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SUBJECT INDEX TO VOLUME XIII

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BOOK NOTICES

THE JOURNAL OF INDUSTRIAL HYGIENE

VOLUME XIII MARCH, 1931 NUMBER 3

A METHOD OF STAINING THE ASBESTOSIS BODIES FOUND IN THE SPUTUM OF ASBESTOS WORKERS*

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THERE is a consensus of opinion that the asbestosis bodies found in the sputum and lungs of asbestos workers do not stain with the ordinary aniline dyes. This failure to stain has been one of the difficulties in working out their relation to the histology of the disease and in determining their composition. By employing the following technic the bodies can be made to take on a definite color which enables them to be better studied.

HEMATOXYLIN

After digestion of the sputum with equal quantities of concentrated antiformin (as described by Stewart and Haddow (1)) and centrifugation, the antiformin is pipetted off and replaced by a 5 per cent. solution of Ehrlich's hematoxylin. Bluing of the hematoxylin immediately takes place owing to the remains of the alkaline antiformin. The mixture is well shaken and allowed to stand for a half to one hour and then recentrifuged and the deposit mounted as a wet preparation. By this means the asbestosis bodies become a dark brown to black color, according to the length of time they have been exposed to the hematoxylin.

PRUSSIAN BLUE REACTION

The reaction of the asbestosis body to Prussian blue was first described by Cooke and Hill (2) and McDonald (3). The foregoing technic is used but the following mixture is substituted for hematoxylin: 2 per cent. potassium ferrocyanide—1 part; 1 per cent. hydrochloric acid—3 parts. With this technic the asbestosis bodies are colored a brilliant blue. A potassium ferricyanide mixture may also be used but the results are variable, some asbestosis bodies being stained, others not.

AMMONIUM SULPHIDE

The same technic is used but ammonium sulphide is substituted for hematoxylin or potassium ferrocyanide. The asbestosis bodies are then colored

* Received for publication Nov. 22, 1930.

black. This color can be removed with hydrochloric acid.

Discussion

When examined microscopically the hematoxylin specimens give the impression of having hematoxylin deposited on them rather than having actually taken up the stain, but after washing overnight the asbestosis bodies still retain sufficient stain to be colored a dark brown. With the ferrocyanide or ammonium sulphide technic the bodies are homogenously stained.

The advantages of this technic are: (1) The minute details of the asbestosis body can be better seen than in the unstained preparation; *e.g.*, the central core of asbestos fiber generally stands out clearly and can sometimes be seen running across a gap between two segments of the asbestosis body rather like the string between beads on a necklace. The fiber takes on the stain only very lightly—sometimes, indeed, not at all—but the contrast with the stained body is sufficient to demonstrate quite clearly its existence. The outlines of the segments are also very clearly seen, and the small subsidiary bosses on the sides of the asbestosis body, and the cracks in the segments are better distinguished by this method than in the unstained preparation. (2) These reactions support the view that iron enters into the composition of the bodies. The Prussian blue reaction is a well-known test for iron; and ammonium sulphide is universally employed as a group reagent for iron. Hematoxylin also has an affinity for iron, but the reaction in this case is inferior to that given by the other methods.

The amount of iron found in raw asbestos varies considerably. According to Merewether (4) the two main varieties of asbestos used in industry are: (1) a larger portion known as chrysotile, a hydrated magnesium silicate with a low percentage of iron oxides (0.7 to 4.4 per cent.); and (2) a smaller portion known as crocidolite, amosite, and tremolite which have a high percentage of iron oxides (3.2 to 44 per cent.). The latter group is the one used in the factory which produces the cases seen at this Hospital.

Cooke and Hill (5) have also suggested that blood may enter into the composition of the asbestosis body. Oxyhemoglobin contains 0.335 per cent. of iron (6).

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THE TOXICITY OF
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Henry

Assistant Professor

Introduction

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* Read before the Sectio
Hygiene of the American
Association, Fort Worth
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as facts quite as significant to our economic and social health as are births and deaths and contagious diseases to our physical public health? The official registration of all cases of employment discharge with *actual reasons* would involve obvious difficulties. Nevertheless some provision under which industrial management might submit to a properly constituted governmental function the undisguised facts of its experience in maintaining employment standards would furnish employment information as fundamental as physical sickness and death rates in sociologic studies. The facts thus revealed should go far toward laying a foundation for practical measures sounder than the impressions and sentiments upon which sociologists and economists and government officials have hitherto been obliged to base their efforts toward the relief of unemployment.

STUDIES ON EXPERIMENTAL PNEUMONOKONIOSIS. VI. INHALATION OF ASBESTOS DUST: ITS EFFECT UPON PRIMARY TUBERCULOUS INFECTION*

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THE experimental investigation of the reaction to inhaled asbestos dust had long been contemplated as a part of the study of pneumonokoniosis carried on at the Saranac Laboratory during the past twelve years. During that time little attention had been paid to the inhalation of asbestos dust as the cause of industrial disease. It was hoped that this substance might be investigated, because it is a relatively soft and soluble silicate, the study of whose action might shed some light upon several of the vexing problems arising in connection with the inhalation of hard silicious dusts. It admirably suited our plans, therefore, to comply with a suggestion of Dr. Frederick L. Hoffman, that we undertake an experimental investigation of the reaction to this substance. At the request of Dr. Hoffman, the Asbestos Corporation of America has furnished the Laboratory with 600 pounds of exceedingly fine asbestos dust from its plant at Thetford, Quebec. The experiment was started in January, 1928, and animals have now been exposed for two years and five months. The study is not yet completed, but since so much interest has recently been manifested in the subject of asbestosis, a preliminary report is submitted at this time.

* Received for publication July 18, 1930.

ASBESTOS DUST

The dust employed in this study when dry is a light, fluffy, gray-white, stringy substance, composed of short fibers and irregular particles. Commercially this grade of asbestos is known as "King's floats." For a proper understanding of its physical characteristics, a brief consideration of its occurrence in nature and its method of preparation is necessary. The Thetford asbestos is known as chrysotile, a member of the serpentine group of minerals. Pure chrysotile is a silky, white, fibrous substance, but the presence of iron in varying states of oxidation usually gives it a greenish or greenish-brown color. It is composed of tightly packed bundles of smooth, flexible fibers, which are about 0.05 micron in diameter, and which vary from 1/8 inch to 6 inches in length. In nature these fibers occur in veins, which are embedded in hard serpentine rock. The thickness of the vein determines the length of the fibers, which run across it.

The King's floats grade of asbestos contains only short fibers which occur in very narrow veins. The hard serpentine matrix, rich in small veins, is crushed, dried, recrushed, screened and pulverized, and finally passed over shaking screens from which the fibers are withdrawn by suction. The material is then graded by screening, and the fraction which passes the finest screen is allowed to settle in a large room. Such material (King's floats) contains not only short fibers, but in addition many small particles of serpentine rock.

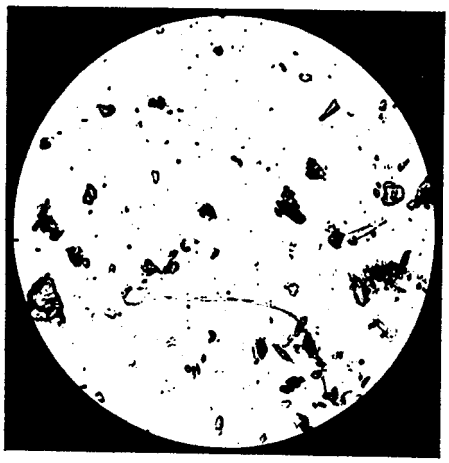

FIG. 1.—Asbestos dust. ×90.

Microscopic examination reveals the fact that particulate matter is far in excess of fibrous material. The particles vary in size from 10 microns to 0.5 micron in diameter. The fibrous traction is less uniform. In length the fibers vary from 1 mm. to 1 micron or less. Many isolated, long, smooth, thin, flexible strands are seen, while others consist of short thick bundles with broken ends. The fibers are highly refractile when viewed by polarized light. (See Fig. 1.)

The dust has a specific gravity of 2.26. It loses only about 1 per cent. of its weight when heated at 110°C., yet in a moist atmosphere sufficient water is absorbed to increase noticeably its tendency to clumping or matting.

In chemical composition, pure chrysotile is chiefly composed of crystalline hydrated silicate of magnesium ($3MgO \cdot 2SiO_2 \cdot 2H_2O$). It is, however, seldom free from impurities which partially replace the magnesium to form more complex silicates. Ferrous iron is the most common contaminant, and it may sometimes constitute as much as 10 per cent. of the mineral as it occurs in nature. A portion of this iron may be oxidized to the ferric state.

The following analysis has been made from samples of the dust used in the study:

	%
Total SiO_2	39.32[1]
Fe_2O_3, Al_2O_3	8.84
CaO	0.67
MgO	35.56
Alkalies and loss	2.87
Combined water	12.74

[1] Free SiO_2 (by rational analysis) = 2.6%.

The material reported as aluminium oxide and ferric oxide was largely the latter. Preparations of the dust stained with potassium ferricyanide and dilute hydrochloric acid indicate that there is ferrous iron in the majority of the fibers; a few exhibit irregular staining with ferrocyanide.

Anderson and Clark (1) have shown that treatment of Thetford chrysotile with hydrochloric acid completely destroys the typical crystalline pattern

of the material produced in Bragg's X-ray diffraction technic.

Careful and repeated search has failed to disclose any yellow structures resembling asbestosis bodies in the dust previous to its residence in the animal. The appearance and method of development of these structures will be discussed later.

Experimental Procedures

The general plan of the experiment is the same as that previously employed in studies on granite (2), marble (3), carborundum (4), and quartz (5). In the present instance, animals are kept in cages along the walls of a room 6 by 8 feet, and 8 feet high, provided with two 3 by 5 foot windows. A cloud of dust is maintained in the atmosphere of this room by apparatus located in an alcove, 6 feet from the nearest animal. This apparatus consists in a horizontal drum 2 1/2 feet long and 1 1/2 feet in diameter, placed 8 inches above the floor. Its top is open, and in it rotates a metal paddle, whose shaft projects through the end of the drum and then through the partition into an adjacent room in which is located an electric motor. By properly selected pulleys and countershafting, the speed is so regulated that the desired dust concentration can be maintained. Ventilation is secured by opening one of the windows an inch or more from the top. The animals are kept, generally in pairs, in 12 by 12 by 12 inch wire cages set on racks at the sides and back of the room. While it will be shown that the dust concentration progressively decreases from the floor to the ceiling, this factor is compensated by frequently changing the position of the cages on the racks.

As measured by the operation of the motor, the daily period of exposure is eight hours, but since the animals remain in this room during the night, the actual exposure is much longer, considerable time being required for all the dust in the atmosphere to settle. In warm weather the period is somewhat shortened by opening the windows when the motor is stopped in the evening. From the commencement of the experiment on Jan. 20, 1928, until the present date, the dust exposures have been continued for eight hours, on six days a week, with the exception of a period of three weeks in the month of January, 1930, when the motor was being repaired.

Dust Concentration

The amount of dust in the atmosphere of this room has been checked with a Greenburg-Smith impinger apparatus.[1] Samples taken on Feb. 14, 1928, one month after the experiment was started, showed the concentrations given in Table 1.

The rate of suction on the sampling apparatus was 1 cubic foot per minute; the sampling times were fifteen minutes and thirty minutes. Owing to the fibrous nature of the dust, the particles were not filtered before the counts were made, but the very large particles (those greater than 100 microns) were simply neglected in counting. Particles over 1.5 microns in diameter, magnified ninety-five times, were counted in the usual manner in a Sedgewick-Rafter cell,

[1] Appreciation is expressed to Mr. Morris Dworski for making these dust determinations.

after being allowed to settle for thirty minutes. The smaller ones varying from 1.5 microns to 0.5 micron in diameter were counted in a hemocytometer chamber at a magnification of 410. The usual blank controls on the distilled water used to collect the dust samples were made, and the number of accidental particles was subtracted before the results were tabulated.

This concentration was maintained with little variation until January, 1930, when the speed of the paddle was accelerated, and the amount of suspended dust was increased approximately ten times. The majority of the animals to be discussed in this report, however, were subjected only to the smaller dust concentration.

In this experiment 128 guinea-pigs, eighteen white rats, and seven rabbits have thus far been used. A portion of the guinea-pigs were infected with tubercle bacilli in an attempt to determine the influence of this dust upon a tuberculous process.

One group of sixty-three guinea-pigs were infected with tubercle bacilli four days before the dust inhalation was begun; forty of them were placed in the dusting room and twenty-three were kept in a normal atmosphere as controls. Two years after the experiment was started, twelve dusted and twelve normal guinea-pigs were infected with tubercle bacilli. This group was then set aside without further exposure to the dust. All the rats and rabbits and fifty-four of the guinea-pigs were used in studying the uncomplicated effects of inhaled asbestos dust. Each of the various groups will be described separately.

TABLE 1.—DUST COUNTS

COUNT NO.	HEIGHT OF INTAKE FROM FLOOR	MILLION PARTICLES PER CUBIC FOOT OF AIR				
		A 100–10μ (× 95)	B 10–1.5μ (× 95)	C 10–0.5μ (× 410)	D 1.5μ or less (C − B)	Total (A + C)
	ft.					
1	2	1.130	8.033	56.666	48.633	57.796
2	2	1.258	6.625	51.600	44.975	52.858
Average..	.....	1.194	7.329	54.133	46.804	55.645
3	4	0.450	4.960	35.000	30.040	35.450
4	4	0.400	4.440	43.333	38.893	43.733
Average..	.....	0.425	4.700	39.166	34.466	39.591

Pathologic Lesions

Non-Tuberculous Guinea-Pigs

Up to the present date, twenty-nine months after the commencement of the dust inhalation, fourteen animals, or 26 per cent. of the group, have died of epizootic pneumonia, and fifteen more succumbed to other conditions, such as enteritis and peritonitis. As this experiment was designed to demonstrate the maximum effects which could be produced by the inhaled dust, relatively few of the ani-

mals have been killed. A number have, however, been sacrificed at 30, 60, 90, 354, 610, 782, and 847 days. Commencing with the eighth month of exposure, the effects of the dust have also been followed radiographically in the living animals.

The pulmonary localization of inhaled asbestos differs from that of any other dust thus far studied. Granite, quartz, carborundum, and soft coal particles penetrate the terminal air spaces of the lung, and large quantities ultimately localize in the subpleural alveoli. Asbestos dust, presumably because it is so largely composed of elongated fibers, is carried by the inspired air only to the distal respiratory bronchioles, and there the major portion of the material comes to rest. Mononuclear phagocytes from the adjacent connective tissues enter the lumen of the air passages and engulf the particles. The phagocytes with their contained fragments of dust are frequently pushed aside into the alveoli which pouch out of the sides of the bronchioles, where many of them remain indefinitely. More dust entering the lung is held up by the partial obstruction created, and further reaction is largely proximal to the point of original localization. A few particles pass beyond into the proximal portions of the alveolar ducts, but in the majority of cases the deposition of asbestos dust occurs within respiratory bronchioles of the second and third orders and in the alveoli given off directly from those structures. (Fig. 2.)

In guinea-pigs killed thirty days after starting the dust inhalation, occasional small mononuclear phagocytes containing a number of brown or black particles and a few short spicules of doubly refractile material are visible in the alveoli budding off from the respiratory bronchioles. A few multinucleated dust cells are

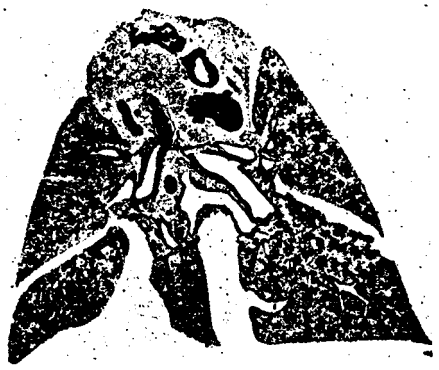

FIG. 2.—Cross section of lungs of guinea-pig exposed to asbestos dust inhalation 840 days. Normal size.

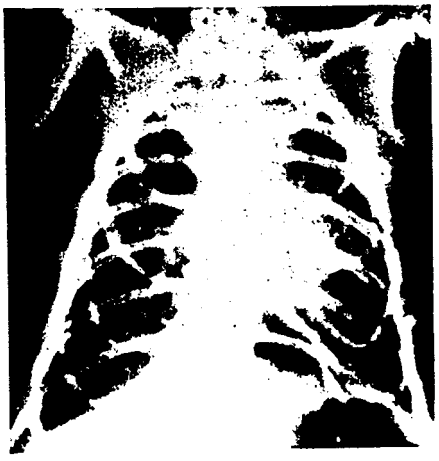

FIG. 3.—Roentgenogram of guinea-pig exposed 880 days to asbestos inhalation.

encountered. The lymphoid tissues of the bronchial tree exhibit a moderate degree of hyperplasia. The lymphatic trunks coursing through the bronchial walls are wide open, but no dust cells or other material can be found in

their lumina. The tracheobronchial lymph nodes exhibit no more dust containing cells than those in any normal animal kept in a laboratory atmosphere.

At sixty days, the number and size of the dust cells in the terminal respiratory bronchioles is considerably increased. The lumina of some of the lateral alveoli are completely blocked by masses of mononuclear phagocytes and larger giant cells. Some of the latter have six or more nuclei. Frequently in Zenker-fixed tissues, these phagocytes have a diffuse yellow-brown color which is presumably due to the presence of dissolved iron in their cytoplasm. In tissues fixed in formalin and stained with acidified potassium ferrocyanide, such cells exhibit a diffuse blue coloration. In addition, there are certain particles in their cytoplasm stained very deep blue which are probably the source from which the iron is dissolved. Doubly refractile intracellular spicules are numerous; they are most readily demonstrated in polarized light. After sixty days' exposure to dust, the first evidence of that peculiar structure which has been called a "curious body" is detected. We prefer to adopt Stewart and Haddow's (6) designation of "asbestosis body," and shall use the latter term exclusively.

After two months the number of asbestosis bodies is small and they are atypical in appearance. The most common form is a club-shaped swelling at the end of a smooth pale greenish fiber. Some present small fusiform swellings along the course of a short fiber. They are seen almost without exception inside of large giant cells.

After ninety days' exposure, the number of these structures has very markedly increased, and they have assumed their typical form. The smaller ones are still contained in giant cells, but many long forms appear to be free in the stroma of the lung. The amount of cellular reaction has not kept pace with the number and size of the foreign bodies. It still consists of collections of mononuclear and giant phagocytes within the lumen of a localized group of air spaces, together with a very slight infiltration of the adjacent septa. Hyperplasia has occurred in the lymphoid tissues associated with the bronchi proximal to the foci of maximum dust reaction, but no phagocytes have carried dust particles into the lymph nodules. The lymphatic trunks are widely distended, but they contain no cells or dust particles. The tracheobronchial lymph nodes also show well-marked hyperplasia, but the number of dust containing cells is still small.

During the next four months, no animals were killed, but nine died of various accidental causes. In them it is found that increasing quantities of dust are accumulating in the vicinity of the respiratory bronchioles, and that the amount of cellular reaction is somewhat increased. Asbestosis bodies are so extremely abundant that as many as eight have been encountered in an oil immersion field. They are practically absent in other portions of the lung. The other changes in the lymphoid tissues and lymphatic vessels remain much the same. There is as yet no evidence that appreciable amounts of dust are being transported to the tracheobronchial lymph nodes.

In three guinea-pigs killed on the 357th day, the amount of reaction has

developed to such a degree as to be visible on gross section of the fixed tissue. Uniformly distributed over the entire surface of both lungs are fine yellowish-white ovoid flecks of granular appearance with ill-defined borders. They are arranged radially on the surface and suggest a relationship to the finer bronchioles. All are of approximately the same size and none exceed 1 mm. in diameter. Microscopically those foci are similar in every way to

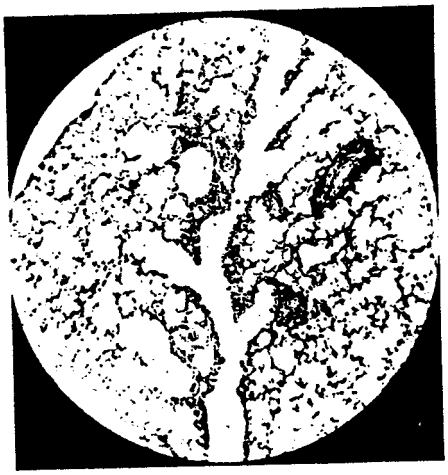

FIG. 4.—Longitudinal section of bronchus and its peripheral branches. Exposure 357 days. Approximately ×45. Note that dust reaction is localized to region of respiratory bronchioles. No reaction in lymphoid tissues.

FIG. 6.—Peribronchiolar dust reaction in normal guinea-pig exposed 840 days. Connective tissue stain. Approximately ×90.

FIG. 5.—Longitudinal section of bronchus and its peripheral branches. Exposure 436 days. Approximately ×45. Note that dust reaction is localized to region of respiratory bronchioles.

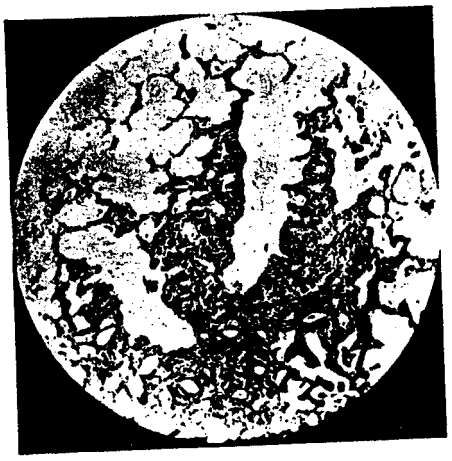

FIG. 7.—Early tuberculous reaction in focus of asbestosis; endogenous extension 357 days after infection. Approximately ×90.

the type of reaction already described. The walls of the bronchioles, proximal to alveolar ducts, are thick, but this is due solely to an excessive local accumulation of phagocytes. There is no evidence that fibroblasts are proliferating. The dust cells have not migrated to any extent from the original foci of localization; none are found in the pulmonary lymphoid tissues, but some have been transported to the tracheobronchial lymph nodes. (Figs. 4–7.) In the medullary sinuses of the latter location there are now definite clusters of brown-stained iron containing phagocytes. In their cytoplasm many irregular black or brown particles and refractile elongated spicules are recognizable. Occasionally a giant cell is seen partially surrounding a very long fiber which may project beyond the limits of the cell. One such fiber measured 25 microns in length. No asbestosis bodies are seen. As yet the only evidence of reaction in these nodes consists in an active proliferation of the follicle cells.

While asbestosis bodies cannot yet be found in the lymphoid tissues, they do occur outside the lung. Two of the 357-day animals had developed a chronic fibrous pleurisy, and occasionally in the connective tissue there are small clusters of phagocytes containing dust and asbestosis bodies. In an isolated field, five of them have been counted.

On the 449th day, two asbestosis bodies are found within a giant cell in the tracheobronchial lymph nodes.

All animals killed or dying on and after the 505th day are characterized by the *proliferation of fibroblasts*. This reaction is confined to the walls of the air spaces adjacent to the deposits of accumulated dust phagocytes. At first only a few cells are involved, but after still another 100 days, a true fibrosis, accompanied by the formation of very considerable amounts of collagen, has developed. The walls become progressively thicker, and encroach upon the lumen of the air spaces. The epithelium of the latter contracts and becomes cuboidal, so that the area of reaction resembles a gland with a heavy connective tissue stroma. The lumina of these gland-like atelectatic air spaces are more or less completely filled with compact masses of dust cells and brown-stained giant phagocytes whose cytoplasm is gorged with dust particles, fibers, and asbestosis bodies. In the thickened septums there are many of the latter, which are generally extracellular. (Figs. 6, 9, and 10.)

The amount of dust carried into the tracheobronchial lymph nodes now becomes more abundant. It consists largely of amorphous or granular black or brown particles with many doubly refractile spicules which fail to stain specifically for iron. Occasionally a few giant cells, sometimes in small clusters, contain typical asbestosis bodies. The stroma of the nodes about the masses of dust cells now exhibits a limited amount of fibroblastic proliferation.

The latest stages of the reaction of asbestos dust thus far produced are manifested in the lungs of five guinea-pigs, of which three were killed on the 782nd day, and one on the 840th day. All five exhibited a large number of subpleural gray-white nodules at least 1 mm. in diameter, uniformly distributed over the surface of the lung.

On section of the organs, sharply demarcated ovoid areas are disclosed in every part of the lung. One animal shows a fibrous pleurisy over

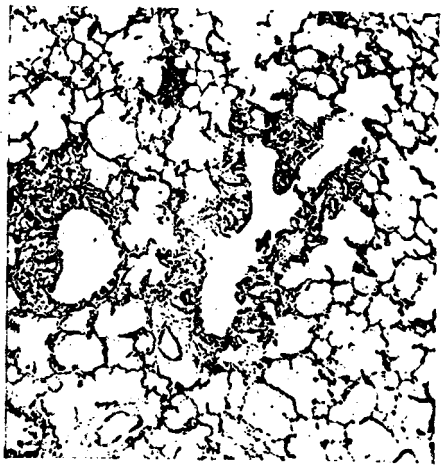

FIG. 8.—Peribronchiolar focus of asbestosis; guinea-pig exposed 782 days. Approximately ×70.

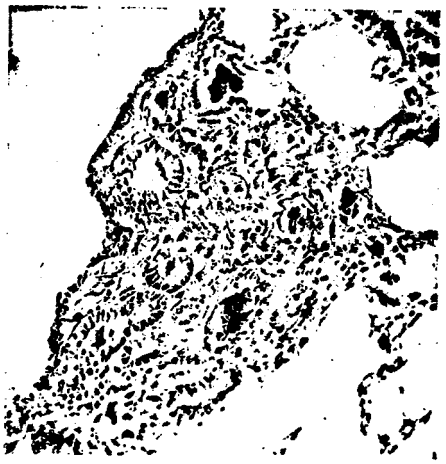

FIG. 9.—Magnified field of Figure 8. Note gland-like air spaces. Approximately ×140.

portions of the lung without evidence of an underlying pneumonia. The tracheobronchial lymph nodes are deeply pigmented in their central portions.

The first radiographic examination to demonstrate definite changes in the lung was obtained after a dust expo-

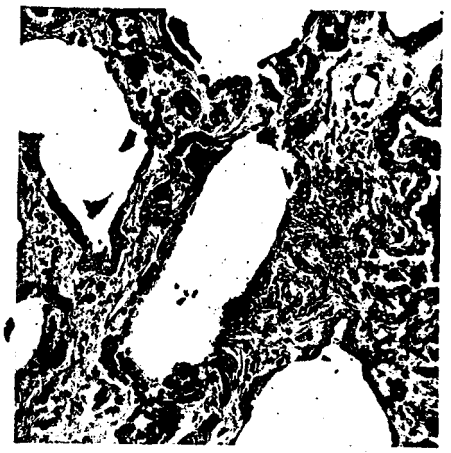

FIG. 10.—Magnified field of Figure 8. Connective tissue stain. Note strands of collagen between gland-like alveoli. Approximately ×140.

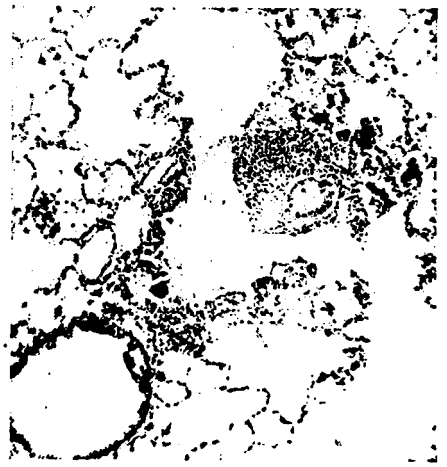

FIG. 11.—Asbestosis in rabbit exposed 149 days. Approximately ×140. Note giant cells, one of which has invaded nodule of lymphoid tissue.

sure of two years. At this time the presence of very fine mottling was detected in the lower portions of the lung fields. After another five months

had elapsed the changes had become much more marked. As illustrated in Figure 3, they consist of strands of coarse mottling which radiate outward and downward from the hilum. The outlines of the mediastinum and the pericardium are obscured by similar shadows. Whether the apexes are also involved cannot be definitely determined.

Pathologic changes in the lungs of experimental animals are much more readily demonstrated radiographically if the lungs are removed from the thorax and inflated before exposure to the X-ray. Roentgenograms have been made in this manner of animals with well-developed asbestosis and the shadows produced are characterized by a pronounced thickening of the linear markings which extend outward from along the main bronchi to the margins of the lung.

Microscopically, the lungs present lesions similar to those already described, but they are more extensive and fibrosis has become more marked. In stains for connective tissue, abundant collagen formation is now apparent in the walls of the respiratory bronchioles and their alveoli. Dust cells and asbestosis bodies are very abundant. The extension of the process from the terminal bronchioles proximally into respiratory bronchioles of greater diameter is obvious.

In addition to these characteristic changes, the lung of one animal exhibits more or less circumscribed foci of fibrosis in the alveolar septums peripheral to the usual reaction zone. The lumina of the included air spaces are normal in size, and apparently fully distended. Their walls are lined with easily visible cuboidal or flattened epithelium which occasionally dips into the thickened septums to form gland-like structures. In marked contrast to the previously mentioned areas of fibrosis in the respiratory bronchioles, these more peripheral foci include practically no dust cells or asbestosis bodies. One lobe of this lung is covered by organized fibrous pleurisy which also fails to exhibit dust deposits.

Examination of the trachea and stem bronchi, both by direct and by polarized light has failed to demonstrate appreciable amounts of dust or local reaction. The only evidence of irritation is the presence of an occasional polynuclear leukocyte on the ciliated surface and the distention of the goblet cells with mucus. More peripherally the connective tissue coats of the bronchi of the second and third orders exhibit considerable infiltration with lymphoid cells, and some engorgement of the blood vessels. The other viscera, the spleen, liver, kidneys, pancreas, and abdominal lymph nodes have been uniformly free of dust or evidence of reaction attributable to it.

In the guinea-pig, the development of the early (two years and five months) response to inhaled asbestos dust may be summarized as follows:

The particles and elongated fibers of asbestos dust do not, during this period, penetrate so deeply into the air passages of the lung as do the other dusts previously studied. The major portion is held up and phagocytosed in the lumina of respiratory bronchioles and the alveoli given off from their walls. Increasingly large masses of phagocytes accumulate in the lumina of these air spaces, and many of the cells migrate into the framework of

the adjacent lung tissue. In this location there develops a low grade chronic inflammatory reaction characterized by infiltration with monocytes and a few lymphoid cells. Approximately 500 days after the commencement of dust inhalation, the connective tissue cells in the walls of the bronchiole and its alveoli begin to proliferate.

Thereafter, the reaction is characterized by increasing amounts of fibrous tissue which develops in the immediate vicinity of the dust cells. The thickening stroma encroaches upon the lumen of the air spaces whose epithelium, being compressed, appears cuboidal, as is the case in pulmonary atelectasis. The picture produced somewhat resembles glandular tissue. In addition to this lesion, which is characteristic of all the animals examined, one of three of the last guinea-pigs killed showed a further change consisting in focal areas of fibrosis in the alveolar septums peripheral in the pulmonary unit to the point of dust localization.

Changes in other structures of the lung are not striking. There is well-marked hyperplasia of the lymphoid tissues in the periphery of the lung, but dust containing phagocytes do not migrate toward and enter these masses, as is the case with quartz inhalation. Dilatation of the large lymphatic vessels in the connective tissues of the bronchi and blood vessels has been a constant finding in all the animals of the series. Even thirty days of dust inhalation would appear sufficient to produce this effect. Its cause has not been discovered; thrombi within the lumen of the lymph vessels are lacking, and a central obstructive lesion in the tracheobronchial lymph node is a late development. Only after 700 days do fibroblasts begin to proliferate in the medulla of the nodes.

Asbestosis bodies have not been found in any animal killed before sixty days of dust exposure. When first discovered, they are small, somewhat atypical in form, and generally contained within the cytoplasm of phagocytes. Within the next sixty days they rapidly increase in number, size, and complexity of structure. The larger ones appear to be liberated from the cells, and ultimately to be free in the air passages or intracellular spaces. In most cases, these structures, presumably because of their size, are not transported from the point where they first develop in the lung. Occasionally they have been found in the tracheobronchial lymph nodes and in areas of chronic fibrous pleurisy. In these instances they are usually intracellular.

Rabbits

Five rabbits exposed to asbestos dust for 40, 53, 149, 253, and 330 days, respectively, have thus far been killed and studied. Within the period of time included, the reaction to the inhaled dust has been characterized by increasingly large focal collections of mononuclear and giant phagocytes. These, as in the guinea-pig, tend to accumulate in and along the respiratory bronchioles, although in the last two animals killed, some collections of dust cells have been seen in the more peripheral air spaces. In marked contrast to their behavior in the guinea-pigs, the phagocytes exhibit a tendency to migrate into masses of lymphoid tissue. This occurs early, and has been observed in all but the

first animal killed. It is probably due to anatomic differences in the two species. In the rabbit, abundant deposits of tonsil-like lymphoid tissue are situated directly beneath the epithelium throughout the course of the bronchial tree; in the guinea-pig the lymphoid nodules are not so readily accessible. The phagocytes are filled with great quantities of doubly refractile dust spicules, but *no typical asbestosis bodies have yet been discovered.* When stained for iron, none of the fibers in the first four animals reacted. In smears of lung tissue from the last animal killed on the 330th day, a few elongated fibers exhibited irregular deposits of both ferric and ferrous iron, and there were occasional globular swellings along their course. But these fibers did not present the usual golden-yellow color of an asbestosis body, and the alterations in structure were in no way characteristic.

No suggestion of fibrosis or even reaction in the framework of the lung adjacent to the collection of dust cells has been discovered, but it is still too early to expect much change. In the guinea-pig, the first indication of fibrosis was found on the 500th day.

Albino Rats

Repeated attempts to study the reaction to inhaled asbestos in the white rat have been defeated by the development of epizootic pneumonia, often complicated by abscess formation. The first series was composed of twelve animals, all of which succumbed to this infection. One survived for 450 days, but in all of them the reaction to chronic pneumonia so obscured the picture that no deductions were possible. In December, 1929, six new, apparently healthy rats were placed in the dust room. During a period of 118 days three have been sacrificed and one has died. All of them have had pulmonary abscesses. In only one animal, which was killed on the seventieth day, could asbestosis bodies be detected, and in this case prolonged search of smears of the lung tissue stained for iron has revealed only two of these structures. One was very small, but typical in appearance. The other consisted of a bundle of fibers frayed at the end, and upon one of the fibrils were a few irregular swellings. In another rat killed after 118 days, no asbestosis bodies have been found.

The Asbestosis Body.

Since the development of the peculiar structure termed an asbestosis body in the lungs of animals compelled to inhale asbestos dust may have an important bearing upon the general problem of pneumonokoniosis, it deserves detailed consideration.

The forms encountered in the lungs of guinea-pigs in every way resemble those pictured in the human cases. While individual specimens exhibit marked variations, there are certain features which are characteristic of all the forms observed. The fully developed body consists of a brilliant golden-yellow, beaded or haustral rod, which may be either straight or curved. Its color resembles that of the hemosiderin deposits found in areas in which hemorrhage has occurred. In length they vary from 1 to 250 microns, and in width from 0.5 micron to 10 microns. The shorter ones are usually straight, but the larger forms are curved, or even coiled. They do not stain with any of the dyes ordinarily used for

tissues, but Wright's blood stain is absorbed to some extent, giving them a greenish cast. Fixing fluids and the usual histologic stains have no apparent effect upon them. Iron in the ferric state may be demonstrated by

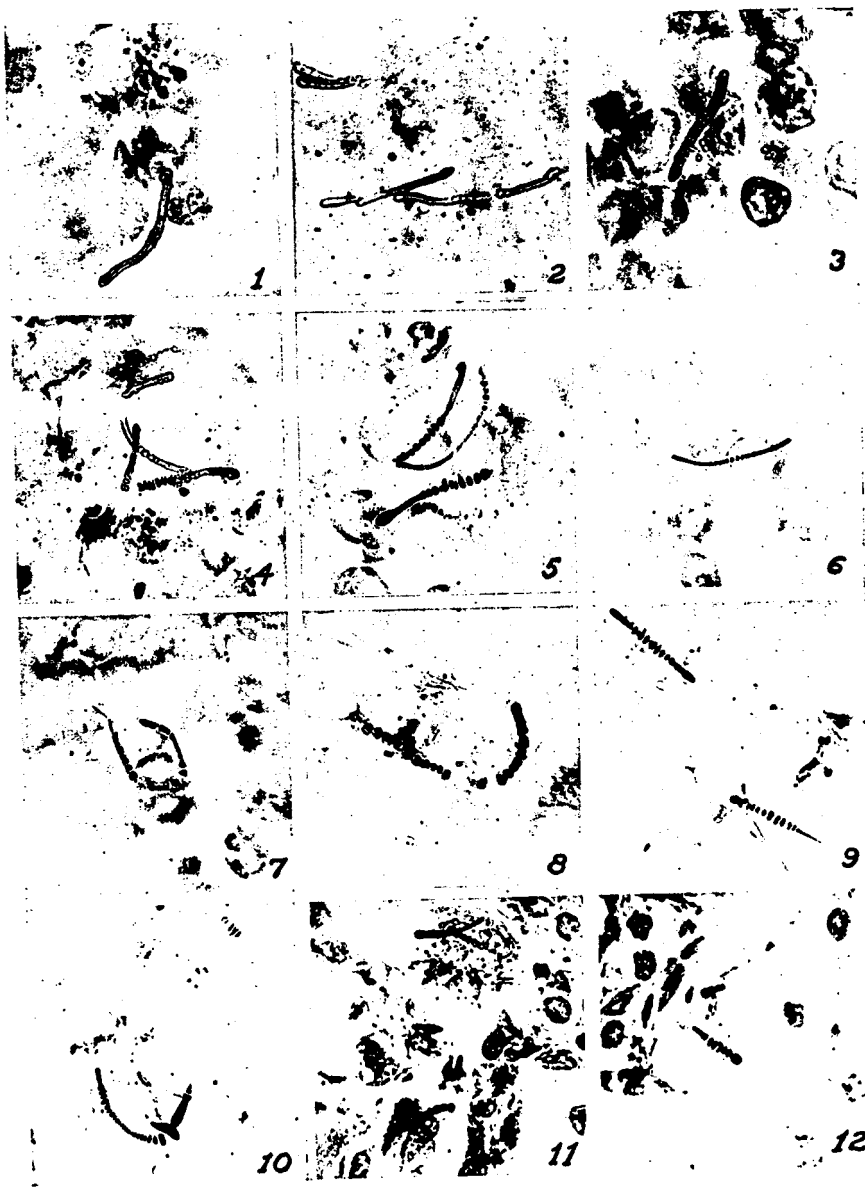

FIG. 12.—Asbestosis bodies in guinea-pigs' lungs. Nos. 1 to 10 from smears of lung tissues; Nos. 11 and 12 in sections. Approximately ×560.
No. 1 shows a smoothly coated fiber; in No. 2, no fiber is visible; No. 7 shows coating material cracked along fiber. Other illustrations show various forms of this structure.

treatment with potassium ferrocyanide in dilute hydrochloric acid (McDonald and Stewart). Examined under polarized light, they are not doubly refractile. The shorter forms are usually found within the cytoplasm of a foreign body giant cell; longer ones the process of preparing sections and smears, cannot be determined. (Fig. 12.)

The lung of the rabbit apparently offers a much less favorable environment for the production of the asbestosis body than that of the human being

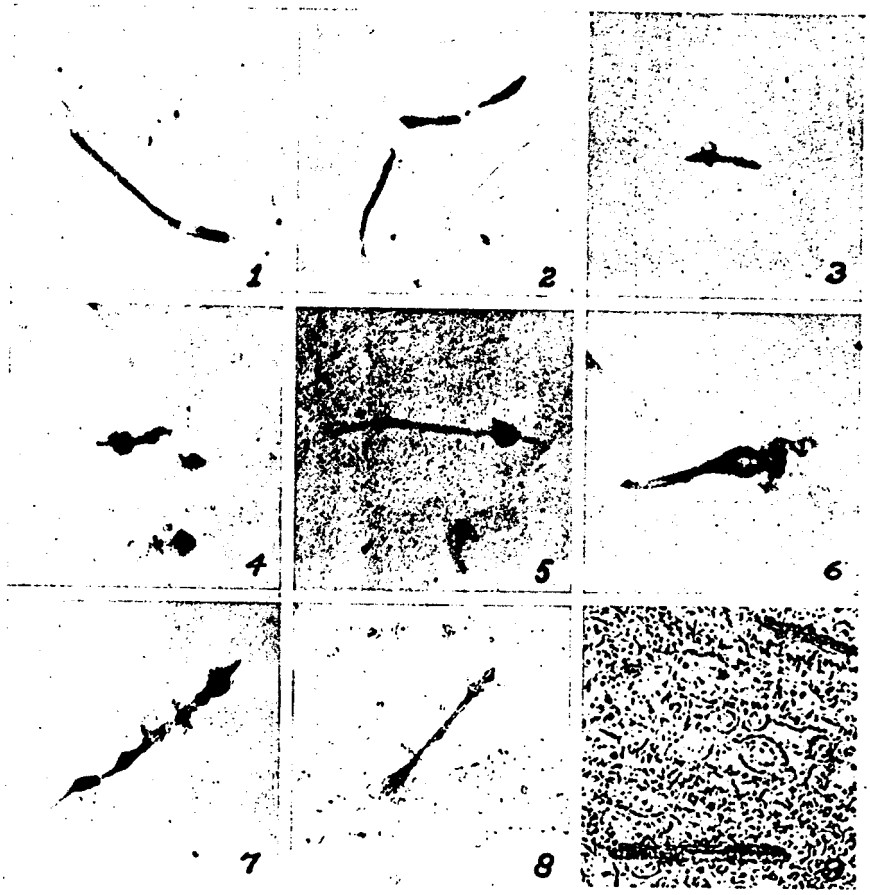

FIG. 13.—Atypical asbestosis bodies from lung of rabbit exposed 330 days. Nos. 8 and 9 are artificially produced asbestosis bodies. ×840.

may be coiled within such cells, but more usually they lie free in the lumen of an alveolus or in the intercellular spaces of the pulmonary framework. Whether they actually exist in the free state during life or whether, owing to their elasticity, they are set free in or the guinea-pig. Nothing faintly resembling one of these structures has been found until the dust exposure has been continued for a period of eleven months. At that time, in hematoxylin and eosin preparations occasional fibers are seen which have a muddy, greenish

hue, but they do not exhibit the regular beading, or the characteristic golden-yellow color seen in the guinea-pig. Preparations stained for either ferrous or ferric iron demonstrate a few very long fibers containing irregular swellings of a deep blue color. Whether typical asbestosis bodies will ever develop in this animal remains to be demonstrated. (Fig. 13, Nos. 3 and 4.)

In the lung of the white rat they would also appear to be very uncommon, although the widespread incidence of chronic pulmonary infection among the animals thus far exposed, in a measure invalidates the results. Thus far, only two asbestosis bodies have been discovered in one animal of this species. If the environment were favorable, it would seem probable that more of these bodies would have been detected, even in the presence of complicating pneumonia.

Our observations have led us to believe that the asbestosis body develops as the result of chemical changes taking place within or about inhaled asbestos fibers. The dust previous to contact with the pulmonary tissues shows no such structures. A period of time which varies with different species of animals must elapse after the fibers have entered the lung, before the asbestosis body makes its appearance. The first forms encountered are different from those seen later. They consist of iron containing, sheath-like or nodular swellings along the sides or at the ends of a fiber. From such points further extensions occur until in some cases the whole filament acquires a uniform coating which is brittle (Fig. 12, No. 1). Movement or other stress causes the coating substance to crack, separating it into segments (Fig. 12, No. 7).

Chemical action continues and the segments tend to elongate in a direction at right angles to that of the original fiber. Extension also takes place at the ends of the fiber, so that it increases in length. Small fragments may also serve as nuclei for chemical activity; about them spherical or ovoid masses develop. The resultant forms exhibit many variations. Perhaps the most common ones consist of an axial fiber traversed at intervals by a variable number of thickened crossbars. Often one end and sometimes both ends are swollen and spindle shaped. In other instances, the central fiber cannot be discovered (possibly it has been dissolved?); the body then consists of a row of globules. Sometimes these are of uniform diameter; frequently they decrease progressively from one end to the other. In guinea-pigs exposed for more than two years, many bizarre branching globoid forms are seen, which resemble clusters of tuberous bulbs.

An observation which merits comment is the scarcity of asbestosis bodies in the tracheobronchial lymph nodes. Presumably because of their size, the majority of the inhaled asbestos fibers are not transported to any distance by phagocytes. Nevertheless, after exposure to the dust has been continued for somewhat over a year, appreciable numbers of doubly refractile non-iron-staining fibers can be found in the lymph nodes of the mediastinum. They are embedded in the cytoplasm of phagocytes which have migrated from the lung. After two years, large masses of such dust cells have accumulated, and yet asbes-

tosis bodies are not found in any number in the tracheobronchial lymph nodes. Those which do occur are located in clumps of giant cells. It is believed that the formation of the few asbestosis bodies found took place in the lung, and that they were then transported to the lymph nodes in emboli of phagocytes.

Why do asbestosis bodies occur so rarely in the material which has been transported to the lymph nodes? Were the fibers during their period of residence in the lung deprived, by solution, of iron or some other substance necessary to their production; or are the transported fibers essentially different from those remaining in the lung; or, again, is the environment furnished in the lung especially favorable for the production of asbestosis bodies?

To answer the last possibility, injections of asbestos dust have been made into other portions of the body. In the peritoneal cavity of the guinea-pig attempts to produce asbestosis bodies have met with but slight success. In one series each guinea-pig was injected with 2 c.c. of a heavy suspension of the King's floats dust, which was so prepared by sedimentation (7) that only particles varying from 2 to 4 microns were present. This material, it will be recalled, contains not only asbestos fiber, but a considerable amount of iron and other material. Another series received a like amount of pure asbestos *fiber* cut and ground into the finest possible state. This fiber was obtained from a vein of Thetford ore. As a control, a third series was injected with a suspension of granite from Lorain County, Ohio. This rock contains free silica and ferrous carbonate, among other constituents. Samples of the peritoneal fluid were withdrawn with capillary pipettes twenty-eight and sixty-four days after the injections. In each series the fluid exhibited large numbers of dust containing monocytes, and in both the asbestos groups large giant cells were numerous. No sign of an asbestosis body could be discovered. Dissolved iron was detected in the cells from the granite series, but none could be found in those from either of the asbestos groups.

On the seventieth day and again on the 110th day, one animal from each group was killed. The amount of reaction was surprisingly insignificant. Careful search revealed minute foci of pigmentation in the omentum of each animal. At seventy days no suggestion of an asbestosis body was discovered, but at 110 days a few very small but typical bodies were found in a smear stained for iron of an omental nodule from one animal injected with the King's floats dust. The asbestos fiber and the iron containing granite animals did not show them. These findings were confirmed subsequently by histologic examination of the tissue. While the remaining animals of this experiment are still under observation, it hardly seems probable that asbestosis bodies will develop in any number. Aside from its failure to favor the formation of these structures, it is surprising that the peritoneal cavity exhibits so little reaction to the injection of very considerable quantities of this foreign material. When more insoluble dusts, such as coal, quartz, and carborundum, are injected, very appreciable deposits are found in the

omentum and beneath the parietal peritoneum.

In the subcutaneous tissues, attempts to form asbestosis bodies have been somewhat more successful. In an uncompleted experiment designed to determine whether certain dusts might cause a dissemination of infection with tubercle bacilli of attenuated virulence, daily repeated injections of asbestos dust suspensions were made into the subcutaneous tissue of the groin of guinea-pigs previously injected with tubercle bacilli in the same area. In all, thirty injections totaling 3 mg. of very fine dust (King's floats) were made. Most of the material has not yet been examined, but in one animal dying in 102 days, and in three more killed 264 days after the dust injections were completed, the subcutaneous tissues exhibited large masses of foreign body giant cells containing many typical asbestosis bodies.

With a view to determining whether the iron of the asbestosis body is derived from the dust or from the animal body, the following experiment has been performed. A mixture was prepared which contained equal parts of very finely divided pure asbestos fiber and fine whole asbestos dust (King's floats), the latter composed of particles between 2 and 4 microns in diameter. Both of these elements were included because the pure fiber from asbestos veins contains so little iron. The mixture was divided into two parts, and from one of them the iron was completely removed by digestion with hydrochloric acid and subsequent washing. Both fractions were sterilized by heating at 100°C. for one hour, and suspended in physiologic salt solution. The iron free portion formed a smooth turbid opalescent suspension, while the untreated portion produced a gray-green flocculent one. Two c.c. of each of these suspensions were injected into the subcutaneous tissues of the groins of each of six guinea-pigs; the untreated suspension on the right side, and the iron free material on the left. When examined thirty days later, all the animals had palpable nodules at the site of injection of the untreated material, and none on the opposite side. At this time one of the guinea-pigs was killed. On the right side there was a nodule 10 mm. in diameter filled with greenish-gray necrotic material, while on the left side there was only a faint suggestion of pigmentation in a very slightly enlarged superficial inguinal lymph node. Smears made from the material on each side failed to demonstrate golden-yellow bodies. When stained for iron with potassium ferrocyanide, numerous uniformly blue fibers were seen in the abscess produced by the untreated material, but only a few short, unstained fibers could be discovered in the smears from the opposite side. There was no suggestion of an asbestosis body. As in the case of the peritoneal cavity, the impression is gained that a part of the dust may have been dissolved in the body fluids. The effects produced at sixty days were identical. The absence of asbestosis bodies on the right side is attributable to the lack of sufficient time for their development; the disappearance of the injected material on the opposite side is most surprising.

(To be concluded)

STUDIES ON EXPERIMENTAL PNEUMONOKONIOSIS. VI. INHALATION OF ASBESTOS DUST: ITS EFFECT UPON PRIMARY TUBERCULOUS INFECTION

(Concluded)

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PRIMARY TUBERCULOUS INFECTION IN PULMONARY ASBESTOSIS

To determine whether inhaled asbestos dust affects the course of tuberculous infection, the same procedures have been employed which were used in the previously reported experiments on other dusts, *i.e.*, granite (2), marble (3), carborundum (4), and quartz (5). For this purpose animals exposed to asbestos dust have been infected by causing them to inhale small numbers of tubercle bacilli of the attenuated strain R_1. By this means, in undusted guinea-pigs a self-limited infection of the respiratory tract is produced with lesions comparable with those of the "primary complex" in man. They consist of a variable number of small discrete subpleural tubercles in the lung, together with a more extensive involvement of the tracheobronchial lymph nodes. The pulmonary tubercles caseate and then the bacilli die. The caseous matter is absorbed and after a period of from eighteen months to two years, complete resolution of the entire lesion takes place (8). Macroscopic disease of the spleen and liver is almost never seen. The course of the infection in such guinea-pigs is generally nonprogressive (Figs. 18, 19, and 20).

During the period from 1920 to 1928, there were three instances of generalized tuberculosis among 251 guinea-pigs infected with this organism as controls to different dust experiments. In one of these three there was some question as to the identity of the animal. In the last three years, however, eleven instances of disseminated disease have been discovered among 148 controls similarly infected. The occurrence has been sporadic, and only one animal in a group of twenty-five or fifty such controls exhibited evidence of spreading disease. The cause of this apparent accentuation in virulence has not been ascertained.

It is hard to believe that after maintaining a constantly low degree of virulence for a period of thirty years the R_1 strain has rather suddenly been altered. As far as is known, the glycerin broth on which it has been cultivated has been prepared in the same manner as heretofore. The dosage used for inhalation infection has been maintained at a constant level. The only discoverable factor which has not

been controlled is the guinea-pigs used for the experiments. They have regularly been purchased from one farmer. On their receipt they are quarantined for a period of three weeks to avoid the introduction of epizootic pneumonia into the animal house. It had not been considered necessary to perform routine intracutaneous tuberculin tests, as no case of accidental tuberculosis had ever been recognized among this stock. It is possible that these recent cases of apparent spread of the

FIG. 14.—Primary subpleural tubercle partially healed by fibrosis. Below it and to the left is a nodule of hyperplastic lymphoid tissue. Slightly removed are foci of dust reaction. No spread because no contact between two lesions is established. Exposed to both dust and infection 357 days. Approximately ×20.

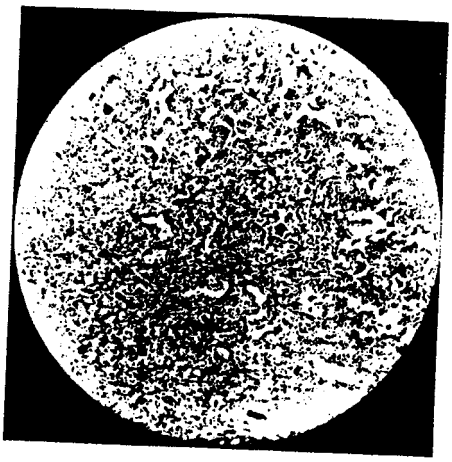

FIG. 16.—Healed fibrous tuberculosis in an area of asbestosis. Simultaneous exposure to dust and infection 838 days. Approximately ×45.

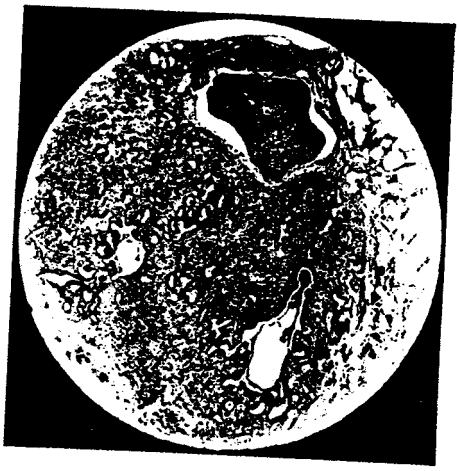

FIG. 15.—Another primary subpleural tubercle from the same lung as Figure 14, which has spread locally into an area of dust reaction. Approximately ×20.

FIG. 17.—Section of uncomplicated asbestosis from same lung as Figure 16, showing more fibrosis than usual. Connective tissue stain. Approximately ×90.

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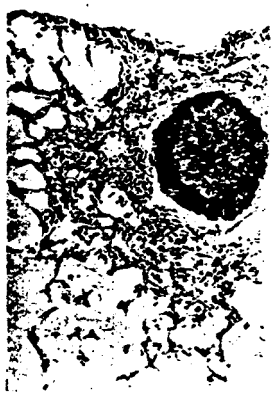

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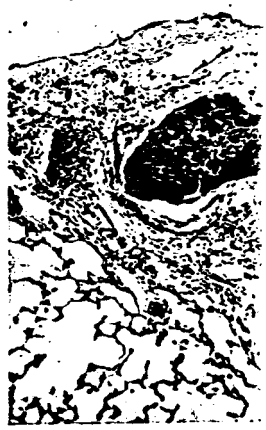

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low virulent artificial tuberculous infection may have been due to previous accidental infection with a more virulent strain. Generalized tuberculosis, however, has always made its appearance only after many months of residence in the animal house. Subinoculation tests are now in progress in an attempt to determine the type of tubercle bacillus responsible for this disturbing manifestation.

But in spite of these occasional instances of disseminated tuberculosis in

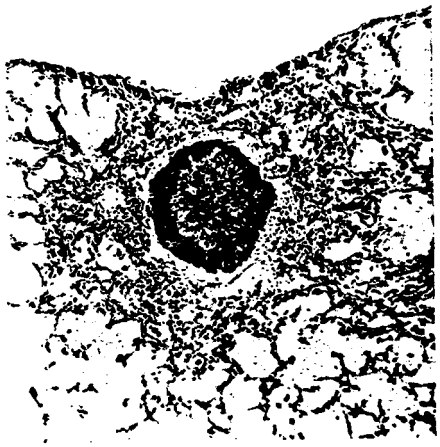

FIG. 18.—Inactive subpleural tubercle in undusted control animal; retrogression has commenced; 654 days after infection. Approximately ×110.

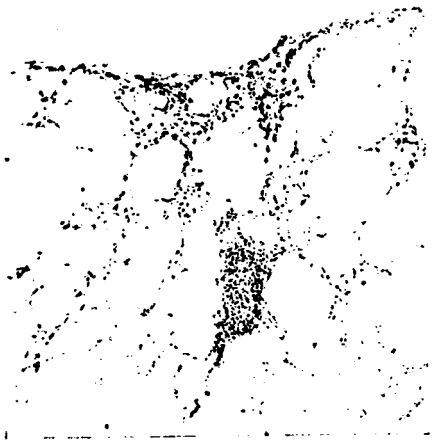

FIG. 20.—Healed subpleural tubercle 654 days after infection. Approximately ×110.

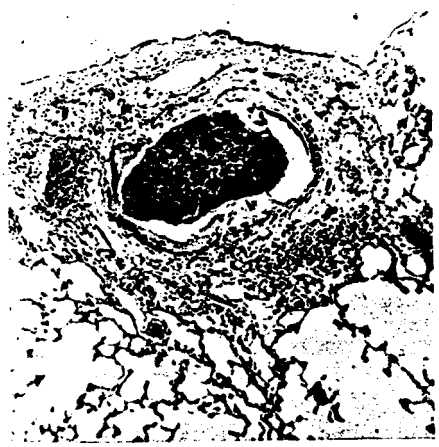

FIG. 19.—Inactive subpleural tubercle in undusted control animal; retrogression has commenced; 654 days after infection. Approximately ×110.

FIG. 21.—Partially healed tubercle in wall of large bronchus. Location atypical; 357 days. Approximately ×130.

the control animals, this method of testing the effect of inhaled dusts upon tuberculous infection is of value. The great majority of the controls not exposed to dust inhalation exhibit nonprogressive pulmonary tubercles which ultimately heal by resolution. On the other hand, almost every animal similarly infected and exposed to the inhalation of quartz dust dies of generalized tuberculosis, unless premature death from epizootic pneumonia, or other causes, supervenes.

In the asbestos dust experiment, two groups of guinea-pigs were infected with the attenuated R_1 strain of tubercle bacilli.[2] One lot of sixty-three normal animals were subjected to inhalation infection, and four days later forty of them were placed in the dusting room where they have been kept under the conditions already described, until death occurred. The remaining twenty-three of this group were set aside in a normal atmosphere as controls to the infection. From this experiment it was hoped that the effect of inhaled asbestos dust upon a tuberculous infection might be determined. In the animals thus exposed, asbestos particles would continue to enter the lungs during the period of tubercle formation. If solution or other chemical reaction should occur, these changes might conceivably affect the activities of the tubercle bacilli.

[2] The method of infection has been described elsewhere (2). The dosage employed for the present infection consisted of six puffs from a DeVilbiss vaporizer containing a suspension of R_1 tubercle bacilli. The water clear suspension was prepared by centrifugation and filtration through paper so that there were from ten to twenty isolated bacilli in each oil immersion field. No clumps were present. The bacilli were grown on glycerin broth, the first group for eight days, the second for twenty-one days.

A second group of twelve guinea-pigs, which had been exposed to asbestos dust for a period of two years under the conditions described above, were infected by the inhalation of an approximately equivalent dose of R_1 tubercle bacilli. At the same time twelve normal animals were infected as controls. Both the previously dusted animals and the controls were then set aside in the general animal room to be allowed to live as long as they would. This second test was designed to demonstrate whether the alterations in pulmonary anatomy and physiology produced by the inhaled dust would affect a tuberculous infection.

Infection Coincident with Dust Inhalation

Of the forty guinea-pigs originally infected and placed in the dusting chamber, thirty-one are now dead. Seven were killed, and the remainder have died of various causes: four of generalized tuberculosis, seventeen with more or less extensive epizootic pneumonia, and the rest from various accidental causes. Nine are still alive and apparently well at the time of this report, two years and three months after infection. Some evidence of spread of the tuberculous process has been observed in ten animals; in six it has been confined to the lungs, while in the other four it involved the abdominal viscera as well. Pulmonary cavity developed in four animals. In most of the cases an extension of the tuberculous infection had occurred at some time previous to death, and subsequent healing resulted in fibrosis of all the secondary lesions. In all the tuberculous animals, even those

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dying with generalized disease, the lesions tend to be fibrous rather than exudative in type.

Of the twenty-three infection controls, twenty are dead. One died after 595 days, of generalized chronic tuberculosis with extensive disease in the spleen, liver, and abdominal lymph nodes. The remaining nineteen succumbed for other reasons. Twelve died of pneumonia and the others from various accidental causes. By the 244th day, the tuberculous lesions in the lungs had healed to such an extent that all evidence of caseation had disappeared. With the one exception noted, the other animals autopsied after this time showed only minute foci of scar tissue at the site of the former tubercles. In two cases there were healed fibrous tubercles of microscopic dimension in the spleen.

The distribution of the primary tuberculous foci in the lungs of the asbestosis group is somewhat atypical; not only are the usual subpleural tubercles formed, but in addition not a few foci are found in the depths of the lung, apparently originating in lymphoid tissues at bifurcation of the bronchial tree (Fig. 21). These pulmonary lesions are associated with the customary lymphatic metastasis to the tracheobronchial lymph nodes, and the development of extensive disease in that location. Many of the pulmonary tubercles are independent of foci of dust reaction and apparently when this occurs, the normal process of resolution is free to proceed. Such foci resolve completely, and ultimately disappear. Others are contiguous to or extend into areas of dust accumulated about respiratory bronchioles. When such contact is established, a reaction much more marked than that produced by either irritant alone is the result. Extensive chronic inflammation and granulation tissue develop, but the dust cells do not migrate into the interior of the tubercle, as in the case of inhaled quartz. Nevertheless, the subsequent course of the tuberculous process is altered. In some instances there is merely an interference with the usual process of resolution, so that excessive fibrosis and calcification of the necrotic central areas result. In other cases, some product is produced (possibly soluble silica) which causes renewed multiplication of the bacilli and a spread of the tuberculous process.

The extension takes place locally about the primary foci of infection (Fig. 15), and there is also metastasis of tubercle bacilli to the peribronchiolar foci of dust reaction (Fig. 7). New tubercles develop in the latter location, which are temporarily progressive and which may even break down to form small cavities. Usually, however, the process tends to come to a standstill, and ultimate healing with fibrosis and considerable anatomic deformity is the result (Fig. 16). The spreading disease is usually confined to limited areas in the lung, and death has with but one exception occurred from other causes. Such endogenous reinfections have first been encountered 203 days after the beginning of the experiment. The last animal of this group studied died on the 838th day, of endemic pneumonia which was strictly localized to one cephalic lobe. The lungs show no trace of subpleural primary foci of infection, but in the deeper portions along the course of the large bronchi are healed fibrous tuber-

cles with plaques of bone and marrow elements in their centers. These have been interpreted as the remains of primary tubercles produced by bacilli which did not reach the periphery at the time of infection because of the obstructing dust in the bronchioles. Elsewhere about respiratory bronchioles are very massive circumscribed foci of fibrosis containing the compressed remains of gland-like air spaces. Whether all of them were once the site of specific tubercle cannot be definitely determined. However, the occasional occurrence of concentric masses of scar tissue enclosing a few giant cells suggests, in some instances, the presence of tubercles. In other organs, the tracheobronchial lymph nodes and abdominal viscera, there are also many non-caseous fibrous tubercles.

Infection Superimposed upon an Established Asbestosis

Of the small group of twelve guinea-pigs infected after two years' exposure to asbestos dust, six died and three were killed during the following forty-eight days. Three of those dying presented an acute non-tuberculous pneumonia involving only one lobe of the lung, and two, an acute hemorrhagic pleural effusion.

Pulmonary tubercles were first found in the fourth animal dying on the thirty-third day; all of the remaining five showed some evidence of pulmonary infection. The majority of the tubercles occurred not in the usual subpleural zone of the lung, but in the areas where dust reaction had already been established. In some instances there are also characteristic subpleural lesions. The peribronchiolar tubercles spread in the preestablished scar tissue, and undergo extensive caseation. Early metastasis to the tracheobronchial lymph nodes occurs and the most extensive foci of reaction are found in this location. In fact, in one guinea-pig dying of an acute pleurisy on the twenty-eighth day no pulmonary tubercles can be discovered, whereas the lymph nodes are heavily infiltrated with masses of epithelioid cells. All the animals dying on and after the thirty-third day show very extensive tuberculosis of the spleen and hepatic lymph.

The infectious process exerts a very noticeable effect upon the reaction to the dust. In all but one of the animals the amount of fibrous tissue about the respiratory bronchioles is much more marked than in non-tuberculous animals exposed for the same period. In two of them, which are uncomplicated by the presence of epizootic pneumonia, the alveolar septums in wide areas peripheral to the foci of localized dust are extremely thick and fibrous.

It is of interest to note the effect of the infectious process upon the asbestosis body. The development of caseation in an area of reaction containing these structures ultimately destroys them. They lose their characteristic golden-yellow color, fail to give a Prussian blue reaction, and are apparently so completely disintegrated that not even a supporting fiber remains. Polarized light fails to reveal refractile elements. In the walls of small tuberculous cavities developing in foci of dust reaction, the various steps in the destruction of the asbestosis body can be studied. The cause of their disappearance has not been determined but it is possible that the change in

hydrogen ion concentration incident to caseation may favor solution of the foreign bodies.

Discussion

The physical and chemical properties of asbestos are so unlike those of any other dust previously studied that, when inhaled, particles of this substance provoke an unusual type of reaction in the lung.

Localization of Dust

The fact that a fiber as long as 100 and even 200 microns can be inhaled and ultimately reach the finer branches of the bronchial tree is surprising and controverts the accepted ideas of the effectiveness of the upper respiratory protective mechanism. Whether such structures enter the lung in full extension, or whether they are partially coiled has not yet been determined. Coiled fibers do not occur in the dust itself. In any case, it is difficult to imagine a structure of such dimension making its way against the normal current of ciliary action. It is generally assumed that prolonged inhalation of dust provokes a chronic bronchitis, but in the case of asbestos dust no morphologic evidence of such a change has been observed within a period of two and one-half years. It is quite possible that the physiologic activities of the ciliated epithelium may be altered without demonstrable anatomic changes. In support of such a view is the fact that very long fibers have not been discovered in the deeper portions of the lung until the dust inhalation has been in progress for several months.

Unlike other dusts, asbestos fibers trate into the ultimate divisions of the primary units of the lung; the major part of them come to rest in the respiratory bronchioles. It will be recalled that these structures are lined, not by ciliated, but by smooth cuboidal epithelium, and that at intervals along their walls are the openings of a variable number of alveoli. As a result, the bronchial tube at this point is no longer smooth walled, but is very irregular in contour. This roughness is probably at least one of the factors responsible for the arrest of the elongated spicules and fibers which catch in the openings of the lateral alveoli. In marked contrast with this is the behavior of a particulate dust like quartz, the major portion of which passes through the lumen of a respiratory bronchiole and enters the alveolar duct and its further ramifications.

Having come to rest, the asbestos particles are ingested by free alveolar phagocytes. As so much of the material consists of elongated fibers, giant cells are very prone to develop. Within the cytoplasm of these cells the chemical changes responsible for the development of that unique structure, the asbestosis body, occur. The process requires a period of approximately two months before the characteristic alterations are produced.

Chemical Reaction and Asbestosis Body

That the changes in the inhaled material are truly chemical in nature is indicated by the appearance of dissolved iron in the cytoplasm of certain phagocytes at a time previous to the appearance of the asbestosis body. The presence of the iron imparts a

and it reacts specifically with potassium ferrocyanide and dilute hydrochloric acid.

As previously noted, study of the structure of the asbestos fibers indicates that iron occurs in intimate combination with silica, and even in the best grade of chrysotile it actually replaces some of the magnesium. Chemical changes involving one constituent of the asbestos molecule must affect its other components. The presence of iron uniformly distributed throughout the cytoplasm of a phagocyte may indicate either hydrolysis of the ingested dust or solution of at least part of the original constituents and a subsequent release of silica. This silica may exist in any of several physical states, as soluble, colloidal, or insoluble silica, or as soluble silicate. By study of the chemical structure and the method of formation of the asbestosis body, it should be possible to discover the actual mechanism by which structural alteration of an inhaled silicate occurs.

The asbestosis body has been subjected to various chemical tests by several investigators. Cooke (9) and McDonald (10) first described this unusual foreign body and stated that it did not stain with aniline dyes, but gave a marked iron reaction. They also noted that it was not doubly refractile. McDonald (10) and Simson (11) also presented a theory for the formation of the golden-yellow bodies from asbestos. Stewart (12) claimed the presence of asbestosis bodies in histologic sections of lung as diagnostic of pulmonary asbestosis. Cooke (13) later called attention to the relation between the iron content of asbestos dust and the iron reaction of asbestosis bodies. He noted that they were not digested by trypsin and that they contained less iron than chrysotile. He also noted that they failed to cast a characteristic pattern when treated by the X-ray diffraction method of Bragg, though a central fiber could be demonstrated with a dissecting microscope. He therefore concluded that they were fibers of vegetable origin covered with colloidal aggregates of adsorbed blood proteins. Stewart (14) replied to Cooke's suggestions, and stated that all the reported cases of asbestosis had exhibited these curious structures. Stewart (15) later noted that antiformin did not destroy them. Gloyne (16) stated that the asbestosis body withstood calcination, but lost its golden-yellow sheath after treatment with concentrated sulphuric acid, leaving a thin central fiber. He reported the body as refractile on dark ground illumination.

We have been able to confirm many of these findings, and we have also attempted to prove conclusively whether or not the asbestosis body contains organic matter. Since it resists calcination without change in configuration or color, and since it is not digested with either pepsin and hydrochloric acid or trypsin, it is not to be regarded as protein in nature. Moreover, asbestos fibers fail to adsorb proteins when placed in blood or peptone broth media for several months. This curious structure is not soluble in any of the usual organic solvents[3] and fails to show charring with sulphuric

[3] It will be recalled that the asbestosis bodies and even their supporting fibers ultimately disappear in an area of tuberculous necrosis. The explanation is not entirely clear but solution may be due to a high degree of alkalinity created in the degenerated cells.

acid. Consequently, it is considered to be an inorganic structure. Inasmuch as a central fiber can be readily demonstrated in nearly all instances, the body is undoubtedly derived from asbestos.

The marked iron reaction of the asbestosis body is not to be confused with that obtained on the dust previous to contact with the animal body. In its original state the iron in the fibers is almost wholly in the ferrous state, while in the asbestosis body only ferric iron can be detected. This structure is therefore regarded as an oxidation product of the original dust.

In an attempt to prove whether the iron of the asbestosis body was already present in the fiber or whether it was derived from animal tissues, the experiment was made in which asbestos fibers, freed from iron by leaching with hydrochloric acid, were injected into the subcutaneous tissues of guinea-pigs as noted above. It was unsuccessful because the acid treatment rendered the asbestos soluble in the body fluids, and no significant reaction occurred. One month after the injection, practically no trace of the fibers could be discovered and only a very slight fibrosis marked the site.

Treatment of asbestos fibers for the determination of free silica disclosed the ease with which the chrysotile molecule could be opened. If enzymatic action or hydrolysis of the fiber is assumed to take place in the presence of body fluids, it is quite possible that the ferrous or ferric silicate existing in the fiber is oxidized and hydrolyzed directly to produce the asbestosis body.

As evidence that hydrolysis or partial solution of the inhaled dust is responsible for the development of the asbestosis body, the following observations may be cited. When studied by Bragg's X-ray technic, asbestos fibers exhibit a characteristic crystalline pattern which is lost upon treatment with acid. Cooke (13), using the same method, showed that asbestosis bodies exhibit no crystalline structure. Ray and Ganguly (17) state that precipitates formed from solutions of ferric chloride and sodium silicates, which are identical in color with the asbestosis body, also yield no crystalline pattern by X-ray. As further evidence of physical alteration is the fact that the asbestos fiber is highly refractile in polarized light, whereas the asbestosis body has completely lost this property.[4]

We have attempted to reproduce the

[4] It has been assumed that the demonstration of iron in the outer coating of the asbestosis body is evidence of hydrolysis of the original asbestos fiber on which the body formed. But actually this finding does not constitute definite proof unless an endogenous source from blood pigment can be excluded. We have thus far failed to eliminate this source of iron. However, the demonstration of magnesium in the asbestosis body would furnish equally convincing proof of hydrolysis and the objection that it was derived from the tissues could hardly be raised, for the amount of this substance in the body is extremely small. An attempt has, therefore, been made to develop a microchemical test for magnesium. It has been found that both asbestos fibers and asbestosis bodies are definitely stained a light blue-green color when treated on microslides with a dilute hydrochloric acid solution of para-nitro-benzene-azo-resorcinol followed by a bath of sodium hydroxide.

The presence of magnesium in the outer layers of the asbestosis body is convincing proof of hydrolysis of the inhaled dust. This color reaction is given only by magnesium, cobalt, and nickel, substances which do not occur in sufficient concentration in the tissues to cause reaction. Therefore, endogenous sources for the coating material of the asbestosis body are assumed to have been eliminated.

asbestosis body from asbestos fibers by immersing them for prolonged periods in buffer solutions of various hydrogen ion concentrations, both above and below neutrality. The solutions have been adjusted with agar and silica gel to a viscosity near that of the cell. Oxidizing agents have been added and the reaction has been allowed to proceed in the incubator for six months. No golden-yellow structures were obtained.

We have, however, been able to reproduce the structure of the asbestosis body quite closely by other means. Iron free asbestos fibers are impregnated with an iron salt by heating to dryness in a dilute ferric chloride solution and ignited. The fibers are then placed in a solution of sodium silicate. The iron salt adhering to the fibers reacts rapidly with the silicate, producing a curiously shaped golden-yellow structure which very closely resembles the asbestosis body (Fig. 13, Nos. 1 and 2).

A similar reaction is involved in the production of the familiar phenomenon, the "silicate garden" (18). If a crystal of ferric chloride is added to a solution of sodium silicate, golden-yellow filaments, often several inches in length, rapidly develop, which exhibit irregular swellings and buds. Ferric silicate is probably formed. This product is partially hydrolyzed, producing a thin wrinkled skin of silicic acid streaked with ferric hydroxide. This skin, acting as a semipermeable membrane, permits diffusion to take place and a high osmotic pressure develops with a consequent rupture of the membrane. Further hydrolysis occurs and the reaction repeats itself until finally the membrane becomes impermeable.

Microscopic structures of fibrous character, suggesting asbestosis bodies, have been produced both with dilute solutions of an iron salt and a soluble silicate, and with iron and silica sols (19).

These observations lead us to conclude that the asbestosis body is a derivative of the crystalline asbestos fiber which has been oxidized and hydrolyzed to a golden-yellow amorphous structure. As such, it can be regarded as the first direct evidence of altered chemical composition in an inhaled silicate dust.

In the animal body, the evidence thus far accumulated would indicate that the lung of the guinea-pig and of man furnishes the most favorable environment for the development of the asbestosis body. Asbestos fibers transported from the lung to the tracheobronchial lymph nodes do not ordinarily appear to produce these structures. Possibly prolonged residence in the lung has deprived them of their capacity for further reaction, or possibly some necessary factor is lacking in the lymph nodes. It is believed that the few asbestosis bodies found in the nodes were transported after attaining full development in the pulmonary air spaces. Injection of asbestos dust into the peritoneal cavity of guinea-pigs has failed to produce characteristic structures in any quantity. In the subcutaneous tissues they do develop, but the period of incubation is nearly twice as long as that required in the lung. Practically no asbestosis bodies have formed in the lungs of rabbits and albino rats. The necessary environmental factors which are lacking in

any of these situations are entirely unknown.

Attempts to determine whether the asbestosis body will develop in the animal when any of the theoretically necessary elements are lacking have thus far met with little success. The experiments *in vitro* indicate that crystalline ferric or ferrous silicate in a medium of proper viscosity and a fiber for support are probably essential to the production of these structures. In our attempt to determine whether iron derived from the tissues could be substituted for the iron inherent in the chrysotile molecule, we have been defeated by the fact that the manipulation necessary to remove the iron from the fiber apparently renders that structure soluble in the body fluids.

The injection and the inhalation of dark Barre granite dust, which contains both free silica and iron, have never resulted in the formation of structures in any way suggesting asbestosis bodies. The solution of iron can be demonstrated by microchemical tests and it generally is assumed that the silica is also ultimately dissolved. Intraperitoneal injections of granite from Lorain County, Ohio, have been made because this material contains iron in the unusual form of ferrous carbonate. No suggestion of an asbestosis body has been discovered. In the light of subsequent studies, it is now recognized that the peritoneum is not a proper location for such a test, and subcutaneous inoculations have already been made with this substance, but it is too early to report on them.

Thus far, it would appear that the mere presence of iron and free silica is not sufficient for the production of asbestosis bodies.

Pulmonary Fibrosis

That the long-continued inhalation of asbestos dust is responsible for the development of pulmonary fibrosis is now unquestioned. From many parts of the world come radiographic reports of fine fibrosis in the lungs of persons exposed by occupation to the inhalation of this substance. The findings from at least ten postmortem examinations have furnished reliable evidence that the shadows seen in the roentgenogram are produced by areas of fibrous tissue (20). In guinea-pig experiments reported in this paper, it has been shown that the fibrosis begins in those portions of the lung where the dust is localized, and that this reaction can be detected in X-ray pictures after about two years' exposure to the concentration of dust used (Fig. 3).

The earliest evidence of proliferation of fibroblasts has been encountered approximately 500 days after the commencement of the dust exposure. It first appears in the immediate vicinity of the largest accumulations of dust cells, which occur in the respiratory bronchiole and its adjacent alveoli. As increasing amounts of dust accumulate in the walls of these structures, the amount of fibrosis is likewise increased. In the otherwise normal guinea-pig, migration of dust cells to intrapulmonary lymphoid tissue has not been encountered, and in consequence the nodular foci of fibrosis, which are so characteristic of the reaction to quartz dust, fail to develop. The occurrence, in one of the last animals killed, of a more diffuse fibrosis peripheral to the point of

maximum dust deposition suggests that collapse induration incident to occlusion of respiratory bronchioles may play an important part in the later stages of the disease process.

Asbestos dust, a silicate of magnesium, is relatively soluble in fluids comparable with those of the tissues. The asbestosis body develops only after solution has occurred in the proper environment. The development of these structures in the lungs of guinea-pigs and of human beings is the first direct evidence of solubility of an inhaled dust known to produce pulmonary fibrosis. It still remains to be demonstrated whether a dissolved substance is the factor responsible for the multiplication of fibroblasts in pneumonokoniosis. In this connection the evidence from asbestos inhalation in the rabbit should prove most valuable. If, after a proper period of exposure, typical asbestosis bodies should still be lacking, and if fibrosis should likewise fail to develop, it would be logical to conclude that fibroblasts were not stimulated because no solution of the dust had occurred. Thus far, the reaction of the rabbit has only been studied during an exposure period of 330 days. The only sign of asbestosis body formation is an irregular swelling of certain fibers which give microchemical tests for iron; evidence of fibrosis is entirely lacking. The 500-day period of exposure, when true fibrosis appeared in the guinea-pig, is anxiously awaited.

Comparison between Reactions to Asbestos and to Other Dusts

Granite dust, which is known to provoke the formation of extensive fibrosis in human beings, appears to act more slowly than asbestos in the guinea-pig. After 910 days, the maximum period of experimental exposure to granite, the lungs show large masses of dust filled phagocytes lying in the lumen of the alveoli along the alveolar ducts and atria. In the adjacent septums there is a slight thickening due to the presence of lymphoid and monocytic cells, but fibrosis is entirely lacking. The significant feature is the *absence of dust particles in the connective tissues of the lung.* In the tracheobronchial lymph nodes, on the other hand, dust accumulates in such quantities that fibrosis develops within one year, and after two years' exposure the lymphoid tissues are largely destroyed by a series of true silicotic nodules. It has been postulated that fibrosis has not developed in the lung of the animal exposed to granite because the dust particles do not come into sufficiently intimate contact with the fibroblasts of the alveolar walls. In the lymph nodes, on the other hand, fibrosis begins early, and typical silicotic nodules are produced because heavy concentrations of dust are brought into close proximity with connective tissue elements.

The conditions of the experiments with granite and asbestos dusts would theoretically favor a greater reaction in the former case. The concentration of granite dust was over eight times as great as that of asbestos (287,700,000 particles less than 1.5 microns in diameter per cubic foot of air for granite and only 34,466,000 particles of the same size for asbestos). However, the greater solubility of magnesium silicate, together with its peculiar localization, probably is the

factor responsible for the production of the more rapid and extensive pulmonary fibrosis by asbestos dust.

Quartz, which is generally accepted as the most active of all the nontoxic dusts which are inhaled in industry, is much less easily dissolved than asbestos, and yet it will produce extensive fibrosis in the lungs of experimental animals more rapidly. In guinea-pigs, pulmonary fibrosis, and even necrosis, has been observed after one year's exposure to quartz dust; in rabbits, typical silicotic nodules are formed in eighteen months. The difference in the rate of reaction to quartz and asbestos has been ascribed to several causes. With equivalent concentrations of dust in two given atmospheres, more quartz than asbestos particles will be inhaled and reach the parenchyma of the lung. This is presumably due to the relative differences in the shape and the surface characteristics of the particles. After phagocytosis, quartz particles seem to possess the ability to stimulate a rapid migration of the dust cells, so that they concentrate large masses of dust about nodules of intrapulmonary lymphoid tissue. Here again, but by a different mechanism, the foreign bodies are collected in circumscribed areas. Subsequently, perhaps as the result of solution of the quartz, a local proliferation of fibroblasts takes place.

Carborundum dust has produced no pulmonary fibrosis after exposure as long as three or four years. In the lung, it is treated much like granite dust, collected in phagocytes which remain within the air spaces, so that the dust cells establish no contact with the underlying connective tissue. In the tracheobronchial lymph nodes, carborundum does excite fibrosis, and structures suggesting silicotic nodules have been discovered. As in the case of granite, proliferation of fibroblasts occurs at the point where they are in intimate contact with sufficient numbers of dust laden phagocytes. Whether solution of carborundum by the body fluids is possible has never been determined.

From these observations on the reaction to various types of dust, an hypothesis has been developed that fibroblasts proliferate in response to sufficient concentrations of a soluble substance liberated by the action of the phagocytes on the included dust particles. The soluble substance probably diffuses through the membrane of the intact phagocytes, but it is only stimulating to fibroblasts in the immediate vicinity. The undefined soluble substance, possibly silica in some form, is rapidly neutralized after leaving the cells in which it is produced, and it exerts no effect upon more remote connective tissue elements. The process of neutralization may be chemical in nature or it may be a result of absorption by some other type of cell which is itself unaffected.

Theoretical Consideration of Pneumonokoniosis

In a previous paper dealing largely with the reactions to granite and carborundum dusts (21), it was suggested that the primary lesion of pneumonokoniosis consists in the development of an obstructive fibrosis in the tracheobronchial lymph nodes attended by stasis in the afferent lymphatics in the lung, and ultimately followed by a perilymphatic fibrosis. When only these two types of dust had

been studied, such an hypothesis looked tempting, for the only trace of fibrosis in the lung in these cases was situated about the large lymph trunks. Masses of dust filled phagocytes lay for many months in the air spaces, and apparently provoked not the slightest reaction of the connective tissues. But subsequent experimental investigation has modified this concept; it is now believed that fibrosis develops wherever sufficient amounts of dust of the proper type come into intimate contact with fibroblasts. The primary obstructive lesion in the tracheobronchial lymph nodes occurs with quartz inhalations but not with asbestos. Undoubtedly such a lesion hastens the development of reaction in the lung, for it reduces elimination and concentrates the dust, but it is not essential to the production of pulmonary fibrosis.

One further point in connection with the state of the lymphatics deserves comment. In experimental asbestosis, both in the guinea-pig and in the rabbit, the lymph vessels are widely dilated after as short an exposure as from thirty to sixty days. Inhaled asbestos dust is not transported to the tracheobronchial lymph nodes in any considerable quantity, and no obstructive lesion has been produced at this time. Therefore in this case the dilatation of these vessels must have some other cause; possibly it is merely a physiologic response to intrapulmonary irritation. Asbestos filled phagocytes do not enter these channels because they are apparently relatively inactive, but epithelioid cells containing tubercle bacilli may leave the lung in great numbers. Apparently the lymphatic channel of escape is open to the asbestos dust cells, but for causes inherent in themselves, they do not migrate to these vessels.

Tuberculous Infection and Asbestosis

Where inhalation infection is instituted simultaneously with commencement of dust exposures, the majority of inhaled tubercle bacilli localize in small peripheral lymphoid masses in a zone immediately beneath the pleura. This is characteristic of such infection with the organism used in the experiment. A certain number come to rest atypically in the deeper lymphoid tissues along the intermediate bronchi, possibly because they are mechanically arrested by inhaled dust particles. The majority of the tubercles formed undergo spontaneous resolution which is the outcome of the infection in most normal control animals. A certain number of tubercles by accident localize in proximity to foci of localized dust. If the contact is sufficiently intimate, these tubercles spread locally and more remotely into foci of dust reaction about respiratory bronchioles. A new crop of tubercles develop in this location, and these may progress and even form small cavities, but the ultimate outcome is usually healing with more or less extensive fibrosis and calcification. The tuberculous process is practically never generalized throughout the lung, but is generally confined to small nodular foci. Blood stream metastasis is usual and macroscopic disease in the spleen and sometimes in the liver is common, an occurrence almost never found in infection controls. In the thirty-one animals of this group dead at the time of this report, a spread of the tuberculous infection occurred in 32.2 per cent. In

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n 32.2 per cent. In 40 per cent. of them, the tuberculosis had subsequently more or less completely healed by fibrosis. It seems probable that in the remaining members of the group a similar result would have been attained had they not died prematurely from accidental causes.

Where inhalation infection was superimposed upon a well-established asbestosis of approximately two years' standing, the primary localization of the tubercles was atypical. Many of the tubercle bacilli were mechanically held up by the reaction to the dust in the respiratory bronchioles. It would appear that many, perhaps the majority, of these organisms were phagocytosed and carried directly into the distended lymphatic trunks. The earliest manifestation of tubercle formation occurred not in the lung, but in the tracheobronchial lymph nodes, a condition which has never before been observed in experimental inhalation infection. Some organisms localized in the foci of dust reaction and then produced tubercles; a certain number of bacilli passed to the periphery, where typical subpleural lesions developed. The major portion of the guinea-pigs comprising this group died or were killed during a period of forty-eight days after infection. Within this time not much extension of the intrapulmonary infection had occurred. The tracheobronchial lymph nodes were heavily involved in all animals dead after the thirty-third day. It is too early to state what will be the ultimate outcome of infection superimposed upon a preestablished asbestosis.

From these experiments, it would appear that inhaled asbestos dust is capable of exerting some stimulating effect upon tubercle bacilli of attenuated virulence. To exert this effect, the dust and the tubercle bacilli must be brought into rather intimate association. This occasionally occurred when the infection and the onset of the dust inhalation were simultaneous; it was much more common where infection was superimposed upon an already established asbestosis. The dust, perhaps by the action of its dissolved products or by alteration in tissue reaction, initiates a renewed proliferation of the tubercle bacilli, and the infection spreads. But this stimulating effect is only temporary and ultimately the foci of new disease tend to heal by fibrosis. In this respect, inhaled asbestos dust differs from quartz, which incites continued and progressive multiplication of the bacteria and consequent spread of disease.

As has been observed with the other types of dust (granite and carborundum), the presence of asbestos in the lung of an animal infected with tubercle bacilli promotes more extensive fibrosis than is produced when either the organism or the dust is acting alone. Where the two irritants are concentrated in the same area, each provokes the formation of granulation tissue which ultimately organizes to form fibrosis. But even in areas of dust reaction remote from the site of tubercle, the fibrosis is excessive, an effect for which explanation is lacking. (Figs. 15 and 16.)

Summary

Guinea-pigs have been exposed for eight hours daily for periods as long as two and one-third years to an atmosphere containing approximately thirty-five million particles per cubic foot of

asbestos dust (Canadian chrysotile) 1.5 microns and less in diameter. Rabbits and albino rats have likewise been exposed for shorter periods (330 days).

The experiments demonstrate that fibrous structures at least as long as 200 microns can pass the protective mechanism of the upper respiratory tract and enter the lung. Anatomic evidence of injury to this mechanism is wanting.

Inhaled asbestos dust does not penetrate to the terminal alveoli of the lung as is the case with a particulate substance such as quartz. The major portion is held up in the respiratory bronchioles. There phagocytosis takes place, and there the material remains localized, at least for a period of two and one-third years. Phagocytes containing asbestos particles migrate into the lateral alveoli given off from the walls of the bronchioles, and considerable numbers ultimately penetrate the adjacent connective tissues. In the guinea-pig, transportation of dust particles to intrapulmonary and mediastinal lymphoid tissues is so slow that changes in these structures play little part in the early development of asbestosis. In the rabbit, dust cells begin to appear in the lymphoid tissues of the lung within sixty days after the commencement of the inhalation; thereafter, they continue to migrate in increasing numbers.

In the guinea-pig, fibrosis in the walls of the respiratory bronchioles and their lateral alveoli is first manifested after 500 days' exposure. Thereafter this type of reaction progressively increases in intensity and extent. The resulting atelectasis is responsible for a gland-like appearance, which is due to the contraction of the included alveoli and a consequent compression of the epithelial lining cells. In the rabbit sufficient time has not yet elapsed for fibrosis to be expected.

In the lungs of guinea-pigs, asbestosis bodies, apparently identical with those described in the human being, have developed after an exposure of approximately seventy days. In the rabbit these structures have not been discovered after exposures as long as 330 days. In the albino rat they are very rare. Only two small typical forms have been discovered in one animal exposed for seventy days. The prevalence of chronic infections of the lung in all members of this series is possibly responsible.

Asbestosis bodies apparently fail to form in the tracheobronchial lymph nodes of guinea-pigs. They may be transported in small numbers to these tissues and to areas of chronic pleurisy. They have not been discovered in the peritoneal cavity 100 days after injection of dust. In the subcutaneous tissue of the groin, typical forms were found 102 days after the injection of 3 mg. of dust.

Asbestosis bodies are not present in asbestos dust previous to contact with animal tissues. They are produced by oxidation and hydrolysis of the chrysotile molecule. The formation of these structures is the first direct evidence that the body is capable of effecting changes in inhaled silicate particles. The chemical processes involved have been discussed *in extenso*. Attempts at artificial production of asbestosis bodies *in vitro* have been partially successful; solutions of ferric chloride and sodium silicate have been made to combine in the presence of a fiber to pro-

duce more or less typical forms. The asbestosis body is therefore analogous to the well-known "silicate garden." Attempts to produce asbestosis bodies *in vivo* by the injection of dusts containing iron salts and silicates have thus far failed. The failure to produce them in tissues other than the lung and subcutaneous tissues of guinea-pigs and man has not been explained.

Comparison between the localization and the reaction to asbestos and other types of inhaled dusts has been shown. The points at which inhaled dust is localized in the lung or lymph nodes vary with the type of dust. Granite remains within the pulmonary air spaces and produces no local reaction of fibroblasts for several years. In the tracheobronchial lymph nodes characteristic silicotic nodules develop within two years. Carborundum likewise has failed to affect the stroma of the lung even in four years, but fibrosis in the lymph nodes has been observed. Quartz is rapidly concentrated by migrating phagocytes in the pulmonary and mediastinal lymphoid tissues. In these places it provokes an early and rapid multiplication of fibroblasts. Asbestos, as it is inhaled, is concentrated in respiratory bronchioles and their lateral alveoli. Phagocytes carry it into the walls, where fibroblasts are stimulated.

Lymph stasis plays little part in early asbestosis; the structure of this dust tends to localize it within the lung from the start. Lymph vessels are dilated in the absence of detectable obstruction. The dilatation may be a direct result of pulmonary irritation.

Primary tuberculous infection is influenced only to a limited degree by inhaled asbestos. This conclusion has been reached after inhalation infection with attenuated tubercle bacilli (strain R_1). In normal guinea-pigs such infection produces tubercles in the lung and tracheobronchial lymph nodes comparable to the "primary complex" in man. The lesions caseate and the pulmonary foci heal by resolution. Spread of the infection with macroscopic disease in other viscera is very rare. In the asbestos experiment, one group of guinea-pigs was infected at the outset of dust inhalation; a second group, two years after the commencement of dust exposure. In the first series, 32.2 per cent. of the animals showed some evidence of spreading tuberculosis. New disease began as a local extension from primary tubercles and metastasis to areas where dust reaction had occurred was common. Rarely small cavities developed in the secondary foci. The tendency to healing by fibrosis was marked; at autopsy 40 per cent. of the cases showed healed fibrous tuberculosis; macroscopic disease in the spleen and sometimes in the liver was common. The contrast with animals similarly infected but exposed to quartz dust is marked. In them every exposure longer than five months resulted in generalized chronic tuberculosis of the lungs and other viscera.

For the second asbestosis group infected, the localization of tubercles was atypical. Many bacilli were trapped in foci of dust reaction. Some produced local tubercles; others immediately entered the dilated lymph vessels and were transported to the tracheobronchial lymph nodes. Tuberculosis in these nodes sometimes occurred without involvement of the lung. Early disease in the spleen and hepatic lymph nodes was the rule.

The ultimate outcome of infection in this group has not yet been observed.

The combined action of asbestos dust and tubercle bacilli in the lung produced more fibrosis than did either agent acting independently.

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THE SO-CALLED CYANIDE RASH

The Editor,
Journal of Industrial Hygiene.

Sir:

Braddock and Tingle's article on "So-Called Cyanide Rash in Gold Mine Mill Workers," in the JOURNAL for September, 1930, interests me because I can add sixteen years' personal experience and observations from New Zealand and the state of Western Australia to the other countries listed. As a cyanide salt we first used potassium cyanide, but this was superseded, as in all countries, by sodium cyanide. The solutions were a stock liquor of up to 20 per cent., from which the working solutions of 0.1 to 0.2 per cent. were made. Ordinarily, these working solutions were cold, but when in some plants the roasted ore was mixed therewith, the solutions became hot and remained warm to the end of the process. An odor of cyanide pervades every gold or silver ore treatment plant, and renders smoking unpleasant. As Braddock and Tingle conclude, the rash appears to be a dermatitis—that is, it is a superficial ailment; the blood is not a factor. I had the rash more or less severely on the arms and face, especially at the hair roots; others had it there and on the legs. Drinkers and nondrinkers, and smokers and nonsmokers alike were affected, but not everyone employed around cyanide. As far as my observation went, as one handling cyanide salts and solutions, also as a foreman and metallurgist, there was no lack of personal cleanliness among the men, as suggested. Some men became immune to the rash after being affected for a time; others had to change their jobs. The wearing of rubber gloves helps, but they induce sweating which often starts a rash. As a rule, we used potassium permanganate solution, but zinc oxide ointment also alleviated the trouble which, as Braddock and Tingle conclude, is probably due to irritation by the strong caustic, excited by lime used in the process. We never considered it as cyanide poisoning, but simply a skin outbreak.

M. W. VON BERNEWITZ

Pittsburgh, Pa.
December 19, 1930.

or from some other source of approved in writing by the local ity of the district in which the is situated, which shall be laid on, or contained in a suitssel:

Except where the water is de- in an upward jet from which rkers can conveniently drink) one suitable cup or drinking at each point of supply, with s for rinsing it in drinking

drinking water supply shall be narked "Drinking Water."

racticable steps shall be taken rve the water and vessels from ination.

e occupier shall make such arnts for first aid treatment of to persons *employed* as will with the requirements laid r factories in Section 29 (i) of rkmen's Compensation Act, d in addition shall see that t aid box is provided with a t supply of ointment and imle waterproof plaster.

very person *employed* shall ined by the *Surgeon* once in urteen days, or at such other as may be specified in writing Chief Inspector of Factories, of which due notice shall be ll concerned, and such examihall normally be made at the r workshop.

ealth Register containing the all persons *employed* shall be form approved by the Chief of Factories.

person after *suspension* shall *ed* without written sanction *Surgeon*, entered in or at- the Health Register.

9. A young person under the age of 18 years shall not be allowed to work at a *bath*.

Provided that this Regulation shall not apply to any young person already so employed on August 1, 1931.

10. The occupier shall see that the official Cautionary Placard as to the effects of chrome on the skin is affixed in the works in such a position as to be easily read by the persons *employed*, and shall arrange for inspection of the hands and forearms of all persons *employed* to be made twice a week by a responsible person, and for a record of such inspections to be kept in the Health Register.

Part II

Duties of Persons Employed

11. No person employed shall misuse or without the concurrence of the occupier or responsible person in charge interfere with any appliance provided in pursuance of these Regulations.

12. Every person *employed* shall wear the protective clothing provided under Regulation 3, and shall deposit the protective clothing when not being worn in the place provided under Regulation 4.

13*a*. Every person *employed* shall present himself at the appointed time for examination by the *Surgeon* in pursuance of Regulation 8*a*.

b. No person after *suspension* shall work in any process involving contact with liquid from any *bath* without written sanction from the *Surgeon*, entered in or attached to the Health Register.

SUBJECT INDEX TO VOLUME XIII

This is a subject index to all the reading matter in the ABSTRACTS OF THE LITERATURE OF INDUSTRIAL HYGIENE, and one should, therefore, look for the subject word. The name of the author follows the subject entry in parenthesis.

For author index, see page 288.

tained in a second wash bottle. By passing a known quantity of air through these two solutions, sulphur dioxide and hydrogen sulphide at concentrations, respectively, of 0.017 to 0.6 mg. and 0.092 to 0.6 mg. per liter can be evaluated with satisfactory accuracy by determining the sulphuric acid formed.—P. D.

INJURIES FROM URSOL IN THE FUR INDUSTRY. *R. L. Mayer and M. Förster. Abstr. as follows from Zentralbl. f. Gewerbehyg., June, 1929, N. S. vol. 6, pp. 171–178, in Bull. Hyg., July, 1930, vol. 5, p. 571.*

Ursol is the commercial name given to metaphenylenediamine and is regarded as a frequent cause of dermatitis. The authors emphasize the importance of functional tests applied to the skin in addition to mere reliance on the family and occupational history. If such testing is applied, the number of cases alleged to be due to ursol falls considerably. The diagnosis "ursol poisoning" from the history is no more to be relied on than a diagnosis of lead poisoning from the presence of punctate basophilia.

Altogether 181 persons employed in the fur trade were examined, of whom 111 in the course of their work had suffered from dermatitis or asthma. Of these 111, 45 per cent. showed existence of eczema and 38.7 of asthma; a combination of the two was found in 16.2 per cent. On testing their skins with a small piece of 2 per cent. paraphenylenediamine vaseline, 44.1 per cent. showed hypersensitization to ursol. Forty-six per cent. of those with eczema gave positive reactions, 30.2 of the asthmatics, and 72.2 per cent. of those who showed presence of both conditions.

The authors regard 44.1 per cent. as directly due to ursol and 55.8 per cent. doubtfully so. The general question of sensitization of the skin is then discussed in particular relation to ursol.—T. M. L.

DUST HAZARDS AND THEIR EFFECTS

COAL-MINER'S LUNG. AN INVESTIGATION INTO THE ANTHRACOTIC LUNGS OF COAL-MINERS IN SOUTH WALES. *S. L. Cummins and A. F. Sladden. Jour. Path. and Bacteriol., 1930, vol. 33, pp. 1095–1132.*

This study of the black lung of coal miners is unusually thorough. It is based on an examination of lungs from thirty-eight cases, many of whom died accidentally. In addition to the pathologic examination, analysis of thirty-four of the lungs was carried out. Details of these analyses are given, and form the most extensive series of such analyses yet published. Eleven excellent illustrations are given of the macroscopic and microscopic conditions seen. The paper opens with a useful historical résumé of earlier references to anthracosis and other forms of dust diseases. The authors hold that the blackness of coal miners' lungs is due to coal; any iron present is quite in subsidiary amounts. Frequently fibrosis is present, caused by dusts other than coal, and particularly by silica from intervening rocks. Such fibrosis blocks the lymph flow of the lungs, and coal dust collects in abundance in such lungs. Normally coal dust is fairly rapidly removed from healthy lungs, but it may so collect in a fibrotic lung as to form a nodule of coal. At times local necrosis takes place, with cavitation quite apart from any tuberculous infection. Discharge from such cavities accounts for the black sputum of miners. Wherever the coal particles were found most concentrated, analysis showed the content of silica to be particularly high. The conclusion is reached that anthracosis is not a simple condition, but exists only as a subdivision of lung fibrosis usually due to silicosis. Probably the lungs of miners interfered with by different dusts account for the high death rates from pulmonary diseases, particularly bronchitis, among coal miners on certain fields, even though their death rate from tuberculosis is usually low. Nevertheless, a condition of anthracosis may be pronounced without interfering with the general health.—E. L. C.

ASBESTOS AND PULMONARY ASBESTOSIS. *V. Dhers. Méd. du travail, July, 1930, vol. 2, pp. 147–172; Sept., 1930, pp. 187–209.*

In this long article the author usefully summarizes information relating to the occurrence of occupational asbestosis. A history of the use of this mineral and its properties is given, together with its chemical composition. Then a description follows of the industrial uses to which it is put, during which dust may be generated, particularly during weaving operations. The lungs of workers become affected in direct proportion to the length of time they have been exposed to it, until after twenty years of work 80 per cent. are affected. Statistics and information as to the occurrence of lung

healthy lungs, but it may so collect in a fibrotic lung as to form a nodule of coal. At times local necrosis takes place, with cavitation quite apart from any tuberculous infection. Discharge from such cavities accounts for the black sputum of miners. Wherever the coal particles were found most concentrated, analysis showed the content of silica to be particularly high. The conclusion is reached that anthracosis is not a simple condition, but exists only as a subdivision of lung fibrosis usually due to silicosis. Probably the lungs of miners interfered with by different dusts account for the high death rates from pulmonary diseases, particularly bronchitis, among coal miners on certain fields, even though their death rate from tuberculosis is usually low. Nevertheless, a condition of anthracosis may be pronounced without interfering with the general health.—E. L. C.

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Diagnosis must depend largely on a knowledge of the occupation of the worker. Prognosis generally is unfavorable, since treatment is unsatisfactory. The only thing to do is to abolish the dangers by suppressing the hazard. Efforts made to this end are summarized. The article is accompanied by a full bibliography containing fifty-six references. It ought to be a useful contribution to which anyone interested in asbestosis will turn.—E. L. C.

PULMONARY ASBESTOSIS. A REPORT OF A CASE AND A REVIEW. *W. B. Soper. Am. Rev. Tuberc., Dec., 1930, vol. 22, pp. 571–584.*

A man of 30 years was admitted to the William Wirt Winchester Hospital, West Haven, Conn., on May 26, 1929, at which time he had been exposed to asbestos dust over a period of about thirteen years. No indications of the severity of the exposures (*i.e.*, dust

concentrations) are given. He was admitted to the hospital four months after he had stopped working.

At that time his weight was 142 pounds, or 8 pounds below his "best weight." Physical examination showed 5 cm. chest expansion, considerable dyspnea particularly on exertion, sputum occasionally blood streaked but negative for tuberculosis, occasional râles, burning pain over the whole chest, nervousness, irritability, and constipation of three months' standing. Several nontender "asbestos corns" were seen on the hands. Blood picture and urine showed nothing unusual. X-ray picture was distinctive of the cobweb appearance noted previously by Wood (see *Tubercle*, 1929, vol. 10, p. 353).

The patient was discharged on July 2, 1929 and reexamined on April 9, 1930. During the nine months' interval he had rested at home. Dyspnea had increased, the burning pain in the chest had been superseded by dull, drawing pain above the left breast, and weight had increased from 142 to 162 pounds. Respirations were 25 and "even ordinary speech produced shortness of breath"; the complexion was leaden, with noticeable cyanosis of the ears, hands, and skin on pressure; chest expansion was 1.5 cm. (as compared with 5 cm. nine months previously). Râles were considerably more definite and more widespread than nine months earlier.

Among the author's conclusions are the following:

"The most common single symptom is dyspnoea. This and the other symptoms are essentially those of a progressive generalized lung fibrosis.

"The physical signs of uncomplicated pulmonary asbestosis are substantially those of generalized fibrosis of both lungs and basal pleurisy.

"X-ray examination is of great value in establishing the diagnosis.

"Asbestos contains but a very small amount of free silica but probably conduces to a more hasty evolution of any accompanying tuberculosis, as in the better understood forms of silicosis.

"An immediate diagnosis at autopsy is said to be made possible by simply squeezing out upon a slide a drop of lung juice from the fibrosed tissue and covering with a cover-glass. The asbestosis bodies in large number are readily visible under the microscope." —P. D.

PNEUMONOCONIOSIS DUE TO FLUE DUST. *W. E. Cooke. Brit. Med. Jour., Nov. 15, 1930, vol. 2, pp. 816–817.*

Detailed analyses are given of boiler scale and flue dust, and also of dust particles found in the lungs of a man who had been a boiler cleaner for 113 months. He died from tuberculosis, while X-rays suggested advanced pneumonokoniosis. The lungs were fibrosed throughout, and dust and dust cells were found in excessive amount. Although the silicious matter in the pulmonary dust was proportionately less than in the flue dust, the occupational exposure is held to have certainly originated the pathologic condition. The process of flue cleaning is not favored; during twelve years twenty-seven men have been employed, and have given up the work. Excepting two of these, one of whom worked only one day and the other one week, the average period of employment was fifteen months, while the nearest approaching the period of the deceased man was thirty-six months.—E. L. C.

A STATISTICAL STUDY OF PULMONARY CHANGES FOUND AMONG MINERS WORKING IN ROCK DUST. *A. Policard and E. Martin. Bull. Acad. de méd., 1930, vol. 104, pp. 333–343.*

A clinical and radiographic examination was made of 175 men using rock drills in mines in the basin of the Loire, some being X-rayed on several occasions. As many men came for examination on account of illness, the percentage of lung trouble found cannot be held to be representative. Nevertheless, when divided according to length of work, nearly 50 per cent. were normal with less than one year of work, as compared with 25 per cent. with ten years or over of work. No information as to age is given, which might quite invalidate the findings. Two certain points emerge: one is that even ten years of exposure to mine dust does not necessarily cause pulmonary fibrosis; and the other, than an unusual number of cases of open tuberculosis were discovered. No X-ray picture diagnostic of silicosis was found; but progressive changes in the appearances were of value in detecting the silicotic condition. The authors hold pulmonary silicosis to be a particular instance of tuberculosis developing under special conditions.—E. L. C.

SOME ASPECTS OF SILICOSIS. *P. Heffernan. Tubercle, 1930, vol. 11, pp. 481–489.*

WOMEN AND CHILDRE

WOMEN IN 5-AND-10-CENT STORES AND LIMITED-PRICE CHAIN DEPARTMENT STORES. *M. E. Pidgeon. U. S.*

A STATISTICAL STUDY OF PULMONARY CHANGES FOUND AMONG MINERS WORKING IN ROCK DUST. *A. Policard and E. Martin. Bull. Acad. de méd., 1930, vol. 104, pp. 333–343.*

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SOME ASPECTS OF SILICOSIS. *P. Heffernan. Tubercle, 1930, vol. 11, pp. 481–489.*

A discussion is presented, rather than new facts. The idea is advanced that silica may react by toughening lung tissue generally, while nodular fibrosis occurs at the site of lesions of which tuberculosis is the most common agent. Such nodules may be radiologic indicators of more extensive silicotic changes taking place, but not casting visible shadows. Silica enters into certain forms of life, and so may be expected to interact with protoplasm. The reaction may be expedited by such a medium as alkaline soap, with acute silicosis as a result; normally the reaction is a chronic process. Its development is associated with increasing dyspnea and dry pleurisy. Should tuberculosis not supervene, cardiac hypertrophy and failure ends the scene. Physical signs alone are not diagnostic; nor is a skiagram; a history of exposure to risk and symptoms must also be present. The fibrotic changes are progressive and cannot be inhibited. Coal and certain other dusts may facilitate the exit of silica; but silica has some power of bringing about the retention of dusts otherwise excreted. Prevention of the risk must be effected; it lies in keeping inhaled air free from a suspensoid system of silica-in-air, which behaves, physically, as a gas. The risk may be lessened by minimizing exposure to tuberculous infection.—E. L. C.

WOMEN AND CHILDREN IN INDUSTRY

WOMEN IN 5-AND-10-CENT STORES AND LIMITED-PRICE CHAIN DEPARTMENT STORES. *M. E. Pidgeon. U. S. Dept. Labor, Women's Bur., Bull. No. 76, 1930, pp. 56.*

This bulletin covers personal infor-

ient conglomeration to form larger
ected shadows and a gradual
escing, phenomena which are asso-
d with stonecutters, wet sand-
e grinders, and sand blasters.
circumscribed shadows appear
clearly in the lungs of stone
rs. Weak, diffuse, and cloudy
ows are characteristic of the coal
lung; silicotic shadows are, how-
for the most part, also evident.
X-ray picture of the schamotte
workers shows less nodule forma-
and a somewhat greater expanse
nected shadows.

the second part of the paper are
ted the results of the examination
enty-five sand blasters, twenty of
1 had indications of silicosis in
ent stages.

E EFFECT OF PROLONGED EXPOS-
OF THE SILICEOUS SPICULES OF A
ER SPONGE (*Spongilla Fragilis*) TO
ACTION OF ANIMAL TISSUES: A
RIBUTION TO THE PATHOGENESIS
OF SILICOSIS IN MAN. *R. G. Mills. Am. Jour. Hyg., Jan., 1931, vol. 13, pp. 224–234.*

The spicules of the fresh-water sponge, *Spongilla fragilis*, are composed of opal, a form of hydrated silica, which is similar to quartz in its chemical reactions. These spicules, when introduced into the tissues of animals, are slowly but definitely dissolved, proving conclusively that silica is soluble in the tissue fluids of animals, and presumably of man. This confirms the assumption held by many students of silicosis that particles of silicious material are gradually converted into the colloidal state and as such exert a fibroplastic influence on the lungs of miners and other exposed industrial workers. Definite fibrosis of the lung of a dog into which the spicules had been introduced suggests that there is a concomitant injury attributable to the disappearance by solution of the silicious elements of the spicules.—*Author's Summary.*

UPATIONAL AFFECTIONS OF THE SKIN AND SPECIAL SENSES

CUPATIONAL ECZEMA. *M. Oppenheim. Arch. Dermat. and Syph., 1931, vol. 23, p. 346.*

e dermatitides may be divided
the following groups: (1) In der-
tis, *sensu strictiori*, the skin is able
al with the irritant; almost every-
skin reacts to certain strong irri-
(*e. g.*, croton oil); even if, with
t variation, the course is acute,
ng soon follows the removal of the
n. (2) In toxicoderma there is a
enital or acquired idiosyncrasy.
slightest irritant evokes it. The
ation period is short. The effect
rked and the course acute. (3) In eczema the entire skin is sensitized. For this reason the intensity of the irritant may be slight. The development of dermatitis is gradual. The course is prolonged and healing delayed.

Occupational eczema is among the most frequent of eczemas, the most frequent of skin diseases, and the most frequent of all diseases. The predisposing factors are important: immersion of the hands in water, soap, alkali or acid, and the influence of heat, cold, and mechanical action. Occupational eczema is allergic, but the predisposing factors mentioned play an important part. Dermatitis artificialis acuta re-

OF INDUSTRIAL HYGIENE

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OF THE SKIN AND SPECIAL SENSES

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Occupational eczema is among the most frequent of eczemas, the most frequent of skin diseases, and the most frequent of all diseases. The predisposing factors are important: immersion of the hands in water, soap, alkali or acid, and the influence of heat, cold, and mechanical action. Occupational eczema is allergic, but the predisposing factors mentioned play an important part. Dermatitis artificialis acuta resembles occupational eczema. The patch test has only a limited value. Attempts at desensitization have produced only slight results.

DERMATITIS DUE TO SENSITIZATION TO CONTACT SUBSTANCES. DERMATITIS VENENATA, OCCUPATIONAL DERMATITIS. *B. Kesten and E. Laszlo. Arch. Dermat. and Syph., Feb., 1931, vol. 23, pp. 221–237.*

In eighteen of a series of twenty-one patients suffering from dermatitis venenata or occupational dermatitis, the etiology was determined or corroborated by patch tests. In the remaining three there was an exacerbation of the dermatitis when the substances were applied to the sensitized skin. In all of the cases there was freedom from dermatitis when the specific substance was avoided.

The sensitizing substances were: paraphenylenediamine, sodium bichromate, novocaine, novol, potassium mercuric iodide, primrose, poison ivy, pyrethrum, mascara, face powder and face cream. In the dilutions used, none of these substances was found irritating to the normal skin.

Passive transfer of sensitization was unsuccessful.

A case of local sensitization and desensitization to potassium mercuric iodide is reported.

In most instances dermatitis venenata and occupational dermatitis result from local cellular sensitization to specific non-proteins acquired by previous contact of the substances with the skin.—*Authors' Summary.*

A CASE OF EPITHELIOMA DEVELOPING RAPIDLY AFTER AN INJURY BY BURNING ASPHALT. *A. Gunsett. Abstr. as follows from Bull. Assn. franç. pour l'étude du cancer, 1930, vol. 19, p. 459, in Am. Jour. Cancer, Jan., 1931, vol. 15, p. 357.*

A workman aged 50 years was burned on the back of his hand by a small piece of burning asphalt. The wound did not heal, and three months later there was a nodule at the site of the injury 1 cm. in diameter. The mass was excised and found to be squamous-cell epithelioma with large keratotic pearls, a few mitoses, and a moderate inflammation of the stroma. Pain in the wound rendered it necessary to remove the sutures, and some small nodules on the border of the scar were submitted to microscopic examination and found to contain some remnants of the growth. After this second operation, the lesion was treated with radium, and healing occurred. The case is too recent to know whether further metastases will take place.

Four similar cases from the literature are referred to. In three, burns were followed by rapid development of cancer; in the fourth, however, the tumor, in this case on the lip, did not appear for two years after the burn, and hence cannot be absolutely correlated with the injury. (Two similar instances of the development of an epithelioma following burning of the skin with sulphuric acid are also on record.)

WARTS FROM MINERAL SUBSTANCES. *A. P. Dewirtz. Abstr. from Roussky Vestnick Derm., March, 1930, pp. 243–247, in Ann. de dermat. et syph., Dec. 30, 1930.*

This writer, when examining workers among asbestos, found a kind of

dermatosis. It is chiefly confined to the palmar surfaces of the hands and fingers; in young people who go about without shoes, it occurs also on the soles of the feet. The right hand is usually more extensively involved than the left. The individual lesions consist of apparently noninflammatory, round or polygonal, rough-topped warts. They vary in size from a millet seed to a pea. Sharp needles of asbestos enter the skin, and thus produce these papillomas. The thin skin of youth and the flexures of the joints are particularly vulnerable, and on these parts the warts are chiefly found. They are most objectionable because of the pain and discomfort they cause when walking, and because of the trouble and inconvenience they give to those who handle tools. These little tumors are well known to the operatives, and are called *verrues d'amiante*, or asbestos warts. The irritation they produce leads the employees to remove the fine spicules of mineral which stick into the skin, either with a pin or a needle, or with the nails. This gives only partial relief, as the little tumors continue to grow or recur on the same place.

The histologic picture was examined and described by Dewirtz. The horny and malpighian strata are largely increased. In the dermis are a large number of round and polymorphic cells, situated especially in the papillary layer. In these warty growths Dewirtz has found the crystals of asbestos. These he accuses of being the cause of the thickening of the rete mucosum and the basal layers, and of the formation of giant cells. The whole condition turns out to be a very slow chronic local inflammation. The author says that this is the first occasion on which these asbestos warts have been brought to the notice of the dermatologist. He suggests that surgical removal is the only advisable course to pursue.—R. P. W.

ERUPTION CAUSED BY RESINS OF TREES. *Longin. Abstr. as follows from Bull. Soc. franç. de dermat. et syph., July, 1930, vol. 37, p. 741, in Arch. Dermat. and Syph., Feb., 1931, vol. 23, p. 333.*

Three cases of eczematiform eruptions produced by volatile constituents escaping from freshly hewn wood are reported. In one case there was an exacerbation when an intradermal injection of an extract of the suspected wood was administered.

OCULAR HYGIENE IN INDUSTRY. *V. de Uzeda. Abstr. as follows from Folha med., 1930, vol. 11, pp. 290–292, in Bull. Hyg., Jan., 1931, vol. 6, pp. 20–21.*

This is a brief sketch of the conditions of interest to the ophthalmologist as they are met with in industry. Reference is made to the risks of working in defective light, in excessive artificial light, and the aggravation which may arise in morbid conditions already existing, *e.g.*, myopia. Secondly, there is a discussion on the irritant effects of certain gases, especially in chemical factories, of dust or larger particles in those working with metal or stone, intoxications as from mercury, phosphorus, nitrobenzene, arsenic, etc.; the effect of heat, as cataract in those attending to furnaces, in glassworkers and others; and finally trauma from fragments of wood, metal, glass or stone, causing various degrees of damage from slight conjunctivitis to

actual penetration of the anterior chamber and its complications and sequelae.—H. H. S.

THE FIELDS OF VISION IN MINERS' NYSTAGMUS. *C. F. Haycraft. Abstr. as follows from Brit. Jour. Ophth., Oct., 1930, vol. 14, p. 523, in Arch. Ophth., Jan., 1931, vol. 5, p. 146.*

From the study of the fields of vision in a series of forty-three cases of miners' nystagmus, of which thirty-five were old and eight were new cases (that is, certified as suffering from the disease within the previous six months), the author arrives at the following conclusions:

INDUSTRIA

SHOULD LAYMEN GIVE INJECTIONS OF LOBELIN AND CARDIAZOL? *L. Teleky. Med. Welt, 1929, no. 2.*

A large number of doctors consider injections of lobelin of extraordinary value in restoring life in cases of apparent death, and Teleky here suggests that as doctors are bound to take time arriving on the scene of the emergency, laymen should be trained to give injections as part of first aid teaching. It is generally objected that it would be dangerous for laymen to give injections, but in giving first aid in industry they often undertake methods which may involve greater risks. Thus in the Silvester and other methods of artificial respiration, broken ribs and injury to the liver have occurred, while the tongue may be injured by drawing it forward and fixing it. In cases of trismus, opening the jaws may cause wounds of the lips and broken teeth. The use of the pulmotor, which is recommended in factories, requires

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In a large percentage of cases of miners' nystagmus there is a definite alteration in the fields of vision. The most common change is a concentric contraction for white. A large number of patients show contraction for red and blue, and interlacing of these colors is frequent. The amount of contraction of the fields is usually but not invariably a measure of the severity of the disease. In the absence of physical signs, the change in the fields described, combined with typical subjective symptoms, can be relied on in diagnosing miners' nystagmus or in determining that recovery is still insufficient to permit work underground.

INDUSTRIAL SURGERY

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Thirty years ago, it was quite common in clinics to give injections without any aseptic or antiseptic precautions, and at the present day many morphinists give injections through their clothing without any serious results. Lobelin is kept in ampoules in emergency aid boxes, and it would not be difficult to teach the giving of injections as part of a first aid course. It has been found in cases of gas poisoning in Düsseldorf that firemen trained in first aid arrive on the scene a half to a quarter of an hour before the doctor, and as every minute is so important, it would be a great advantage if these men were able to give injections of lobelin and even of camphor or cardiazol if necessary.—A. J. C.

those who are employed in the mills where the dust is prepared. Since our practical experience goes back only a short time, as is true also of Schultze's work, there is nothing positive to be said concerning the action of this kind of dust on the lungs of men engaged in this type of work. Dust with a high quartz content or clay slate dust mixed with a high content of silica should, however, be eliminated as far as possible. Further research is necessary in order to show how pure clay slate dust behaves experimentally and, especially, to determine the degree of hazard with varying silica content.

Our next study will be devoted to the dust problems involved in rock dusting. If clay slate dust should actually prove to be injurious to the lungs, there are available several other kinds of dust which are less harmful and which satisfy the requirements of mining authorities. We may mention, for example, limestone dust which contains only about 3 per cent. of silica and has a high lime content. Moreover, official tests have shown that it meets all the requirements of the industry. Our animal experiments with it have been completely satisfactory. An exhaustive report concerning this subject will appear in our next publication.

The relatively slight injury caused by cement dust in our experiments is in complete agreement with previous practical experiences and statistical studies. Only a few authors have ascribed a tuberculosis promoting action to this dust, and their views are no longer significant since statistical studies have nowhere established a high tuberculosis mortality with certainty. The fact that mild degrees of lung injury (Schott, Sommerfeld, and Kästle) are found among workers exposed for a number of years, and that other health derangements occur as a result of severe exposure in industry, together with the results of our experiments, show that cement dust is not entirely harmless. Care must be taken, therefore, to avoid the development of too large a quantity of dust in manufacturing and to insure efficient removal of the dust by suction.

At first glance our experimental results with tobacco dust appear to be at variance with previous experimental results as well as with the statistics on the incidence of tuberculosis in tobacco trades. That tuberculosis occurs frequently among tobacco workers cannot be denied, but the opinion at the present time is that this is not due entirely to employment in dusty work but is brought on by other causes of a social and economic nature. We cannot convince ourselves, however, that tobacco dust is entirely harmless. We therefore stress the importance of improving hygienic conditions, especially of women workers, of furthering vocational selection, of prohibiting employment of young persons, and particularly of installing efficient dust removal systems, and of eliminating the possibility of infection. These observations on tobacco dust inhalation clearly show that other factors are responsible for the dust injuries and particularly for the tuberculosis. They demonstrate the correctness of K. B. Lehmann, the Nestor of industrial hygiene, in his assertion that poor nutrition, bad living conditions, weak constitution, and susceptibility

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to infection play a more important rôle in the production of tuberculosis than do moderate dust concentrations.

We hope that we have shown by these observations that it is possible by means of animal experimentation, especially with tuberculosis immune animals, to evaluate the danger of different occupational dusts by extensive parallel studies and to reach conclusions which are in agreement with statistical and practical results. Ickert confirms our opinion by a comparison of the findings of Jötten and Arnoldi with recent and old statistics. The statistics show a scale of dust risk which Ickert states agrees exactly with the experimental findings of Jötten and Arnoldi.

Further studies on the relation of occupational dust and pulmonary tuberculosis will be of value, especially if they are extended over a long period of time and include observations on chronic dust inhalation. The correct evaluation of such animal studies can result only from extensive series of comparable experiments with various kinds of dust; furthermore, statistical and other research findings, as well as the social and economic conditions of the various groups of workers, must be taken into consideration. If studies are carried on this way, it is our opinion that it will be possible eventually to reach a definite decision in regard to the industrial dust problem. —M. F.

ASBESTOSIS BODIES IN SPUTUM AND LUNG. *K. M. Lynch and W. A. Smith. Abstr. as follows from Jour. Am. Med. Assn., Aug. 30, 1930, vol. 95, pp. 659–661, in Arch. Path., Feb., 1931, vol. 11, pp. 291–292.*

In microscopic sections of lung from the body of a worker in an asbestos factory, who died from a gunshot wound, numerous asbestosis bodies were found in the alveoli, the walls of the alveoli, the deeper pleural tissues, the bronchi, and the interlobular framework, in thrombi in the veins and in the peribronchial lymph glands. Associated with them were black granular pigment, in the lymph glands a yellow-brown granular substance, a reaction of mononuclear and polymorphonuclear giant cell phagocytes, and in the framework structures a cellular increase in fibrous tissue. The asbestosis bodies were seen in the sputum of three people who had been workers in an asbestos factory, one as long before as six years. In the sputum, these bodies had a central filament of a transparent, slightly greenish-tinged, needle-like crystal. On this were deposited nodules, blebs, and segments of a homogeneous refractive substance. These bodies were from 12 to 140 microns long and from 1 to 12 microns thick. They did not take the ordinary dyes for tissue and sputum. They could be stained by the Prussian blue reaction for iron. It is suggested that the iron content of the deposit was of tissue origin, probably from the blood.

absorption of the tar. On the other hand, removal of fat from the skin by preliminary treatment with petroleum ether produced an opposite effect, the number of tumors being decreased.

As the authors point out, other investigators have obtained results directly contrary to those described in this paper.

FURTHER INVESTIGATIONS ON THE TREATMENT OF TAR TUMORS IN MICE WITH CERTAIN AMINO-ACIDS. *F. Vlès, A. de Coulon, and J.-L. Nicod. Abstr. as follows from Compt. rend. Acad. d. sc., 1930, vol. 191, p. 350, in Am. Jour. Cancer, April, 1931, vol. 15, p. 898.*

One hundred and seven mice with tar cancer (verified by biopsy) were given an equimolecular mixture of alanine, cystine, and proline by mouth, subcutaneously, or by both routes. The dose was 0.03 to 0.075 gm. daily. In twenty-six cases the tumor disappeared entirely; in thirty-seven there was partial regression; in nine the tumor continued to grow, and in thirty-five animals it remained stationary. This last group, however, contained a number of mice that died less than fifteen days after treatment was begun and before it had had time to exert its full effect. Among forty-two controls not a single case of regression had been discovered.

A mixture made up in the proportion of two molecules of d-glutamic acid to one of l-cystine promised to be even more successful. Among twenty mice treated, the carcinoma disappeared in ten and regressed partially in six more; three tumors continued to grow, and one remained stationary.

DUST HAZARDS AND THEIR EFFECTS

CONTRIVANCES FOR DUSTLESS FILLING AND PACKING OF DUST PRODUCING MATERIALS. *Beihefte z. Zentralbl. f. Gewerbehyg., no. 19, 1930, pp. 48. Reviewed as follows in Bull. Hyg., Nov., 1930, vol. 5, p. 897.*

This publication on a question of very great hygienic importance deals with the engineering side of the subject and as such is too technical to be of direct service to the medical officer of health. The author lays stress on the dual aspect of the problem: first, the importance of catching up the dust as soon as it is formed and rendering it innocuous; and secondly, the method of dealing with it afterwards. Naturally, the treatment will differ according to the industry, the nature of the dust, its quantity, and whether it is of sufficient commercial value to recover, or whether it has to be got rid of as a waste product. The work is amply illustrated both by photographs, and diagrams, all of which are well and clearly reproduced.—H. H. S.

RECENT VIEWS ON PNEUMONOCONIOSES. *E. L. Collis. Proc. Roy. Soc. Med., March, 1931, vol. 24, pp. 531–540 (Epidemiology and State Medicine, pp. 13–22). (Abstract by author.)*

This article presents a summary of work done with regard to dust diseases since the author's Milroy Lectures, 1915. Studies have shown that silicosis may be advanced without impairing health; but it may itself end fatally. Generally superimposed

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THE PRESENCE OF ASBESTOSIS BODIES IN THE FAECES IN A CASE OF PULMONARY ASBESTOSIS. *S. R. Gloyne. Tubercle, April, 1931, vol. 12, pp. 158–159.*

This short note describes how asbestos bodies in cases of pulmonary asbestosis may be found by emulsifying the feces in four to five times their volume of 5 per cent. formalin in saline and then centrifuging the product, which will be found to contain a scanty number. The bodies, which have probably been swallowed in sputum, show less than usual of the typical deep-yellow coloring matter, as though the pigment were partially destroyed by intestinal juices.—E. L. C.

SILICOSIS AND COAL-MINING. *J. S. Haldane. Tr. Inst. Min. Eng., 1931, vol. 80, p. 415.*

In earlier papers[1] the author concluded (*a*) that no danger to health would arise from stone dusting, provided suitable shale or other material was employed; and (*b*) that the unusually high bronchitis mortality rate among colliers in the higher age groups is due mainly to the strain on the lungs caused by muscular exertion. In the present paper Dr. Haldane reviews his conclusions in the light of the full data contained in the Registrar-General's Decennial Supplement for 1921 to 1923.

The phthisis death rates for the various groups of underground workers are distinctly lower than those for all occupied and retired civilian males. Even in that group engaged in making and repairing roads, which includes the work of ripping stone roofs and driving roads in stone, the death rate from phthisis at all ages above 25 is lower than for the standard population. It is mentioned, however, that in exceptional cases great risk may occur among men driving roads in highly silicious rock, particularly when machine drills are used. The Mines Act of 1911 required certain precautions in the use of these drills, but the clause was practically ignored. As a result, cases of silicosis have been discovered in the Somerset and South Wales coal fields.

The thesis is advanced that the inhalation of coal dust and shale dust, as among coal miners, coal boat loaders, or cement workers, stimulates

[1] The Effects of Dust Inhalation. Tr. Inst. Min. Eng., 1917–1918, vol. 55, p. 264. The Health of Old Colliers. *Ibid.*, 1915–1916, vol. 51, p. 469.

DUST HAZARDS AND THEIR EFFECTS

CONGRESS OF INDUSTRIAL MEDICINE. *Foreign Letter (Italy), Jour. Am. Med. Assn., Feb. 14, 1931, vol. 96, pp. 542–544.*

This letter contains an account of the Ninth Congress of Industrial Medicine held in Rome. The subject before the Congress—"The Problem of the Respiratory Pathology of Dusts"—was divided into several parts. Caccuri of Naples discussed the etiology and pathogenesis of respiratory diseases due to dust; Coppa of Naples, the pathologic anatomy and the clinical aspects of respiratory dust diseases; Pastena, also of Naples, radiologic research in pneumonokoniosis. Abstracts of these papers are included in the letter. Communications were also presented concerning the respiratory diseases of coal heavers and of workers in hemp.—K. R. D.

ASBESTOSIS BODIES IN THE SPUTUM: A STUDY OF SPECIMENS FROM FIFTY WORKERS IN AN ASBESTOS MILL. *F. W. Simson and A. S. Strachan. Jour. Path. and Bacteriol., Jan., 1931, vol. 34, pp. 1–4.*

The result is reported of examining sputum from fifty workers who were intensively exposed to asbestos dust in a mill in South Africa. Asbestosis bodies were easily demonstrated by direct thick films. They were found best by examining specimens taken early in the morning; in the evening the mouth and nasal pharynx were too loaded with dust for the bodies to be easily detected. The sputum was always mucoid in character, often resembling egg albumin. No tubercle bacilli were found. The asbestosis bodies were intracellular, and their study suggested that they were formed by the deposition on asbestos fibers of iron containing substance elaborated by the cell. The shortest exposure to be followed by the appearance of the bodies was five months.—E. L. C.

FURTHER OBSERVATIONS ON PULMONARY ASBESTOSIS, WITH SPECIAL REFERENCE TO ASBESTOS DUST AND THE CURIOUS BODIES FOUND IN THE LUNGS. *W. E. Cooke and C. F. Hill. Abstr. as follows from Jour. Roy. Micr. Soc., 1930, vol. 50, p. 15, in Physiol. Abstr., Feb., 1931, vol. 15, p. 626.*

In a case of suspected pulmonary asbestosis sections of the lung or macerations of the tissue revealed a large amount of fine granular black dust, but the fine spicules of fiber which make up the bulk of asbestos dust were not found. There were present, however, large fragments (5 to 360 microns) closely resembling in size, shape, and color various constituents of asbestos dust. These large fragments are found in the lung embedded in fibrotic or necrotic areas of which they are the cause. In addition, curious bodies were present which are believed to be diagnostic of pulmonary asbestosis. These bodies were eventually shown to consist of a central core of asbestos fiber enclosed in adsorbed débris.—C. K. D.

ANTHRACOSIS, SILICOSIS, AND TUBERCULOSIS IN COAL-MINERS. *S. L. Cummins. Lancet, Jan. 31, 1931, vol. 1, pp. 235–238.*

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is retained in the lungs owing to a state of fibrosis with lymph blockage. The pathologic condition arising from dust inhaled together with the coal and also chemical analyses are similar, so far as the content of silica, to those found in cases of pure silicosis. In certain cases of "hard heading" work, where rocks rather than coal are mainly tackled by the miners, silicosis develops which is indistinguishable from that seen in other cases of silica risk. But when coal has been the chief dust inhaled, no tendency to succumb from tuberculosis is found; and the suggestion has been offered that coal dust exerts a protective influence against tuberculosis. This idea is, however, not definitely accepted; at least, the suggestions to explain why the coal miner has a low mortality from tuberculosis, although his lungs show definite fibrosis, are not accepted. Professor Cummins now puts forward the possibility that carbon particles in the lungs adsorb the active principle of tuberculin. He points out that such adsorption occurs *in vitro*, since he has found that finely powdered dust of anthracite coal is capable of adsorbing a large proportion of the active principle from old tuberculin diluted with normal saline solution. Whether or not carbon dust particles bathed in the tissue juices retain this adsorbing power requires further investigation. Some clinical facts appear to favor the theory. Certainly, negative sputums are more common in clinically tuberculous coal miners than in other clinically tuberculous adult males. Although any excessive liability to tuberculosis is absent in the case of coal miners, a high mortality from bronchitis among old colliers is present, which, in all probability, is closely associated with the life of exposure, not only to coal dust but to stone dust as well.—E. L. C.

OBSERVATIONS ON THE DIFFERENTIAL DIAGNOSIS OF SILICOSIS BY MEANS OF THE ROENTGENOGRAM AND AN INVESTIGATION INTO THE RISKS OF SAND BLASTERS. *Lochtkemper. Abstr. from Arch. f. Gewerbepath. u. Gewerbehyg., 1930, vol. 1, pp. 271–302, in Ber. ü. d. ges. Physiol. u. exper. Pharmakol., Oct. 8, 1930, vol. 56, p. 182.*

The author distinguishes roentgenologically the various forms of silicosis, pneumonokoniosis caused by quartz dust. The first stage is characterized by enlarged hilum glands and by increased vascular markings; the second stage, by numerous infiltrated and isolated nodules and increased induration; the third stage, by the so-called "snowstorm" effect, which is partly an isolated and partly a confluent mottling.

The rate of dust inhalation and the concentration of the quartz content are important in the resulting roentgen picture. Among workers in industries whose dust contains free silicic acid—sandstone grinders, stonecutters, sand blasters, porcelain workers, and stone hewers—there are found in the X-ray picture of the lung, near the enlarged hilum, small, sharply defined shadows from pinhead to pea in size, some of which are isolated and others joined by fine streaks. The thickness of the nodules is greater in sandstone grinders and stonecutters than in porcelain workers and stone hewers, and in occupations in which a mixture of quartz and clay dust is inhaled. In the further development there is a gradual increase in the small shadows with an

of the dust particles and on the air current; in fine dust the brownian movement plays a part. Calcium, silica dust, and coal dust are considered especially. While the histologic reaction in the air passages consists principally in hyperemia and round cell infiltration, in the alveoli phagocytosis prevails. The coal particles are taken up without cytoplasmic change, while quartz slowly exerts a toxic effect on the phagocytosing cell. The article contains numerous details which it is impossible to cover in an abstract.

PNEUMONOKONIOSIS AND TUBERCULOSIS. *H. S. Willis. Abstr. as follows from Medicine, Dec., 1930, vol. 9, pp. 413–506, in Am. Jour. Pub. Health, May, 1931, vol. 21, p. 565.*

This is a review of the whole subject of pneumonokoniosis and tuberculosis in approximately ninety pages divided into seven portions as follows: (1) historical résumé of pneumonokoniosis; (2) types of dust; (3) pathology; (4) diagnosis; (5) prognosis; (6) relationship between tuberculosis and pneumonokoniosis; and (7) prophylaxis and treatment.

It is quite impossible in a brief abstract to do justice to the paper, since in itself it is an interpretation and very complete summary of all the important contributions in this field.

Anyone who is interested in the problem of dust and its effects will find this an invaluable reference work. The paper concludes with a bibliography of 238 references.

PNEUMONOKONIOSIS IN BOLIVIAN MINERS. *G. Orosco et al. Abstr. as follows from Semana méd., 1931, vol. 38, no. 10, pp. 601–634, in Bull. Hyg., June, 1931, vol. 6, pp. 467–468.*

This is a long article containing many points of importance and is worthy of study in the original by those interested in the subject. The chief features only can be referred to here. The whole, like Caesar's description of Gaul, is divided into three parts. The first presents in considerable detail the conditions under which the industry is carried on. The workers use pneumatic drills but, except those engaged in the grinding process later, do not use any protecting masks. Illustrations of the district, the mines, and the different processes and machinery are well reproduced, showing the actual working conditions of the employees. The second part gives clinical histories of typical cases and an account of the pathologic state of the lungs with microphotographs of the lesions produced. The third part details the chemical investigations of the pulmonary tissue, and shows the presence of silica, iron, aluminium, and tin (no lead). Quantitative estimation gave 10.9 gm. of tin per kilogram of the dried tissue and 2.7 per kilogram of the moist. Of iron there were 3.3 parts per thousand of dried substance estimated as ferric oxide, or 2.5 gm. per kilogram expressed as iron; in the undried tissue there was 0.45 gm. per kilogram as ferric oxide, or 0.34 as iron.

The symptoms produced and the resulting disablement from fibrosis of the lungs and the consequent cardiac mischief need not be detailed, but the author rightly demands that prophylactic measures should be put in force to reduce the sickness in an industry which employs a large proportion of

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✓ PULMONARY ASBESTOSIS II. INCLUDING THE REPORT OF A PURE CASE. *K. M. Lynch and W. A. Smith. Am. Rev. Tuberc., June, 1931, vol. 23, pp. 648–660.*

In a survey of all available literature on the subject up to the present time we have collected 172 cases of pulmonary asbestosis. There are references to this subject in one or two abstracts, notably those of Bridge and of Sir Thomas Oliver, but specific cases are not enumerated. In four cases belonging to Wood's series the diagnosis was doubtful, and in the majority of others the diagnosis was based entirely on clinical and roentgen findings. There were twenty-seven in which the diagnosis was confirmed by the finding of the asbestosis bodies in the sputum, in the lung juice by puncture, or by necropsy. Necropsy has been made on eighteen cases. In three of these the disease was complicated by pulmonary tuberculosis, three by lobar pneumonia, three by bronchopneumonia, and one was a traumatic death. In four the authors failed to give a complete report, stating only that the necropsy confirmed the diagnosis. Including the very first case recorded, that of Murray in the Charing Cross Gazette of 1900, which apparently received little attention until resurrected by Cooke, there are now four records of necropsy on uncomplicated pulmonary asbestosis. Except those reported by ourselves, and those by Pancoast and Pendergrass, and four others by Simson from South Africa, these cases have all developed in the British Isles.—*Authors' Summary.*

✓ A CASE OF PULMONARY ASBESTOSIS. *H. E. Seiler and M. D. Gilmour. Brit. Med. Jour., June 27, 1931, vol. 1, pp. 1112–1114.*

The pathologic findings are reported of a fatal case of asbestosis uncomplicated by pulmonary tuberculosis. The man died, aged 42, after twenty-three and one-fourth years of occupational exposure to asbestos dust in a textile mill. Death was due to cardiac failure secondary to back pressure from massive generalized fibrosis. Before death, cyanosis was pronounced; and diffuse fine mottling of a silicotic type was detected on X-ray. The macroscopic appearances were typical of dense pulmonary fibrosis, with other organs secondarily affected—dilated heart, nutmeg liver, and indurated spleen and kidneys. The fibrosis was generalized, with no nodules or whorls, as in silicosis; no polymorphonuclear cells were to be seen in the bronchi or elsewhere. Asbestosis bodies were abundantly present, and also a great deal of yellow pigment in the form of granules and globular masses. No tuberculous lesions were found.—E. L. C.

✓ THE FORMATION OF THE ASBESTOSIS BODY IN THE LUNG. *S. R. Gloyne. Tubercle, June, 1931, vol. 12, pp. 399–401.*

Pictorial presentation is given in this short note of the formation of asbestosis bodies. They appear to be formed by the deposition of some organic material around an asbestos fiber; this material then fissures or cracks, giving rise to the appearance of segments; finally, fragmentation from the asbestosis body may separate portions. There is evidence that iron

is a component of the material deposited on the inhaled fiber. During the reaction which takes place, solution of a fraction of asbestos occurs; but evidence is lacking as to how the long asbestos particles, which are far longer than the diameter of a dust cell, are introduced into the pulmonary tissues. —E. L. C.

PNEUMONOCONIOSIS. THE DELAYED DEVELOPMENT OF SYMPTOMS. *J. A. Britton and J. R. Head. Jour. Am. Med. Assn., June 6, 1931, vol. 96, pp. 1938–1939.*

Most clinical and statistical studies of silicosis have been made on groups of men still employed in dusty trades. From such statistics one cannot say what is the late effect of short exposures. In this paper we have reported four cases of silicosis or silicosis and tuberculosis which developed many years after relatively short exposures. These instances suggest the necessity of revising the conception of the length of exposure necessary to produce the disease and make it seem probable that after relatively short exposures sufficient dust must be deposited in the lungs to set up a progressive fibrosis, which only after many years becomes sufficiently extensive to produce symptoms. They tend to indicate that men in the work develop symptoms only after many years of exposure, not because that length of exposure is necessary but because it takes a long time for the disease to develop. —*Authors' Conclusions.*

SILICOSIS. *T. H. Belt. Canadian Med. Assn. Jour., Dec., 1930, vol. 23, pp. 802–804.*

This is a general discussion of silicosis and of the various theories as to the method of action of silica dust in the lungs.—M. C. S.

DIAGNOSIS OF PULMONARY SILICOSIS. *C. Garin. Abstr. as follows from Presse méd., April 18, 1931, vol. 39, p. 568, in Jour. Am. Med. Assn., July 11, 1931, vol. 97, pp. 143–144.*

Garin states that most of the authors cited by him reported cases of silicosis in which tuberculosis was present. None of them attempted to bring out the differences between the two conditions. He stresses mostly the roentgen side of the question. In his roentgen studies he found that about 85 per cent. of the cases are those of a granular silicosis. He believes that the granular aspect of chest roentgenograms is not positively that of pure silicosis and it should not serve as an exclusive base for diagnosis of silicosis. The diagnosis between simple silicosis with a granular picture and pulmonary tuberculosis is, however, easy: the patients with silicosis have no fever and the condition is progressive. On the other hand, diagnosis becomes almost impossible in cases of silicotuberculosis, in which the tubercle bacillus interferes with the development of a pure silicosis. In such cases it is impossible to pronounce the patients sick with silicosis or with pure tuberculosis. One can only make a diagnosis of silicotuberculosis.

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OCCUPATIONAL INFECTIOUS DISEASES: OCCURRENCE, TREATMENT, AND PREVENTION

CASE OF ANTHRAX IN MAN. *C. Rasch. Abstr. as follows from Ugesk. f. Laeger, March 19, 1931, vol. 93, p. 307, in Jour. Am. Med. Assn., June 13, 1931, vol. 96, p. 2080.*

Rasch reports the case of a man on whose hands two lesions developed after he had handled a cow with anthrax. A scraping made under the crust on the larger plaque, when stained with methylthionine chloride, revealed numerous typical anthrax bacilli. This result is almost always obtainable, he says, if examination of untreated primary anthrax is made during the first three days. Treatment with 0.75 gm. of neoarsphenamine three times daily, at intervals of from three to five days, together with hot local applications, was followed by rapid recovery.—C. K. D.

PNEUMONIA IN BROWN IRON ORE MINERS. *W. Schopper. Abstr. as follows from Arch. f. Hyg., Sept., 1930, vol. 104, pp. 175–183, in Bull. Hyg., April, 1931, vol. 6, p. 322.*

In this paper, Schopper, after referring to the well-recognized peculiar symptoms of chronic manganese poisoning, has followed up the other aspect of its action, namely, the association with pneumonia. He describes the postmortem appearances of two miners who had died of this. In addition to the ordinary signs of pneumonia, he found throughout the lungs extensive deposits of foreign material rich in manganese which had led to fibrosis of the lungs.

He considered that his findings, together with the clinical experience of the medical men in the district of Giessen, where the manganese ores are mined, explained the prevalence of the pneumonic symptoms, but the classical symptoms of chronic manganese poisoning are unknown in the district in question.—T. M. L.

ULTRA-VIOLET RADIATION AND RESISTANCE TO INFECTION: INTRANASAL INFECTION WITH THE PNEUMOCOCCUS AND WITH BACTERIUM LEPISEPTICUM IN THE RABBIT. *M. Hardy and J. Chapman. Am. Jour. Hyg., Jan., 1931, vol. 13, pp. 255–280.*

Exposure of rabbits to direct sun and to artificial radiation from a mercury arc had little or no effect on mortality rate, and on resistance to pneumococcus and *Bacterium lepisepticum* infection, and little effect on blood counts and antibody formation.—C. P. Y.

OCCUPATIONAL AFFECTIONS OF THE SKIN AND SPECIAL SENSES

DERMATITIS FROM CELLULOSE VARNISHES. *J. Rousset. Méd. du travail, May, 1931, vol. 3, pp. 76–82.*

The occurrence of outbreaks of skin troubles in a furniture factory led to investigation of the composition of the varnishes used. The composition of the fluids used for filling and for cleaning the wood, and for diluting the varnishes is given. These fluids contain a number of volatile grease solvents. Experiments by applying them to the skin failed to reproduce the condition which occurs in the workers; but wood vinegar and benzene, two of the constituents, did cause some ery-