across the alveolar epithelium by migrating macrophages and as a result of endocytosis by type 1 alveolar cells.

Quartz appears to be most toxic when freshly fractured, suggesting that surface properties are important in toxicity. This concept is supported by experimental evidence that various clay minerals and other chemicals that occlude the surface reduce the toxicity of inhaled quartz when inhaled simultaneously in mixtures of dust. The recognition that a coating of aluminium reduced the *in vitro* toxicity of quartz led to the inhalation of aluminium being trialled as a potential therapeutic agent in both the United Kingdom and Canada (MacIntyre Powder), although this was later abandoned.

Macroscopic inspection of silicotic lungs shows fibrous pleural adhesions, enlarged lymph nodes that contain fibrotic nodules, often calcified, and grey nodules throughout the lung. These nodules vary from a few millimetres to several centimetres in diameter and are more profuse in the upper zones. They may rarely be calcified, and they have a typical whorled, collagenous appearance when cut across (Fig. 18.13.15). The largest lesions consist of many such nodules that have become confluent, and as in CWP, this progressive massive fibrosis may undergo ischaemic necrosis and cavitate. Under the microscope the silicotic nodule consists of concentric layers of collagen surrounded by a zone of refractile silica particles, macrophages, and fibroblasts. The nodule may contain the remnants of the respiratory bronchiole and arteriole, destroyed by fibrosis.

Extremely high exposures to crystalline silica may be followed by the development of an alveolar lipoproteinosis-like reaction (silicoproteinosis). In these cases the macroscopic appearance is similar to pulmonary oedema, but under the microscope the alveoli are seen to be filled with eosinophilic fluid and the alveolar walls contain plasma cells, lymphocytes, fibroblasts, and silica. The condition is characterized by excessive secretion of surfactant, which the macrophages attempt to phagocytose, leading to the appearance of foamy cytoplasm that stains strongly positive with eosin and periodic acid-Schiff.

Clinical features

There are three main clinical presentations of silicosis: classic silicosis, accelerated silicosis, and silicoproteinosis.

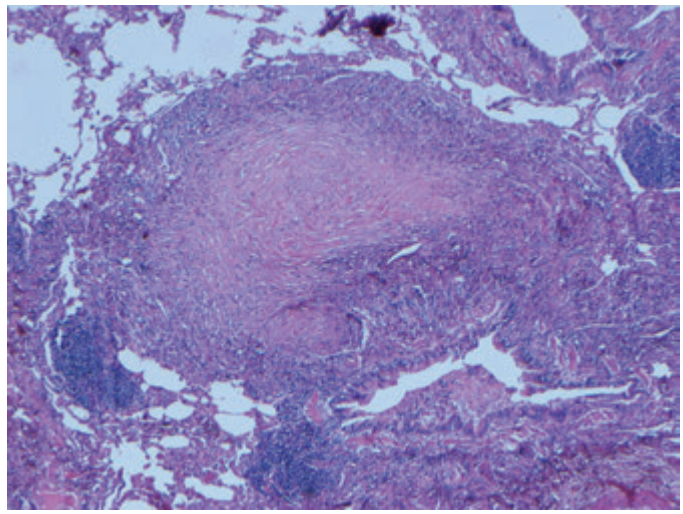

Fig. 18.13.15 Silicotic nodules, showing the typical whorled appearance. Photograph kindly provided by Dr William Wallace, Consultant Pathologist, NHS Lothian.

Classic silicosis

This is the most common presentation and typically appears following 10–20 years of continuous silica exposure, usually associated with exposure to dust containing 10–30% silica. The condition may both develop and progress in the absence of symptoms, physical signs, or any demonstrable lung function abnormality, being only identified on a chest radiograph taken for surveillance purposes. However, as the condition progresses, increasing levels of breathlessness and lung function impairment can be anticipated. The typical pattern of lung function defect is a restrictive ventilatory defect in the presence of reduced lung volumes and impaired gas transfer.

The diagnosis of silicosis is usually based on a history of exposure and the typical radiographic appearances. The typical plain chest X-ray appearances are similar to those of coal worker's pneumoconiosis, but owing to the greater fibrogenicity of silica, the nodules, which are generally between 3 and 5 mm in diameter, and concentrate in the upper and mid-zones, are usually more pronounced (Fig. 18.13.16). Silica cleared to the regional nodes results in hilar enlargement that eventually calcifies. Eggshell calcification in the hilar nodes (Fig. 18.13.17) is often held to be a pathognomonic feature, but may be observed in sarcoidosis.

HRCT provides greater diagnostic and prognostic information. The technique is considerably more sensitive at detecting the presence of nodules, whose upper lobe posterior centriacinar and subpleural bias may be more easily appreciated (Fig. 18.13.18). The presence of PMF, which may be present in the absence of symptoms, is more readily defined and is often seen to be accompanied by cicatricial emphysema. Greater resolution of lymph node anatomy shows enlargement of the hilar and mediastinal nodes, which may show calcification as described earlier. In addition, HRCT allows an assessment of the contribution of any additional pulmonary pathology, such as emphysema, that may confound assessment of reported functional limitation and the interpretation of lung function tests.

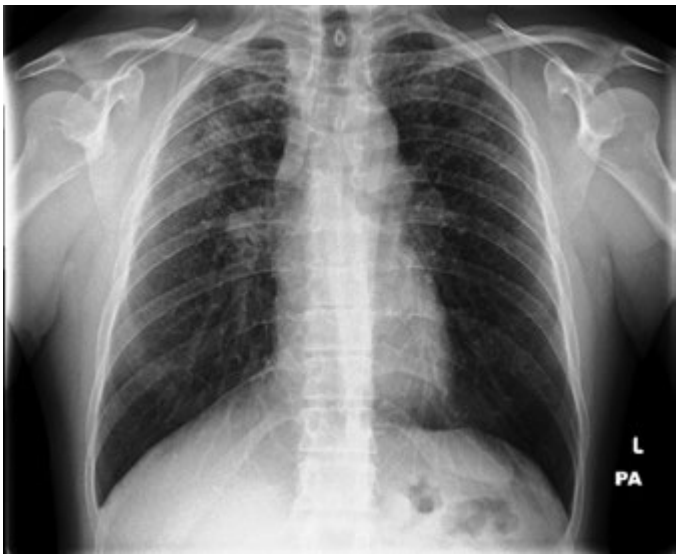

Fig. 18.13.16 Chest X-ray appearances of silicosis demonstrating upper and mid-zone nodules and hilar lymphadenopathy. In this case, loss of volume in the upper lobes has occurred.

Fig. 18.13.17 Radiograph of a hard-rock miner, showing massive fibrosis in right mid-zone and eggshell calcification of hilar nodes.

Biopsy may be considered when the diagnosis is uncertain on clinical and radiographic grounds alone. Sarcoid represents a challenge for the unwary: silica exposure can be associated with bilateral hilar lymphadenopathy, lymphopenia, and elevated serum angiotensin converting enzyme. The typical silicotic nodule is acellular and consists of hyaline collagen arranged in a whorled pattern. Polarizing filters demonstrate birefringent crystals within

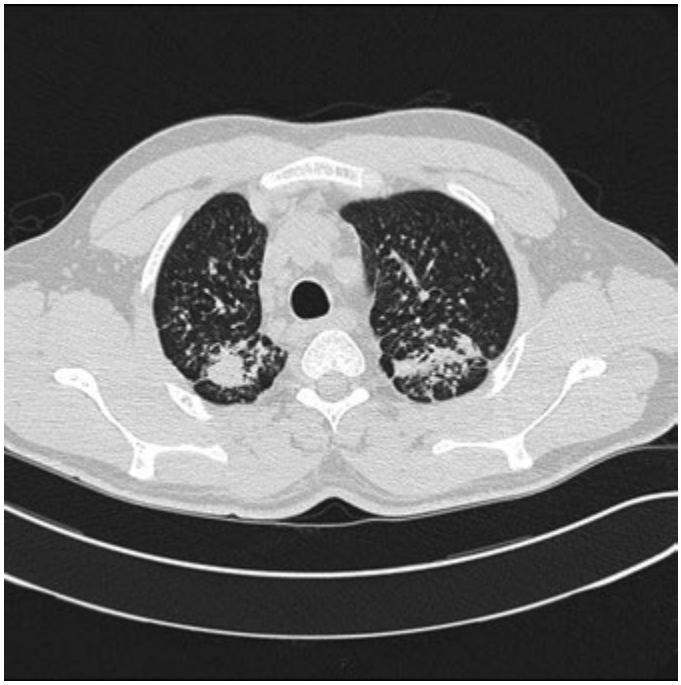

Fig. 18.13.18 HRCT scan from a stonemason showing the presence of nodules with an upper lobe posterior bias and the occurrence of progressive massive fibrosis.

the nodules confirming the presence of silica and other silicates. Silicotic nodules develop in the lymph nodes, but silicosis should not be diagnosed unless lung involvement is present. Lung tissue between the nodules is usually normal. Occasionally, in cases of mixed dust exposure, a diffuse fibrosis may be present.

Accelerated silicosis

This is associated with a much shorter duration of dust exposure (typically 5–10 years) and, as the name suggests, a faster rate of disease progression. Clinical presentation may be as early as 1 year after exposure. Otherwise the clinical, radiographic, and pathological features are similar to classic silicosis. The pathology may show less established collections of macrophages, more loosely arranged than the classical silicotic nodule with relatively little collagen.

Silicoproteinosis

This an acute, rapidly progressive disease following very high-level exposure. Presentation within one year of exposure and death within 5 years of exposure have been reported. The radiograph shows appearances resembling pulmonary oedema.

Prognosis

The biopersistence of silica in the pulmonary interstitium may lead to progression of the disease, even following cessation of exposure (Fig. 18.13.19). In the most severe cases may be complicated by the development of pneumothorax, pulmonary hypertension, respiratory failure, and cor pulmonale. In addition, those exposed to high quantifies of silica have increased risks of several other pulmonary and extrapulmonary conditions.

Inhalation of respirable silica appears sufficient to increase the risk of developing pulmonary tuberculosis, but the risk is greatest when silicosis has developed and the occurrence may be termed silicotuberculosis. The prevalence of silicotuberculosis is particularly high among South African gold miners, who undoubtedly share other risk factors common to the contraction of pulmonary tuberculosis (TB), including a high prevalence of HIV infection. However, there are theoretical reasons to suggest that silica exposure increases the risk of contracting TB. First, silica is toxic to macrophages that are an important defence mechanism to mycobacteria, and secondly, experimental evidence suggests silica may promote the growth of mycobacteria. The physician should be aware of this close relationship between silicosis and pulmonary tuberculosis, as both the clinical and radiological manifestations of silicosis may mask the appearance of this complication. In addition to mycobacterium tuberculosis, individuals with silicosis are also susceptible to infection with nontuberculous mycobacteria.

Crystalline silica has been recognized as a carcinogen by the International Agency for Research on Cancer since 1987. An increasing number of epidemiological studies support an increased prevalence of lung cancer in individuals with silicosis and in the

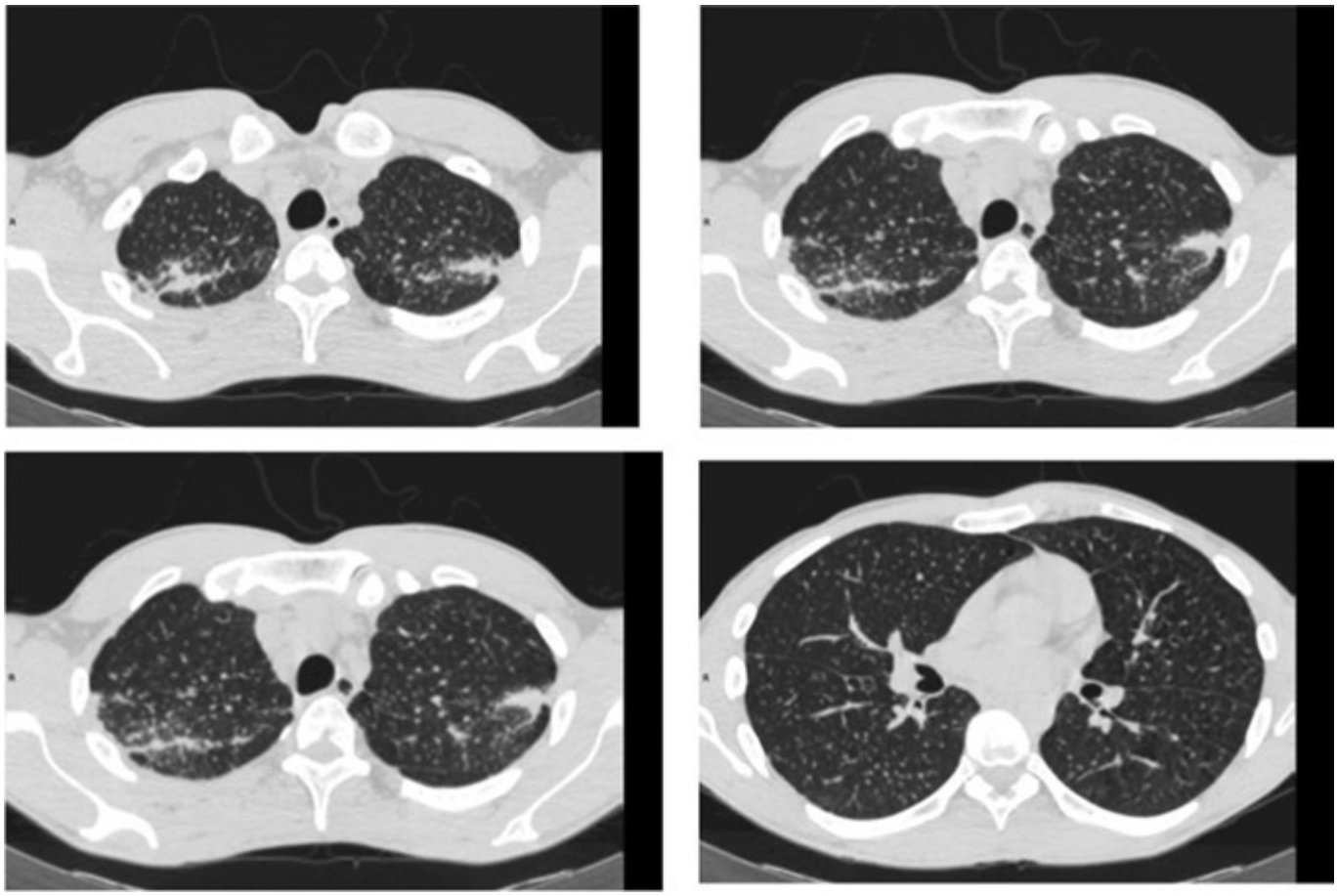

Fig. 18.13.19 These images are taken from the same stonemason 8 years apart following cessation of exposure to stone dust and illustrate the progression of silicosis.

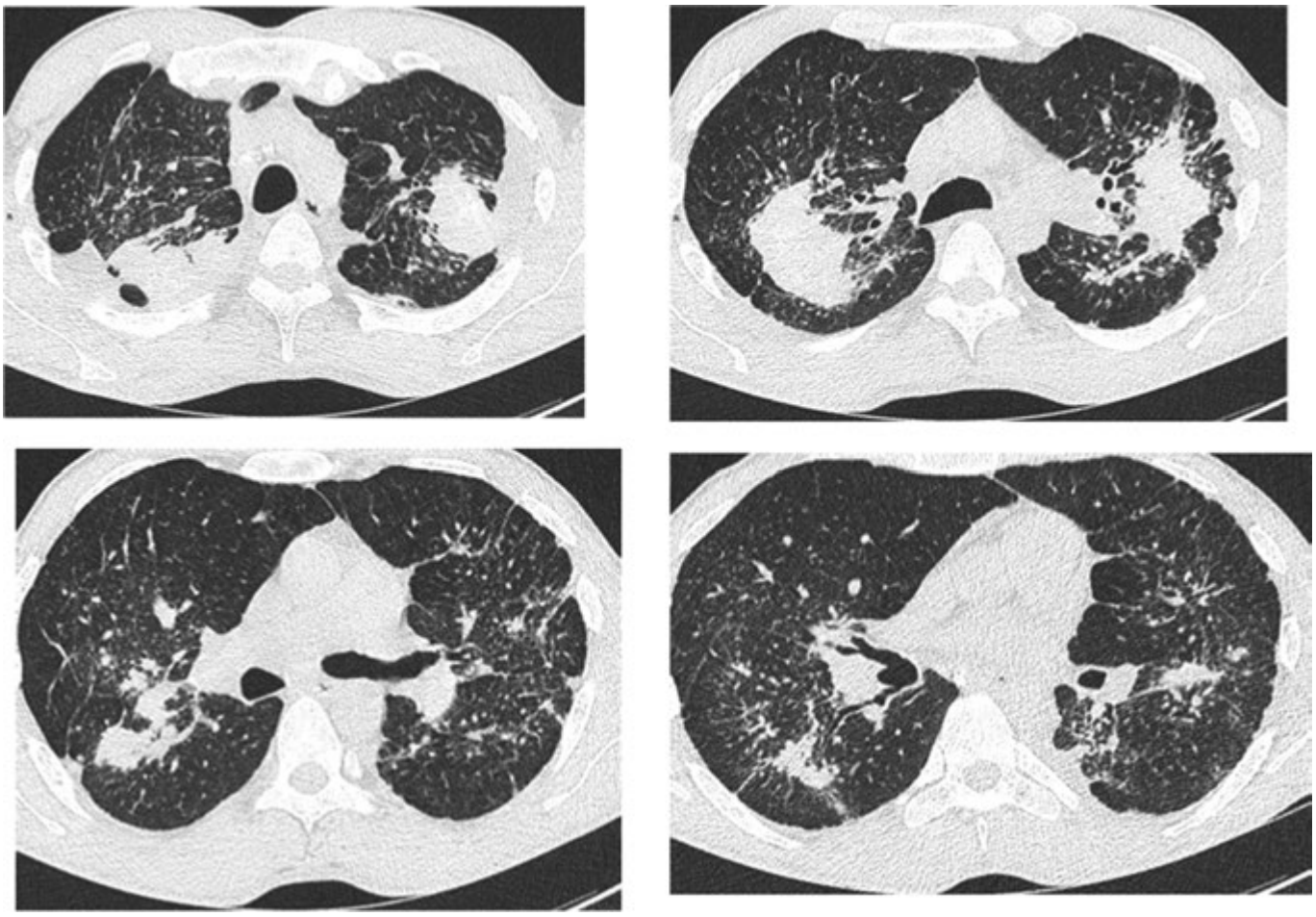

Fig. 18.13.19 Continued

United Kingdom, the occurrence of lung cancer in individuals with silicosis is recognized as an occupational disease.

In common with coalminers, epidemiological studies of workers exposed to respirable silica dust suggest that cumulative exposure to silica is related to the development of airflow obstruction and emphysema. Hence, silica exposure is a recognized cause of chronic obstructive pulmonary disease (COPD) and potentiates the effects of cigarette smoking.

Numerous publications have drawn attention to the development of hypergammaglobulinemia, rheumatoid factor, and autoantibodies and the association between silica exposure and scleroderma, known as the Erasmus syndrome, has been recognized since the turn of the twentieth century. Several studies have suggested that the prevalence of systemic lupus erythematosus is greater than would be expected in a comparable general population, particularly in men. Other immunologically mediated conditions, such as autoimmune haemolytic anaemia, and dermatomyositis/dermatopolymyositis have also been described in individuals following silica exposure. Exposure to respirable silica has also been associated with the development of glomerulonephritis, even in the absence of silicosis.

Prevention and management

The epidemiological evidence suggests that workers exposed to levels of respirable silica in excess of 1 mg/m^3 have a high risk of silicosis, and that a risk may still exist at levels of around 0.1 mg/m^3. The United Kingdom maximum exposure limit is 0.1 mg/m^3, and industry is obliged to keep the exposure of workers as far below this level as is reasonably practicable. This is achieved by control measures such as appropriate ventilation, extraction, dust-suppression measures, and personal respiratory protection.

A worker who has developed the disease should be prevented from working with silica again. In the United Kingdom, workers with silicosis (whether or not complicated by lung cancer) should apply to the Respiratory Diseases Board of the Benefits Agency for industrial injuries benefits. The only medical management necessary is regular sputum examination for tubercle bacilli, as tuberculosis accelerates the lung damage, but responds normally to chemotherapy. In areas where TB is particularly prevalent, it may be sensible to consider prophylaxis in individuals with silicosis. Advanced silicosis is an indication for consideration of lung transplantation. Whole-lung lavage may be contemplated for sufferers of alveolar proteinosis, but its role in other forms of silicosis remains unclear.

Silicates

Silicates are complex compounds in which silicon and oxygen (combined as an anion) bond with any one of several cations.

While less fibrogenic than silica, many of these are believed to cause pneumoconiosis. However, as silicates are commonly contaminated with asbestos, silica, or both, this has confounded the understanding of their fibrogenicity. The pathological reaction is similar to that of silicosis, but the nodules are invariably less well demarcated. Silicates are identified on pathology as plate-like, birefringent crystals that produce foreign body granulomata.

Talc pneumoconiosis

Talc (hydrated magnesium silicate) is mined as soapstone in the United States, China, Australia, Austria, and the Pyrenees. It is milled and has many uses including in cosmetics, the rubber industry, paints, ceramics, and pharmaceuticals. Talc may be contaminated with silica and asbestos (tremolite) and when these are present, talco-silicosis and talco-asbestosis display a clinical picture similar to silicosis and asbestosis, respectively.

Talcosis refers to the inhalation of pure talc. It is an uncommon cause of pneumoconiosis, but continues to be reported in miners, millers, and soapstone artisans. 'Samosa' pneumoconiosis has been reported in a worker with considerable exposure to talc during preparation of 'samosa'. Bronchoconstriction may occur in children following aspiration of high concentrations of cosmetic talc, but the more usual presentation in adults is the radiological occurrence of rounded and irregular opacities in the mid-zones, often with a perihilar distribution. Exceptionally, very small, widely disseminated opacities (about 2–3 mm in diameter), similar to the miliary lesions of sarcoidosis or tuberculosis may be observed.

Talcosis may also be observed in intravenous drug abusers who crush and inject oral medications in which talc is used as a bulking agent or lubricant. The radiographic findings are more typically those of large, irregular, nodular densities, or consolidation in the upper parts of the middle lung fields. Widespread irregular nodules may appear accompanied by a permanent loss of lung volume. Lymph node enlargement is common and may be massive. Lung biopsy shows foreign body granulomata and free intracellular birefringent deposits and multinucleate giant cells. In particular, talc particles longer than 5 microns in length should raise suspicion of intravenous drug abuse.

Kaolin pneumoconiosis

Kaolin (hydrated aluminium silicate), often referred to as China clay, is quarried in southwest England, Georgia (United States of America), Japan, Egypt, Germany, and the Czech lands. Kaolin causes a pneumoconiosis similar to coal worker's pneumoconiosis with small, discrete nodular lesions initially and a tendency to produce massive fibrosis. It has been described in workers involved in the drying and milling processes in the production of china clay and in those working in the manufacture of ceramics, paper, and paint. Kaolin may also have been the component of the dust responsible for pneumoconiosis in the now defunct Scottish shale oil industry.

Fuller's earth (montmorillonite) pneumoconiosis

Fuller's earth (hydrous aluminium silicates of varying composition, including altered volcanic ash, mainly calcium montmorillonite) is an adsorbent sedimentary clay, which takes its name from Fullers who trod or pounded newly woven cloth placed in large vats of water and detergent to remove grease and dirt, and to thicken and soften the cloth. Quarrying in the United Kingdom has been discontinued on economic grounds, but it continues to be mined in the United States of America, and Germany. Nowadays it has found extensive use in cosmetic and pharmaceutical industries, but it also finds a use in special effects departments where the use of Fuller's earth in explosions results in an impressive particle plume allowing a smaller safer charge to be used. Fuller's earth pneumoconiosis has been described in workers extracting this clay. It is a benign nodular pneumoconiosis similar in pathological and radiological appearance to simple coal worker's pneumoconiosis.

Mica pneumoconiosis

Mica is a complex aluminium silicate occurring in two forms, muscovite and phlogopite. Large reserves are found in Africa, South America and India, Canada, Russia, China, and the United States. Muscovite, the most common mineral of the mica family, is mined in the United States of America and India and used in fire-resistant windows and the manufacture of paper and paint. Other forms of mica include phlogopite, mined in Canada for use in the electrical industry because of its resistance to heat and electricity. The role of mica in the development of pneumoconiosis has recently been reported in muscovite miners working in a pure muscovite milling unit. Dry cough and breathlessness were accompanied by bilateral micronodular ground glass opacities and mediastinal and hilar lymphadenopathy. Histological analysis showed giant cell granulomas without typical silicotic nodule with high concentration of birefringent particles consistent with mica.

Berylliosis

Beryllium is an alkaline earth metal mined in the United States, Brazil, Russia, India, and Madagascar. The ore occurs in two forms: bertrandite, a silicate, and aluminosilicate beryl. The first descriptions of chronic berylliosis occurred in fluorescent light bulb workers who applied a beryllium oxide coating. Classically, occupational exposure to beryllium may be encountered in aerospace, nuclear, and military settings. However, its use is widespread in automotive, electronics, and telecommunications industries. Alloys may be used as tubing for oil and gas drilling, tools, jewellery, bicycle frames, and dental appliances. Recycling of electronics, computers, and scrap alloy to recover copper also results in beryllium exposure.

Beryllium causes granulomatous ulcers on contact with the skin and is highly toxic when inhaled. Inhalation of high concentrations, which is rarely seen nowadays, causes an acute pneumonitis, which can be fatal or complicated by fibrosis in survivors. Chronic exposure to beryllium may be followed by sensitization, subclinical disease, or clinically apparent disease. The susceptible individual, who may be identified by HLA-DP2 haplotype, typically develops sensitization within two or three months following exposure.

Clinical, radiological, and pathological features

The clinical, radiological, and pathological presentation of chronic berylliosis is very similar to that of pulmonary sarcoid. The patient

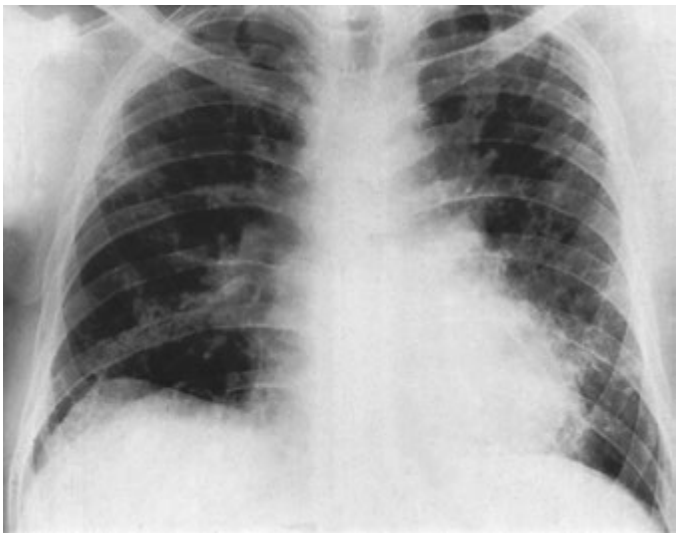

Fig. 18.13.20 Radiograph of a beryllium refinery worker, showing the diffuse fibrosis of berylliosis.

presents with cough and shortness of breath accompanied by bilateral pulmonary mottling, upper lobe fibrosis, and bilateral hilar lymphadenopathy. The pathological lesion also shows noncaseating granulomata and varying amounts of interstitial fibrosis. Hence, a diagnosis of sarcoidosis may be incorrectly applied if the occupational history has not been noted and awareness of the effects of beryllium exposure known. When berylliosis is suspected, the diagnosis may be confirmed with a beryllium lymphocyte stimulation test in blood or bronchoalveolar lavage.

Treatment and prognosis

The progress of the disease can be controlled with corticosteroid therapy, but this needs to be continued indefinitely in most cases. The disease typically progresses to diffuse fibrosis (Fig. 18.13.20), but the rate of progression is very variable. Beryllium is a class A human carcinogen, hence individuals with beryllium sensitization or disease must be advised to stop smoking.

Prevention and surveillance

The risk of berylliosis is reduced by keeping exposures below the threshold limit value (2 ng/m^3), although cases have occurred in in individuals with apparently low (trivial) levels of exposure (e.g. in wives exposed to dust from their husbands' clothes, and in people living near the factories). Efficient respiratory and skin protection should also be provided for workers in these industries. Biomonitoring for beryllium by measurement of beryllium in the urine has recently become possible. However, further validation of these assays is required to remove uncertainty regarding the toxicokinetics of beryllium excretion.

Aluminium

The role of aluminium as a cause of pneumoconiosis remains uncertain. On the one hand, its use has been linked to a rapidly progressive pulmonary fibrosis in alumina abrasive workers (Shaver's disease) and on the other, the inhalation of aluminium powder has been advocated to ameliorate the fibrogenic potential of silica. There has been little evidence of interstitial lung disease associated with primary aluminium production (Bauxite mining, aluminium refining, and aluminium smelting) and long-term follow-up of China Biscuit placers from Stoke-on-Trent exposed to respirable aluminium found no evidence of pneumoconiosis. Nonetheless, the potential role of aluminium continues to be reported with the documentation of sarcoid-like granulomas induced by aluminium dust and the occurrence of desquamative interstitial pneumonia in aluminium welders, the development of pulmonary alveolar proteinosis in an aluminium rail grinder and the recent reporting of pulmonary fibrosis associated with aluminium trihydrate (Corian) dust.

Other pneumoconioses

Siderosis occurs in workers exposed to iron oxide: iron ore miners, welders, iron foundries fettlers, steel workers, boiler scalers, haematite miners, and crushers. The condition is benign and is usually only detected when radiology is performed for purposes of surveillance. The radiological lesions often regress after exposure ceases. Pathologically, the lungs are coloured red. An increased risk of lung cancer has been reported but is probably due to radiation in mines. Baritosis occurs in workers processing barium. Although benign, the appearances may be dramatic owing to the radiodensity of barium. However, some resolution may occur following cessation of exposure, such as stannosis occurring in tin smelters and argyosiderosis occurring in silver polishers (Fig. 18.13.21). Graphite pneumoconiosis, occurring in those exposed to graphite dust, has

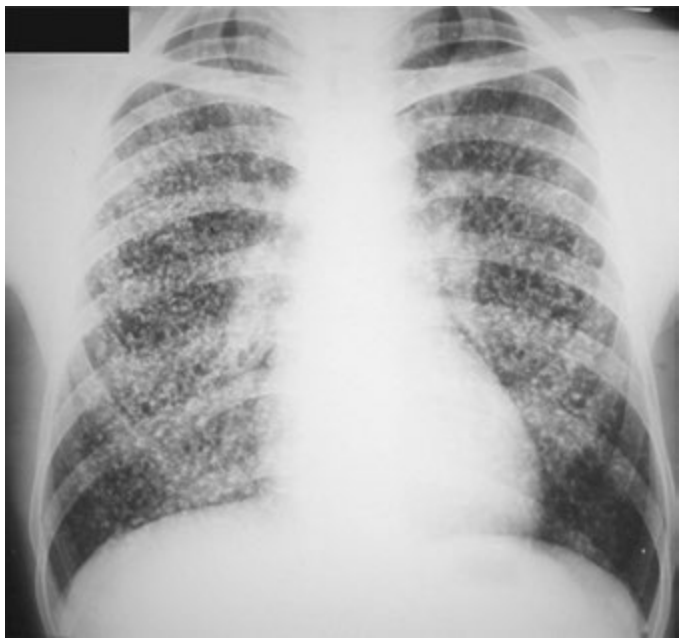

Fig. 18.13.21 Radiograph of a worker exposed to tin oxide fume in refining. He was completely symptom-free and had normal lung function. The radiological appearances reflect radiopaque dust in macrophages.

similar appearances to coal worker's pneumoconiosis including miliary and nodular opacities, conglomerate shadows, emphysema, and Kerley B lines.

Conclusion

Despite being an entirely preventable condition, pneumoconioses remain common and, when standards of occupational hygiene lapse, resurgent. The continued production and use of coal, asbestos, and silica in many countries suggests that coal worker's pneumoconiosis, asbestosis, and silicosis will continue to dominate the literature. However, new technology creates new risks for lung disease, and the rapid increase in the nanoparticle technology has raised concern regarding nanoparticle toxicity because these particles may easily reach the alveoli. Carbon nanotubes have been shown to cause pulmonary fibrosis in rats, and the occurrence of breathlessness, pleural and pericardial effusion has been described in seven young women working in a print plant and exposed to polyacrylate consisting of nanoparticles.

There is also an increasing awareness of the potential role of inhaled particles in cardiovascular disease. Concern regarding air pollution has been reflected in the cardiovascular and public health literature for some time, but more recently publications have focused on the potential links between silica exposure and increased risks of cardiovascular disease and stroke. Finally, the recognition that moon dust is rich in respirable crystalline silica has prompted interest in the behaviour of particles in microgravity, and early results suggest that there is increased pulmonary deposition of smaller particles in microgravity environments.

Acknowledgements

The author would like to acknowledge the original author of this chapter, Professor Anthony Seaton. Much of what is written continues to reflect his input. In addition, I would like to acknowledge the helpful comments from Dr William Wallace, Consultant in Pathology, NHS Lothian for provision of histopathology material and helpful comments on the manuscript. Dr Richard Attanoos, Llandough Hospital, Vale of Glamorgan kindly provided several examples of the histopathology of asbestosis. Dr Michael Rubens and Dr Arnie Debaraj from the Royal Brompton and Harefield NHS Trust provided images on asbestosis and Caplan's syndrome, respectively.

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