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THE PNEUMOCONIOSES

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THE pneumoconioses include all chronic changes in the lungs induced by prolonged inhalation of dust with no implication as to type or severity of tissue reaction. The latter may vary from simple phagocytosis to progressive fibrosis. Excluded from this category are the responses to living bacteria and fungi which are occasionally inhaled as dust.

A variety of specific terms has been introduced to indicate the kind of dust responsible for the pulmonary condition. The use of such terms is only desirable when the character of the reaction is distinctive and leads to significant clinical symptoms. In the group of pneumoconioses belong *silicosis*, the condition produced by inhaling quartz or other forms of free silica, *asbestosis*, the condition resulting from inhaling various fibrous silicates, and a few others not yet specially designated.

Since most other forms of dust in pure state have essentially the same effects upon the lungs and since none of them appreciably influences respiratory function the writer has proposed that reaction to them be designated by the common term, *simple benign pneumoconiosis*. Included under this term are uncomplicated *anthracosis* from coal, and *siderosis* from iron. When these minerals are mixed with quartz a modified type silicosis may develop which is properly designated as *anthraco-silicosis* and *sidero-silicosis*.

Dusts of vegetable origin, like tobacco, grain, cotton fiber, and so on may be inhaled but probably they cause little anatomical change. They may, however, sensitize tissue and give rise to allergic symptoms. Although these conditions produce insignificant structural alteration in the lungs, their

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special designations, like *tobaccosis and thresher's fever*, are not infrequently listed as forms of pneumoconiosis.

This group of conditions almost invariably develops in industry because only in its environment are the necessary concentrations of fine dust particles constantly maintained. In the state of nature there is dust, but the concentrations are rarely excessive, the particles are relatively coarse, and exposures are intermittent. The human race has evolved in such an environment and its lungs are protected against ordinary amounts of dust. The tortuous upper respiratory passages exclude most of the contaminants of inspired air, the ciliated epithelium lining the nose, trachea, and bronchi carries back to the pharynx many of the particles that lodge on its surface. It is estimated that at least 50 per cent of the dust in the air we breathe fails to reach the depths of the lungs. The free phagocytes wandering over the surface of the air spaces ingest and carry off particles that pass these barriers. The lymphatics of the lung remove phagocytosed and probably free particulate matter and deposit it in lymphoid tissue where it is no longer in contact with respiratory membranes. These mechanisms are adequate to protect man against all but extraordinary concentrations of dust.

Evidence of such protection may be seen at almost any autopsy where the heavily pigmented tracheobronchial lymph nodes attest the amount of carbon and other minerals removed from the lungs. Not infrequently the nodes of persons who have been exposed in industry to moderate concentrations of fine quartz reveal clusters of microscopic silicotic nodules while the lungs themselves remain free of such reaction.

ETIOLOGY

To have significant effects, the atmospheric concentrations must be excessive, the exposure to dust must be prolonged over periods measured in years, and the particles must fall within a particular size range. Within limits these factors bear a reciprocal relationship to one another, but under no circumstances is it possible to reduce the time factor much below *two years* even in the case of the most potent dusts. It takes time for effective quantities of dust to accumulate

within the lungs and more time for the particles to react upon the tissues.

The Size of Particles.—The size of the particles must be small enough to permit them to remain suspended in the air and to pass the barriers of the upper respiratory tract. The latter prerequisite is influenced by their shape and flexibility. Of the particles that are roughly spherical, few larger than 10 microns in diameter are found within the air spaces, but fibers of asbestos as long as 60 microns are relatively common and some have been seen that measured 200 microns. On the other hand, even short fibers of fine glass wool seem to be practically uninhalable because they are stiff and inflexible.

Where a mineral is chemically irritating, the factor of size has further importance because the smaller it is the greater the surface area exposed to contact with the tissue. Experiment has demonstrated that there is little reaction to particles of quartz between 3 and 10 microns in diameter, but that below the critical size of 3 microns the intensity of tissue response increases as the size of the particles decreases. There is probably a lower limit of effective size which is determined by the amount of retention within the air spaces. Particles smaller than this unestablished limit are exhaled with the air or eliminated through the blood and urine and hence do not accumulate to produce effective concentrations.

PHAGOCYTOSIS AND DISTRIBUTION WITHIN THE LUNG

Regardless of the character of the minerals in a dust the particles inhaled into the terminal air spaces are ingested by free phagocytic cells that develop in the adjacent walls. The subsequent disposition of the foreign bodies is more or less influenced by their *nature* and *quantity*. Small amounts of inert particulate matter like soot, coal, and iron are transported by the phagocytic cells through the lymphatic vessels to lymph nodules within the lungs. Here they may remain but there is a tendency for most of them to be carried on to the nodes about the bifurcation of the trachea. After the latter have accumulated excessive amounts of dust, more particles begin to collect in the lymph nodules within the

lungs themselves. This order of disposition suggests stasis from obstructive reaction in the nodes at the root of the lung. It is practically never complete, however, for even sclerosed silicotic lymph nodes become involved in a superimposed lobar pneumonia or pulmonary cancer.

When larger amounts of dust of the same type are inhaled all of the phagocytes do not remain within the lymphatic vessel; many accumulate within the surrounding connective tissue. This is evidenced by the delicate perilymphatic pigmentation which outlines the lobules presenting on the pleural surface and by similar deposits in the walls of blood vessels traversing the depths of the lungs. On exposure to excessive atmospheric concentrations of dust the protective mechanisms are entirely inadequate and dust-filled phagocytes remain in the alveoli for years.

The *solubility* of particulate matter also influences its disposition. Readily dissolved particles like those of marble and gypsum quickly disappear either before or after they have been ingested by phagocytic cells and leave practically no evidence of their presence. Toxic substances like fine quartz, on the other hand, exert their first effects upon the phagocytes. The cells undergo a series of changes comparable to those excited by the tubercle bacillus, including epithelioid alterations and giant cell formation. Necrosis occurs but it rarely involves the large numbers of cells seen in tuberculosis so that the gross appearance of caseation is lacking. However, numerous isolated phagocytes are killed, liberating the quartz that they have already ingested and thus creating a demand for more cells of the same kind. As a consequence the picture of early silicosis is a much more active one than that of the corresponding stages of any other form of pneumoconiosis. Phagocytes not killed but injured tend to adhere to one another and hence there is a pronounced tendency to form tubercle-like nodules.

Fibrous material, like asbestos, is not handled so effectively. The same type of phagocytes attempt to ingest inhaled asbestos but the fibers are so long that they project beyond the margins of the cell. This appears to impede ameboid activity and as a consequence there is little or no transport to

the lymphatic system. Asbestosis, accordingly, begins about the terminal respiratory bronchioles, where most of the inhaled fibers come to rest.

SIMPLE BENIGN PNEUMOCONIOSIS

Gross Anatomy

In the absence of associated infection the pleural surface is smooth and free from adhesions. There is usually *pigmentation* distributed in small focal areas, in linear deposits along the pleural lymphatics or diffusely, the amount varying with the intensity of the exposure. The sectioned lung again reveals varying amounts of pigmentation. In the slighter degrees one sees scattered flecks of black pigment, not over 2 or 3 mm. in diameter, in the centers of the lobules or fine linear deposits along the lymphatics in the walls of smaller arteries and in the septa between lobules. The old soft coal miner's lung may be uniformly black in color with here and there a small collection of emphysematous air spaces. Regardless of size or intensity, none of these pigmented areas is fibrous and palpation fails to differentiate them from the surrounding lung. Inspection with a lens reveals normal structure underlying the pigmentation.

The microscope demonstrates that the pigment is largely contained within phagocyte cells which may be located within the air spaces or in the areolar framework of the lung. In the latter situation these *dust cells* are often elongated and simulate connective tissue cells but as Haythorne has demonstrated, the development of edema separates the supporting cells and permits the phagocytes to assume their primitive rounded or oval forms. In marked cases heavy collars of pigmented cells will be found about the smaller arterioles. In cross section these deposits simulate ill-defined nodules but closer scrutiny reveals the central blood vessel. When cut longitudinally their true nature is more obvious. While such tissue changes are not infrequently associated with appreciable amounts of newly formed connective tissue, chemical analysis generally demonstrates unusual quantities of free silica. In such cases it is the invisible silica which has been responsible for most of the tissue reaction. More rarely no excess of silica is demonstrable and in these instances it seems probable that a healed infectious process may have produced a fibrosis in which the inhaled pigment has accumulated. This interpretation seems logical in view of the paucity of such cases and the repeated demonstration in animals of the lack of fibrosis on exposure to pure minerals of this class.

Roentgenologic Findings

A roentgenogram of the chest of a subject with simple benign pneumoconiosis reveals that the linear shadows normally cast by the blood vessels are thicker than usual and extend further into the periphery of the lung. No new shadows are observed. This picture is confusing to observers not thoroughly familiar with possible variants of the "normal" pattern. It is probably safe procedure to regard nothing

but very well defined linear exaggeration as evidence of reaction to inhaled dust. In no case should it be so regarded where the change is not uniform throughout all parts of both lungs. A further source of confusion arises from the fact that exposure to free silica dust, insufficient to produce definite and characteristic nodular roentgenographic patterns, may also cause exaggeration of the linear markings. Since it is impossible to distinguish between "early" silicotic reactions and those of nonspecific origin, it is unsafe to classify such films as presilicotic. In surveys or in annual reexaminations of large groups of men whose industrial exposure is thoroughly understood, such a diagnosis is a reasonable probability, but in an isolated case, seen on a hospital ward, the chances of error are great.

Clinical Picture

Simple benign pneumoconiosis ordinarily causes no symptoms. Disability is hard to imagine in view of the distribution of the dust reaction in the framework of the lung. *Physical signs* are usually absent although in some instances those indicative of chronic bronchitis may be elicited. The diagnosis depends upon a *history of adequate exposure* to dust supported by evidence of definite alterations in the roentgenographic pattern. But it should always be borne in mind that the latter is not pathognomonic, that inhaled dust is only one of the possible causes. Healed infections may also produce slight degrees of linear exaggeration, but in this case the distribution is apt to be less uniform.

Complications

Susceptibility to infection is not appreciably modified by simple benign pneumoconiosis although the nature of the causative dust influences the frequency of this complication. Acute pulmonary infections are no more common than in the population at large; the incidence of chronic infections like tuberculosis may be slightly elevated in the case of persons breathing dusts containing an adequate mixture of free silica. Where dusts of calcium compounds are concerned the frequency of tuberculosis is generally very low.

SILICOSIS

Gross Anatomy

The characteristic lesion of silicosis is a *localized nodule* of dense, hyaline, fibrous tissue not over 3 or 4 mm. in diameter. Inspection of typical silicotic lungs reveals nodules of this nature seeded over the pleural surface and uniformly scattered throughout all parts of the depths of both organs. Where the condition is of long standing there may be a zone of emphysema, free of nodules, over the diaphragmatic surfaces and where there are scars of old infections the uniformity of the distribution is invariably disturbed.

In the absence of infection the pleural surface is free from adhesions and, except for the elevated nodules, is smooth. *Pigmentation* is variable but in most cases there is enough associated carbon or other colored minerals with the silica to produce a diffuse or localized black color. In such cases the slightly raised centers of the colorless silicotic nodules stand out in sharp contrast. As silica tends to accumulate more rapidly in this location, the pleural manifestations may be the only definite evidence of early silicosis. However, palpation of the foci of pigmentation in the deeper parts of the lung usually reveals some that are firm enough to be differentiated from the surrounding tissue. Inspection of such foci with a lens demonstrates local obliteration of the normal structure. In well marked cases the uniform distribution of the firm discrete nodules constitute unmistakable evidence of silicosis.

Where the proportion of associated minerals is relatively large, the form of the silicotic nodule is often modified. About each is an ill-defined zone of heavy pigmentation which may communicate with similar deposits along arterioles or other structures containing lymphatic trunks. Sometimes the pigmentation is so intense that the firm, hyaline nodules are almost obscured. These modifications produce general patterns more suggestive of a linear network than the typical nodulation. They are most common in anthraco- and sidero-silicosis.

The tracheobronchial lymph nodes are practically always deeply pigmented from associated colored minerals. In the early phases of silicosis the nodes are enlarged but later, as the fibrosis matures, they contract to a size only slightly larger than normal and become as hard as the sole of a shoe.

The *reaction* to silica particles is progressive to the extent that nodules of microscopic dimensions increase until they attain a diameter of 2 to 4 mm. regardless of further exposure. However, on attaining their maximum size the lesions remain stationary and new ones do not develop. From then on only the development of associated infection is likely to involve new portions of the lung.

Many cases of silicosis fail to conform to this classical pattern. The pleural surface is obscured by *dense fibrous adhesions* and on sectioning the lung large, black masses of rubbery consistence have replaced variable amounts of air-containing tissue. Discrete nodules usually occur elsewhere but sometimes they are detectible only along the borders of the massive fibrosis. Coarse emphysema, not infrequently of bullous type, is a usual complication. The large *conglomerate lesions* most often occur in the upper thirds of one or both lungs. Sometimes bilaterally symmetrical masses radiate from the hilum into each lung involving perhaps portions of two

or more lobes with obliteration of the fissures. At other times a solid prism of such scar is discovered parallel to but 3 or 4 cm. beneath the lateral pleura of an upper lobe. In such cases a zone of coarse emphysema separates the mass from the overlying pleura. On sectioning such a mass the knife creaks as though passing through tough leather but the gritty sensation often mentioned is rare unless obvious calcification is encountered. Deep within these areas of conglomerate fibrosis one frequently sees irregular zones of necrosis filled with inky fluid. There are no definite walls of a different color such as those surrounding a tuberculous cavity; the black fibrous tissue simply becomes granular and then liquefies. As there is no communication with a bronchus this debris remains *in situ*.

Massive fibrosis of this type replaces and obliterates all normal structures in the portion of lung involved. Along the irregular borders of such a lesion there may be included islets of dilated air spaces. Blood vessels are obliterated and thrombosis is common. The writer has seen four instances in which the main branches of the pulmonary artery were completely obstructed by organizing clots. All but the larger cartilaginous bronchi are likewise compressed and obliterated.

Microscopic Appearances

Microscopic examination of the *simple, discrete, silicotic nodule* reveals a characteristic picture. The lesion is composed of concentric laminae of thick, hyaline connective tissue fibers whose nuclei are thin and compressed. Around the outside of this main mass is a layer of more cellular connective tissue of variable thickness. Usually the latter is more or less infiltrated with phagocytes containing black carbon or other colored particles and the center of the hyaline nodule may also be pigmented. Contraction of the fibrous elements in the nodule causes some distortion of the air spaces in the immediate vicinity but there is little or no exudate. Variants of this picture are (1) central areas of necrosis in nodules produced by exposure to excessive quantities of very fine quartz in practically pure state and (2) the much more common tendency for several contiguous nodules to become surrounded by a common capsule, thus forming small conglomerate lesions.

Similar study of the *massive conglomerate areas of fibrosis* reveals a diffuse matrix of hyaline fibrous tissue in which nodular foci are more or less easily defined. The matrix sometimes presents an arrangement of fibers suggesting an origin in an organizing pneumonic process; in most cases there is no particular pattern. The necrotic foci exhibit simple degeneration of the scar without leukocytic reaction. This becomes understandable when it is noted that the blood vessels throughout the mass are either thrombosed or more or less occluded by endarteritis. The bronchi, when still patent, usually display variable amounts of chronic inflammatory reaction but most of the smaller branches are compressed beyond recognition.

It is not uncommon in persons that have been exposed to low concentrations of silica dust to find silicotic nodules only in the vicinity of old tuberculous scars with none in the other parts of the lungs. This observation, in contrast to the generalized distribution of the nodules in persons with no evidence of infection, has led to the hypothesis that the massive conglomerate types of fibrosis are the result of localized injury. The resultant lymph stasis would explain local retention of excessive quan-

tities of the irritant particles. This concentration would in turn cause more reaction of the tissues. If the infection was still active while dust was being inhaled the pneumonic process could organize to produce the form of scar tissue sometimes observed. The silica would then act upon newly formed connective tissue to produce the diffuse type of fibrosis of the matrix between nodules. Such theory has support in experimental observation where both tuberculous and nontuberculous infections have been observed to heal with resultant massive fibrosis of similar appearance. Other elements may influence the development of these massive lesions. All of them show dense pigmentation from accumulated nonsiliceous mineral particles. Whether this is merely a result of the local lymph stasis or whether such minerals actually initiate multiplication of connective tissue cells which are further stimulated and hyalinized by the associated free silica is not clear. Finally, the element of collapse incident to bronchial obstruction may play some part, although not a primary one, as this factor is not introduced until the fibrosis is well advanced. The writer is convinced that the most probable basis for massive conglomerate fibrosis is a healed infection which distorts the structure in a localized portion of the lung and disturbs its functional activity. Tuberculosis is the most likely kind of infection to occur in the upper parts of the lungs.

Roentgenologic Findings

Roentgenographic manifestations of silicosis, of course, vary with the character of the pathological process. In cases of *simple discrete nodulation* the diagnostic feature is the uniform distribution of the small, sharply defined shadows of nodules. Unless they are so distributed throughout both lung fields the presumption is that some other condition is responsible. In the very early cases the nodulation is fine and without stereoroentgenograms may be confused with an advanced stage of linear exaggeration. Watkins-Pitchford aptly compared the appearance of the latter to the leafless tree and when early nodulation supervenes, to the tree in bud. As the nodules increase in size and number, their shadows become larger and more numerous. Only the main branches of a tree in full leaf can be identified.

On inspecting a single film of an advanced case of nodulation there are so many small round shadows that it is hard to imagine that much uninvolved tissue is left. However, one should remember that the shadows of all the nodules in an organ from 4 to 9 inches in thickness have been projected onto one plane. Stereo-films will do much to dispel the impression of their number and an examination of the lung itself still more. Rarely are there more than eight to ten nodules

to the square inch in any plane of section. Emphysema is responsible for a variable amount of shadowless lung fields in the costophrenic regions. In moderately advanced cases the mediastinal shadow is broad and dense due to the enlarged lymph nodes; in the mature stages the density persists but the width of this shadow is again less because of the contraction of the nodes.

Cases of *massive conglomerate fibrosis* present a diagnostic problem because they simulate tuberculo-silicosis in which the infectious element is merely dormant and because sometimes they do not even reveal anything indicative of silicosis. The typical conglomerate case presents one or more dense massive shadows upon a background of generalized nodulation with variable amounts of peripheral lung fields black because of emphysema. Distortion of the diaphragmatic shadows and other evidences of chronic pleurisy are common. The massive shadows may radiate as large fans from the hilum into each lung field or they may involve the root of only one lung. Another common manifestation is the sharply defined block-like shadow located beneath the clavicle, crossing the anterior second and third ribs at right angles a few centimeters beneath the lateral pleura. Peripheral to it there is usually evidence of emphysema. Occasionally massive shadows occur in the lower thirds of the lungs but these are less common. Overexposed films fail to demonstrate much structure within these extremely dense areas and even the foci of anemic necrosis lack sufficient definition to be visualized.

The contraction of these sclerotic masses, fixed to the chest wall by pleural adhesions, pulls much of the lung tissue upward and in so doing the discrete nodules in the lower lung are brought into close proximity to the massive lesion. Coincidently the air spaces in the lower lungs become overdistended to keep the pleural cavity filled. The combination of compensatory emphysema and a contracted lung may completely obscure the shadows of the discrete nodules so that they fuse with that of the large mass nearby. As a consequence the film may reveal only the massive shadows, emphysema, and chronic pleurisy with no discrete shadows to suggest the silicotic origin of the condition. These cases present a most difficult problem in diagnosis.

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Complications

Relationship to Infection.—Silicosis definitely increases susceptibility to tuberculosis; it is frequently associated with chronic bronchitis that may lead to terminal bronchopneumonia. The incidence of lobar pneumonia is high in certain industries with silica hazards but when conditions like exposure to sudden and extreme changes in temperature have been corrected the pneumonia rate has fallen. Such experience suggests that factors other than the silicosis are responsible.

Tuberculosis

Incidence.—While a few writers have expressed skepticism there is little reason to doubt that silicosis predisposes to tuberculosis. Statistics from every industrial country in the world indicate rates for this infection in the silica industries four to twenty times that in adult employed males. Autopsy statistics reveal complicating tuberculosis in *60 to 75 per cent* of silicotic subjects. Animal experiments demonstrate that exposure to silica dust is unique in causing infection with tubercle bacilli of low virulence for various species, which progresses and produces chronic tuberculosis. The skeptics base their opinions on clinical impressions of isolated cases, but for reasons to be presented such evidence may be misleading.

Factors Affecting Incidence.—While there is more tuberculosis among silicotic subjects than others, the frequency of this infection varies with the *opportunities for contact* with the tubercle bacillus in particular communities. In a modern foundry in the city of Milwaukee where a program of control has been in operation for seven years, Sander now reports no excess of this infection. Among Rand gold miners in South Africa in 1937–38 only five new cases of tuberculosis were discovered on periodic examination of 28,414 men with silicosis. In the years 1917–18 there were 116 similar cases among 13,474 silicotics examined. Many other examples of such contrasts could be cited but they are hardly necessary. The point to bear in mind is that while prevalence rates may vary from community to community it is as necessary for silicotics to come in contact with the disease in order to

develop tuberculosis as for other subjects. The presence of silicosis merely enhances the probability of effectiveness of such contact.

In groups of persons exposed to silica dust the incidence of complicating infection increases with the *severity of the reaction.* For one large group of 2612 miners, Cummings reported the following rates per 100,000:

No evidence of dust reaction	0.5
Linear exaggeration, 1st degree	1.0
Linear exaggeration, 2nd degree	2.0
Silicotic nodulation, 1st degree	6.0
Silicotic nodulation, 2nd degree	12.0

The frequency of tuberculosis in silicotics also increases with *age* which has led to the belief that most of the infections are of exogenous origin. This is true in many instances, but an appreciable number result from reactivation of preexisting latent foci of reinfection type disease. The probabilities of reactivating a so-called primary or Ghon tubercle are much more remote. While this possibility has been demonstrated experimentally in animals, annual reexamination of large groups of human subjects has demonstrated the great rarity of its occurrence. The calcified or fibrous parenchymal tubercles of the primary complex remain unchanged through years of exposure to silica dust although in some countries men with such lesions are rejected on the preemployment examination. In the United States the general practice is to admit them unless, of course, the primary focus shows evidence of recent activity.

Pathological Anatomy.—The pathological anatomy of tuberculosis in the silicotic subject is usually materially different from that in other individuals. In its commonest manifestation as *tuberculo-silicosis* it may be almost indistinguishable from the massive conglomerate form of simple silicosis, already described. Many sections may be necessary to disclose an isolated focus of caseation or a small tuberculous cavity. When such an area is exposed it is usually recognized easily by the gray-yellow color of the caseous matter which offers sharp contrast to the surrounding black fibrous tissue. In some instances the microscope must determine whether the infectious process is still active and even this method may require inspection of several square inches of section for the foci of activity may be few and far between. More often, however, the tuberculous complication is obvious at the time of autopsy. In 60 per cent of the conglomerate cases, large cavities have destroyed much of the massive scar and about

its borders the air-containing lung is invaded by a very chronic, fibroid type of tuberculosis. There may be a few clusters of isolated tubercles in the lower lung but usually bronchogenic and hematogenous extensions are rare. Similarly complications in the larynx, intestines and other organs are most exceptional. This very chronic form of tuberculosis is the usual one in silicotic subjects and since both its pathological and clinical manifestations are atypical it properly deserves its special name of tuberculo-silicosis.

Quite exceptionally tuberculosis may behave in a typical manner in persons with minimal or very old silicotic nodulation. In such cases, a chronic apical focus progresses slowly and finally excavates with resultant bronchogenic or hematogenous dissemination through the lungs and perhaps extrapulmonary complications.

Roentgenographic Appearances of Tuberculo-silicosis.—These are often indistinguishable from those of massive conglomerate fibrosis on first examination. *Annual films*, however, may demonstrate a gradual extension of the process. In many cases the time ultimately arrives when the activity of the infectious element is manifested; cavities may then be visualized and progression becomes much more rapid. Death may be anticipated within a period of two or three years. The rarer typical tuberculosis on a background of silicotic nodulation presents no unusual features.

Clinical Picture in Silicosis

One of the most characteristic features of simple, discrete, nodular silicosis is the paucity of symptoms and clinical signs in comparison with the extent of the roentgenological manifestations. Many subjects are entirely unaware of their condition until it is revealed by a routine roentgenogram. They continue to perform hard physical labor with no complaints and no diminution of output. Only severe and unusual exertion demonstrates some *dyspnea*. Some, on the other hand, will report constriction or burning sensations in the chest. Not infrequently there is an *unproductive cough*, probably due to bronchial irritation and not to changes in the lung proper. It seems probable that certain susceptible individuals may have symptoms even in minimal stages of the disease although this subject needs further investigation. The stethoscope often detects a *harsh respiratory note* and expiration is apt to be prolonged. In this type of disease chest ex-

pansion and the excursion of the diaphragm may be somewhat limited.

In the presence of *massive conglomerate fibrosis* the picture is different. These men are definitely short-winded. Although many of them continue to work, their production is much below par. Unusual exertion precipitates an attack of severe dyspnea from which they recover slowly. They frequently suffer pleuritic pain and cough, which is particularly troublesome in the morning. In some it is severe enough to precipitate vomiting. Theirs is the picture of advanced emphysema with the physical signs of that condition.

When the conglomerate lesion is due to an unhealed tuberculous infection *toxic symptoms* are so late in making their appearance that diagnosis is difficult. Not until the terminal breakdown do these cases manifest symptoms ordinarily associated with tuberculosis. Before that time they are short of breath but well nourished or even overweight from restricted activity. They have no fever, loss of appetite, or increase in sedimentation rate. Tubercle bacilli do not appear in their sputa. It is necessary to follow them carefully year after year to note the first hint of symptoms or the development of a *positive sputum.* On occasion, monthly guinea-pig tests may demonstrate the presence of tubercle bacilli followed by many negative specimens. Usually, however, the sputum remains positive after the organisms finally appear. For economic as well as medical reasons most of the closed cases are better off if they are allowed to do some work compatible with their strength. If put on rest treatment they are discontented and their dyspnea seems to become more severe. But they should not be neglected; as soon as any evidence of activity, and particularly a positive sputum, makes its appearance, they must be removed from contact to protect their fellow workmen.

Diagnosis of Silicosis

Diagnosis depends upon *a history of adequate exposure* in an industry with a free silica hazard, a *chest roentgenogram* showing a shadow pattern characteristic of this disease, and *physical signs* of the nature already described. The film often suggests the presence of silicosis but to establish a diagnosis

corroborative history must be obtained. This involves a complete record of a man's occupational life, including not only the plants at which he worked, but the kind of job and the materials used. The physical examination is important for two reasons: (1) It may show almost complete absence of abnormal signs, which, in conjunction with the extensive roentgenographic changes, is almost pathognomonic of silicosis; and (2) it may reveal evidences of activity of an infectious process. As already indicated, the most difficult diagnostic problem is the determination of the latent element of infection in a lesion of massive conglomerate type. Only repeated examination can settle this question.

Other Complications of Silicosis

The effect of silicosis upon the circulation is a subject that has been discussed without definite conclusion. Both silicosis and heart disease are most frequent in mature adult life. Many believe that obstructive fibrosis in the lungs results in *cor pulmonale* with characteristic hypertrophy of the right side of the heart. If this result does follow it is probably limited to cases of massive conglomerate silicosis. Discrete nodulation seems to produce little anatomical change in the pulmonary blood vessels. But even with conglomerate disease cases are rare in which only the right side of the heart is affected. Most of them have generalized *cardiovascular lesions* which might easily have originated independently. Obstructive fibrosis in the lungs places an added burden on the overworked heart but the writer questions whether it is a primary cause of heart disease.

While some authors have claimed that soluble silica, liberated in pulmonary lesions, circulates through the body to poison other tissues, there is nothing to support this purely hypothetical reasoning. Any excess of *nephritis* that may occur can be explained by the higher incidence of arteriosclerosis at the age periods when silicosis is common. Silicotic involvement of lymph nodes at the head of the pancreas is a regular finding and occasionally nodes along the abdominal aorta are involved. Only once has the writer known them to cause symptoms.

Prognosis

Prognosis in *uncomplicated, discrete, nodular silicosis* is good. In the absence of infection such lesions reduce the reserve capacity of the lungs but do not seriously interfere with ordinary work. Persons with simple silicosis should be kept under observation and given an annual x-ray examination to detect early evidences of tuberculosis. In the absence of this complication their life expectation is not greatly impaired.

Massive conglomerate silicosis is a more serious condition. It causes disability in its own right and it is hard to differentiate from tuberculo-silicosis in an inactive phase. Men with small conglomerate lesions often work with little difficulty but after exertion dyspnea is much more obvious than in those with the discrete form of the disease. The large conglomerations are usually incapacitating because of associated emphysema.

Tuberculosis in any form is a serious complication of silicosis as it is responsible for most of the disability from this disease. Detected early and promptly subjected to treatment it need not terminate fatally in the cooperative patient. The advanced tuberculo-silicotic lesions are another matter; those in whom there is an element of active infection quite regularly progress and although death may occur from other causes, many ultimately succumb to their infection.

Treatment and Disposition of Cases

There is no known treatment for silicosis; the condition must be prevented by control of the dust in the environment and by the proper selection of persons who are to be employed. Good plant housekeeping, the use of water, adequate general ventilation and local exhaust systems are usually sufficient to maintain safe concentrations of dust in the air of working places. *Medical control* involves a preemployment examination to exclude persons with tuberculous lesions from exposure to silica dust and periodic examinations to detect evidences of disease in those already employed.

Independent observations by Robson, Denny, and Irwin in Ontario, and by the Saranac Laboratory in this country have demonstrated that *aluminum and certain of its compounds*

will prevent the development of silicosis. The Canadian observers obtained their results with finely divided aluminum powder. The Saranac Laboratory's experiments were made with the hydroxides of aluminum. Immature silicotic lesions are aborted and regress, but fully developed nodules are not affected. To be effective, a large quantity of the inhibitor must reach the same location and probably the same phagocytic cells that contain the quartz particles. Chemical reaction results in a coating of the silica whose toxic effects are completely neutralized. Experiments are now in progress at the Porcupine Silicosis Clinic in Timmins, Ontario, to discover whether aluminum inhalation therapy has any influence upon symptoms. As a prophylactic measure aluminum inhalations might be effective, but difficult of application to a large group of workmen. There is no reason to believe that it can ever be substituted for engineering methods to reduce atmospheric concentrations of dust.

The *disposition of employees* in whom the periodic examination discloses different manifestations of pulmonary disease depends upon a number of factors: the effectiveness of dust control in the plant, the condition and age of the man, the opportunities for transfer to other jobs, and so on. Medical recommendations in each case must be particularized and will depend upon a thorough study of the individual. In general, men with simple discrete nodulation may continue at their regular work in a plant with a good program of dust control. Exception should be made in the case of the young employee who manifests signs of early silicosis after a short exposure. He is probably more susceptible than others and should be transferred to another job, but there is no medical reason why he should stop all work. The same may be said of the case with a small focus of conglomerate fibrosis without much dyspnea. More advanced cases of the same character seem to have less dyspnea if they are allowed to do light work instead of being laid off with no exercise. Management, however, is often embarrassed to find enough jobs of this character in the heavy industries like mining.

Of course all of these men require *constant observation* to detect the earliest evidence of activity in an infectious com-

plication. Open tuberculosis means segregation for the protection of the rest of the group; early tuberculosis should be given full sanatorium treatment, and recovery is quite possible in the cooperative patient. The chronic tuberculosilicotic is best cared for on a modified regimen of exercise. Ultimate recovery is rare.

RAPIDLY DEVELOPING SILICOSIS

A rare and atypical manifestation of silicosis has occurred in a few groups of persons exposed to excessive concentrations of very pure and very fine quartz dust. This condition was first identified in persons manufacturing and packing abrasive soap powders and it was assumed that free alkalies associated with the silica caused rapid solution of the inhaled quartz. Animal experiment finds no justification for this hypothesis and subsequent observation has demonstrated similar cases in sandblasters working in enclosed tanks and certain tunnel workers whose exposure included no alkalies. After periods as short as eighteen months some of these operatives have developed severe dyspnea. *Chest roentgenograms* reveal only a fine diffuse haziness throughout the lung fields with no suggestion of the classical nodulation. A few have died within a year or so and a number of autopsies have been obtained. Many of them showed a *complicating tuberculosis*, and in most of the others the cause of death was a *nonspecific bronchopneumonia*. But apart from these infectious lesions, all of the lungs have presented a generalized induration which, in gross, suggested an organizing pneumonic process, but on microscopic examination was revealed as a diffuse silicotic reaction. Irvine aptly described it as a "dust pneumonia."

Practically the same picture is seen in guinea pigs exposed to excessive amounts of pure quartz dust of very fine particle size. Innumerable silicotic nodules of microscopic dimensions occur throughout the walls of the pulmonary air spaces. There is also a generalized proliferation of all connective tissue elements in the lungs and the formation of plugs of similar tissue within some of the alveoli. Tracheobronchial lymph node reaction is minimal. Apparently the lung is so nearly

overwhelmed with the large amount of a potent irritant that the lymphatic system is entirely inadequate to remove it. Reaction begins simultaneously throughout the functional portions of the organ. However, even under such circumstances, time is essential for the quartz to produce any gross change. In guinea pigs nothing can be seen for the first six months of exposure. Therefore it seems ill advised to describe this condition as an "acute" silicosis.

The *diagnosis* depends upon the history of an unusual exposure which must be verified in all essential details, upon the roentgenogram with its barely identifiable haziness and the clinical picture of marked dyspnea. These cases need careful protection against infection.

ASBESTOSIS

Pathological Anatomy

The characteristic features of well marked asbestosis are (1) *diffuse, non-nodular fibrosis* involving ill-defined portions of the parenchyma of the lung, (2) moderate sized *emphysematous blebs* often located in fibrous strands beneath the lateral and interlobar pleura, and (3) *adhesive fibrous pleurisy*. Such a lung has a doughy consistence but can be partially collapsed by moderate pressure.

The diffuse involvement is frequently associated with fibrous thickening of the interlobular septa so that these structures are clearly demarcated on the cut surface of the lungs. In the center of each lobule one usually finds an ill-defined collection of gray dust pigment; in sections cut in a proper plane the fanlike branches of a terminal bronchiole are seen to enter the pigmented area. The emphysematous blebs often occur in rows roughly parallel to the pleura. Most of them are less than 5 mm. in diameter with smooth, glistening gray walls; sometimes they are much larger and project through and above the thickened pleura as bullae. The tracheobronchial nodes are blue-black in color, small and moderately firm.

Microscopic sections of the lungs reveal a diffuse fibrosis, not as dense or hyaline as in silicosis. It extends from the terminal bronchioles into the parenchyma, replacing many but not all of the air spaces in an included plane. Animal experiments and the few cases of early disease in man that have come to autopsy reveal that such fibrosis begins about the terminal bronchioles and slowly spreads into the periphery of the lung. Apparently most of these fibrous foreign bodies are caught in the respiratory bronchioles whose walls are irregular because of lateral alveolar pouches. Just proximal to these structures the lining epithelium of the bronchial tree changes from ciliated to low columnar cells, another factor which may influence retention. As fibrosis develops in the walls of these bronchioles the lateral alveoli are closed or stretched so that the internal contour of the tube becomes smooth. Subsequently inhaled fibers now pass deeper into the lungs and there cause more fibrosis. Patent air

spaces in the midst of a fibrous zone are apparently supplied by uninvolved bronchioles outside the plane of section. It is probably these air spaces which dilate after being cut off and appear as emphysematous blebs.

A characteristic feature is the presence of large numbers of *asbestosis bodies*. These structures result from the deposition of albuminous material and iron upon the surface of the inhaled fibers. They vary in size and shape from minute globules 1 micron or less in diameter to haustrated rods 5 to 60 or more microns in length. They are golden-yellow in color and exhibit many bizarre forms. Most have swollen, club-shaped ends and many show beading or smooth, lateral projections. They occur in clusters within air spaces or widely scattered throughout the scar tissue.

Roentgenologic Findings

Roentgenographic appearances of moderately advanced, uncomplicated asbestosis are much less obvious than the anatomical changes would suggest. Inspection of the film reveals a light, diffuse haziness overlying the lower third of both lung fields. Evidences of pleurisy may or may not be visualized. As the fibrosis matures the haziness is more pronounced until it reaches the so-called "ground glass appearance" which obscures all lung markings. The upper thirds remain relatively clear. The failure of the fibrosis to cast a more dense shadow is probably due to the relatively large number of patent air spaces persisting throughout it. As histological examination reveals as much reaction in the upper lungs as in the lower thirds, it is inferred that the distribution of the x-ray shadows is due to the greater thickness of the lower lung. Very advanced cases may show a fine stippling and a certain amount of reticulation superimposed upon the ground glass background. In such cases pleuropericardial adhesions are responsible for the so-called "porcupine heart shadow."

Relationship to Infection

American surveys reveal no such general excess of tuberculosis as occurs in the free silica industries. In England much more infection has been reported and autopsy statistics from all countries reveal many instances of *terminal tuberculosis*. Animal experiments demonstrate no special tendency for tuberculosis to progress upon a background of asbestosis. The infections frequently heal, accentuating the fibrosis provoked by the dust. It seems probable that socio-economic factors

may outweigh those of the dust and that selection has influenced the incidence in the postmortem cases. Persons with asbestosis who contract tuberculosis are apt to be sent to sanatoria where autopsies will be secured because of the special interest in the occupational origin of their disease. Those dying elsewhere are less apt to come to autopsy.

Course of the Disease

The course of the disease is somewhat obscure as most of the patients who could be followed continued to work with more or less dust exposure in spite of the excellent programs of dust control in most American factories. Cases that were quite well developed when first observed now reveal more intense x-ray shadows; those with little change at the outset seem to remain in approximately the same condition. In animals no progression occurs after complete cessation of exposure. Any fibrosis originally present tends to become denser but it does not increase in area. Asbestosis bodies disappear between two and three years after an injection of asbestos into the lungs of guinea pigs.

Clinical Picture

A case of asbestosis exhibits dyspnea which seems entirely out of proportion to the severity of the roentgenographic changes. These patients are very short of breath, have a dry unproductive cough, and are said to have a somewhat bluish color. The latter symptom is not invariable. Signs of cardiac injury are not generally elicited. Occasionally asbestos bodies can be detected in the sputum but they rarely appear in the absence of associated infection.

Complications

As already indicated *tuberculosis* may be superimposed on this condition, but there is little to indicate an excessive prevalence. Bronchopneumonia is a commoner cause of death. Reported autopsies from various countries have demonstrated ten cases of *primary bronchogenic carcinoma* among persons with asbestosis but in comparison with the number exposed to this dust this incidence would not appear at all surprising.

The character of the pulmonary fibrosis would seem to be ideal to create a *cor pulmonale* because large amounts of capillary bed are obliterated. However, neither clinical nor pathological evidence seems to indicate a high frequency of cardiac involvement.

A complication of the occupation although not of the pulmonary disease is the so-called *asbestos corn* on the skin. This is a localized focus of chronic inflammation provoked by relatively coarse splinters of the mineral that may penetrate into the subcutaneous tissue. No asbestosis bodies are formed in these lesions.

Diagnosis

Diagnosis depends upon a history of exposure to dust of asbestos fibers, characteristic chest roentgenograms and physical findings. Dust exposure occurs usually in fabricating plants where fireproof textiles, brake linings, and similar materials are manufactured, or among those using asbestos fiber for insulating purposes. Strangely enough experiment has demonstrated that the longer fibers are much more dangerous than very finely powdered asbestos. This probably explains the absence of the condition at the mines where, in formerly very dusty plants, the mineral was ground, separated, and the finest products collected for insulating purposes. An average exposure of about eight years seems necessary to produce roentgenographic evidence of asbestosis.