State of the Art

Silicosis[1-3]

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Contents

History

The effects of silicosis, the chronic fibrosing disease of the lungs produced by prolonged and extensive exposure to free crystalline silica, have been recognized for centuries. Pulmonary disease produced by dust is mentioned by Agricola in his *Treatise on Mining* (1556) and is described in stonecutters by van Diemerbroeck (1672) and Ramazzini (1713) (1). The physical evidence of previous occupational exposure to sources of free silica abound in old mines, abandoned quarries, and ancient flint tools and weapons (2). The disease can be acquired during direct operations with siliceous materials or in mineral extraction in which the free silica is contained in the residual rock. The exposure in such operations produces contact with high concentrations of dangerous fibrogenic material. Technologic advances that have supplied powerful sources of energy to industry have greatly increased the dust exposure of the worker. The pneumoconioses became more frequent and developed more rapidly after the introduction of steam machinery into factories at the turn of the nineteenth century. Zenker (1866) gave the general name pneumoconiosis to the group. Kussmaul (1866) demonstrated silica within the lungs. The specific name silicosis (Latin, *silex*, flint) was applied by Visconti (1870) (3). Intensive mining using pneumatic drills and modern energy sources made mining even more dangerous at the turn of this century. The gold mines in South Africa were opened in 1886 and clinical disease and pathology were described in this location in 1902 (3). Haldane (1902, 1914) stated that silica created the dust hazards for tin miners, and Collis (1915) proposed the theory that crystalline silica was the cause of most serious lung disease and predisposition to tuberculosis related to dust exposure (1). Increasing interest in industrial hygiene led to more intensive study of traditional trades carrying a dangerous free silica exposure, such as work in potteries, quarries, brick yards, and foundries. The frequency of the disease in metal grinders was known in the early nineteenth century. The high risk of work with granite was recognized almost a century later (4). Rapidly developing disease ("acute silicosis") was reported in scouring powder workers in 1929 after a short, intense exposure to high concentrations of free silica (5). The same course of illness has been described in runnelers (6) and sandblasters (7).

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The great increase in frequency of pneumoconiosis in coal miners and associated workers in this century led to special studies that have advanced our understanding of the pathogenesis, pathology, roentgenographic appearances, and progression of silicosis (8). Epidemiologic studies of involved workers have thrown light on the determinants of group disease (9). The relation of dust exposure to tissue reaction as visualized on chest roentgenograms and alterations in pulmonary function is under continuing study. Experiences with the coal workers has established the importance of the concept of mixed dust exposure and has made it possible to some degree to distinguish changes produced by prolonged coal dust exposure from those created by free silica (10). This concept has been of great importance in deciding the part that silica plays in the development of diffuse pulmonary fibrosis and pleural changes. It appears that admixed free silica accounts for the pulmonary disease produced by bentonite and montmorillonite. To a lesser degree, free silica may produce disease in workers exposed to talc and kaolin. In those instances where the workers are exposed to industrial combinations of asbestos and sand, variable degrees of nodular silicosis have developed. Mixing of substances containing free silica with other dusts or chemical substances has maintained the silica hazard in industry. Understanding of chemical changes has demonstrated that certain substances become increasingly dangerous in the course of industrial processes. The heating of diatomaceous earth produces high concentrations of cristobalite and tridymite which are forms of crystalline silica more dangerous than the commonly encountered quartz (11). In the course of industrial development throughout the world, problems of production have led to the revival of dangerous industrial processes. Abrasives for the cleaning of metal surfaces before painting are in constant demand in construction and shipbuilding. In older industrial regions, the use of sandblasting for such purposes has been forbidden by law (United Kingdom, 1949, and European Economic Community, 1966). Sand as an abrasive has been extensively used in the United States in shipbuilding operations and in preparation and maintenance of oil rigs for offshore drilling since the termination of World War II. This has produced a resurgence of accelerated silicosis in sandblasters, leading to a large number of injuries and legal claims. Health and financial costs have therefore increased and have engendered a great need for modern protective devices and preventive work practices. Protective measures adopted in the past have almost eliminated clinical silicosis in quarry workers (12) and metal miners (13). At this time, the use of metal grit and coal ash residue promises to eliminate silicosis in abrasive blasters.

The early literature on silicosis is relatively limited. Important accounts were supplied by writers working for official institutions in South Africa (14), Australia (15), and Great Britain (16). In the United States, the earliest reports came from the U. S. Public Health Service (17). A pioneer monograph on roentgenology in pneumoconiosis was written by Americans (18). The early situation in the roentgenography of silicosis is described with personal reminiscences by Cole in a valuable and entertaining book (19). Descriptions of the pathologic features of silicosis are encountered in the works of Gardner (20), Gloyne (21), and the South Africans, Simson and Strachan (22). The earliest works on general studies of miners' diseases are given in varying detail by Rosen (23) and Meiklejohn (24). The enlarging literature contains valuable accounts of national experiences with silicosis. A French monograph (25) and a large Swedish text (26) described the situation before 1960. In the encyclopedic volumes on occupational health and safety published by the International Labour Organization (27), there are substantial sections devoted to silicosis. Valuable material will be found in the latest edition of Hamilton and Hardy's textbook (11). The experience of the U. S. Public Health Service is brought up to date in the recent criteria document on crystalline silica published by the National Institute of Occupational Safety and Health (28). There is a large section on silicosis that includes historic data in Hunter's *The Diseases of Occupation* (2). Modern clinical accounts of silicosis are found in 2 excellent recent books by Parkes (29) and Morgan and Seaton (30). In Baum's textbook (31), Kleinerman writes a full account of silicosis and the other pneumoconioses. A monograph on experimental pneumoconiosis includes extensive material on silicosis (1). The proceedings of the International Pneumoconiosis Conference (32) and of the International Symposia on Inhaled Particles and Vapors (33) review current epidemiologic, experimental, and environmental work.

Geology and Occupational Sources

Most of the earth's crust consists of compounds

of silicon and oxygen. The place of silicon in the inorganic world is similar to that of carbon in the organic sphere. The compound that is responsible for the development of silicosis is silicon dioxide, which occurs in nature in 3 different crystalline forms: quartz, with hexagonal crystals; cristobalite, with cubic crystals; and tridymite, with hexagonal crystals. Quartz, a hard, colorless substance, is the most common of all minerals and is a constituent of many rocks, such as granite and sandstone. The structure of quartz is described as consisting of SiO_4 tetrahedra, with each oxygen atom serving as the corner of 2 of the tetrahedra. To break a crystal of quartz, it is necessary to divide some silicon-oxygen bonds. The structure of quartz accounts for the hardness of the mineral (34).

The uncombined forms of silicon dioxide are called, collectively, "free silica" to distinguish them from silicates, which contain cations. The silicates are found in chains and in more complex structures.

The ubiquitous presence of silicon dioxide in the earth's crust is the prime factor responsible for the frequent contact of workers of various occupations with the substance. The silica-rich rock or mineral may be directly quarried for purposes of construction or may be the matrix in which a desired material is embedded. Residual rock is sometimes used for industrial purposes, notably in construction; but when the special properties of free silica are needed for abrasives, relatively pure forms of the crystalline material are used. Crypto-crystalline flints have been used since pre-recorded history, and with other materials containing silicon dioxide in high concentrations are used in those industries in which hard, heat-resistant materials are required for production of pottery and porcelain and in casting metals. Crystalline silica may be present in lesser concentrations (up to 10 to 24 per cent) when silicates such as fuller's earth and bentonite are mined. The noncrystalline (or amorphous) forms of silica are regarded as having little or no fibrogenic properties but may acquire these if heated or calcined.

The history of industrial development shows how the silica hazard has increased with the application of new and more powerful sources of mechanical energy to the earth's crust. In mining and quarrying, the introduction of pneumatic drills and blasting increased production and produced larger dust clouds that contained high concentrations of respirable particles (< 10 μm in diameter). The danger of using such methods in enclosed spaces while handling substances containing high concentrations of crystalline free silica is demonstrated in tunneling and in sandblasting (35, 36). Rapid development of complicated silicosis was vividly illustrated at Gauley Bridge, W. Va., in 1931 (6). Unprotected tunnelers encountered a vein of quartz and developed fatal silicosis after short exposures, in some cases less than one year. The same pattern of rapidly developing disease occurred in abrasive powder workers, who also worked in enclosed spaces with no respiratory protection.

Free silica is widely used in industry, but the dust risk may be unsuspected because of its admixture in rock structure or clay. Combination of free silica with other minerals is a common industrial practice: The silica is often added to asbestos in asbestos-cement mixtures for the production of pipe, tile, and roofing, and to cement and concrete for use in heavy construction.

The following list of principal industrial sources of free silica is modified from Parkes (29):

(*1*) Mining, quarrying, and tunneling. The mining of gold, tin, copper, and mica produces a dust containing high concentrations of free silica. Sandstone is a rich source of quartz that may be encountered in the development of gold mines. Quarrying of quartz leads to exposure to dust containing 10 to 30 per cent of free silica. The quartz content of dust from quarried slate may approach 20 to 30 per cent. Tunneling through stone containing quartz or digging graves in sandstone has been associated with the production of silicosis.

(*2*) Stonecutting, dressing, polishing, and cleaning monumental masonry. In this work, the stones used, sandstone and granite, contain high concentrations of quartz and are dangerous because of both the silica content and the difficulty in protecting the worker, who is in close contact with the material and frequently removes his protective devices to inspect his work. Pneumatic hand tools are used for cutting and smoothing; abrasive blasting for lettering and decoration increases the risk of the procedure.

(*3*) Abrasives and abrasive blasting. Sandstone grindstones are now rarely used, but sandpaper and scouring powders still contain flints and quartz. The use of abrasive soaps and scouring powders was recently discontinued in the United Kingdom. The risk from abrasive blasting is greatest when sand propelled by compressed air is used. This has been largely re-

placed by steel grit in the United Kingdom. However, shot blasting of sand cores on metal castings creates dust containing high concentrations of respirable free silica.

(4) Glass manufacture. Limited use of sand in slurries to grind glass has continued in the operations of small companies.

(5) Foundry work. The free silica used in foundry work contaminates the atmosphere because of the development of molds containing sand and clay. The work is carried out at high temperatures and there is some conversion of quartz to cristobalite. There is a trend toward sand substitutes that do not contain quartz; olivine is said to be in general use in Sweden. The widespread use of sand molds and the use of blasting, hammering, and chiseling create a dusty environment containing iron oxide and quartz and lead to a form of pneumoconiosis to which silica probably makes the most important contribution.

(6) Pottery, porcelain, and lining bricks. The combination of materials containing free silica in concentrations varying from 2 per cent to 30 per cent and the high temperatures used creates a serious silicosis risk.

(7) Boiler scaling. High energy sources are used in this work creating mixed dust clouds with variable concentrations of respirable quartz particles.

(8) Vitreous enameling. All such occupations produce contact with significant amounts of free silica. Because of the use of high temperatures and pneumatic air jets or other high pressure techniques, a dusty environment is produced that will expose workers to excessive concentrations of free silica.

Characterization of Exposure

The development of silicosis depends on the inhalation of respirable free silica particles < 10 μm in diameter. The size range for maximal alveolar deposition is 1 to 3 μm. Free silica concentrations vary greatly in materials that enter into industrial processes. Concentrations usually exceed 60 per cent in sand, but this material is not hazardous under ordinary conditions because the particles are coarse and unrespirable. Where powerful desert winds whip up sandstorms, clinical silicosis does not occur; definite hyaline nodules have not been demonstrated in the lungs of inhabitants of the desert.

The silica content of natural substances can be studied in several ways. The traditional method in petrology is to use the polarizing microscope to examine small particles of the material (37). In analysis of finely divided material roentgenographic diffraction may be used if the sample contains more than 200 μg of free silica but the error of current methods is about 30 per cent (38). In the absence of other silicon compounds (silicates or amorphous silica), a wet chemical method can be used in which hydrochloric and hydrofluoric acids separate the free silica, which is read by colorimetry (39). Infrared spectrophotometry is also used in analysis of dust containing free silica (40).

Measurement of the degree of exposure to respirable free silica is necessary to determine the risk of disease within the industrial environment. Standards have been published through the years that were originally based on a unit of one million respirable particles in a cubic foot of air (mppcf). Current standards are usually expressed in milligrams of respirable dust per cubic meter. The current threshold limit value for respirable dust containing free silica (American Conference of Government Industrial Hygienists, 1973) is (*1*) $\frac{300}{\%\ \text{quartz} + 10}$ in mppcf, or (*2*) $\frac{10}{\%\ \text{quartz} + 2}$ in mg per m^3. This calculated threshold limit value is divided by 2 if the dust contains cristobalite or tridymite instead of quartz. For respirable nuisance particulates containing less than 1 per cent of quartz, the threshold limit value is 30 mppcf or 10 mg per m^3. A new standard for silica exposure has recently been proposed (28).

A number of methods have been used to measure the concentration of dust in the atmosphere. These include (*1*) settlement by gravity or centrifugation, (*2*) filtration, (*3*) impingement, (*4*) electric precipitation, and (*5*) thermal precipitation.

The method of impingement was modified successively to serve as a field method for sampling industrial dusts. An early technique was the konimeter method, in which the dust particles were sucked onto a plate covered with a thin film of petroleum. The number of particles collected within a given time was calculated by magnification of a microscopic grid. Readings of this instrument were high because fragmentation of particles by impingement exaggerated the relative dust hazard. A related instrument, the impinger, was originally described in 1932 (41); more recently, it has been modified by Greenburg and Smith to produce a practical field instrument known as the midget impinger, in

which particles were entrapped by high velocity impingement and collected in water and alcohol. In the portable midget impinger, particles impinge at a velocity of 70 per sec, and the air flow for sampling is 0.1 cu ft per min. The instrument can be operated by hand or by electric pump, with the particles being collected in a liquid volume of 10 ml. The midget impinger reduced the risk of shattering large particles or the loss of particles after impingement, but aggregated particles that broke up on contact with the fluid within the collection chamber increased the dust count.

The instrument that is in general use in field operations today is the personal gravimetric dust sampler. The sampler is composed of a cyclone assembly and filter holder containing a preweighed millipore filter that is attached to a battery powered pump. In the Mine Safety Appliance sampler the pump draws air through the assembly at a flow rate of 1.7 liter per min. Nonrespirable particles (> 10 μm) are discarded and the smaller particles adhere to the filter (42). The total weight of dust on the filter is established and the weight of the sample is obtained by subtraction. The dust is analyzed by one of the methods previously described.

Pathogenesis

Events in the pathogenesis of silicosis include (1) inhalation of silica particles, their penetration to the lung periphery, and their retention; (2) ingestion of the particles by macrophages; (3) death of the macrophages; (4) release of the contents of the killed cells, including silica particles; (5) ingestion of silica by other macrophages and their deaths; (6) gradual accumulation of other cells; (7) production of collagen; (8) hyalinization; and (9) (possibly) complication.

Particles deposited in alveoli are readily ingested by macrophages, the process resulting in creation of a phagosome from invaginated cell membranes. Silica particles at first lie within the phagosomes, which receive enzymes from the lysosomes. Within hours, however, the phagosome ruptures and silica particles can be demonstrated lying free in the cytoplasm (43). The lysosomal enzymes, discharged into the cytoplasm in activated forms, are probably responsible for the rapid death of the macrophage and extracellular loss of its contents including the particulate silica (44). More macrophages accumulate in the area, ingest the silica, and are killed. This cytotoxic effect of silica is a necessary step in the production of silicotic fibrosis. For a variety of mineral dusts, good correlation between macrophage toxicity and fibrogenicity has been demonstrated (45, 46).

The relative ease and speed with which one may expose macrophages to dust and detect phagosomal rupture and cell death have led to a number of studies of the relative cytotoxicity of various dusts. This assay system circumvents problems of particle penetration and retention in studies of relative pathogenicity and allows studies relating particle size and composition to actual cell toxicity (47). A number of substances are ingested by macrophages and lie undigested in phagosomes but fail to alter permeability of the phagosomal membrane. Macrophages may become "choked" with such dusts and yet retain mobility as well as structural integrity. Carborundum and diamond dust fail to show macrophage toxicity, although they are angular and sharp (48). These experiments, in fact, demonstrate on a cellular level the basis of earlier animal studies that disposed of the "angularity theory" of silicogenesis. Stishovite, a rare form of crystalline free silica, also accumulates harmlessly in macrophages and fails to produce fibrosis (49). This material is octahedral; only the tetrahedral forms of silicon dioxide possess cytotoxic and fibrogenic properties. Coesite is another high temperature, high pressure form of silica. Quartz is more soluble than coesite, but the 2 minerals possess equal fibrogenic activity (50). In other experiments, differing quartz specimens with similar particle sizes and solubilities have shown significant differences in fibrogenicity (51). The foregoing have led to the rejection of the solubility theory of silicogenesis and to increased interest in stereochemical hypotheses. The importance of silanol groups on the surfaces of silica particles has recently been emphasized (51). The formation of hydrogen-bonded complexes between silica particles and active groups of the phagosomal membranes (such as quaternary and phosphate ester groups of phospholipids) may be the mechanism producing rupture of the phagosome (52). The hydrogen donor hypothesis has another attractive feature, namely, that most of the compounds that protect against experimental silicosis behave as hydrogen acceptors (53, 54). Experiments relating the particle size of colloidal silica to its activity in rupturing erythrocyte membranes lend support to a stereochemical rather than a simple "energy-transfer" explanation for membrane toxicity. The larger particle sizes of

colloidal silica are more hemolytic; 3 μm particles lack hemolytic effect and, in fact, protect against the effects of subsequent exposure to the larger particle sizes even after repeated washing of the treated erythrocytes. The implication is that the smaller particles can become firmly attached to the cell membrane but lack sufficient surface area to effect membrane rupture (54). Further support for a stereochemical hypothesis comes from the fact that stishovite, lacking cytotoxic or fibrogenic properties, does possess surface silanol groups (51). Apparently, the octahedral configuration of stishovite prevents the orientation of silanol groups that produces membrane disruption. The proposed membrane toxicity of particulate silica is thus more geometric than energetic; however, this does not require that the silica be in crystalline form (55, 56).

Other recent work has examined the induction of fibrosis by products of dusted macrophages. In these experiments, macrophages are harvested from dusted animals or are exposed to particulate silica *in vitro*. The cells may then be lysed by ultrasound and separated into fractions that are subsequently injected subcutaneously into animals of the same species to assay for fibrogenicity. Control experiments have shown that residues from lysed nondusted macrophages produce little if any fibrosis. To exclude a direct effect of silica the mineral was added to the residue of lysed but undusted macrophages, and this mixture also produced little fibrosis. Using these methods, Heppleston and Styles (45) found a fibrinogenic factor in the supernate of a centrifuged suspension of dusted lysed macrophages. They considered this factor soluble. Kilroe-Smith and associates (57) used similar experimental methods but much higher speeds of centrifugation. They found the fibrinogenic activity in the residue, not the supernate. This fibrogenic factor was not a lipid, because it was not extracted by methanol-chloroform; the factor was also resistant to treatment with acetic-trichloracetic acid.

Further work on macrophages *in vitro* has demonstrated a toxic basis for the impaired resistance of silicotic patients to certain infections. *Mycobacterium tuberculosis* grows more rapidly in macrophages that are fed sublethal doses of quartz particles, and the bacilli are released more rapidly into the surrounding medium (58).

At this point, it is useful to consider some differences between these experimental models and human silicosis. The models require high silica doses, administered for relatively brief exposure times, to produce rapid biologic responses. These are exactly opposite to the usual conditions leading to human silicosis. Differences in individual exposures, in anatomic and physiologic factors governing particle retention, in exposures to other noxious agents, and in host responses to retained silica must separately and together be important determinants of which exposed persons will actually develop disease. Experimental models may therefore exclude some mechanisms that ultimately prove to be of considerable importance in human silicosis. Although these models have provided useful data on limited aspects of silicosis and have indicated promising areas for new research efforts, they have yet to provide an inclusive theory of silicogenesis. Recent work has challenged the apparent simplicity of explaining fibrogenesis by a factor released from dusted cells (59).

Autoimmunity may be important in several phases of development of silicosis. Interest in immunologic mechanisms is based on several observations: (*1*) silicotics show increased prevalence of autoantibodies (60–63); (*2*) silicotic lesions contain plasma cells and immune globulins (64–66); (*3*) gamma globulins are increased in the plasma of silicotics (64); (*4*) there is an increased prevalence of autoimmune diseases in silicosis (67–69); (*5*) the presence of a collagen disease may influence the course of the pneumoconiosis (70). Immune mechanisms probably do not participate in the killing of macrophages by silica, or in the induction of fibrosis by the residues of the dusted macrophages. Immune reactions may, however, be responsible for providing a large and continuing supply of macrophages to the area and may thus occupy a central role in the pathogenesis. Established silicotic nodules (in rats) may become more active in the presence of remote tuberculous foci (71), and Caplan's observations (70) suggest a similar effect of immune globulins in man. Another area of possible importance is the role of lipids in silicosis. The initial attack of silica on the phagosomal membrane may involve hydrogen bonding to lipids. The finding that lipid residues of dusted macrophages lack fibrogenicity does not vitiate the importance of lipids in the intact animal. Lipids may have an active part in macrophage accumulation and may also have passive effects in rendering silica particles less wettable (72). In any case, striking alterations in lipid content (and metabolism) characterize silicotic tissues (73).

Pathology

Three types of tissue reaction have been distin-

guished (74): chronic, in which moderate exposure extends for a period of 20 to 40 years; accelerated, with increased particle dose for a period of 5 to 15 years; and diffuse, in which there is a heavy alveolar deposition of particles for a period of less than 5 years.

Chronic reactions are encountered in industries in which the proportion of quartz in respirable dust is less than 30 per cent. In such cases the nodules are seen after approximately 20 years of exposure. These are usually rounded but may take oval or slightly lobulated forms. The distribution is uneven, with lesions usually more prominent within the upper lobes, probably relating to better clearance of dust from the lung bases. Studies of postmortem material have shown that practically all of the silica particles visualized within the lungs are 1 to 2 μm in diameter. Careful studies of human and experimental material have demonstrated that the particles can reach the supporting tissue of the finer air spaces either through macrophages or less commonly as a result of the movements of the lungs. The particles pass toward the hilar lymph nodes, where free silica is concentrated. The death of macrophages usually leads to the formation of nodules containing free silica in the fixed interstitial tissue near the respiratory bronchiole. Here the nodules lie in relation to bronchioles and small arteries. They are also found near the lymphatics of the small veins. In chronic disease, the nodules surround a central hyaline zone that contains a variable amount of dust. This is in turn surrounded by a concentric zone of cellular connective tissue that contains no particles; it is surrounded by a halo of dust containing crystalline silica in a zone of irregularly dispersed connective tissue, which also contains crystalline silica. It is from the peripheral zone that silica is carried to enlarge the nodules and set up new silicotic nodules. A typical hyaline nodule is shown in figure 1.

Variations in the formation of the nodules have been noted. Alveolar wall involvement can lead to denudation of the overlying layer and the formation of a lumpy cellular lesion protuding into the alveoli (figure 2) that resembles bronchiolitis fibrosa obliterans (75). In the simple stage of silicosis, with few nodules larger than 5 mm, the surrounding air spaces are usually not violated. The hyaline material shows some resemblance to amyloid (74). Serum globulins within the hyaline material have been demonstrated by Vigliani and Pernis (64).

Silicosis is often complicated by the formation of massive fibrotic lesions that usually develop within the upper lobes. They are composed of nodules matted together by fibrosis and contain obliterated blood vessels and bronchi. Ischemic slit-like cavities may be demonstrated, but in the past the most important type of cavitation reported was produced by associated tuberculosis.

In coal miners with rheumatoid arthritis, Caplan (70) noted an increased prevalence of massive fibrosis. The larger masses were associated

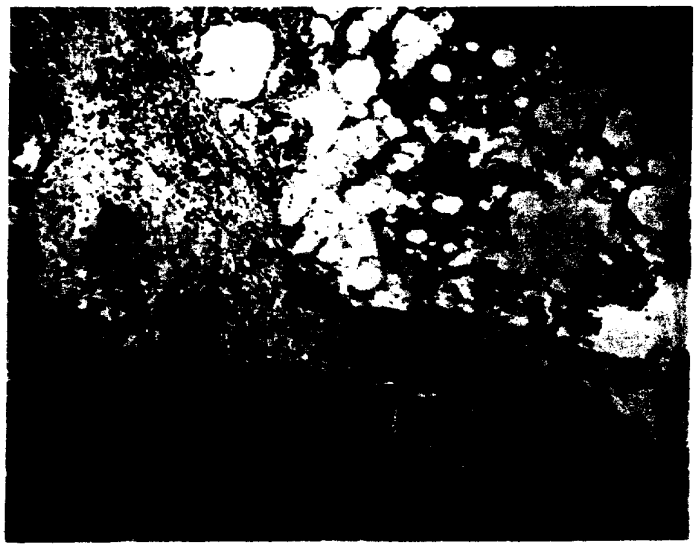

Fig. 1. Classical silicotic hyaline nodules associated with adjoining parenchymal scarring and limited lymphoid exudate. (Original magnification: × 40)

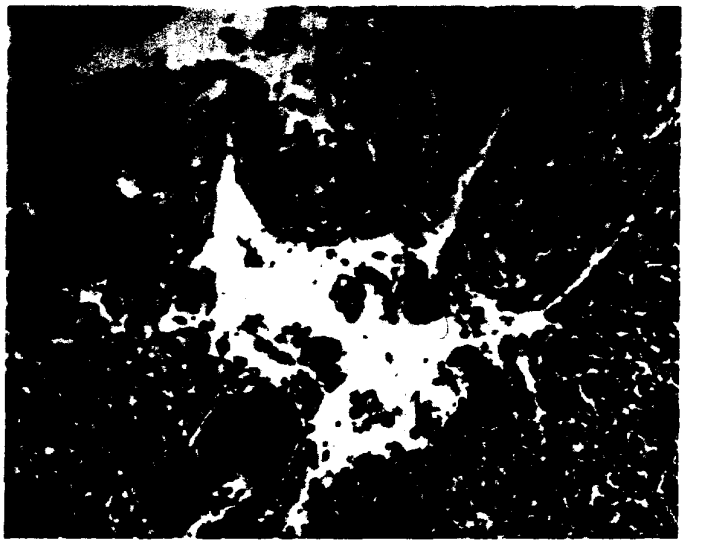

Fig. 2. Diffuse alveolar wall thickening by histiocytes with air space encroachment (Original magnification: × 140).

with a crop of round, rapidly developing opacities larger than simple silicotic nodules. Cavitation and calcification in the larger nodules has been described. Pathologic examination has demonstrated that Caplan's nodules contain necrotic materials surrounded by palisading connective tissue cells as seen in rheumatoid subcutaneous nodules. Complicated silicosis is characterized by distortion of the structure of the lungs with contraction of upper lobes and the development of emphysematous changes in the lower lobes, often with large bullae. Pleural adherence is common in this form of the disease. The enlarged lymph nodes often contain peripheral layers of calcium producing the fairly characteristic eggshell appearance. The masses can occupy one-third or more of the upper lobes. The disease has been noted to cross the interlobar fissure. The amount of dust within the masses is variable. In tuberculosis, occasional caseating granulomas may be found, but the histologic reactions may be nonspecific. There are numerous complications of silicosis. Cor pulmonale has been frequently mentioned but is not often confirmed on pathologic examination. Calcified lymph nodes, often the result of previous tuberculous infection, have produced the following changes in neighboring structures: the superior vena cava syndrome, esophageal compression, perforation of the bronchial tree with infection and hemorrhage, and paralysis of the phrenic nerve and, less often, the recurrent laryngeal nerve (76).

Data concerning the residual ash from silicotic lungs have been published (37, 77). The upper limit of normal content of free silica in human lungs is 0.2 g, whereas in disease, the quantity of free silica may rise to 15 to 20 g. McCrae showed that in the normal person the average percentage of silica in ash was 14.7 per cent. This rose to the range of 29.4 to 48 per cent in patients with silicosis. The silicon percentage of dry matter was 4.7 in the most severe cases (78). Patients with silicosis usually had at least twice as much free silica in their lungs, in percentages of dry matter, than did normal persons. Others have shown that the lungs of normal persons contain less than 0.12 per cent silica but that the fibrosis in silicotuberculous patients is excessive for the amount of silica in their lungs (79). The importance of the silica content in relation to fibrosis has been shown by Rossiter: The amount of visible reaction on the chest roentgenograms was related to the total amount of coal dust, except in those instances in which the percentage of free silica was increased (80).

The changes that have been described in chronic silicosis are also seen in accelerated silicosis, but the rate of progression is more rapid and the lesions usually become visible on chest roentgenograms after 4 to 8 years of exposure. Much of the information on this group has been

obtained from studies of sandblasters. In these men well-formed nodules developed, but there was a tendency for nodules to form in relation to the walls of the alveolar space, instead of near the respiratory bronchiole at the orifice of the acinus (81). The disease leads more frequently to massive fibrosis, and the large opacities are seen more often in the middle and basal portions of the lungs than in chronic silicosis. Cavitation is as frequently the result of atypical mycobacterial infection as of human tuberculosis (82). Ischemic cavitation may also occur.

"Acute" silicosis is a rare condition related to exposure to heavy concentrations of respirable free silica in enclosed spaces with minimal protection. The disease develops rapidly and clinical features appear after an exposure of approximately 1 to 3 years. On autopsy, there is consolidation with maintained lung volume. The lungs have a gravish white airless appearance with thickening related to diffuse interstitial fibrosis. The nodulation and massive changes of the more chronic forms of silicosis are not grossly demonstrable.

Because of terminal pulmonary edema or exudation, fluid flows from the cut surfaces. The disease is usually complicated by mycobacterial or other infections that produce thickened and adherent pleura. A striking microscopic change is the presence of acidophilic fluid, containing fine granules and many macrophages, within the alveolar spaces (figure 3). There is also cuboidal transformation of the alveolar cells. Interstitial fibrosis is prominent, but silicotic nodules are poorly demarcated and small (6). The fluid within these spaces contains lipids and proteins and gives a strongly positive reaction to periodic Schiff reagent (7). Quartz crystals are present within the lungs and the hilar lymph nodes. The cells seen within the alveolar spaces are macrophages, but it is possible that in the course of the disease, type 2 pneumocytes are desquamated into the alveolar spaces as well.

The reaction of silica has been elucidated by experimental exposure of laboratory animals. Silica has been introduced into the respiratory tract by dusting or by direct intratracheal injection. Subcutaneous, intravenous, and intraperitoneal routes of administration have been used. Silica has even been placed in the anterior chamber of the eye. Important studies have been carried out on macrophages exposed to free silica in tissue culture media. Lesions produced in animals have been studied for silica content by the sensitive spectrophotometric colorimetric method in which silicomolybdate is formed.

A number of animal models have been used for these studies. Examinations at various intervals have demonstrated the course of silicotic lesions. Typical compact nodules have been produced in rats after exposure in dust chambers for periods as long as one year (83). Collagenous nodules have also been produced in chronically dusted monkeys (84). In the hamster, nodulation

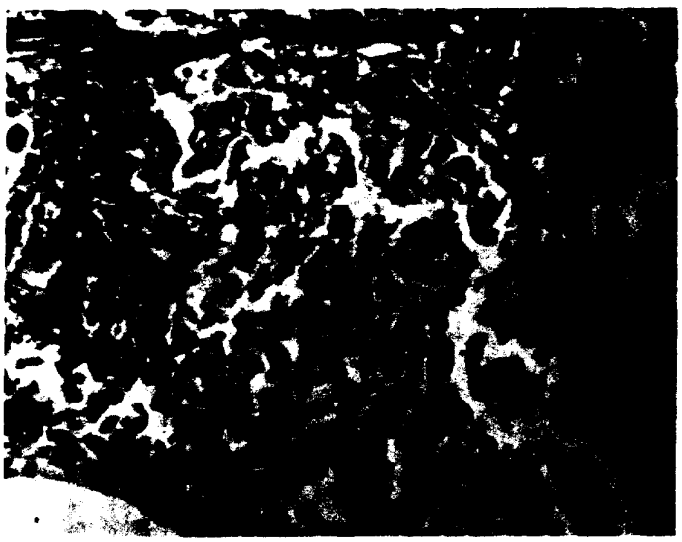

Fig. 3. Silico-proteinosis. The alveolus is filled with macrophages associated with pigment granules and proteinaceous material. The alveolar margins are demarcated by congested capillaries.

occurs early, is widespread, and is associated with diffuse pulmonary fibrosis. This is probably related to numerous foci in lymphoid tissue scattered throughout the lungs (85). Intratracheal injection of a massive dose of free silica usually produces acute cellular reaction, which fills the air spaces and only later leads to the formation of nodules and fibrosis. This reaction is well illustrated in the guinea pig (86). The sequence of focal collection of dust cells followed by the concentration of fibroblasts leading to definite collagen nodules has been demonstrated in monkeys chronically exposed to small particles of quartz, 3 μm or less. Under similar conditions, amorphous fused silica dust produced only limited fibrosis.

The resistance to mycobacteria of dusted animals, often guinea pigs and rats, has been studied by experimental methods. The native resistance of both species was altered by silica. The disease was produced more readily by virulent organisms and by attenuated strains that ordinarily would not produce infection. *Mycobacterium marinum* produced progressive disease in guinea pigs after their exposure to silica by both intratracheal injection and dusting techniques.

Clinical Features

Silicosis is usually a chronic disease, and the principal symptoms develop late; it is rare for the chest film to become positive before 20 years of exposure. In the past, the average duration of life after first exposure has been approximately 40 years for those whose exposure to free silica was moderate, as in foundrymen, quarrymen, miners, and potters (87). An earlier, more rapid onset of the disease would be an indication of heavier exposure due to unusual circumstances of employment (lack of protection and work in enclosed spaces), or an infectious or immunologic complication.

The earliest symptoms in chronic cases are cough and expectoration, which can usually be explained by a history of cigarette smoking extending back to early youth. The principal symptom of established silicosis is shortness of breath on effort. This is usually associated with roentgenograms showing complicated, rather than simple pneumoconiosis. Significant dyspnea on effort is almost invariably related to massive changes within the lungs, contraction of lobes, or cavitation of infectious or ischemic origin. Distortion of the bronchial tree under these circumstances leads to increased cough and expectoration, but these symptoms will be more se
if cavities are present. Hemoptysis and c
pain due to infection are not uncomm
Weight loss is a characteristic finding in sil
tuberculosis and other types of infective pn
moconioses. Mycotic infections, including
cardiosis, cryptococcosis, and sporotrichosis, ha
complicated this pneumoconiosis. Infections
particularly common when silicosis is accelera
or acute.

Respiratory failure is the most important co
sequence of complicated silicosis. Ventilato
failure may be aggravated by the developme
of pneumothorax, which resists successful trea
ment because of the difficulty in obtaining r
expansion of the shrunken, fibrotic lung and i
sealing the leak in the poorly retractile tissue.

There have been a number of reports dealing with the increased prevalence of scleroderma in pneumoconiosis and silica exposure. In our experience, autoimmune disease has often been associated with the accelerated type of silicosis seen in sandblasters: About 10 per cent developed connective tissue disorders, including scleroderma, rheumatoid arthritis, and systemic lupus erythematosus. The role of the complicating disease is uncertain but is usually associated with more rapid progression of roentgenographic and functional abnormalities. It is in these cases that some response to adrenal corticosteroids may be noted. The evolution of silicosis associated with auto-immune disease can be very rapid, producing marked structural and functional changes within the course of 1 or 2 years.

In accelerated silicosis, the major features of the disease are identical to the chronic disease, but the chest roentgenogram usually becomes positive within 4 to 8 years of first dust exposure. The over-all course of deterioration is rapid and the average exposure to free silica is approximately 10 years in fatal cases of sandblasters' silicosis. Mycobacteriosis affects 25 per cent of the workers; half of these infections are due to atypical organisms. In Wisconsin, the common atypical mycobacterium complicating silicosis is *M. intracellulare* (Battey bacillus) (88). This is the organism usually associated with rural residence. In the coastal zones, and near the larger cities of the southwest, *M. kansasii* has been the atypical mycobacterium usually associated with silicosis.

Most of the disease described above has been related to high doses of free crystalline silica. Smaller doses of quartz produce a rather mild

disease of long duration. This may occur in patients exposed to minor amounts of quartz contaminating other minerals.

Silicoproteinosis is the name applied to a variant of rapidly developing silicosis in which there are characteristic histologic changes. It is the result of heavy exposure to respirable silica dust. Dyspnea on effort may develop within 6 months of first exposure. There is associated weakness and weight loss and, in more severe cases, cyanosis and diffuse rales. Complication by mycobacterial infection is the rule, but in one case treated with steroids there was terminal nocardiosis. Progressive deterioration may be temporarily and partially suppressed by corticosteroids. Death is due to intractable hypoxemia.

The prevalence of mycobacterial infections may be declining for chronic silicosis but remains high for the accelerated and acute forms. The roentgenographic appearance varies from characteristic cavitary infiltrates to massive disease, with or without cavitation in which tuberculous elements may be difficult to distinguish. In those with positive sputum cultures the rate of sputum conversion is high; but the massive disease and conglomerate lesions will often progress despite appropriate chemotherapy (89).

A number of investigators indicate that tuberculosis tends to complicate silicotic disease of long standing and that it tends to be more severe in the more rapidly progressive types of the disease. Can prior silica exposure, insufficient to produce nodulation on the chest roentgenogram, predispose a person to tuberculosis? In persons who have had years of silica exposure and negative roentgenograms active tuberculosis may suddenly appear. In some instances, the disease may continue to progress and produce massive lesions without visible associated nodular foci. Macrophages are of undoubted importance in immunity to mycobacterial infections; it is precisely these cells that demonstrate exquisite susceptibility to the toxic effect of particulate silica. Watkins-Pitchford (90) found an association between work as a gold miner for 3 to 5 years and the subsequent development of tuberculosis, even though silicosis was not demonstrated on the chest roentgenograms. This potentially important observation has not been confirmed. The progressive and massive changes produced by mycobacterial infection in silicosis have not been described for mycotic superinfection. A study of the relation of silicosis and silica exposure to histoplasmosis would be of theoretic and practical interest.

There is no indication that silicosis is associated with increased risk for the development of cancer of the respiratory or other systems. When there is combined exposure to silica and other substances such as arsenic, nickel, or chromate, the increased susceptibility to cancer appears to be related to the other material. There is no indication of a synergistic increase of susceptibility to cancer after exposure to such other dusts and silica.

Diagnosis

The diagnosis of silicosis usually depends on historical and roentgenographic evidence. A history of significant exposure to free silica is required. This is usually obvious, but occasionally the source of silica may not be apparent, particularly in mixed exposure. In the case of brickyard workers, the exposure to silica brick that lines the kilns may be overlooked; the clay bricks contain little or no free silica. In another instance, an apparently safe amorphous silica (e.g., diatomaceous earth) may be rendered toxic by heating to near or above the temperature of crystallization (55).

Roentgenographic changes provide the evidence that exposure has in fact produced lung disease. The individual elements that combine to form the pathology of silicosis are seen on chest roentgenograms as characteristic shadows. The roentgenographic features of silicosis have been known for more than 50 years (18, 19, 91). In the simple forms of the disease, rounded nodules are the basic elements (figure 4). In the complicated forms, massive densities predominate (figure 5). Because of the diagnostic and epidemiologic value of distinguishing these changes, there has been a continuous effort to standardize descriptions of the abnormal shadows. Originally, the descriptions were based on patterns composed of small rounded opacities, as seen typically in silicosis and coal worker's pneumoconiosis. It was later recognized that mixed disease was common and that a more useful classification should also include the small irregular opacities produced by asbestos and other noxious inhalants (92). The current Union International Contra Cancre–International Labour Organization classification provides for identification and grading of both rounded and irregular opacities. Four grades of profusion (0-1-2-3) are used. After assigning a grade, the reviewer has an opportunity to reconsider his or her original choice and to designate a second grade of greater, equal, or lesser magnitude, as

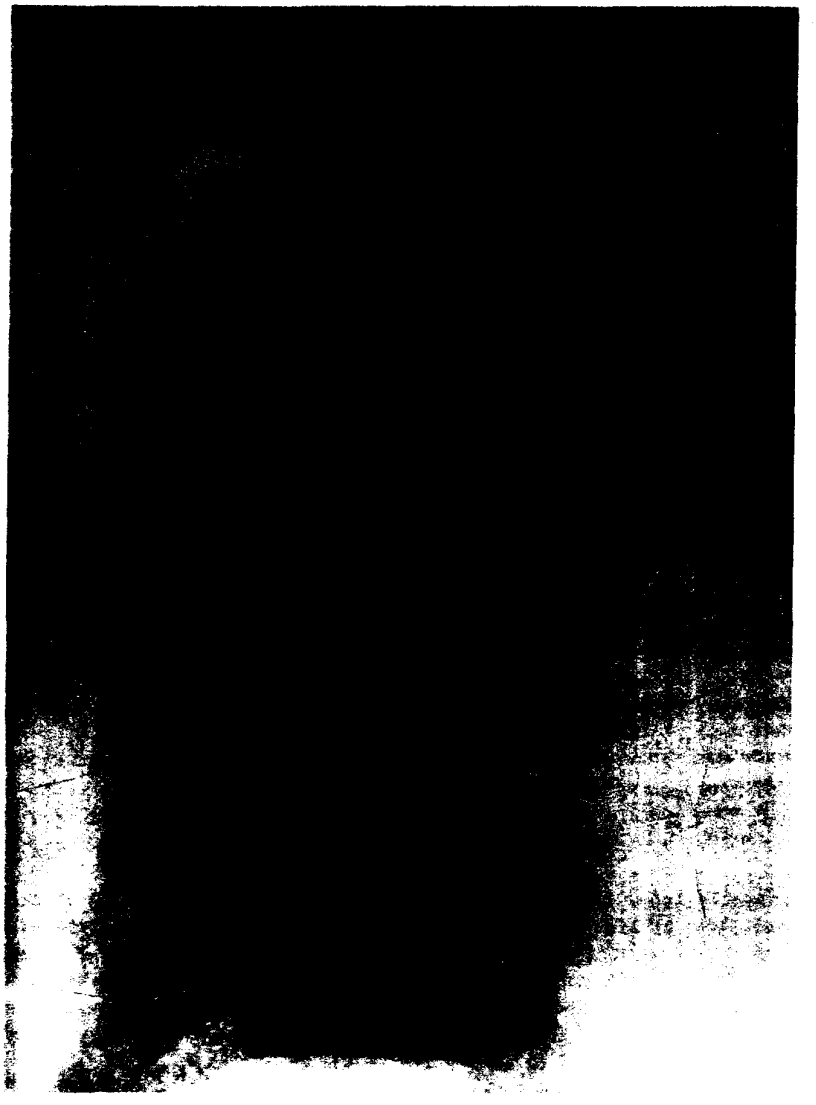

Fig. 4. Simple nodular silicosis.

appropriate. In this manner, 12 possible subcategories of profusion can be selected, producing a 12-point scale that results in greater precision and sensitivity when a panel of readers is used (93). The resulting data can then be compared with exposure, clinical, functional, and pathologic data (94). In addition to this grading of simple opacities, the current scheme allows description of complicated disease on the basis of the size of opacities > 1 cm. The classification also provides for grading of pleural changes, a modification of special value in dealing with the effects of asbestos exposure.

The lesions of silicosis are usually more prominent within the upper lung fields. They may be difficult to distinguish in the early forms of the simple disease and at this stage may be more readily detected on 15° oblique projections (95). The same effect may be obtained on standard oblique views or on lateral views in which the fine lesions are superimposed. The nodules, which are rounded and fairly uniform in size in simple disease, may later show coalescence as a result of infection or the beginning of massive fibrosis. As mentioned above, the development of massive change may itself be an indication of

complication by mycobacterial infection. In miners with rheumatoid arthritis, massive changes are more prevalent and opacities of one to several centimeters may enlarge more rapidly than expected. A third form of rheumatoid pneumoconiosis is rapid enlargement of disseminated small opacities (96).

Roentgenographic progression of simple disease or from simple to complicated disease, can usually be expected within 5 years (26). Masses usually occur within the upper lobes and are often associated with contraction of the lobes, elevation of the lung roots, and the development of emphysematous changes at the bases.

Although calcification of pulmonary nodules is rare, lymph nodes may calcify, producing an "eggshell" appearance. Enlargement of lymph nodes is common and may occur before pulmonary nodulation. Within the mediastinum enlargement may be extreme, leading to compression of the superior vena cava and the esophagus (76). Massive disease with contraction of the upper lobes is frequently associated with thickening of the pleura, and with pleural adhesions. Pneumothorax is not unusual in silicotuberculosis or massive fibrosis and is often a pre-terminal complication.

The so-called acute form of the disease is characterized by widespread involvement of both lungs. The air spaces are filled; there are associated interstitial changes, with poorly defined nodulation demonstrable at the periphery. The lung volumes are obviously small and the diaphragm is high. Although infection is often present, cavities can rarely be demonstrated, and the infectious exudates are concealed within the larger exudates produced by reaction to the dust. This applies to fungal as well as mycobacterial infections; nocardia can complicate silicoproteinosis as well as idiopathic pulmonary alveolar proteinosis.

In mixed exposures to respirable silica and asbestos, patients may show roentgenographic changes associated with either or both types of dust. It is not unusual to see both rounded and irregular opacities within the lung fields, as well as fibrous and calcified pleural plaques (97).

Exposed workers without roentgenographic

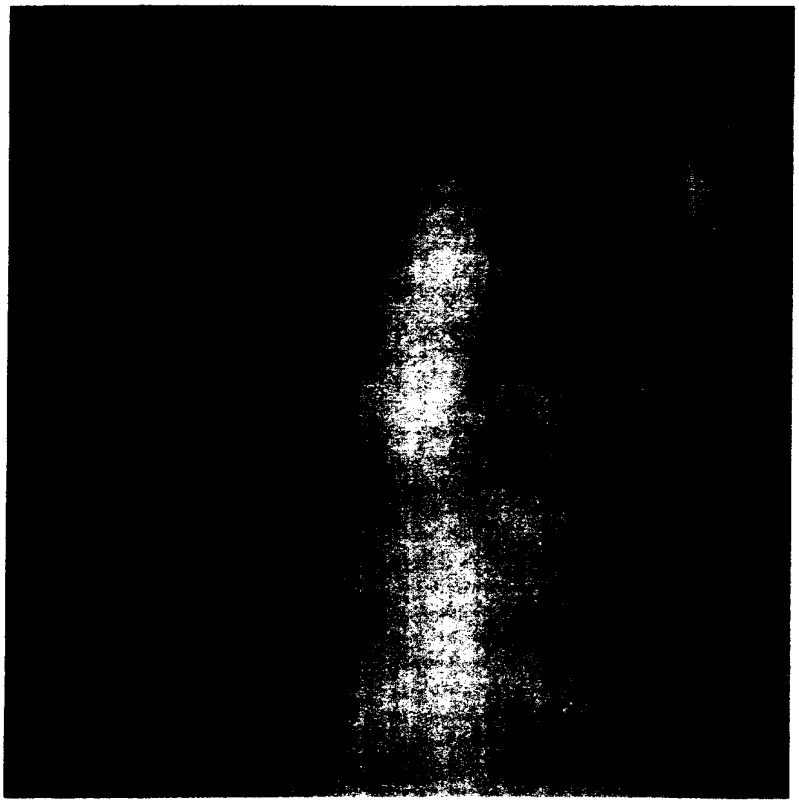

Fig 5 Complicated silicosis with conglomerate massive shadows.

...alities should receive regular follow-up examination, because well-established nodulation may become evident within a year. This may occur even though silica exposure has terminated.

Silicosis must be differentiated from disorders producing similar roentgenographic abnormalities. Sarcoidosis shares with silicosis a tendency to produce widespread nodulation, often more profuse in the upper zones, and hilar lymphadenopathy. Advanced cases of sarcoidosis may also show small lung volumes, conglomerate densities, and emphysematous changes. Sarcoidosis may exhibit characteristic extrapulmonary clinical findings and often shows roentgenographic improvement with corticosteroid treatment. Massive opacities of silicosis have been mistaken for cancer and vice versa. It should be noted that clubbing of the digits is most unusual in silicosis. Diffuse carcinomatosis and simple silicosis may have similar roentgenographic appearances, but the patient suffering from carcinomatosis ordinarily shows severe clinical and lung functional abnormalities. Infectious granulomas may provide problems of differential or simultaneous diagnosis. Large opacities in the upper zones that are clearly separated from the pleura (producing the characteristic "angel's wings" appear-

Fig. 6. Conglomerate shadow, often described as "angel's wing" appearance.

ance) favor a diagnosis of silicosis (figure 6). With similar densities in mycobacterial infection, greater contact with the pleural surface is expected; remote pleural reactions favor a diagnosis of mycobacterial infection. The simultaneous diagnosis of silicosis and mycobacteriosis can be extremely difficult. The silicotic nodules may be caught up in the tuberculous process, and emphysematous basilar changes may spread the remaining nodules, making them difficult to detect. In the presence of massive tuberculous changes, silicosis may be suspected only when there is widespread uniform small nodulation, remote from the tuberculous foci. Other pneumoconioses may mimic the roentgenographic appearance of silicosis. In this connection it should be remembered that welders, for example, may work near sandblasters and develop silicosis (figure 7), siderosis, or both.

Ordinarily, a lung biopsy is not required to establish the diagnosis of silicosis; the combination of a history of significant silica exposure and a characteristic roentgenogram will suffice. Biopsy must sometimes be undertaken in exposed persons because the roentgenographic abnormality is thought to be atypical. This has been the case in some patients who have diffuse alveolar filling or diffuse interstitial reactions as the result of heavy dust exposure (figure 8). Biopsy may be needed when there is complicating auto-immune disease, or in other cases showing progressive and rapid deterioration (figures 9A, 9B). Biopsy may also be needed where there has been exposure to more than one type of dust. Under any of the above circumstances, histologic information may be of crucial importance in legal proceedings.

When lung biopsy is required, an open chest procedure is preferable. Needle biopsy is inadvisable because of coexisting emphysematous changes. Needle and transbronchoscopic biopsies do not yield sufficient tissue for the special studies that are often necessary. Conventional histologic examination is sufficient for diagnosis when it shows the cellular reaction and hyaline nodules in differing stages of formation.

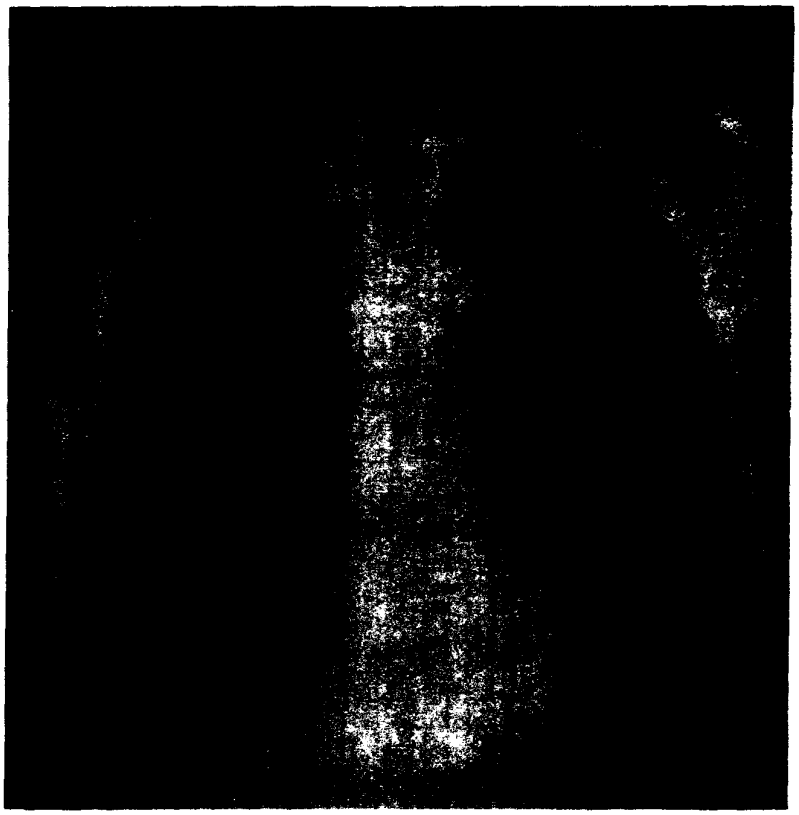

Fig. 7. Welder with complicated silicosis who was employed in sandblasting operations.

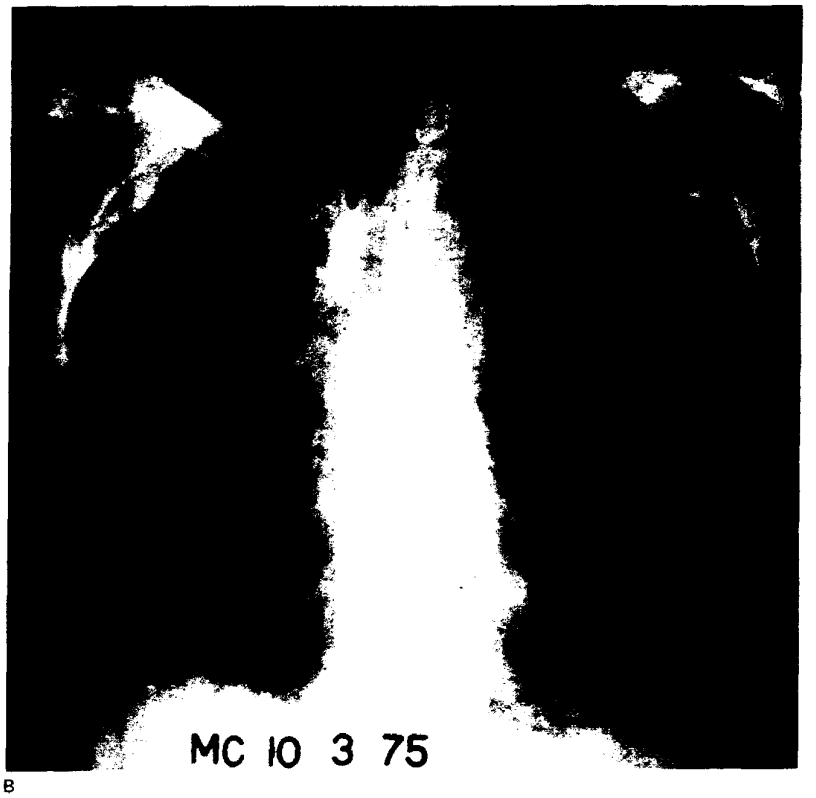

Fig. 9. Sandblaster with scleroderma exhibiting rapid progression of silicosis in less than one year.

When the tissue pattern is not characteristic, examination under polarized light may demonstrate doubly refractile particles of silica. When further characterization is required, fine particles of quartz can be demonstrated by scanning electron microscopy. The presence of excess silicon may be demonstrated by x-ray energy spectrometry. High silicon-sulphur ratios determined by this method are diagnostic for pneumoconiosis and are strongly suggestive of silicosis. When tissues contain silicates rather than free silica, x-ray energy spectrometry may disclose the presence of unusual amounts of associated elements such as calcium, magnesium, or iron (98). These elegant methods should be applied to all biopsy and autopsy specimens from dust-exposed persons that show obscure or atypical changes on routine tissue examination. These methods will not only provide improved diagnosis in individual cases but will widen our awareness of known hazards and disclose unsuspected sources of dust exposure.

Lung Function

It is difficult to propound general statements about lung function in silicosis. This is due to the wide variety of clinical and pathologic forms of the disease. This variation is due partly to the exposure variables of intensity and duration and to the type of silicious dust. Infections and immune reactions may complicate the disease and affect lung function. The effects of age and tobacco are not easily assessed, because most silicotics are older men who have smoked for many years.

To add to the confusion, most of the cross-sectional studies of lung function and silicosis have examined miners, quarrymen, or foundry workers. Mixed dust exposures are the rule in those occupations, and free silica usually comprises less than half of the total and respirable dust exposure. Industrial bronchitis is common in such populations, and symptoms and functional abnormalities may correlate better with smoking than with dust exposure (99–101).

Heavy exposures to relatively pure, respirable free silica, on the other hand, produce the less common accelerated or acute forms of silicosis (87, 102–104). These forms are rapidly progressive, and lung function data differ from that

found in the more ordinary form of silicosis (105). Animal studies are even more limited in applicability. Enormous doses of dust are generally given in a short period, or in a single dose. The experimental pathology frequently differs greatly from human tissue changes, thwarting from the outset any attempt to relate directly the animals' functional change to the human disease. The foregoing seem to express an "uncertainty principle" wherein the more confident one is that he is studying pure silicosis, the less confident he may be in applying his results to the ordinary human disease.

It is not surprising, then, to find apparent contradictions in the literature of lung function. Investigators have focused on the fibrotic or emphysematous aspects of silicosis (106–111). Lung diffusing capacity in various studies has shown a rather wide range of correlations with other measures of functional impairment (112–119). Static and dynamic compliance are often reduced in silicosis (120–121). The difficulty of applying invasive tests (such as compliance and arterial gas studies) to working populations has retarded study of the early phases of development of pneumoconioses. Arterial oxygen tensions may be normal both at rest and during exercise (122). Measurement of resistance of the lower airways requires a plethysmograph, substantial time, and good subject cooperation, so has not been widely applied to exposed populations. The procedure yields limited additional information when the forced expiratory spirogram is abnormal. Pulmonary mixing is impaired in a large percentage of silicotics but is more sensitive to bronchitis (123).

These varied functional abnormalities are easier to understand if the lung pathology is reviewed. Focal dust collections are often peribronchiolar, in excellent location for producing a disturbance of ventilatory distribution, and, later, obstruction of the acinus. Focal fibrosis can obliterate peripheral airways. Overall, more generalized fiberosis tends to reduce lung size, whereas obstruction of expiration leads to enlargement of lung volume. When conglomerate masses form, they not only produce restriction per se (as does any space-occupying lesion), but they commonly distort, compress, and even obliterate larger airways. Vessels are similarly affected. The discontinuous, asymmetric lung changes in silicosis contrast with those in asbestosis and explain the wider range of functional abnormalities in silicosis.

Despite the complex pathophysiology, however, the following statements seem to have wide support. (*1*) In simple silicosis, clinical tests of ventilatory function are often normal (30, 100, 111, 120, 124). We found this to be true even for a group of sandblasters with heavy exposure to pure quartz: The relative youth of that group (mean age, 37 years) probably minimized the effect of smoking (105). (*2*) Series of symptomatic silicotics will include patients with restriction, obstruction, and mixed patterns of ventilatory impairment (105, 111, 122). (*3*) Complicated cases show reduced diffusing capacities and exercise-induced hypoxemia (125). (*4*) Lung compliance is usually reduced (120). (*5*) Terminal cases have severe restrictive impairments. (*6*) Severe hypoxemia dominates the last phase of the disease.

Selection of lung function tests has recently been reviewed (126, 127). Aside from simple spirometry, a test may have differing utility in clinical, survey, or disability evaluation testing. No functional measurement, or combination of measurements, is specific for silicosis. Serial testing of silicotics is highly desirable because the course of progression in the ordinary form of this disease has not received adequate study.

Treatment

Unfortunately, there is no specific treatment for silicosis and current therapy is directed entirely at complications. Anti-tuberculosis drugs are effective in sterilizing the sputum of infected patients, but massive changes have frequently progressed after institution of the appropriate drugs. Drug treatment should begin with suspicion of infection and should not await confirmation by cultures. A positive tuberculin test constitutes strong evidence of mycobacterial infection. The high proportion of atypical mycobacteria warrants the initial use of 3 anti-tuberculous drugs, including rifampin. The physician should not be anxious to discontinue treatment after 2 years, especially if there is cavitation or continued roentgenographic progression. The physician must also be alert to the possibility of other infections and vigorous in their treatment. When auto-immune diseases complicate silicosis, corticosteroids should be tried. When obstruction forms part of the functional impairment, bronchodilators may be used; a surprising percentage of obstructed patients will show significant improvement. Pneumothorax is treated with chest tube drainage, but with poor results in the advanced case. Heart failure is treated in the ordinary way, but this may produce only

modest relief of chronic dyspnea. Digitalis should be used carefully to avoid complicating rhythm disturbances. Phlebotomy is rarely required. The need for supplemental oxygen is a prominent feature of the later stages of the disease. Ventilatory failure, unless precipitated by acute infection or sedation, is a terminal event.

A number of compounds have received experimental study in prevention or treatment of silicosis. Of these, polyvinyl pyridine N-oxide has shown the greatest promise; a related drug is receiving clinical trial (29).

Prevention

Where silica exposure is moderate, as in mines, quarries, potteries, and foundries, workers may be protected by improving ventilation and by the use of wet techniques. In some cases, materials may be substituted for those containing free silica. In many instances, however, such substitutes are not available or suitable or are adopted slowly because of their costs. Respirators are required when the concentration of respirable free silica exceeds the threshold limit value by more than 5 times. At such levels, dust masks can be useful if the work is carried out for short periods of time. When the work is prolonged, such respirators produce too great a resistance to air flow and become intolerable. All masks used in work with free silica must completely exclude the ambient, unfiltered air. Defects along the seams and eyeglasses greatly reduce the value of the masks. With very high concentrations of free silica, as produced by blasting with white sand, workers require air-supplied abrasive blasting hoods. These devices must be checked to be sure that the air flowing through the hoods is not contaminated by dust or oil, that the pressure is reduced sufficiently to prevent excessive noise within the hood and that the flow rate is still high enough to exclude entry of ambient air. Flow rates should be in the range of 3 to 6 cu ft per min. Work practices should prescribe the wearing of hoods during periods of blasting and for sufficient time afterwards to allow dispersal of the dangerous cloud of suspended respirable silica. Associated workers should (but often do not) wear appropriate protective equipment.

One can be optimistic about the eventual control of silicosis despite national statistics from industrial countries that show thousands of new cases as late as 1965 (27). Recent results from the United Kingdom and from certain industries in the United States indicate that the disease can be controlled. With better control of the environment and the observance of modern standards for air quality, workers will be exposed to lower concentrations of free silica. This approach will eliminate most of the cases produced by the traditional sources of silicosis. For dangerous operations such as sandblasting, the only effective solution can be the substitution of less noxious abrasive materials. New potential sources of exposure will appear with additional uses for silica. The risk of silicosis will always be present in mining; recent advances in mine safety should be universally applied. With continued progress in occupational health, it is our hope that silicosis will become a medical curiosity rather than an important cause of disability and premature death.

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