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THE PATHOLOGY AND ROENTGENOGRAPHIC MANIFESTATIONS OF PNEUMOCONIOSIS

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To the pathologists who coined it, the term pneumoconiosis was useful to describe all pulmonary reactions due to the inhalation of dust. Under the impetus of compensation laws this group of conditions has received so much attention that today pneumoconiosis is almost a household word. But too few are aware of its original significance and even some medical writers use it interchangeably with the specific term silicosis. As a pathologist I prefer to retain the original meaning and use pneumoconiosis as a generic term to describe all forms of pulmonary reactions to inhaled dust, with no implication as to character, severity or effect on function. The two clinically important forms of pneumoconiosis that are known as silicosis and asbestosis are respectively due to inhaled free silica and asbestos dusts. Other forms have been given special names to indicate the kind of mineral that produces them, but such terms have little practical significance because most pure substances other than free silica and asbestos cause little irritation and provoke essentially the same kind of tissue changes. Available information would make it more logical to classify most of the other known pneumoconioses in two general categories. Those which are characterized by appreciable degrees of fibrosis will yield free silica on analysis and hence should be designated as "modified silicosis." For the remainder I would suggest the name "benign nonspecific pneumoconiosis."

Illustrative of the latter are simple anthracosis and siderosis produced by inhaling relatively pure coal or iron dusts. By themselves these minerals provoke no significant fibrosis but merely pigmentation, which has no influence on pulmonary function. When they are mixed with free silica there is a fibrous reaction, but it is due to the contaminating silica. The resultant diseases are then more properly designated as anthracosilicosis and siderosilicosis.

Badham [1] suggested the term "silicatosis" to designate reaction to any silicate dust, but as there are hundreds of different silicates and only the fibrous varieties, collectively called asbestos, are known to provoke serious reaction his suggestion has not been generally adopted. In nature some silicates are commonly mixed with quartz, but it is probably the latter which is responsible for pulmonary damage. Hence reactions to such dusts are properly designated as modified silicosis. Possibly other silicates whose effects have not yet been evaluated may subsequently prove to be dangerous in their own rights, but if they are it will not be because they are compounds of silicon but because of some special peculiarity of structure or composition.

In the temporary category are the pneumoconioses that are known chiefly from shadows cast on a roentgenogram. They may have a foundation of pathologic reaction, but it has not yet been adequately defined. However, the changes in the film are associated with so few authentic symptoms that their influence is viewed with skepticism. Here belong the so-called baritosis seen in men who are exposed to dust of barium sulfate and the false nodulation of arc welders. The former, described by Arrigoni,[2] may be nothing but the shadows of compact collections of radiopaque barium particles in the lungs. Likewise, Enzer's [3] report of a single autopsy on an arc welder makes it seem probable that similar collections of iron particles rather than foci of fibrous reaction are responsible for the "nodular" shadows seen in occasional roentgenograms.

Finally there is the whole group of reactions to organic dusts that are properly included under the term pneumoconiosis. One form said to be due to cotton fiber has been named byssinosis but no good description of its pathologic manifestations can be found in the literature. In general it is assumed that most of the organic dusts may cause bronchitis with or without sensitization phenomena resulting in a variety of allergic symptoms. Moreover the reaction to dust composed of living organisms is in one sense a pneumoconiosis, but such conditions are generally classified as infections. They are beyond the scope of this paper. Likewise, definitely toxic dusts such as lead are excluded. Even without this group it will be appreciated that the term pneumoconiosis includes many different conditions and does not necessarily imply disabling disease of the lungs.

The first paper of the series [4] dealt with specific causes. It reviewed some of the complex factors which govern the behavior of fine mineral particles suspended in air and attempted to point out how they influenced the inhalation of dust. It discussed the varying capacities of different kinds of minerals to provoke reaction once they had accumulated in sufficient quantities within the lungs and indicated that some might inhibit the dangerous effects of free silica. It considered the influence of coexistent infection and the

From the Saranac Laboratory for the Study of Tuberculosis of the Edward L. Trudeau Foundation.

1. Badham, Charles: [illegible]

2. Arrigoni, Arturo: Pneumoconiosis from [illegible]

subject of individual susceptibility with a review of the factors proposed to explain this phenomenon.

The present paper will be concerned with the pathologic reactions to different minerals in normal and in infected human lungs. It will take up the evolution of the various disease processes and, when possible, describe the shadow pattern cast on roentgenograms of the lungs.

PROTECTIVE MECHANISMS

When one considers that in quiet respiration the average human being inhales some 12,000 liters of air every twenty-four hours and then recalls the varying degrees of atmospheric pollution created in our industrial civilization, it is apparent that the lungs must be protected against dust or they could not escape becoming clogged with foreign material. In all the higher animals, at least, two sets of mechanisms have developed designed to keep their lungs clean: one prevents dust particles from entering the lungs; the other removes the particles that elude the first barriers.

Dust particles are caught in the mucus secreted by the membrane lining all parts of the tract. Ciliary action then transports them to the nasopharynx, from which they are excreted.

Lehmann [5] has suggested that such activities play only a minor role in the removal of dust in the nose and thinks that the shape of its cavities has much more effect. He has pointed out that the nasal passage consists of dilated anterior and posterior portions separated by a narrow constriction in the vicinity of the turbinates. He recalls that when dust-laden air is blown through a glass tube with a central constriction the particles all come to rest in the distal, dilated portion owng to the sudden cooling and expansion of the air. He believes that deformities due to faulty development, disease or injury change the shape of the nasal cavities and lower their efficiency for the removal of foreign particles. The technical difficulties encountered in measuring the quantities of dust retained in the nose have prevented confirmation of his observations.

It is generally assumed that at least half of the foreign matter in inspired air will be removed by these mechanisms in the normal nose, trachea and bronchi. There has been considerable speculation but little proof of the influence of disease in these organs. It is argued that the chronic bronchitis often associated with silicosis probably permits unusual quantities of dust to enter the lungs. As a matter of observation, the lungs of animals with purulent bronchitis actually contain much less dust than those of normal ones exposed to the same concentration. The heavy plugs of secretion in the larger air passages mechanically prevent the ingress of foreign particles. It has also been pointed out that one of the manifestations of chronic bronchitis is epithelial metaplasia with the formation of a smooth lining membrane that should permit freer passage of dust particles into the lungs. One should remember, however, that such metaplasia is practically never generalized and that it almost always involves one or two bronchi immediately adjacent to a focus of chronic disease inside the lung. Such a condition might account in part for the unusually heavy deposits of dust in the localized pulmonary focus of infection, but it would have little influence on the rest of the lungs. Thus some phases of tracheitis and bronchitis may be protective mechanisms, and until their influence has been evaluated it is best to refrain from inference.

The discussion thus far has dealt only with particulate foreign bodies, but where fibrous materials are concerned the upper respiratory protection would seem to be less adequate. Since asbestosis constitutes one of the dangerous forms of pneumoconiosis to be discussed, certain exceptions to what has been said must be noted at this point. Apparently many of the long asbestos fibers succeed in sliding over the surface of ciliated epithelium, for the lungs contain plenty in excess of from 10 to 20 microns in length, and occasional ones as long as 200 microns have been discovered. These fibers seem to pass through the smooth walled bronchi quite readily, but when they reach the respiratory bronchioles the alveolar pouches given off from the sides of these tubes entrap and retain them. Whether the same is true of all fibrous foreign bodies has not been established.

Little is known about the primary distribution of inhaled foreign particles within the lungs or the factors which govern it. It has been observed that carmine particles reach the subpleural alveoli within half an hour after animals have been exposed to heavy atmospheric suspensions of such material. The path of these particles, the influence of tidal and residual air, the effect of deep or shallow breathing all remain to be investigated. Posture and specific gravity probably have little influence on particles as small as 3 microns or less in diameter.

Secondary deposition of inhaled inert particles, on the other hand, has been investigated more extensively. Gross inspection of the lungs often shows streaks of pigmentation in the pleural surface, arranged in bands that are opposed to the intercostal surfaces, with little or no deposit in the intervening grooves formed by the ribs. Likewise the diaphragmatic surfaces are practically free of dust. Such distribution implies that pressure of overlying parts has prevented local deposition. Furthermore the heaviest deposits tend to occur in the upper two thirds of the pleura, suggesting that the greater excursion of the lower portion of the lung may have limited retention. Examination of a section of the lung is not so informative because the various structures are cut in so many planes. However, inspection with a lens will usually demonstrate fine linear deposits along the connective tissue septums, between lobules and around the medium sized blood vessels. The walls of the bronchi always show much less pigmentation. In very severe cases of pure anthracosis the entire lung may be uniformly black. Almost always the lymphoid tissues within the lungs and those of the nodes at their root are more or less heavily pigmented.

To understand this distribution of inhaled pigment one must appreciate the mechanisms provided for its elimination from the air spaces. These mechanisms include the mobile alveolar phagocytes and the pulmonary lymphatic system.

Alveolar Phagocytes.—These originate in the walls of the air spaces, become detached and are capable of independent ameboid activity. Their origin is still debated, but it is my own belief [6] that they belong to the general group of wandering cells of connective tissue, variously known as histiocytes, clasmatocytes and the like. Others think that they may be modified epithelial cells from the alveolar lining and some observers consider them monocytes that have wandered out of the blood vessels. This is not the place to discuss the evidence for these views. Whatever their origin, these

5. Lehmann, Gunther: Die Filterung der Atemluft und deren Bedeutung für Staubkrankheiten, Berlin, Julius Springer, 1938.

6. Gardner, L. U., and Smith, D. T.: The Origin of the Alveolar Phagocytes, Am. J. Path. 3:445-460 (Sept.) 1927.

cells appear in the alveoli in numbers corresponding to the quantities of inhaled foreign bodies. As chance contacts are established, the particles of dust are ingested by the cells.[7] The process may be repeated so often that many phagocytes contain enough foreign material to obscure their internal structure. Often the cell enlarges as it engulfs more particles. The phagocyte moves slowly over the inner surface of the air space until it finally comes to rest in the vicinity of a lymph vessel. Whether there is any force which guides its course has never been established.

Lymphatic System.—The final stage in the process of freeing the air spaces of accumulated foreign particles is a function of the lymphatic system. Space forbids a complete description of the pulmonary lymphatics but it should be recalled that the lungs are provided with two sets of lymph vessels, one coursing through the pleura and another located in the connective tissue sheaths of blood vessels and bronchi. The superficial and deep sets communicate with one another by means of short thick vessels situated in the septums between subpleural lobules; these permit lymph to flow from the interior of the lung to the pleura in case of obstruction in the deep system. Wherever lymphatic trunks communicate with one another inside the lung there are masses of lymphoid tissue. These points are located in the pleura, at the distal ends of the alveolar ducts and where blood vessels or bronchi bifurcate. The lymphoid nodules increase in size as the hilus is approached. Both superficial and deep lymphatics discharge most of their lymph into large nodes located about the bifurcation of the trachea, referred to in this communication as the tracheobronchial nodes. Efferents from the lower portion of both lungs pass through the crura of the diaphragm to nodes situated along the esophagus and cardiac end of the stomach.

Dust particles are carried into the lymphatic vessels either by mobile phagocytes or in the free state. The mechanism in the latter case is not understood.[8] Many come to rest in and about intrapulmonary lymphoid deposits; more are borne along and deposited in the tracheobronchial nodes. In experimental animals the first deposition is in the nodes, and as these structures become filled increasing quantities are found in the successively peripheral nodules of pulmonary lymphoid tissue. Strachan and Simson [9] described similar deposition in human lungs.

Not all the inhaled material is removed to the lymphoid tissues; in most lungs considerable pigment is also found in the areolar tissue surrounding the lymph vessels. These deposits often seem to be made up of elongated collections of free particles packed between the fibers of connective tissue. Haythorn, [10] however, has demonstrated that many of these particles are actually contained within the bodies of compressed phagocytes. On production of an edema that separates the fibers and allows the "dust cells" to assume their more familiar spherical form, the intracellular distribution of the particles again becomes recognizable.

It is not known whether such perilymphatic deposits are composed of material that is temporarily stored in the areolar tissue until it can be carried off through the lymphatic vessels or whether, having entered a vessel at some peripheral point, it has subsequently escaped into the surrounding tissue. In any event such deposition occurs in the pulmonary framework, a location where the foreign body can exert no influence on respiratory function.

These perilymphatic and lymphoid tissue accumulations of particles are responsible for the pigmentation seen on gross inspection of the lungs. On the pleural surface the delicate tracery of lines is made up of accumulations in the areolar tissues about the superficial lymph vessels; the focal collections occur in lymphoid tissues at the junction of communicating and superficial lymph vessels. Similar relationships exist in the depths of the lungs. The generalized diffuse pigmentation often seen in the lungs of persons dying during exposure to dust is due to free and phagocytosed particles still within the air spaces. In cases in which diffuse pigmentation is still present years after exposure has ceased, the "drainage" mechanisms have been inadequate to remove the excess of inhaled particles. However, the next section will indicate that even within the air spaces most kinds of particles produce no apparent changes that could interfere with respiratory function.

THE HISTOGENESIS OF PNEUMOCONIOSIS

Phagocytosis and Concentration of Dust.—It is in the phagocytes that foreign bodies first exert their specific influences on living cells and that differences due to physicochemical composition of the irritant become manifest. Inert substances like garnet, silicon carbide and aluminum oxide have no effect on the structure of the cell, although they may retard or stop its locomotion by their mass within its cytoplasm. Frequently such overloaded phagocytes are found within the alveoli years after exposure to dust has ceased.[11]

Toxic free silica, on the other hand, quickly injures the phagocytes, and its effect is directly proportional to the number and size of the ingested particles. Such effects are most readily observed in experimental animals killed at intervals during exposure to high concentrations of siliceous dust, but they can also be seen in human cases of rapidly developing silicosis. No changes are visible in the cell that has taken up a few large fragments 4 or more microns in diameter, but when the particle size is under 3 microns the number ingested by each cell is much greater and, as a consequence, the amount of surface in contact with cytoplasm is greatly increased. Degenerative changes closely simulating those in the "epithelioid" cells of tuberculosis then become manifest. The cell enlarges, droplets of visible lipoid appear in the cytoplasm and the elements stained supravitally with neutral red are rearranged to form patterns indistinguishable from those in tuberculous epithelioid cells.[12] With the proper concentration of the irritant, the nucleus divides repeatedly as the cytoplasm increases in extent; the result is a giant cell in every way comparable to the Langhans giant cell of tuberculosis. In animals injected with extremely fine silica, such giant cells may attain astounding size with several hundred nuclei. Under very potent stimulation the cell is killed and undergoes

7. Fenn, W. O.: The Phagocytosis of Solid Particles, J. Gen. Physiol. 3: 439-464 (March) 1921.
8. Drinker, C. K., and Field, Madeleine E.: Lymphatics, Lymph and Tissue Fluid, Baltimore, Williams & Wilkins Company, 1933.
9. Strachan, A. S., and Simson, F. W.: A Preliminary Study of the Pathology of Silicosis as Seen on the Witwatersrand: Silicosis, International Conference at Johannesburg, Geneva, 1930, pp. 221-248.
10. Haythorn, S. R.: Experimental Edema as an Aid to Histopathologic Studies, Warthin Ann. Vol., pp. 491-502, 1927.
11. Gardner, L. U.: Studies on the Relation of Mineral Dusts to Tuberculosis: III. Carborundum, Am. Rev. Tubere. 7: 344-357 (July) 1923.
12. Gardner, L. U.: The Similarity of the Lesions Produced by Silica and the Tubercle Bacillus, Am. J. Path. [illegible]

a process that Mavrogordato [13] described as "mummification." It retains its normal size and the limiting membrane is intact, but all internal structures fail to stain with histologic dyes. Some of these "ghost cells" preserve their identity, but others probably break up and liberate their contents, which are then taken up by new phagocytes.

The great similarity between the effects produced by crystalline silica and tubercle bacilli [12] has puzzled many observers, but Fallon [14] has proposed a hypothesis and already published preliminary experiments which may contain the explanation. He conceived the idea that the action of both these primary irritants on the phagocytes liberates toxic phospholipids and that these substances are responsible for the further proliferation that results in the formation of the granulomatous nodule. He demonstrated that such lipids, at least partially freed of silica, were actually capable of producing tubercles.

Finally there is a suggestion that small quantities of silica taken up by phagocytes tend to stimulate ameboid activity,[15] for in early silicosis the cells seem to migrate to lymphoid tissue more rapidly than in any other form of pneumoconiosis. However, it is difficult to be certain whether the clusters of cells observed in and about the nodes have actually migrated there or whether new ones may have proliferated under the stimulation of the toxic material.

The response of the phagocytes to fibrous asbestos requires special comment, as it is treated in a different manner from particulate material. The fibers are often too long to be completely ingested by a mononuclear or giant phagocyte. Frequently one end will project beyond the border of the cell, or sometimes several phagocytes will attach themselves to a single fiber. Giant cells do not migrate far and most of them are either applied to the walls of the bronchiole or at most have penetrated its substance. It is practically impossible to discover fibers or asbestosis bodies in the more remote intrapulmonary or mediastinal lymphoid tissues.

For all dusts the mechanisms of phagocytosis and concentration have many common features but, as indicated, even the initial cellular responses are modified by the properties peculiar to the three classes of minerals under consideration. Because these changes are microscopic, it has been convenient to consider them together. We are now in a position to consider the three generally recognized anatomic forms of reaction to mineral dusts under the headings benign nonspecific pneumoconioses, silicosis and asbestosis.

THE BENIGN NONSPECIFIC PNEUMOCONIOSES

In the category of benign nonspecific pneumoconiosis is included every known reaction to mineral dust except that to the soluble poisons such as lead, the specific diseases, silicosis and asbestosis, and "roentgenologic conditions" such as baritosis and the pseudonodulation of arc welders, previously mentioned.

We have seen that the action of the alveolar phagocytes and the lymphatic system tends to concentrate particulate mineral matter, regardless of its chemical composition, in the lymphoid tissues of the lungs and mediastinum and that there are also appreciable accumulations in the areolar tissues about lymphatic trunks. The reaction that will be produced in these locations is determined by the physicochemical properties of the minerals concerned. As shown in the first paper, on etiology,[4] most of them exert no appreciable effects on connective tissues; a few can produce low grade chronic inflammation which is not progressive and does not terminate in fibrosis appreciable on gross examination. All these reactions occur in the framework of the lung. The only secondary effect is the dilatation of the few air spaces that directly abut on the pigmented connective tissues. Such emphysema never involves other parts of the lung and is too restricted in extent to have functional significance.

Gross appearances are determined largely by the color of the inhaled dust. If it has no color, no abnormality may be detectible. If in masses it appears black, the diagnosis will probably be "anthracosis" in the absence of a history of exposure to a specific kind of mineral; really it makes little difference. The pleural surface of the lung is flecked with focal and linear deposits of pigment. The cut surface shows the linear collections in the septums between lobules, the thin streaks along branches of the pulmonary arteries and the rounded flecks scattered here and there which a lens identifies as perivascular accumulations about cross sections of arterioles. The air spaces are always visible in the colored areas, a feature which distinguishes the benign pneumoconiosis from all silicotic reactions. Both the intrapulmonary and the mediastinal lymphoid tissue stand out in sharp contrast by reason of their color. In extreme cases the pigmentation is diffuse and the entire pleural and cut surface of the lung may be black. But in no case is there enough reaction to be detected by palpation or gross inspection.

The shadows cast by such changes on a roentgenogram tend to exaggerate their importance. Except in the most advanced cases the pattern is merely one of exaggeration of the normal lungmarkings. Since most of the latter are due to the blood vessels, their shadows become heavier and the finer branches are visualized when they are thickened by a sheath of dust and chronic inflammatory reaction. In advanced cases the film may present a reticulated appearance due to the thickening of peripheral arterial twigs and the interlobular septums. The diffuse haziness observed in certain cases may be caused by the presence of great numbers of phagocytes scattered throughout the air spaces. Enough of them in superimposed planes of tissue will intercept some of the x-rays and register a haze on the film.

Since the blood vessels may be thickened from causes other than deposits of dust in their outer coats and since such thickening becomes increasingly frequent with advancing age,[16] there is a great possibility of error in ascribing the exaggerated linear markings seen in a film to occupational factors. In older persons particularly one must beware of diagnosing benign nonspecific pneumoconiosis from a roentgenogram and a history of exposure to dust.

It is hard to imagine that pulmonary symptoms or disability could be produced by reactions of this character. There is generally no involvement of the alveolar walls at all. While in advanced cases there may be a little emphysema, it is confined to only a few air spaces immediately about the pigmented connective tissues of the lung. Even in extreme cases presenting

13. Mavrogordato, A.: Studies in Experimental Silicosis and Other Pneumonokonioses, South African Institute for Medical Research, No. 15, 1932, pp. 1-58.

14. Fallon, J. T.: Specific Tissue Reactions to Phospholipids: A Suggested Explanation for the Similarity of the Lesions of Silicosis and Pulmonary Tuberculosis, Canad. M. A. J. 36: 223-228 (March) 1937.

15. Gardner, L. U.: Studies on Experimental Pneumoconiosis: VIII. Quartz Dust, J. Indust. Hyg. 14: 18-37 (Jan.) 1932.

16. Gardner, L. U.; Durkan, T. M.; Brumfiel, D. M., and Sampson, H. L.: Survey in Seventeen Cement Plants of Atmospheric Dusts and Their Effects upon the Lungs of 2,200 Employees, J. Indust. Hyg. & Toxicol. 21: 279-318 (Sept.) 1939.

diffuse pigmentation the lung is still elastic and the respiratory membranes show no abnormality. If symptoms are associated with such reactions they are in all probability due to causes outside the lungs.

As far as can be learned from statistical and experimental evidence, the dusts other than free silica are not responsible for alteration of natural susceptibility to tuberculous infection. There is no proof that their inhalation increases the probability of infection with other organisms. In some of the dusty trades, investigation is disclosing that other factors than the dust are responsible for pulmonary infection.

Scars or imperfectly healed infections in the lungs of persons exposed to these inert or practically inert minerals are sometimes a cause of confusion. They attract and retain abnormal quantities of inhaled dust particles and it is possible, though not yet proved, that such deposits may maintain a preestablished chronic inflammatory reaction. Hence there may be less contraction and less tendency for the area of disease to disappear. Such an outcome is not inevitable, but many more cases will have to be followed in serial roentgenograms before its frequency is established.

Much more puzzling are the patients with obvious fibrosis whose history records only exposure to inert minerals. In most of these instances a review of the facts and a chemical examination of the tissues will disclose that there has been free silica either in the last or in previous exposures. An apparently comprehensive occupational history and the histologic evidence of a single autopsy specimen does not warrant the inference that a mineral other than free silica has caused the fibrosis. Quartz dust masquerades in unsuspected places where much ingenuity may be needed to detect it.

SILICOSIS

Initial Phase.—As already intimated, silicosis begins like the reaction to any other particulate dust, but the peculiar properties of free silica are responsible for subsequent modifications of the standard pattern. Migratory phagocytes concentrate silica in and about the lymphatic system of the lungs. The toxic particles, directly or indirectly through the released lipoids, stimulate connective tissue cells in their immediate vicinity and proliferation ensues. The ultimate result is a nodule composed of connective tissue whose fibers are characteristically modified by the effect of the silica. The location of these nodules, situated in the immediate vicinity of the lymphatic trunks, impedes the free flow of lymph. Such a development of microscopic silicotic nodules in the tracheobronchial lymph nodes and intrapulmonary lymphoid tissues constitutes the primary phase of silicosis.

Grossly these early nodular lesions are invisible or recognizable only with a magnifying glass. Usually there is enough carbon or other colored dust inhaled with the silica to produce the linear and focal pigmentation previously described for inert nonspecific pneumoconiosis. Obviously a roentgenogram of such a lung will reveal the shadows of the perivascular desposits but not those of the nodular lesions that are too small to be seen without a microscope.

A history of exposure to a dust rich in free silica with a roentgenogram showing only exaggeration of the linear lung markings presents a problem in diagnosis. I myself believe that if other causes can be eliminated the case should be classified as a benign nonspecific pneumoconiosis, for there is nothing pathognomonic about the film and there is at least only one chance in four that the disease will subsequently progress to nodulation. Others will argue that the history should be given more weight, and they would call such cases presilicotic.

If silicosis in this early state is not definitely diagnosable during life, has it any significance? Will it progress? Does it increase susceptibility to tuberculosis? The probabilities of progression to a stage of generalized nodulation are slight if the exposure should be interrupted at this stage. This is not necessarily true in the case of a worker such as a sandblaster whose exposure has been heavy and who has attained the stage of linear exaggeration rapidly. With ordinary exposures, however, there would not be enough silica accumulated in the air spaces to produce fresh nodules if no more dust were inhaled. With regard to susceptibility to tuberculosis, statistics on groups of men exposed to relatively high concentrations of silica show a slightly higher incidence of this infection in those with exaggerated linear markings than in those with no visible evidence of reaction to dust. The odds are against a silicotic origin in an individual case, but it could not be proved that silica was not a factor, particularly when atmospheric concentrations of this mineral may have been high.

If there is no probability of progression or no increase in susceptibility to tuberculosis, does early silicosis of this degree have any influence on the body? The only effect thus far discovered is the increased probability that continued exposure to silica dust will ultimately result in more advanced stages of silicosis.

The latter raises problems of administration, the answers to which depend on local conditions and the status of the subject. If the individual is young and linear exaggeration has developed quite rapidly in an environment heavily polluted with free silica dust, he should probably be transferred to some other position. If he is older and serial roentgenograms have shown that such changes have been present for a long time, he can unquestionably remain where he is, especially when an enlightened management is making every effort to reduce the concentration of dust in the working atmosphere. His roentgenographic changes may be due to other causes and hence will not progress because of these conditions.

At this stage of the disease there is no disability or any limitation of respiratory function because the lesions do not encroach on those portions of the lung in which respiration occurs. If physical examination discloses evidence of disability, the cause must be found outside the lungs.

Discrete Nodulation of Classic Silicosis.—After enough silicotic reaction has developed in the lymphoid tissue to retard the flow of lymph, fresh increments of inhaled silica are not as readily removed from the pulmonary air spaces. The phagocytes still ingest particles and migrate with them over the surface of the alveolar lining. Unexplained conditions in the lymphatics (possibly increased lymph pressures) now seem to prevent the cells from entering the vessels. As a matter of observation, most of them collect in groups scattered here and there on the walls of the air spaces. Again the high local concentration of silica results in proliferation of connective tissue cells. Parenchymatous nodules now develop, which ultimately attain a diameter of 3 or 4 mm. They are characterized by the sharp definition of their borders, by their uniform composition of hyaline collagen fibers arranged either

in concentric laminas or in coarse basket weave and by their regular distribution throughout all parts of both lungs. Certain variations are encountered, but these do not cause difficulties in diagnosis. The centers of young nodules may be necrotic when the disease evolves rapidly. Peripheral accumulations of nonsiliceous dusts may cause a fringe of more cellular connective tissue that more or less modifies the usual sharpness of the border. The costophrenic portions of the lungs may contain no nodules owing to the development of emphysema in these areas subsequent to the contraction of the many fibrous foci in other parts of the lung. In the early case the tracheobronchial lymph nodes are enlarged, but as the scar tissue contracts they shrink and become exceedingly hard.

The shadows of these larger nodules uniformly distributed throughout the parenchyma of both lungs form a characteristic roentgenographic pattern. When associated with a history of adequate exposure to silica dust and an absence of any very marked physical signs, such a film constitutes an adequate basis for the diagnosis of silicosis. Clinicians generally classify cases of silicosis in three stages, defined by the number and size of the nodular shadows. In stage 1 the linear markings are markedly exaggerated and the nodulation is barely visible; in stage 2 the linear shadows are obscured and each nodule is from 2 to 3 mm. in diameter; in stage 3 the nodules measure from 3 to 6 mm., are less well defined and show a tendency to confluence in certain areas. There is generally a suspicion of associated infection in films interpreted as stage 3.

The clinical significance of generalized discrete silicotic nodulation is not nearly as great as inspection of the film might indicate. Roentgenographic surveys always reveal many cases which have developed entirely unsuspected by the subjects, who have continued to perform their habitual work with no symptoms of respiratory embarrassment. Only shortness of breath on sudden and unusual exertion demonstrates that the respiratory reserve has been reduced. In other words, there is still so much uninvolved lung tissue that normal respiration is unimpaired. Persons with nonclinical silicosis are not disabled and from a medical point of view are employable. Since they are usually skilled by virtue of long experience, the management would generally prefer to keep them at work. However, liability for compensation has complicated the picture and has been responsible for a lamentable rejection of many able workmen.

The nodular stage of silicosis is associated with a definite increase in susceptibility to tuberculosis. This is attested by the old South African figures, which showed tuberculosis of the lungs in 75 per cent of the silicotic miners who died. In the Saranac Laboratory autopsy series active tuberculosis was present in 65 per cent of the lungs of persons exposed to free silica dust and in only 15 per cent of those working in other dusts. Official figures from the Factory Department of the British Home Office[17] disclosed evidence of tuberculosis in 59.4 per cent of the autopsies on silicotic subjects.

The infection may develop as a result of reactivation of a preexisting latent tuberculous focus, but opinion today is unanimous that new infections from without are a more common cause. A contact with the tubercle bacillus, which in normal subjects would perhaps be quite harmless, is apt, in the silicotic lung, to result in chronic progressive infection. Obviously such contacts cannot occur unless there are open cases of tuberculosis in the locality. In areas in which general living conditions have improved and routine antituberculosis hygienic measures have been put in practice the tuberculosis rate has fallen, among the silicotic as well as among the other members of the community.

The case for nontuberculous infections is not so clearly documented and today it would be well to turn back to Collis's Milroy Lecture of 1915,[18] in which he took great pains to show that pneumonia is relatively uncommon with silicosis though prevalent with "the pneumoconioses that cause bronchitis." Other statistics were published subsequently, however, that showed high frequencies of pneumonia in different dusty trades, and autopsies on silicotic subjects demonstrated the common occurrence of massive areas of fibrosis which closely simulated the end result of an organized pneumonia. Most observers came to believe that the same mechanisms which increased susceptibility to tuberculosis also favored the growth of pneumococci and other bacteria. Thoughtlessly silica was accepted as the common etiologic factor.

But new investigations of silica industries showed that excessive pneumonia rates did not prevail in all of them. Then the importance of exposure to extremes of temperature, humidity and the like assumed proper significance in the silica industries as in others. In mining groups it was shown that the pneumonia rate dropped to approximately that of the local community when the change house was moved to the head of the shaft so that the sweaty, overheated miner no longer had to expose himself to winter weather on coming to the surface. Similarly it is now believed that in the foundry the influence of sudden changes of temperature is much greater than the silica dust, to which only a few of the employees are exposed in dangerous concentrations. In many modern mining areas the incidence of pneumonia is no higher than that in the general population, and the course of the disease when it does develop is usually normal.[19]

Pathologic material uncontrolled by a knowledge of general clinical experience may be misleading, owing to selection of cases submitted for examination. It may well be true that some of the massive conglomerate foci seen in lungs are the result of organized pneumonia, but serial roentgenograms of certain silicotic groups make it appear doubtful whether organization is the common outcome.

Experiments by Vorwald, Delahant and Dworski[20] show that in rabbits silicosis alters in no way susceptibility to type III pneumococcus or the course of the resultant pneumonia. It is anticipated that similar tests will be made with other types of this organism.

Until accurate statistics based on reliable clinical and bacteriologic data for pneumonias of different origins become available, it would be unwise to generalize. At the present time, however, American experience does not seem to indicate that silicosis has an appreciably unfavorable influence on lobar pneumonia. Possibly infections due to organisms outside the pneumococcus group are in a different category.

17. Merewether, E. R. E.: A Memorandum on Asbestosis, Tubercle 15: 109-118 (Dec.) 1933, 152-159 (Jan.) 1934.

18. Collis, E. L.: Industrial Pneumonoconioses with Special Reference to Dust Phthisis, Milroy Lectures, 1915, Pub. Health 28: 252-259, 1914-1915; 29: 11, 1915-1916.

19. Pierpont, D.: Fourth Saranac Laboratory Symposium on Silicosis, 1939, Employer's Mutuals Insurance Company, Wausau, Wis.

20. Vorwald, A. J.; Delahant, A. B., and Dworski, M.: Silicosis and Type III Pneumococcus Pneumonia: An Experimental Study, to be published.

Rapidly Developing Silicosis.—Whereas most cases of silicosis require at least from three to six and more often from ten to twelve years of exposure for their development, there are isolated industries in which exposures of from twenty to twenty-four months have produced a modified form of the disease. Under conditions that liberate excessive quantities of exceedingly fine pure silica the ordinary protective mechanisms fail to cope with the situation and an unusual kind of reaction develops. The initial phase of lymphatic involvement is lacking. The overwhelming deposits of silica seem to stimulate connective tissues in every part of the lung at the same time, and as a consequence the alveolar walls become thickened and nodules of microscopic proportions develop throughout the pulmonary framework. The air spaces are filled with actively proliferating phagocytes. Irvine[21] has aptly described the picture as a "dust pneumonia."

Gross examination reveals no nodules visible to the naked eye; there is merely a generalized partial consolidation of the lungs. All the postmortem specimens that I[22] have seen have been complicated by infection which completed the solidification of the involved areas. Because the nodules are too small to be seen without a microscope they do not cast discrete shadows on a roentgenogram. Except when infection complicates the picture, the film generally shows little but a heavy diffuse haze because most of the air spaces contain enough air to permit the passage of some of the x-rays. The diagnosis in these cases rests not on the film but on the presence of extreme dyspnea in a case in which other causes have been eliminated and on the history of an exposure to excessive quantities of exceedingly fine and pure free silica. This diagnosis is never warranted except in the case of unusually severe exposures such as those in unprotected sandblasting or in drilling pure quartz without the ventilation found in ordinary mining practice.

Most of the fatal cases terminate in tuberculosis, as indicated by Middleton's[23] summary of English experience. Foci of necrosis produced by the excessive concentration of fine silica in the microscopic nodules throughout the lungs furnish the most favorable medium conceivable for the growth of the bacilli. A few patients have succumbed to nontuberculous bronchopneumonias, and very rarely it is possible that the silicosis itself may cause death. However, it should always be remembered that evidences of infection are not uniformly distributed and may be hard to distinguish on gross examination of a lung heavily involved with such a reaction to dust. Review of a few small sections in one of Chapman's[24] "soap powder cases" failed to disclose evidence of tuberculosis, but so little tissue was available that the possibility of localized infection could not be excluded.

Modified Silicosis.—When the atmospheric dust is composed of a mixture of particles of free silica with those of other minerals such as coal, iron and various silicates the characteristic nodular reaction is modified in varying degrees. When the dust contains enough free silica, nodular fibrosis develops in the pulmonary parenchyma although the collagen may not show its characteristic hyaline, laminated appearance. The other minerals in the dust tend to be deposited in the interlobular septums and walls of arteries as they would in benign nonspecific pneumoconiosis, but they also collect around the margins of the parenchymatous nodules. The result is a combination of nonspecific pneumoconiosis and silicosis with the specific lesions of each modified by the presence of another type of dust. The linear perilymphatic deposits are heavier and tend to be fibrous; the nodules are larger and lack definition because of fringes of cellular connective tissue. Frequently projections from the nodules are continuous with chronic inflammation about vessels and septums. Reaction about adjacent nodules may replace considerable numbers of air spaces, giving rise to a small conglomerate focus. However, patent air spaces are always present in the involved area. The fibrosis is never of the massive obliterative type to be described later, in which the tissue is uniformly hard and rubberlike in consistency.

Generally the roentgenologist does not attempt to differentiate between these modified forms of silicosis and those produced by purer silica. In occasional extreme cases, however, the nodular shadows may lack their characteristic definition and uniformity in size, the vascular markings will be unusually heavy and there may be a background of more or less uniform reticulation.

Susceptibility to tuberculosis may be more or less favorably modified in these cases. In siderosilicosis due to hematite, tuberculous infection in both man and animals progresses for a time and then in many cases heals with the formation of masses of scar tissue. The same is apparently true of anthracosilicosis, which often requires prolonged search to discover evidence of the tuberculous element in the healed focus. In granite silicosis, tuberculous infection is much more apt to progress and terminate in cavity formation with disseminated infectious lesions.

Since most industrial dusts are mixtures, modifications of the classic picture of pure silicosis are the rule rather than the exception. It cannot be too strongly emphasized that both the pathologic and the clinical manifestations of silicosis in different industries are not identical in all details. Observations that are perfectly valid for anthracosilicosis may be inapplicable to miners of other hard rock, granite cutters or porcelain workers.

Massive Conglomerate Fibrosis.—This pathologic feature of the disease is the common cause of most of the disability in silicotic subjects. Unfortunately it presents vexatious problems in diagnosis and administrative treatment. During life it may be difficult to differentiate it from the simple conglomerations just described under modified silicosis. In this country and in South Africa most observers think that massive conglomerate fibrosis is due largely to associated infection. In recent years I have come to feel that a third essential factor may be the presence of minerals other than free silica. At the present time it is impossible to classify all areas of conglomerate fibrosis on an etiologic basis. Microscopic examination reveals an element of tuberculosis in 60 per cent of the cases; in the remainder this feature is either absent or escapes detection because it is obscured by the silicotic fibrosis. Although most or perhaps all of these massive fibrous lesions may have developed on a background of tuberculosis th

21. Irvine, L. G.: Report of the Commission to Enquire into the Possible Prevalence and Origin of Cases of Silicosis, in the Colony of Southern Rhodesia, Salisbury, Government Stationery Office, 1938.
22. Gardner, L. U.: Pathology of So-Called Acute Silicosis, Am. J. Pub. Health 23: 1240-1249 (Dec.) 1933.
23. Middleton, E. L.: Industrial Pulmonary Disease Due to the Inhalation of Dust with Special Reference to Silicosis, Lancet 2: 1-9 (July 4), 56-65 (July 11) 1936.
24. Chapman, E. M.: Acute Silicosis, J. A.M. A. 98: 1439-1441 (April 23) 1932.

problem is to recognize the ones in which the infection is still active. For them some form of treatment is indicated. No treatment in use today is ideal, for all of them tend to promote healing by fibrosis and it is the scar tissue that causes the disabling dyspnea.

Names were coined by the Miners Phthisis Medical Bureau of South Africa to indicate reciprocal relationships between silicosis and tuberculosis in these chronic forms of the disease. "Tuberculosilicosis is the modification produced in silicotic lesions by a chronic tuberculous infection." Here the dust factor is dominant. "Silicotuberculosis," on the other hand, is a clinical term used to indicate that the infectious element is more prominent. On the suggestion of Dr. L. G. Irvine, chairman of the bureau, the last International Silicosis Conference in Geneva adopted the pathologic term "tuberculosilicosis" as the standard one to describe this specific chronic lesion. It is not applicable to every manifestation of tuberculosis in the silicotic lung. When the infection develops typically, as it does in nonsilicotic subjects, the diagnosis should be "silicosis with tuberculosis." Such cases are rare, however.

The anatomic picture of massive conglomerate fibrosis is variable, although there are certain features that characterize all such lesions. The involved area is hard and rubber-like, is blue-black or gray-black, has rather sharply defined borders and is practically always associated with high grade compensatory emphysema. If the area of involvement extends to the surface of the lung there is always chronic fibrous pleurisy with adhesions. Most cases occur in organs showing a background of generalized discrete nodulation, but there are some in which this diagnostic feature is lacking. In the latter case it is possible that contraction of the mass has drawn most of the original nodules into its orbit and that the more peripheral portions of the organ have subsequently been distended by emphysema.

The distribution and extent of the fibrosis varies. The massive scars occur most often in the upper part of one or both lungs. Some radiate from the hilus; some assume the form of wedges with their bases on the pleura; others grow as tumor-like masses in the depths of the lung. They may involve the whole of a lobe and even extend across an obliterated interlobar fissure.

The cut surface of the conglomerate focus generally shows a more or less well defined nodular structure, but at times this is recognizable only with a magnifying glass. Some show central areas of caseation and cavity formation indicative of their tuberculous origin; others are traversed by irregular slitlike openings filled with inky fluid. The latter have no well defined walls and are not differentiated by color from the surrounding fibrosis.

Microscopic sections reveal nodules embedded in a matrix of heavily pigmented hyaline fibrous tissue that replaces practically all normal pulmonary structures. Blood vessels show high grade obliterative endarteritis and often their lumens are filled with dust-containing connective tissue. The larger bronchi are compressed and distorted. When patent, they present advanced chronic inflammatory changes. Tuberculous reaction may be obvious in widespread caseation, but in cases in which the infection has healed it has sometimes been necessary to search over 200 square centimeters of section to discover isolated noncaseous tubercles. In a few cases even this evidence is lacking, but clumps of acid-fast bacilli without cellular reaction are found in areas of softening. Guinea pig inoculation has supplied proof that the organisms are tubercle bacilli. Examination of the black slitlike cavities has generally revealed no suggestion of tubercle and these cavities have been interpreted as areas of anemic necrosis resulting from the obliterative endarteritis.

In view of the difficulties of diagnosis it would appear unwise to draw any conclusions as to the frequency of nontuberculous massive conglomerate fibrosis.

The shadows of such changes on the roentgenogram offer an easier problem in diagnosis when they occur on a background of generalized nodulation. When this is lacking even the silicotic nature of the disease may be in doubt. Stereoscopic films may permit visualization of discrete nodules otherwise obscured. Overexposed films may bring out tuberculous cavities in the midst of massive shadows, but often none can be seen. The behavior of the shadows in serial examinations over periods of years is perhaps the most reliable index of activity of the process.

The clinical manifestations in many of these cases may likewise be confusing. Often severe dyspnea is the only prominent symptom. Perhaps there has been no loss of weight. The sputum may be repeatedly negative or on rare occasions prove positive by culture or guinea pig inoculation, but if followed long enough the infection in many of these cases will become manifest. Toxic symptoms then suggest tuberculosis; bacilli are constantly present in the sputum; roentgenograms may reveal cavity formation and more rapid extension of the massive lesion. When this is the case death from tuberculosis is the outcome, but the individual in whom the infection has completely healed succumbs to other causes.

Cardiac Involvement.—The question as to the relationship between silicosis and disease of the heart is still debated. Observers primarily interested in silicosis who are following the course of the disease in groups of employed workmen are unanimous in their opinion that cardiac complications are not unusually common. They admit that some silicotic patients exhibit symptoms referable to the heart but point out that the age group in which silicosis develops is also the one in which arteriosclerosis and myocarditis are general. The clinician whose experience is limited to the general hospital, on the other hand, is confronted with a selected group of silicotic subjects. These men have applied for hospitalization because they are sick and often about to die; those who are obviously tuberculous may be transferred to sanatoriums. Thus the internist is naturally impressed by the high proportion of cardiac conditions among his silicotic patients. The pathologist's views are likewise colored by the source of his material. Cardiac complications are rare in able-bodied workmen killed by accidents, but they are not at all exceptional in the older men who die in hospitals at the age of 55 or 60 years. Furthermore, both clinician and pathologist may form unusual concepts of the disease if their material is drawn from a single industry. For example, the anthracosilicosis of the hard coal miners is especially prone to manifest itself as massive conglomerate fibrosis, and it is quite probable that such disease may cause more cardiac complications than the discrete nodulation of sand pulverizing or some other kind of mining.

Cor pulmonale is primarily a disease of the right side of the heart resulting from obstruction to the circulation in the lung. One of the most common

causes of such obstruction is high grade emphysema. Silicosis of the massive conglomerate type is liable to produce such emphysema. No one doubts that many patients with long-standing silicosis complicated by conglomerate lesions caused by associated tuberculosis finally die of congestive heart failure. But the same is also true of patients with uncomplicated tuberculosis, and yet one rarely speaks of this infection as a common cause of "heart disease." Personal experience and the reports from the literature have convinced me that in most fatal cases of silicosis the heart is already damaged by arteriosclerosis or other causes and that the presence of a conglomerate area of fibrosis with emphysema merely adds to its burden. At the autopsy table hypertrophy of the right side of the heart without arteriosclerosis and even greater involvement of the opposite side is a rarity. Clinically no one has ever demonstrated evidence of increasing strain on the right side of the heart as the successive phases of simple discrete nodulation make their appearance. Even in the case of massive conglomerate fibrosis cardiac symptoms are relatively late manifestations. Further clinical and pathologic studies will be valuable as far as they differentiate between the types of pulmonary lesions that are alleged to have affected the condition of the heart muscle.

Carcinoma of the Lungs and Silicosis.—General interest in the subject of pulmonary cancer has been responsible for special effort in securing autopsies in such cases. The discovery of coexistent silicosis or even a benign nonspecific pneumoconiosis has led to the deduction of causal relationships that are not supported by statistical evidence. Vorwald and Karr [25] collected from the literature the results of roentgenographic examinations of 57,362 persons at work in industrial plants creating dust of various kinds. Although the group contained 12,206 with silicosis, there were only three cases of cancer of the lung. In the Saranac Laboratory surveys of five different industries, films of 15,587 individuals were reviewed with the discovery of 1,357 cases of silicosis. In the total group there were only three cases of pulmonary cancer, one in a silicotic subject and two in nonsilicotic subjects. The authors' most impressive autopsy statistics were quoted from the 1930 Report of the Miners' Phthisis Medical Bureau of South Africa. This official publication cites postmortem figures on 4,510 adult males including 3,117 European miners and 1,393 European males with no underground exposure. The frequency of pulmonary carcinoma was as follows: 1,393 European males, no underground work, 0.93 per cent; 1,679 European miners, no silicosis, 0.71 per cent, and 1,438 European miners with silicosis, 0.70 per cent.

Theoretically, silica should be less likely to initiate a malignant proliferation of epithelium than the tubercle bacillus. The latter not infrequently does cause metaplasia of bronchial epithelium and sometimes carcinoma eventually results. In uncomplicated silicosis, however, there is no effect on the epithelial elements that give rise to cancer. The silica stimulates only the fibroblast or connective tissue cell. If anything there should be an excess of pulmonary sarcomas, but these have not been reported.

In spite of the occasional coexistence of silicosis and primary carcinoma of the lung indicated by published autopsy reports, it is felt quite definitely that the silica has no etiologic significance. The only dusts known to cause pulmonary carcinoma are those of the radioactive ores in Schneeberg.[26] Possibly, as Campbell's [27] experiments have suggested, the tar in road dust may also be significant; but this awaits proof.

25. Vorwald, A. J., and Karr, J. W.: Pneumoconiosis and Pulmonary Carcinoma, Am. J. Path. 14: 49-57 (Jan.) 1938.

ASBESTOSIS

It will be recalled that protective mechanisms of the upper respiratory tract appear to be less effective against fibrosis than against particulate foreign bodies and that mobile phagocytes do not remove long fibers from the pulmonary air spaces. As a consequence the greatest accumulation of inhaled asbestos fibers occurs in the lumen of the respiratory bronchiole, the point at which they first come to rest. Almost none are found in the areolar tissues about lymphatic trunks or in the lymphoid tissues inside or outside the lungs. Reasons for believing that the stimulus from inhaled asbestos may be mechanical rather than chemical have been discussed in the first paper on etiology.[4]

Microscopic Appearance.—As long as asbestos fibers continue to be inhaled, scar tissue develops as a gradually thickening sleeve about the respiratory bronchioles. Either because the bore or the tube is smoothed out by the obliteration of the lateral alveoli or because of changes in the lining epithelium, subsequently inhaled fibers then pass on into the alveolar ducts. Here a similar sleeve of fibrosis develops, and this formerly irregular tube likewise permits fibers to pass farther into the lungs. Reaction in the walls of the terminal air spaces ultimately results in a localized patch of obliterative fibrosis of the parenchyma of the lung.

A random microscopic section through an area of fibrosis does not reveal a uniform obliteration of every air space. Here and there are many that still contain air; some are of normal size, some are compressed and many are greatly dilated. These patent air spaces are apparently supplied by other bronchioles that did not happen to be involved in the primary fibrosis. Their intrusion into the area of scar formation is easily understood on reference to Miller's [28] models of the terminal branches of the bronchial tree. His diagrams show that the terminal air spaces of different bronchial systems are packed together in such a manner that a single section will contain alveoli given off from widely separated bronchi. Many writers have described this condition as bronchiectasis, but emphysema would seem to be a more apt term as the larger bronchi and bronchioles are never involved.

The scar tissue of asbestosis is in no way peculiar. Unlike that of silicosis, it fails to show a characteristic hyaline swelling of the collagenous fibers. Its arrangement is usually diffuse rather than nodular, although occasional cases such as those reported by Lynch and Smith [29] may present a few nodules. Their presence suggests that there may have been an unrecognized contamination of the inhaled dust with free silica.

Because the fibers are not transported, the asbestosis bodies which develop from them will be found very

26. Saupe, E.: Bemerkungen zur Beurteilung der Silikose als entschädigungspflichtige Berufskrankheit, Klin. Wchnschr. 9: 1352-1356 (July 19) 1930.

27. Campbell, J. A.: Cancer of Skin and Increase in Incidence of Primary Tumors of Lung in Mice Exposed to Dust Obtained from Tarred Roads, Brit. J. Exper. Path. 15: 287-294 (Oct.) 1934.

28. Miller, W. S.: The Lung, Baltimore, Charles C. Thomas, Publisher, 1936.

29. Lynch, K. M., and Smith, W. A.: Pulmonary Asbestosis: II. Report of Case, Am. Rev. Tubere. 23: 643-660 (June) 1931.

largely within the scar tissue around bronchioles and the air spaces which they supply. But, as Gloyne [30] has pointed out, commercial asbestos usually contains particles of various contaminating minerals. Physiologic mechanisms within the lung are responsible for the sorting out and removal of much of this particulate matter to the pulmonary framework and lymph nodes. There it sets up a nonspecific pneumoconiosis the color and intensity of which depend on the quantity and character of the contaminant. After the development of parenchymatous fibrosis the particulate matter is not removed so readily. Its retention in the patches of reaction due to the asbestos is responsible for the pigmentation seen in advanced cases of asbestosis.

Gross Appearance.—These observations make it easier to appreciate the variable gross picture in asbestosis. The obvious changes consist of patches or strands of dense scar, which are irregular in size, shape and distribution. In advanced cases they are gray or black and included in all of them are thin-walled, dilated air spaces that vary from a few millimeters to a centimeter or more in diameter. Fibrous pleurisy plus a variable amount of pigmentation in the walls of the pulmonary arteries and interlobular septums complete the grosser changes.

More careful inspection, perhaps with the aid of a magnifying glass, demonstrates numerous minute, ill-defined patches of fibrosis widely scattered throughout the parenchyma. If they happen to be sufficiently pigmented by minerals other than asbestos, such foci will stand out sharply like those illustrated in color in Gloyne's [30] article, but only one of the twenty-eight cases in my collection even approximates this picture. The borders of these lesions invariably lack the sharp definition of the silicotic nodule. Here and there the plane of section will cut one of these areas in such a manner that the thick-walled bronchiole with its peripheral fan of fibrosis is clearly recognizable. The lens demonstrates the presence of dilated air spaces within each fibrous area if these are not already large enough to be seen with the naked eye. Elsewhere the air spaces will be visible, but their walls are much less prominent. The patches of fine fibrosis, scattered throughout the lung, are not sufficiently large or dense to be palpated individually, but they increase the general consistency of the organ and limit its crepitation.

It is now felt that the fine, diffuse fibrosis with emphysematous dilatation of included air spaces constitutes the characteristic feature of asbestosis. Whether the grosser patches of scar tissue represent merely an intensification of the same process in localized areas or whether they are due to reaction to dust in the scars of healed infection is not altogether clear. Sometimes they occur as a thin zone beneath and paralleling the pleura, an arrangement hardly suggestive of infection; at others, more localized patches of scar simulate old foci of infection. The chronic pleurisy is probably not a reliable index of infection, as it seems to occur whenever subpleural air spaces are involved. The thickening of blood vessels and interlobular septums are variable accompaniments due to accidental contaminants in the inhaled dust. The same is true of reaction in the tracheobronchial nodes.

Roentgenograms.—Compared with the microscopic appearances, the roentgenographic shadows of early or even moderately advanced asbestosis are surprisingly slight. A faint haziness throughout the lower lung fields together with more or less evidence of chronic pleurisy are the only unusual features of these cases. Pleural manifestations may be limited to visualization of the transverse fissure of the right lung. There is also more or less exaggeration of the linear markings, but the specificity of this reaction is questionable. As shown by Gardner, Durkan, Brumfiel and Sampson,[16] in cement workers the frequency of such exaggeration tends to increase more with age than with dust exposure. Dreesen, DallaValle, Edwards, Miller and Sayers [31] concurred but found more of this type of reaction in old asbestos operators than in persons not exposed to dust and less than in those of the same age exposed to kaolin dust. As suggested in the section on pathology, linear exaggeration is probably an accidental accompaniment of asbestosis and in my opinion should not be considered as an index of early reaction to the fibrous silicates.

In far advanced cases there is a heavier diffuse shadow throughout the lung fields, whose appearance has been compared to that of ground glass. Its uniformly fine granular texture is undoubtedly due to the superimposed shadows of the small patches of fibrosis in the parenchyma alternating with patches of radiotranslucent patent air spaces. The very advanced case may show in addition many small flecklike shadows on the generally hazy background. The shadows never present the sharp definition of silicotic nodulation. The so-called porcupine heart, said to characterize advanced asbestosis, is manifested by heavy linear shadows that radiate into the lung fields from the surface of the heart. They may be cast by pleuropericardial adhesions.

Clinical Symptoms.—The symptoms most commonly reported are an irritative cough and dyspnea; some would also include weakness and chest pains. A dusky color suggesting cyanosis, clubbed fingers and blood streaked sputum are symptoms of advanced disease whose frequency apparently varies in different locations. Dreesen and his associates [31] find that cough and dyspnea are by far the most common symptoms and that their frequency increases with the intensity of change visualized in the roentgenogram. Of the patients with far advanced cases 82 per cent had both; of those with moderately advanced cases 72 per cent complained of cough and 68 per cent were short of breath. Since the dyspnea must be due largely to associated emphysema, it is quite conceivable that this symptom should appear early and explain the incidence of dyspnea in 33 per cent of persons whose films showed only second degree linear exaggeration. These observers discovered no greater frequency of cardiac involvement than in industrial groups in general. Others have reached the opposite conclusion, but here again allowances must be made for the source of their material. Theoretically there would seem to be greater reason to suspect cardiac involvement in cases of simple asbestosis than in simple silicosis. Further study is needed to elucidate this point.

Merewether,[17] who gave a classic description of this disease, reports that a minimum of seven years' and more commonly eleven years' exposure to high concentrations of asbestos dust was necessary to produce a serious degree of reaction in the English plants. In this country Dreesen and his associates [31] found the

30. Gloyne, S. R.: Morbid Anatomy and Histology of Asbestosis, Tubercle 14: 445-451 (July), 493-497 (Aug.), 550-558 (Sept.) 1933.

31. Dreesen, W. C.; DallaValle, J. M.; Edwards, T. I.; Miller, J. W., and Sayers, R. R.: A Study of Asbestosis in the Asbestos Textile Industry, U. S. Pub. Health Bull. 241, 1938.

minimum duration somewhere between five and nine years, depending on the character and concentration of the dust inhaled. At this time 27 per cent of exposed workers were involved, and among those with more than fifteen years of employment the percentage rose to 60.

The question of progression after cessation of exposure has had various answers. Merewether [17] and Ellman [32] both believe that asbestosis invariably progresses to a fatal termination once enough fiber has been entrapped in the lungs. The former reports one case in which a mattress maker died eight years after ceasing an employment of four years and five months. An autopsy revealed far advanced asbestosis, but unfortunately there had been no films to indicate the extent of the progression. Mills [33] reported a case in which a man died of congestive heart failure approximately thirty-two years after an intermittent exposure of three years. I was privileged to study sections from this patient, but if there had been any progression it had not involved much of the lungs. There were a few small patches of pulmonary fibrosis containing rare atypical asbestosis bodies. Lanza [34] is of the opinion that "it is by no means certain that asbestosis progresses as does silicosis after withdrawal from dust exposure." In experimental asbestosis of guinea pigs the pulmonary reaction retrogresses after removal from the dust rooms. On the basis of mechanical injury there should be no progression, for the rounded surfaces of the asbestosis body would produce less trauma than the rough ends of the freshly inhaled fibers.

Diagnosis depends on a history of adequate exposure, evidence of characteristic roentgenographic changes and the clinical picture. Asbestosis bodies in the sputum are confirmatory but alone they do not indicate disease. Any one may inhale a few asbestos fibers, but their number is too small to be significant. In routine examination of sections of the lung I have discovered occasional asbestosis bodies in a dozen or more cases in which no history of exposure to this dust could be obtained.

Susceptibility to pulmonary infection in asbestosis is not nearly as well defined as in the case of silicosis. English writers like Merewether,[17] Ellman [32] and Gloyne [30] are impressed by the high incidence of tuberculosis among the disabled patients and those who died. American statistics based on surveys of employees in different plants, on the other hand, show relatively little tuberculosis. Dreesen and his associates [31] reported only two cases of active infection among 541 persons exposed in the asbestos fabricating plants of North Carolina. However, some 150 employees had been discharged fifteen months previously. Of the latter, seventy-one were examined by Shull,[35] who reported eight cases of tuberculosis, only two of which were active at the time. In the entire group "the degree of infiltration was only slight to moderately advanced, and one or both upper lobes were involved." He found that thirty-five of the patients had moderately advanced asbestosis, of whom two subsequently died or were dying of tuberculosis, twenty had far advanced asbestosis with two more cases of tuberculosis. This would make a total incidence of 7.2 per cent for the discharged group. The figure for the entire group of employed and discharged subjects cannot be computed as so many of the latter have not been traced. McPheeters,[36] among 210 employees from the same district, found an incidence of active tuberculosis of 2.8 per cent. In Pennsylvania, Fulton, Dooly, Matthews and Houtz [37] discovered two cases of healed tuberculosis among fourteen persons with asbestosis. In 1936 Lanza [34] summarized all the available evidence and failed to find convincing evidence of a great excess of tuberculosis.

The autopsy statistics are more suggestive. Egbert [38] reviewed the cases reported up to 1935 and found that six out of twenty-eight showed complicating tuberculosis. Merewether [17] reports an incidence of 35.7 per cent in forty-two fatal English cases. Dreesen and his associates [31] include autopsy reports in three cases with no tuberculous complications. My own series, which includes twenty-eight specimens, most of which have been previously reported elsewhere, contains nine cases of active chronic tuberculosis. While these autopsies reveal a high incidence of such infection, their number is too small to compensate for the factor of selection. The data from the surveys probably constitute a more reliable index.

In experimental animals asbestos dust [39] has nothing like the effect of free silica on associated infection. Like gypsum, iron oxide and other nonsiliceous minerals, asbestos may cause tuberculous infection to progress for a time, but it subsequently heals with a marked tendency to scar formation. The fibrosis from the infection then retains excessive amounts of inhaled asbestos and unusually large patches of scar develop in the pulmonary parenchyma.

The cause of death in the remaining cases has been certified as nontuberculous pneumonia, myocarditis, pulmonary cancer and a miscellany of other conditions.

Tuberculosis may be an unusually frequent cause of death in certain groups of asbestos workers, but at present it seems more probable that nonspecific hygienic factors and general living conditions are responsible. The actual frequencies of nontuberculous infections and primary cancer of the lungs are unknown. One must not be misled by a comparatively small number of postmortem reports.

7 Church Street.

32. Ellman, Philip: Pulmonary Asbestosis: Its Clinical Radiological and Pathological Features and Associated Risk of Tuberculous Infection, J. Indust. Hyg. 15: 165-183 (July) 1933.
33. Mills, R. G.: Pulmonary Asbestosis: Report of Case, Minnesota Med. 13: 495-499 (July) 1930.
34. Lanza, A. J.: Asbestosis, J. A. M. A. 106: 368-369 (Feb. 1) 1936.
35. Shull, J. R.: Asbestosis: A Roentgenographic Review of Seventy-One Cases, Radiology 27: 279-292 (Sept.) 1936.
36. McPheeters, S. B.: A Survey of a Group of Employees Exposed to Asbestos Dust, J. Indust. Hyg. & Toxicol. 18: 229-239 (April) 1936.
37. Fulton, W. B.; Dooly, Allan; Matthews, J. A., and Houtz, R. L.: The Nature and the Amount of Dust Encountered in Asbestos Fabricating Plants on the Health of a Group of Workers, Commonwealth of Pennsylvania, Department of Labor and Industry, Harrisburg, special bulletin 42, 1935.
38. Egbert, D. S.: Pulmonary Asbestosis, Am. Rev. Tuberc. 31: 25-34 (Jan.) 1935.
39. Gardner, L. U., and Cummings, D. E.: Studies on Experimental Pneumoconiosis: VI. Asbestosis, J. Indust. Hyg. 13: 65-81 (Feb.) 1931.

Effect of Flying on the Ear.—Flying has no significant effect on the external ear, but the middle and inner ear are the source of a great amount of difficulty. The magnitude of the ear problem in aviation may be judged from the fact that pilots suffer more frequently from occupational disturbances of this organ than from all other occupational diseases combined and that it is the most frequent cause of discomfort among passengers on commercial air lines. The conditions of flight which most affect the ear are changes of atmospheric pressure during ascent and descent, noise, and possibly vibration. At the present time the former is increasing in importance as a result of the increased climbing ability of modern aircraft, while the two latter conditions are decreasing in importance as a result of recent advances in aircraft design.—Armstrong, Harry G.: Principles and Practice of Aviation Medicine, Baltimore, Williams & Wilkins Company, 1939.