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The Effects of Inhaled Talc-Mining Dust on the Human Lung

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Talc belongs in the group of silicates that have been under suspicion for many years as a cause of pneumoconiosis. The literature contains a number of reports of studies which indicate that industrial workers exposed to talc dust sometimes develop changes in the lungs, and several investigators have used the term "talcosis" to describe the pulmonary condition produced in those exposed workers.

Pure talc, a hydrous magnesium silicate, is a specific mineral, but, as Schulz and Williams [1] pointed out, the word "talc" as used in industry usually refers to a product which meets certain physical requirements rather than to a substance of definite chemical composition. In commercial talc, the mineral talc itself may be only a minor component. Schulz and Williams found that in 51 samples of commercial talc the amount of the talc component, based on the count of particles smaller than 10μ, never exceeded 52% of the sample. Other prominent minerals in their samples were serpentine, dolomite, and tremolite. A review of the data on 35 "talc" samples received at The Saranac Laboratory for routine analysis revealed that the composition varied widely. In 8 of the 35 samples there was no more than a trace of the mineral talc present, and all the 35 contained a substantial amount of one or more other components, such as tremolite, mica, carbonates, and clay minerals.

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The extent to which the mineral talc is responsible for the changes in the lungs is still in doubt. Certainly the experimental and clinical evidence incriminating pure talc as the principal etiologic agent in so-called talcosis has so far been much less convincing than similar evidence supporting the views that silicosis is caused by inhaled quartz dust or that asbestosis is provoked by inhaled asbestos fibers. Nor is there complete certainty yet concerning the pathognomonic features of the specific talc disease.

In spite of these uncertainties, reports on 21 clinical and roentgenological and 13 autopsy studies exist in the literature, commencing with the first paper by Thorel [2] in 1896. Jaques and Benirschke [3] have recently reviewed these cases. The main emphasis appears to be on a radiological pneumoconiosis, ranging from diffuse bilateral reticulation without predisposition to tuberculosis to conglomerate massive shadows frequently tuberculous in nature. Clinically the disease varies from a benign to a rapidly developing fatal process, with emphasis on cor pulmonale as the cause of death. There may be a prolonged symptom-free induction period. Tuberculosis, emphysema, and bronchitis vary in their prevalence. Pathologically the condition has been described mainly as a dense type of fibrosis, with peribronchial and perivascular prevalence and sometimes with nodularity. Talc has been demonstrated in the tissues of some cases, and the suggestion has been advanced that the talc shows certain erosion changes in the human tissue not present in the original state. A point which has by no means previously been settled concerns the role of substances inhaled in association with the talc as the cause of the disease process. Speculation has mainly concerned the effect of the quartz, which has frequently been demonstrable. On the other hand, cases

exist in which neither quartz nor talc have been demonstrable.

Passing reference should also be made to the extensive literature on the granulomata associated with the surgical use of talc and the fact that talc lesions have been observed not only in the lungs but also in the pericardium, the epicardium, and the gastric mucosa, besides surgical wounds. It is evident that a great deal may yet be added to the sum total of our current knowledge concerning this dust disease. With this object in mind, observations are presented in this paper on dust surveys conducted by The Saranac Laboratory of certain mines and mills of the talc industry of Northern New York State, together with the chemical findings and histopathology of eight deceased employees from that same industry.*

SURVEY OF DUST CONDITION IN CERTAIN MINES AND MILLS OF THE TREMOLITE TALC INDUSTRY OF NORTHERN NEW YORK

The rock mined and milled in the area in Northern New York studied by The Saranac Laboratory, although sold as talc, is a mixture of talc and tremolite accompanied by a smaller amount of anthophyllite. All three minerals are silicates. The talc usually develops in thin, flexible, white laminae that are characteristically greasy to the touch, but in some samples from this area it occurs in fine fibers instead of the usual plates. The tremolite and anthophyllite normally occur as coarse crystal grains, but in the area studied and elsewhere those minerals sometimes break up into long narrow fibers and then exhibit the structure and properties of asbestos. It should be pointed out that the term "asbestos" does not refer to one specific mineral but rather to any mineral capable of splitting into long, thin, flexible fibers and resistant to heat and chemical agents. Two distinct types of mineral are used commercially as asbestos: the bulk of the product is chrysotile, which is a fibrous variety of the silicate mineral serpentine; the important remainder belongs to the group of silicates known as amphiboles and includes the varieties amosite and crocidolite. Tremolite and anthophyllite are also members of the amphibole group. Since the experience in South Africa shows that at least one of the asbestiform amphiboles—crocidolite—is capable of causing typical asbestosis, there is reason to suspect that the fibrous amphiboles from the area studied by The Saranac Laboratory also might cause reaction of the asbestosis type. It is likewise possible that any portion of the talc which may be present in fibrous form might have a similar effect on tissue.

Representative samples of the mine product from three mines and of ground talc from two mills in the area were analyzed by chemical, petrographic, and x-ray diffraction techniques. The results appear in Table 1. At the same time samples of air-borne dust were collected with an electrostatic precipitator in two of these three mines, near a miner operating a jackhammer drill, and in the working area of both mills. Later precipitator samples were collected in the third mine also. Analysis revealed that the distribution of minerals was somewhat different in the atmospheric samples (Table 2) than

* These cases are part of a series collected by the late Dr. L. U. Gardner. A manuscript under preparation by Dr. Gardner had not been completed by the time of his death. The present account is an independent study of the material without reference to this manuscript.

TABLE 1.—*Composition of Mine Product and of Milled Talc from Tremolite Talc Industry of Northern New York*

Mineral	Mine Product			Milled Talc	
	Mine A, Per Cent	Mine B, Per Cent	Mine C, Per Cent	Mill D, Per Cent	Mill E, Per Cent
Talc	20	40	50	12	30
Tremolite	40	30	35	55	55
Anthophyllite	35	3	7	20	7
Serpentine	1	3	5	8	6
Calcite	<1	4	3	2	2
Quartz	4	20	<0.1	3	0.2

Mill D used the mine product of Mines B and C, and Mill E was supplied by Mine C.

TABLE 2.—*Composition of Atmospheric Dust Collected with Electrostatic Precipitator in Mines and Mills of Tremolite Talc Industry of Northern New York*

Mineral	Atmospheric Dust					
	Mine A*		Mine B, Per Cent	Mine C, Per Cent	Mill D, Per Cent	Mill E, Per Cent
	Per Cent (a)	Per Cent (b)				
Talc	15	25	22	15	25	25
Tremolite	60	55	15	40	55	50
Anthophyllite	2	2	2	40	13	13
Serpentine	1 (?)	1 (?)	7	3	3	10
Calcite	20	10	50	2	2	2
Quartz	2	7	9	0.1	2	0.2

* The two samples of atmospheric dust from Mine A were collected in different levels of the mine. They were taken several months later than those from Mines B and C and Mills D and E.

in the mine product and in milled talc. This finding is in agreement with previous observations [4] that the composition of air-borne dust may differ considerably from that of the source material from which the dust originated. Even in the same mine there may be substantial difference in the composition of the air-borne dust: one atmospheric sample collected in Mine A had a quartz content of 7%, while for another sample, taken at about the same time but in a different level, the quartz value was only 2% (Table 2). This variability in the quartz content is illustrated again by comparing the analyses of various samples of rock, mine-product, and air-borne dust taken in Mine A and in Mine B (Table 3). It will be noted that the per cent of quartz in the Mine A samples ranged from 21% to 0.3%, and in the Mine B samples from 41% to 9%.

This matter of quartz content is mentioned in some detail: first, because previous investigators [5] have reported that they found only a negligible amount of quartz in samples of rock and of ground material from this area; second, because it has been demonstrated (Table 4) that at least some quartz was present in the lungs of one miner and one miller from this local industry who had no other industrial exposure to dust, and, third, because quartz is a known pulmonary pathogen. The quartz may not be uniformly distributed throughout the entire tremolite talc bed, but the analyses in Table 3 show that it can be present in substantial amount. Owing to erratic distribution, the quartz deposits may be missed by random sampling.

In attempting to take cognizance of the potential pathogenic role which may be played by the quartz in the talc, sight must not be lost of the fact that the quartz found in the lungs of deceased miners who had also worked in other industries may have been derived from exposures in those industries.

CHEMICAL AND PETROGRAPHIC STUDY OF THE LUNGS OF EIGHT DECEASED TALC-INDUSTRY EMPLOYEES

The series of autopsy specimens studied consisted of the lungs of seven miners and one miller from the tremolite talc industry. All the miners had been engaged in drilling rock for periods ranging from 10 months to 27 years. The mill worker (Case 3) had been employed for six years, but, as his body had been exhumed for study 18 months after his death, the findings are only of limited value. A portion of the autopsy material was taken for gross specimens and for histologic examination, and the balance was reserved for chemical, petrographic, and x-ray diffraction examination. For the component chemical analysis and a few of the mineralogical analyses, samples of tissue

TABLE 3.—*Quartz Content of Rock, of Mine Product, and of Atmospheric Dust from Mines A and B*

	Quartz Content											
	Mine A, Per Cent						Mine B, Per Cent					
Rock chips	0.3	11	11	19	..	..	13	..	..	41	..	..
Mine product	..	..	..	..	4	21	..	..	..	..	20	21
Atmospheric dust	2	7	9	..	..	..	10	17	9	..	..	..

TABLE 4.—*Analysis of Lungs of Industrial Workers Exposed to Dust in the Tremolite Talc Industry of Northern New York*

Autopsy Case No.	1	2	3	4	5 Right	5 Left	6 Right	6 Left	7	8
	%	%	%	%	%	%	%	%	%	%
Ash, per cent of dried tissue	17.41	11.22	17.60	8.50	12.41	13.02	6.47	7.45	4.69	5.72
Mineral Constituents, Per Cent of Ash										
Minerals										
Quartz	33.1	8.5	2.3	7.5	14.9	....	8.0	....	3.2	2.4
Talc	Tr	50	25	18	10	....	5	....	11	19
Tremolite	Nf	8	14	18	14	....	2	....	4	2
Anthophyllite	Nf	2	12	8	4	....	3	....	4	7
Feldspar	45	....	....	....	Tr	....	Tr	....	....	....
Mineral Constituents, Per Cent of Dried Tissue										
Minerals										
Quartz	5.8	1.0	0.4	0.6	1.8	....	0.5	....	0.2	0.1
Talc	Tr	5.4	4.4	1.5	1.2	....	0.3	....	0.5	1.1
Tremolite	Nf	0.9	2.5	1.5	1.7	....	0.1	....	0.2	0.1
Anthophyllite	Nf	0.2	2.1	0.7	0.5	....	0.2	....	0.2	0.4
Feldspar	8	....	....	....	Tr	....	Tr	....	....	....
Component Analysis, Per Cent of Ash										
Components										
SiO_2	63.1	40.0	51.6	36.0	52.1	52.6	59.4	53.5	17.9	56.1
Fe_2O_3	4.4	4.8	1.5	5.6	11.0	9.2	14.1	15.9	6.1	7.1
Al_2O_3	11.9	6.4	10.5	9.1	8.1	7.9	4.4	6.0	0.9	2.1
P_2O_5	6.7	21.2	6.1	16.1	8.8	8.3	21.4	17.2	31.3	25.3
CaO	0.8	4.8	3.7	3.4	2.5	2.1	3.0	2.0	3.0	4.8
MgO	2.3	13.3	13.8	16.2	12.0	12.9	3.4	4.7	7.8	8.4
Na_2O	4.5	3.2	5.6	5.3	4.7	2.5	5.9	5.8	11.9	9.5
K_2O	4.0	4.9	3.1	10.0	3.2	3.2	6.6	6.4	11.8	8.9

Nf—none found.

were removed from representative portions of the lungs and mixed. The samples were then dried overnight at 105 C and ashed in a muffle furnace. Most of the mineralogical determinations were based upon other mixed portions of tissue digested with 30% hydrogen peroxide by the method of Sundius and Bygden [6] to avoid the alteration in mineral structure sometimes caused by dry ashing. The results of the chemical and mineralogical determinations are shown in Table 4. It should be pointed out that the values given for some of the minerals are only approximate estimates. The quartz content was determined by a special chemical and petrographic method and is fairly accurate, but the values in the table for talc, tremolite, and anthophyllite may be somewhat above or below the true value.

PULMONARY HISTOPATHOLOGY ASSOCIATED WITH TALC-DUST EXPOSURE

Though our series of eight cases appears limited, we were particularly fortunate in having available for study such a diversified range of dust exposures and lung lesions (Table 5). At the one end of our scale we have Case 1, with but 10 months' exposure to talc dust as a miner and 17 years' general mining. At the other extreme is Case 8, with 27 years' talc mining exposure and 10 years' general mining.

The associated exposures included service as miners of zinc, lead, coal, and iron pyrites. This helps to elucidate the essential talc reaction, as the normal result of exposure to dust hazards in mines of the latter types is fairly well understood.

Our best fortune, however, for the present purpose is Case 7, a person who had worked 23 years only as a talc miner before dying from an unrelated cause without any intercurrent superimposed pulmonary disease. This case may therefore serve as a classical example of a talc miner pneumoconiosis.

Case 3 would have been equally valuable, as this worker had been exposed during his six years of employment as a surface crusher man and mill sweeper. Unfortunately, the studies were not made until his body was exhumed 18 months after burial, and so not much detail was preserved. However, it confirms certain essential points.

FUNDAMENTAL PULMONARY TALC REACTION

The primary reaction present in Case 7 consists of multiple irregularly shaped foci (1 to 3 mm. in diameter) comprised of virtually pure fibrocytic proliferation and macro-

TABLE 5.—*Industrial Exposures, Causes of Death, and Pulmonary Pathology in Eight Deceased Tremolite Talc-Industry Employees*

Case No.	Dust Exposure: Talc	Dust Exposure: Other	Age at Death	Cause of Death	Dominant Pulmonary Lesions: Talc Pneumoconiosis	Dominant Pulmonary Lesions: Silicosis	Dominant Pulmonary Lesions: Infection
1	Mine ? 10 mo.	Zinc mine 10 yr. Unknown ? yr.	?	Cor pulmonale	Fibrocellular, with perivascular granulomatosis	Advanced diffuse, with hyalinization; isolated nodules	Nil
2	Mine Drilling 4 yr.	Lead mine ? yr. Iron mine 1 yr.	38	Cor pulmonale	Massive diffuse fibrocellular	Diffuse with focal necrosis	? Histoplasmosis
3	Surface Crusher ? yr. Sweeper 4 yr.	.....	48	?	Diffuse dominantly cellular perivascular	Nil	Basal lobes tuberculosis
4	Mine Drilling 14 yr.	Zinc mine 8 yr.	49	Tuberculosis	Massive fibrocellular	Massive confluent and multifocal	Chronic basal tuberculosis with bronchogenic spread
5	Mine Drilling 16 yr.	Coal mine ? yr. Iron mine ? yr.	51	Cor pulmonale	Multifocal massive fibrocellular	Confluent nodular and massive fibrocellular	Tuberculosilicosis with necrosis
6	Mine ? 17 yr.	Zinc mine ? yr. Pyrites 8 yr.	52	Tuberculosis	Diffuse massive fibrocellular	Tuberculosilicotic	Tuberculosilicosis with cavitation
7	Mine ? 23 yr.	.....	57	Nephritis with cardiac failure	Perivascular discrete focal	Nil	Nil
8	Mine ? 27 yr.	Mining 10 yr.	60+	Congestive cardiac failure	Diffuse fibrocellular	Massive multifocal	Nil

phage accumulation. The cellular deposit tends to be arranged in a stellate manner around medium-sized and smaller blood vessels (Fig. 1*A*). There is fairly abundant visible pigment, which either is found within isolated koniophores or seems to lie in the interstices between the fibrocytes. Some of these particles are brilliantly birefringent and may be present as spicules, some of which measure 0.5μ by 5μ (Fig. 1*B*).

These characteristic macules are easily distinguished from isolated mature silicotic nodules which are also present. Some of the latter possess a halo of cellular elements and are probably composite talc and silicotic lesions (Fig. 4*B*).

Elongated terminally clubbed bodies, measuring 20μ to 50μ long and in no obvious respect distinguishable from asbestos bodies, are present in fair abundance (Fig. 7), mainly within alveoli, where they tend to occur in clusters held together by koniophores (Fig. 8*A*). A moderate number also occur among the fibrocytes, and in these sites where there are fewer dumbbell types, there are also more instances of degenerative changes. The intra-alveolar "talc bodies" are generally stained intensely by means of Prussian blue, while those which lie among the fibrocytes may be losing their iron-containing sheaths as the Prussian blue reaction is fainter and more widely dispersed. Many of the koniophores in the alveoli show this blue staining too.

The larger blood vessels trapped within these foci do not show much deviation from the normal. It should be clearly appreciated that the focal lesions appear as isolated macules in section only and really represent cellular sheaths accompanying the blood vessels for variable distances. The smaller arterioles may show some endarteritis obliterans, and rarely a talc body may be found embedded in the vascular walls. The fibrocytic infiltrate abuts directly on the vascular adventitia. However, there is no appreciable modification of the lamina elastica of the blood vessels. Capillary circulation through the fibrocytic masses is poorly developed.

But little collagen is laid down among these fibrocytes. The supporting stroma instead consists of a delicate web of reticular fibers embracing groups of fibrocytes rather than subtending individual cells (Fig. 2*A*). Elastic tissue is absent from the centers of the cellular areas (Fig. 4*A*).

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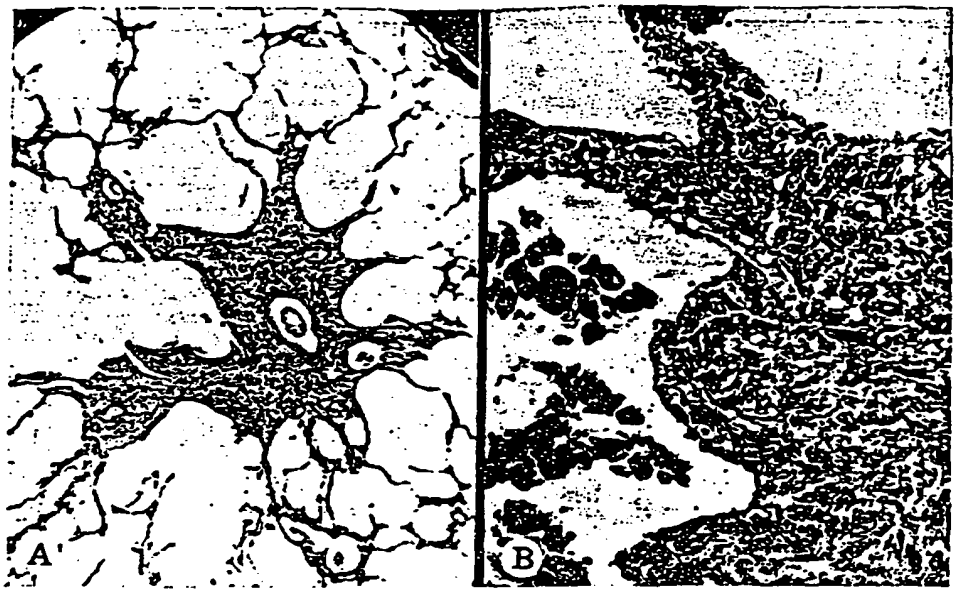
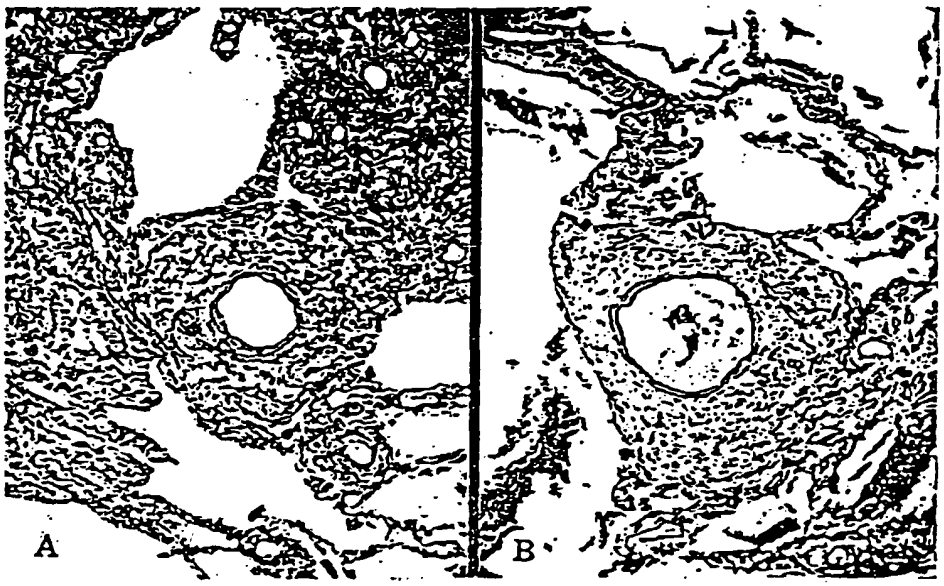


Fig. 1.—Primary lesion: talc mine dust exposure only. *A*, perivascular cellular aggregation. *B*, high-power view, showing massed macrophages and fibrocytes and talc particles.

Fig. 2.—Stroma of perivascular deposits of talcosis. *A*, reticulum supporting the macrophages and fibrocytes in the primary lesion, with talc components only (low quartz content in lung ash). *B*, collagen abundantly deposited with fewer cells (high quartz content in lung ash).



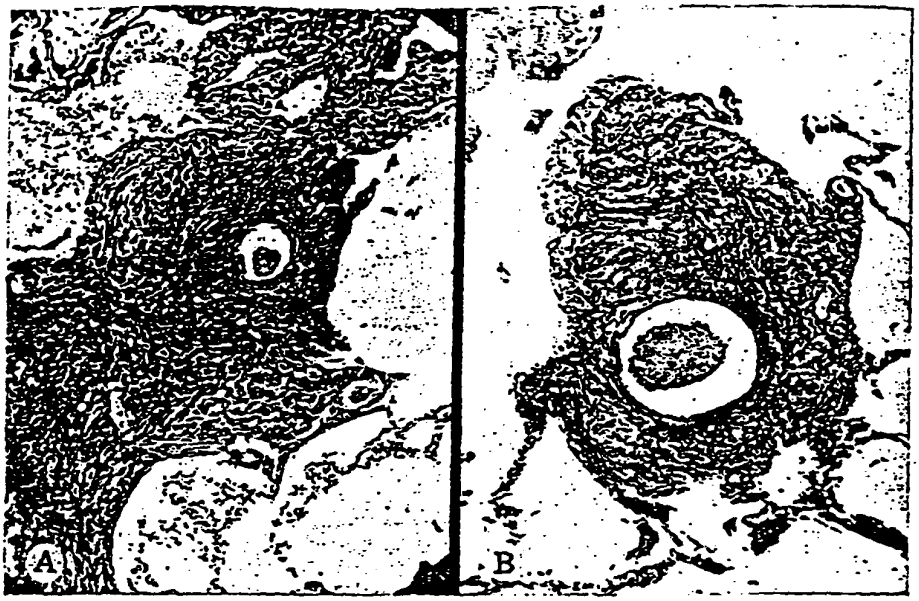


Fig. 3.—Perivascular fibrosis in talcosis. *A*, abundant fibrocellular reaction around vessel (moderate quartz content in lung ash). *B*, marked collagen deposition with paravascular nodule (high quartz content in lung ash).

Fig. 4.—Parenchymal nodules found in talcotic lung. *A*, dominantly cellular nodule, with central amorphous change and talc bodies (low quartz content in lung ash). *B*, hyalinized whorled nodule, with peripheral cellular reaction (high quartz content in lung ash).

around vessel
scular nodule

nodule, with
, hyalinized

At isolated sites focal necrosis has supervened within the cellular areas. There is no apparent zonulation around these necrotic areas or any tendency to collagen deposition or caseation. No suggestion of tuberculosis exists, and the cause may be ischemic in view of topographically evident arteriolar occlusion or luminar narrowing. On the other hand, the histological features are highly suggestive of histoplasmosis.

The perivascular fibrocytic deposits tend not to invade adjacent alveolar walls in massive columns, though large numbers of alveolar walls are moderately thickened owing to cellular infiltrates, and this change is the more evident at the points of junction of individual septa. At isolated points the alveolar walls are inclined to be thin, but there is only a slight tendency toward rupturing, as alveolar spaces are inclined to be moderately reduced in diameter. The resultant tendency to atrophic emphysema is most distinct toward the lung periphery.

Septal cells are not conspicuously developed, and there is no evidence of macrophage or septal cell catarrh into the alveolar spaces. Virtually no excessive collagen is present within these alveolar walls, but a delicate reticular skeleton supports its center. Elastic bundles are poorly represented and occur in a fragmented fashion among the fibrocytes. Alveolar wall capillaries are occluded along some stretches where fibrocyte deposition is particularly abundant, but more generally the capillary circulation is undisturbed.

Columns of cellular reaction accompany the interlobular septa to the pulmonary periphery, thus producing a coarsely webbed sectional effect. There is more collagen in these septa than elsewhere (Fig. 11*B*). The pleura shows slight cellular infiltration and mild collagen deposition internally to the lamina elastica. Numerous talc bodies may be found here, and some can be seen to partially penetrate the elastica. Superficial to the latter, a vascular zone of fibrocellular reaction of variable thickness is to be seen. Isolated silicotic nodules occur in this zone. It is covered by mesothelium (Fig. 12).

Lymphoid tissue is scantily present in the lungs, and the granulomatous reaction appears to avoid these foci almost completely, though these granulomata may abut on such lymphoid tissue. The hilar lymph nodes show hardly any hyperplasia and exhibit minimal pigmentation only. No talc bodies are to be found. However, minute circumscribed silicotic nodules are present.

Many of the bronchioles and some of the smaller bronchi are markedly distended and distorted and are the seat of chronic inflammatory change without, however, any material impairment of the epithelium (Fig. 9*B*). The latter indeed tends to be hypertrophic, with goblet cells predominating. The bronchial glands are also somewhat hyperplastic. A little plasma cell infiltration into the mucosa is evident, but there is no collagen deposition. The muscularis mucosae does not seem to be hypertrophic, because its component columns are so widely separated. However, this is illusory, and there is in reality fairly well-marked muscular hypertrophy. Sometimes this is focal in distribution (Fig. 9*A*). How effectively this muscular system may operate is left in some doubt, in view of the patent invasion of the bronchiolar adventitia by fibrocytes at many sites, as the peribronchial veins and arteries are similarly invested by the proliferating reaction.

MODIFIED TALC LESIONS

The basic lesion just described may be recognized throughout this series of cases, though modified by the associated pathological processes induced by other dusts. It is the more remarkable to note that the cellular proliferative phenomenon is present even in Case 1, where the history of talc-dust exposure is as short as 10 months, and persists in virtually similar form not only in Case 7, with a history of 23 years of talc exposure, but also in the instance of Case 8, where there was a 27-year talc-exposure history,—together with 10 years' exposure to dusts encountered in zinc and lead mining.

There may be a greater tendency toward the formation of massive lesions and subpleural reaction where there is an associated

Fig. 5.—Parenchymal cellular deposits in talc miners. *A*, loose cellular web, with atrophic alveoli (moderate quartz content in lung ash). *B*, pigmented iron-staining stellate cellular deposit (moderate quartz content in lung ash).

Fig. 6.—Stromal reactions in talcosis. *A*, pigmented fibrocellular granulation tissue, with atrophic alveoli (moderate quartz content in lung ash). *B*, dense diffuse fibrosis, with surviving elastic skeleton of occluded blood vessel (high quartz content in lung ash).

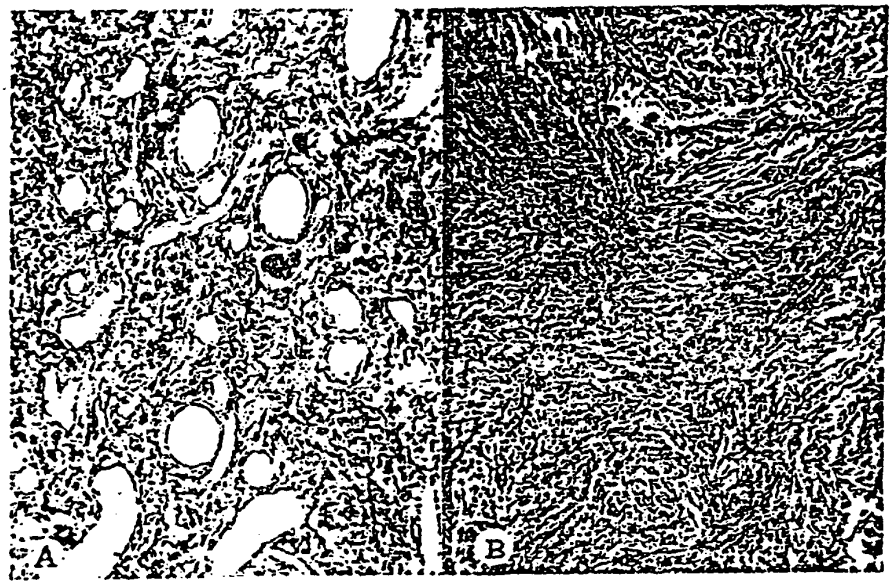
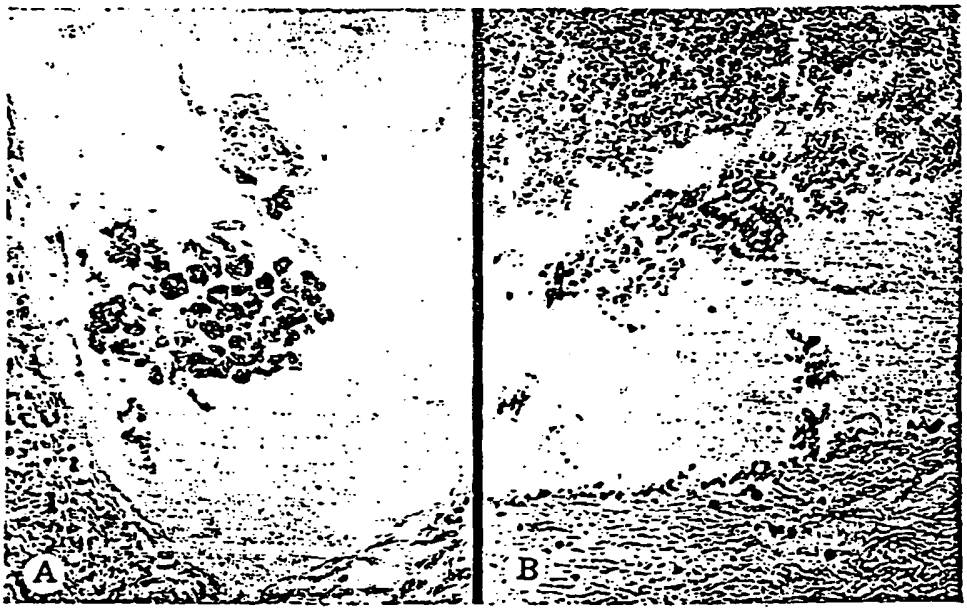


Fig. 7.—"Talc" bodies in human lung tissue. *A*, slender elongated "talc" bodies embedded in fibrous tissue. *B*, short dumbbell body partly engulfed by a macrophage and showing intense iron staining.

Fig. 8.—Talc bodies in human lung tissue. *A*, accumulation of koniophores, showing a high degree of iron staining and containing short lengths of talc fibers. *B*, talc body among erythrocytes within the lumen of a blood vessel.



quartz reaction. In Cases 2 and 6, collagen formation is restricted to a minimum and the supporting stroma tends to be of a reticular nature of variable density. In Cases 1, 5, and 8, there is a greater tendency toward collagen formation. It is to be noted that of these cases Cases 1 and 5 yielded a relatively high value for quartz in the lung tissue but Case 8 showed a very low quartz level. Birefringent quartz particles are a prominent feature of the tissues in Cases 1 and 5 and are but poorly demonstrable in other instances.

The interstitial alveolar wall reaction is also more marked in the cases with heavy quartz-dust exposure, and there is considerable collagen deposition even with some hyalinization in Cases 1, 2, 5, and 8. Indeed, in these cases the alveolar wall involvement is so pronounced as to overshadow somewhat the essentially perivascular distribution of the underlying talc reaction.

The damage sustained by the alveolar walls is further modified by the presence of quartz particles which involve marked macrophage and plasma cell infiltration, marked enlargement and proliferation of the superficial septal cells, often associated with cellular catarrh into the alveolar spaces, and finally moderate to marked impairment of the capillary circulation through these alveolar walls. The latter is not, however, a constant phenomenon, and there may be advanced alveolar wall disease without appreciable loss of capillaries (e. g., Case 6).

When collagen is present, it fails to be arranged in the form of silicotic nodules in all but rare locations (e. g., Cases 1 and 5). Incipient fibrous whorls are present also in Cases 2 and 8. Some lie against blood vessels (Fig. 3*B*). It seems possible that the abundantly cellular talc reaction is incompatible with the complete evolution of the nodular silicotic lesions.

Subpleural deposits follow the same pattern, being most marked where exposures to both talc and quartz have been considerable. The resultant lesion is, however, an exaggeration of the primary talc reaction except for the greater prominence of the collagen where quartz is abundantly present. Essentially, then, there are three cortical zones, viz., a fibrocellular internal component which may be variably pigmented and which may contain distended bronchioles, an intermediate exaggerated lamina elastica, and an external highly vascular fibrocellular layer usually covered by mesothelium (Fig. 12*B*).

The parenchymal stroma is considerably exaggerated in the presence of a quartz reaction superimposed on the talc phenomenon (Fig. 5). This is largely a perivenous change, and within these linear columns of fibrosis partially or wholly occluded blood vessels may be seen, sometimes so effectively incorporated within the scars as to be betrayed only by their residual elastic tissue skeletons (Fig. 6).

Vascular damage is indeed very much more in evidence in those cases with the longest history of hard-rock mining or where the highest free-silica content was discovered. Two essential processes are present, namely, an endothelial proliferation in the least vessels ending as endarteritis or endophlebitis obliterans and a periarteriolar fibrocytic proliferation, with fibrotic stricturing or partial invasion of the muscular coats (Figs. 2*B*, 3*B*, 10, 11). This process is present in its most exaggerated form in Cases 1 and 6, in which multiple periarteriolar granulomata may be found. Such lesions cause marked pulmonary ischemia, the more so as the lesions are not limited to the pulmonary circulation but may also involve the bronchial vascular system at numerous points, thus effectively precluding establishment of any collateral circulation.

While the essential reaction to talc appears to include exaggerated distention of bronchioles and smaller bronchi, this change, though present in a variable degree in all cases of the present series, is not universally observed throughout the lungs where reaction to quartz dust is concurrently present. Instead, there is a tendency toward narrowing of the bronchial lumen, epithelial desquamation, mucosal hypertrophy, sometimes with papilloma formation, and inflammatory infiltration, with adventitial fibrosis and cicatrization at multiple sites where exposure

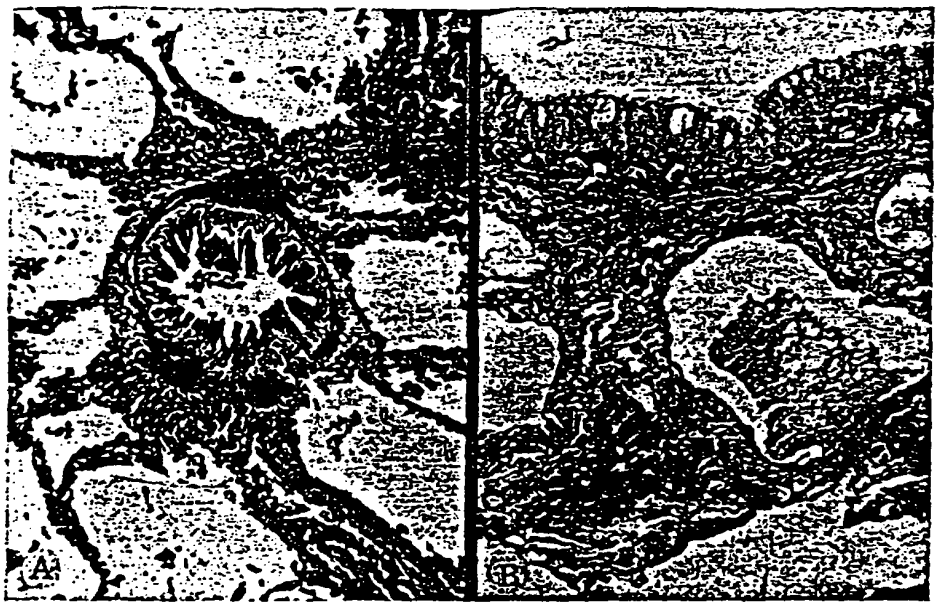
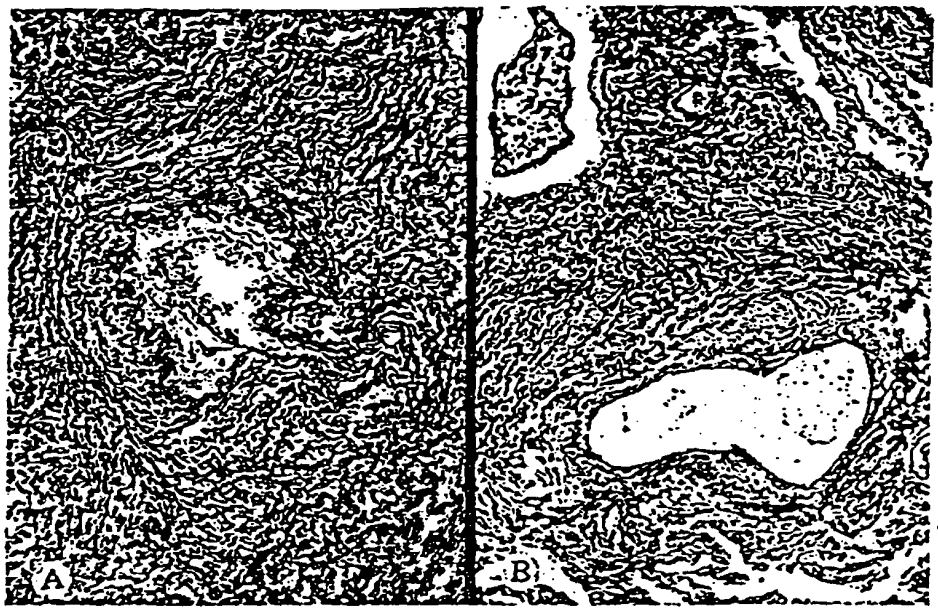


Fig. 9.—Bronchial damage in talcosis. *A*, irregular focal proliferation of muscularis mucosae (low quartz content in lung ash). *B*, submucosal fibrosis, with lymphatic distention but no injury to the epithelium (moderate quartz content in lung ash).

Fig. 10.—Vascular damage in talcosis. *A*, perivascular fibrosis and intimal swelling (high quartz content in lung ash). *B*, talcotic nodules in the walls of blood vessels (low quartz content in lung ash).



to quartz dust was adequate. This combination of chronic hypertrophic bronchitis, obliterative bronchiolitis, and the peripheral bronchiolectasia superimposed on the fibrocellular changes throughout the lungs may lead, on the one hand, to extensive areas of partial atelectasia of the relevant lung fields or, on the other, may be associated with the development of multiple epithelium-lined peripheral cysts. The latter are essentially ballooned-out terminal segments of the respiratory passages and may be readily distinguished from emphysematous bullae by the presence of the epithelial lining, the residual basement membrane, and the irregular presence of supporting muscle fibers. True emphysema is relatively infrequently seen and, when present, consists of the atrophic vesicular variety.

The differential involvement of lymphoid tissue in the reaction to talc dust and to talc dust combined with quartz dust is clearly demonstrated in the present series. Whereas the talc reaction tends sedulously to avoid the lymphoid tissue, the contrary condition prevails when quartz is abundantly present or where there is an associated tuberculosis. Talc bodies are, however, never seen in the lymph nodes, and the reaction present in most instances is limited to medullary macrophage infiltration and pigmentation. Silicotic or tuberculosilicotic nodules are present in but a few instances (Cases 1 and 5). Despite the fact that multiple nodules and necrotic foci are present in the lung substance, the hilar node involvement is not marked. This state of affairs is the reverse of what prevails in the presence of exposure to quartz dust unaccompanied by an exposure to talc dust. One is consequently inclined to infer that the simultaneous presence of talc dust and quartz dust in the lungs militates against the transportation of the quartz dust to the hilar nodes. Alternately, though talc bodies are not seen in the hilar nodes, their liberal transference is not yet precluded, and the inhibitory tendency of the talc on the silicotic reaction, which is manifest in the lung substance of this series, may prevail also in the lymphoid tissue.

Necrotic foci were observed within the areas of cellular proliferation in Cases 2, 4, 5, 6, and 7. In Case 2 histoplasmosis is the obvious answer, while in Cases 4, 5, and 6 the lesions are more suggestive of tuberculosis or tuberculosilicosis. There is some tendency toward inflammatory reaction at the periphery of the lesions in the latter three cases only. On the other hand, the necrosis also involves the stromal elements, favoring histoplasmosis once more. In the majority of other cases, it seems possible that the necrosis may be explicable on an ischemic basis, either because the cellular hyperplasia had outstripped its vascular supply or because the latter had been cut off through regional vascular occlusion. However, as all these cases came from the St. Lawrence Valley area at the time of an epidemic in that region, it is possible that histoplasmosis may be a factor.

The process seen in Cases 4, 5, and 6, if tuberculous, has been modified considerably by the abundance of fibrous tissue and cells. A large thick-walled cavity, without a distinctive fibrous capsule or even components, is present in the latter instance. Atypical tubercles are present within this wall at the edge of the broad inflammatory zone. While the temptation exists to interpret this cavity as tuberculous, it may represent merely a chronic discharging abscess. The lesion is also compatible with a diagnosis of histoplasmosis. Attention may also be drawn to the marked peribronchitis and ulcerative bronchitis in the passage draining this cavity. No tubercles were observed here.

Pneumonic areas were observed in the cases with exposures to both quartz dust and talc dust, especially Cases 2 and 4, but not where only talc dust was the responsible etiological agent. This pneumonic process tends to show healing by organization in various stages of progression, and numerous talc bodies are thus trapped. It seems likely that those present in the formed lesions may have been incorporated in this manner through earlier episodes of inflammation.

COMMENT

The chronic or long-term effects of the inhalation of dusts, such as are generated in talc industries, are thus demonstrated by this

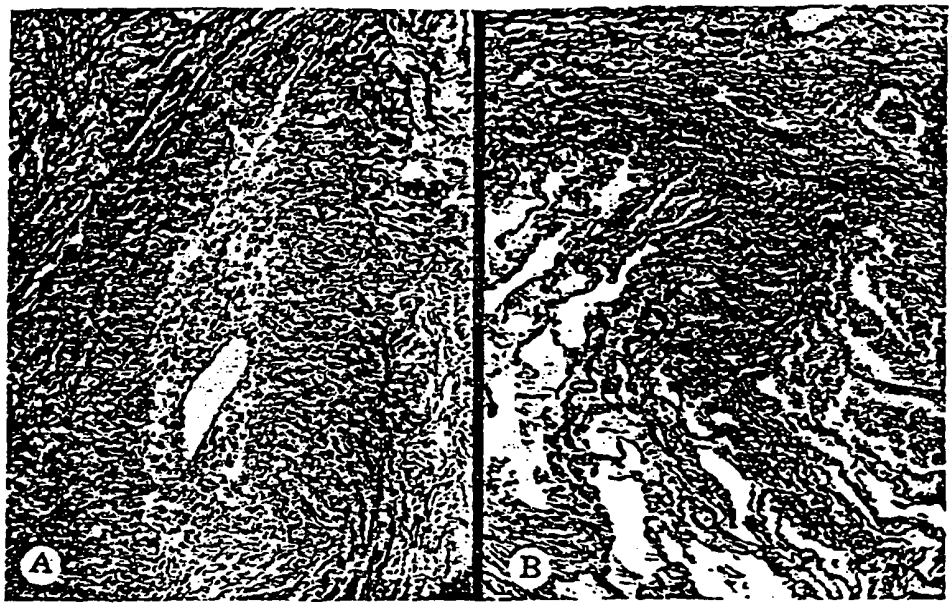
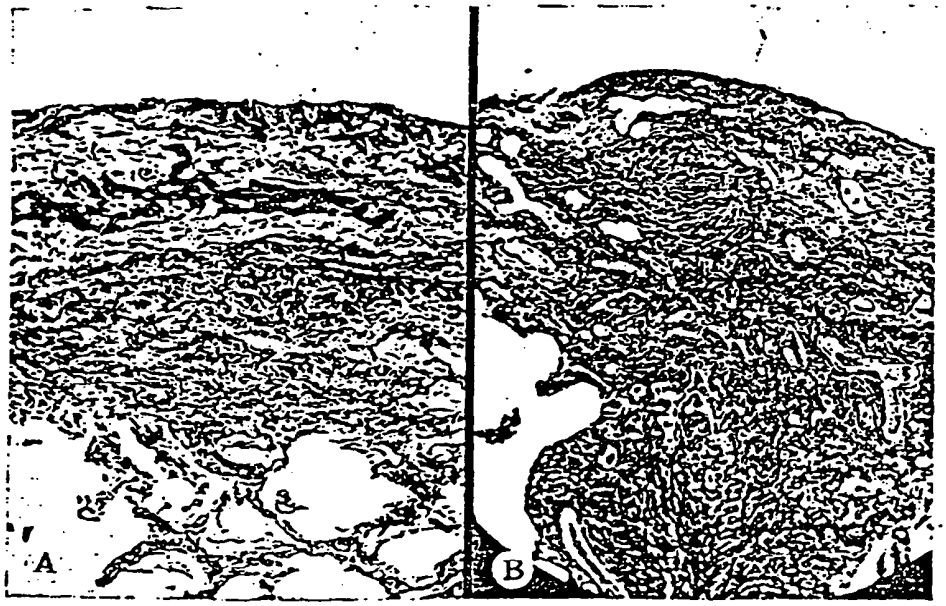


Fig. 11.—Vascular damage in talcosis. *A*, progressive loss of venous lumen through progressive proliferation of intima (moderate quartz in lung ash). *B*, fibroelastic scar in interlobular septum, representing the remains of obliterated blood vessels (moderate quartz in lung ash).

series of cases to vary considerably according to the extent or nature of associated dust in other industries to which the person may have been exposed, either preceding or suc-

Fig. 12.—Pleural damage in talcosis. *A*, diffuse fibrocellular, partly pigmented, and highly vascular reaction (low quartz content of lung ash). *B*, loose fibrous proliferation external to lamina elastica, with whorled nodules; talc plaque (high free-silica content of lung ash).



ceeding the period during which talc dust was breathed.

The histopathological features enumerated are almost entirely explicable in terms of the mineralogical analyses of the lung ash presented in Table 4.

It is seen, for instance, that for both of our key cases of pure talc pneumoconiosis (Cases 3 and 7) the quartz content of the lung ash (2.3% and 3.2%) was about the same as the corresponding value for many normal persons never exposed industrially to quartz dust. Among this series, the amount of lung ash of Case 7 is particularly low (4.69% of dried tissue), and so is the total silica content (17.9% of ash) which includes the silica in the silicates present in these tissues.

Quartz was present in Cases 1, 2, 4, 5, and 6 in concentrations compatible with nodular silicosis. Indeed, the average quartz content of the silicosis cases studied at The Saranac Laboratory is 9.3% of the lung ash. Cases 1 and 5, therefore, had unusually large amounts of quartz dust lodged in their lungs. Yet nodular silicosis was conspicuous by its absence in Cases 2, 4, and 6 and only sparsely present in Cases 1 and 5.

Attention is drawn to the demonstrated presence of talc, tremolite, and anthophyllite in the lung ash of Case 7. There is no apparent correlation in this series between the length of exposure and the concentration of these minerals in the lung ash.

The factor which seems most obviously to be responsible for the modification of the essential reaction to talc dust is the abundant amount of quartz dust coexistent with the talc in the pulmonary tissues. Five of the eight deceased talc employees had been miners also of lead, zinc, or pyrites. Attention is drawn to the minor differences in the mineral components of the lung ash. While we do know that quartz is an active pulmonary pathogen, we do not yet know whether the additional substances demonstrated (e. g., feldspar) are capable of playing a material role in modifying the response to either the quartz or the talc or are themselves pathogenic.

It does seem permissible, however, to infer that the presence of talc dust in its turn modifies appreciably the type of reaction to the quartz dust. Though considerable quantities of free silica were demonstrable in the lung tissue (Table 4) in some instances (Cases 1, 2, 4, 5, and 6), there was not in this series a clear-cut tendency to nodular silicosis.

Tuberculosis or histoplasmosis may have been a factor in the pneumoconiotic reaction in some of these cases. While doubt persists as to the diagnosis of a true infective process, it does seem certain that if the latter diagnosis has to be accepted the presence of the talc reaction induced an aberrant type of chronic inflammatory process.

While it has been postulated that the foregoing observed deviations from the primary process may all be due to coincidental quartz exposure to tuberculosis or histoplasmosis or to nonspecific pneumonia, reference should be made to the fact that there is insufficient knowledge in the present instances concerning the differences in the talc dusts to which the men were exposed or to the concentration and rate at which the talc dust was deposited in their lungs. The latter factors alone are known to influence the nature of the silicotic reaction which may follow exposure to quartz dust, and the precise composition of the talc may therefore necessarily be a factor too. In this connection it is interesting to note that the majority of talc bodies were in a range of 20μ to 50μ, being somewhat longer and thinner than the asbestos bodies generally found in asbestosis. In rare instances some slender fibers, measuring up to 200μ, were also present. Terminal clubbing was a factor in all but two cases (Cases 2 and 3), and occasionally an intermediate bead could be seen. Segmented forms were but rarely seen. In all cases the mantle of the body showed an intense iron-staining reaction, but degeneration of this coat was demonstrable in most cases where the talc bodies were present in the newly formed fibrocellular tissue.

In addition to the talc bodies and the chemically demonstrable quartz, there were in most instances pigment granules and birefringent particles, spicules, and crystals within the interstitial tissues and in the koniophores trapped within alveoli. The variable abundant

presence of such elements at sites of maximal fibroid or cellular reaction may undoubtedly bear some relation to the differential pathological effects observed in the present series. The pigmented particles, though present in all cases, were most abundant in Cases 1, 3, 6, and 8. Brilliantly birefringent particles, on the contrary, were conspicuous features mainly in Cases 2, 3, 4, and 8, and in this series large numbers of such particles were dispersed among the fibrocytes comprising the pulmonary lesions. These particles were identified as talc.

The "talc bodies" described may be an indication of the main pathogenic agent in the present series of cases or may be merely incidental features. Were the former to be the case, it would perhaps be advisable to rename them "tremolite bodies."

They were relatively sparsely represented in Cases 1, 6, and 8, and it is interesting to find that in these very three cases the tremolite content of the lung ash was least. They were present in greatest profusion in Cases 3, 4, and 5, and once more the mineralogical analysis confirms the relatively high incidence of tremolite in these three cases (Table 4). The anthophyllite values, on the contrary, do not correspond with the histopathological findings. It may therefore be fairly safely inferred that the "talc" bodies are of tremolite origin.

In view of the fundamental similarity between the talc reaction seen in this series and the histopathological changes present in asbestosis, one is constrained to speculate whether the tremolite component, being an asbestiform mineral, is not after all the main source of mischief. It remains for animal experiments to shed some light on this subject.

SUMMARY

A survey of the talc industry in Northern New York State revealed that the talc mined and processed there consists of a mixture of talc, tremolite, and anthophyllite. Quartz is also present in moderate amounts in the dust generated in mining and processing the commercial talc.

A mineralogical analysis of the lung ash from eight deceased talc-industry employees revealed the presence of appreciable quantities of talc, tremolite, and anthophyllite. Quartz was present in significant amounts only in the cases where the men had been additionally exposed to dust in mining industries other than in the talc industry.

The histological features suggest that tremolite may be the main pathogenic agent in provoking the characteristic "talc" lung lesion. The role of talc and of anthophyllite has not been wholly excluded.

The presence of quartz modifies materially the nature of the "talc" reaction.

The presence of "talc" dust in the lungs modifies both the response to quartz dust and the course of associated infection.

Marked pulmonary vascular damage was present in the cases where the quartz content of the lungs was highest, and this feature is in harmony with the tendency to cardiac deaths.

Bronchitis, bronchiolitis obliterans, and bronchiolectasis are associated major findings in this series.

The chemical analyses presented in Table 4 were made by A. J. Redlin, chemist, Saranac Laboratory. E. S. Larsen, 3d, Ph.D., of the U. S. Geological Survey, formerly petrographer of The Saranac Laboratory, made the petrographic and X-ray diffraction analyses.

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