Final Report

INVESTIGATION CONCERNING THE CAPACITY OF INHALED KAYLO DUST TO INJURE THE LUNG

to the

Owens-Illinois Glass Company

b CONFIDENTIAL

The Saranac Laboratory

January 30, 1952

CONFIDENTIAL

Final Report

INVESTIGATION CONCERNING THE CAPACITY OF INHALED ASBESTOS DUST

TO INJURE THE LUNG

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to

Owens-Illinois Glass Company

Toledo, Ohio

by

The Saranac Laboratory

Saranac Lake, New York

January 30, 1952

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INVESTIGATION ABOUT THE [illegible] OF INHALED KAYLO DUST

IN MONKEYS AND RATS

I. INTRODUCTION

In 1942 the Owens-Illinois Glass Company had developed to the pilot plant stage a new industrial product, known as Kaylo, which could be used as a thermal insulating material and for other applications. According to information supplied by the company, this product was prepared by heating under steam pressure a suspension of calcium hydroxide, silica, and asbestos to form a hydrated calcium silicate. Studies at The Saranac Laboratory showed that although the principal component of Kaylo was the hydrated calcium silicate, some unchanged raw materials, including asbestos and free silica in the form of quartz or diatomaceous earth, were also present in the final product. Before Kaylo was used commercially on a large scale, it was important to determine whether or not any dust liberated from this product during manufacture, handling or fabrication would be likely to constitute a respiratory hazard to exposed individuals. Therefore, a comprehensive investigation was undertaken in which the effect of inhaled Kaylo dust on animals was studied. The investigation was started in February 1945 and was carried on for more than five years. It explored the nature of the pulmonary tissue reaction to inhaled Kaylo dust in normal animals and in animals harboring a tuberculous infection. In this final report of the study the principal findings given in previous interim reports will be reviewed briefly and the conclusions derived from the entire experimental program will be stated.

II. TESTING MATERIAL USED

The material used for producing atmospheric dust in the experimental cubic room was finely-divided [illegible] obtained from the dust collectors of the Corning, New York, plant, in which Kaylo is manufactured. The material was received in separate shipments, as follows:

Lot #1 - Received in February 1945.
" #2 - " " February 1947.
" #3 - " " January 1949.

A. Composition: The results of chemical and petrographic analysis of a representative sample of the material as received at the Saranac Laboratory, are given in Table 1. It will be noted that the only asbestos mineral revealed by the petrographic examination of this sample is chrysotile. Since Kaylo is a commercial product, it is possible that minor alterations in composition may occur from time to time in accordance with changes in the raw materials used. For example, the quartz value for lot #1 of Kaylo was less than 1 per cent but the quartz content of lots #2 and #3 was between 2 to 5 per cent. In the final shipment of Kaylo, received in January 1949 and first used in this experiment in September 1949, the asbestos component contained the mineral amosite as well as chrysotile. The fibers of amosite, in comparison with those of chrysotile, are less flexible and have a higher iron content. However, since experiments with animals have shown that both amosite and chrysotile are capable of causing asbestosis, it is unlikely that the substitution of the one mineral for the other in Kaylo would cause a significant change in the toxic properties of the final product.

B. X-Ray diffraction studies: The X-ray diffraction pattern of samples of two different shipments of Kaylo are shown in fig. 1. The principal lines present are probably those of a hydrous calcium silicate, which is the principal component of Kaylo. Comparison of patterns a and b discloses that the quartz line is stronger in b than in a, indicating that the Kaylo received in January 1945 has a higher quartz content than has the earlier product, received in January 1946. Faint lines representing calcite and chrysotile are visible in both patterns. Diffraction lines produced by anosite are also present in pattern b.

C. Size-frequency studies: The size-distribution of Kaylo dust is shown by the graph in fig. 2. The lines of the graph represent the parent material in the dust machine and two samples of atmospheric dust collected in the dust room on different days. A magnification of 1200X was used in making the size-frequency counts. It will be noted that about 83 per cent of the particles in the parent material visible at that magnification are smaller than 5 microns in size; the corresponding values for the samples of atmospheric dust are 90 and 96 per cent. This difference in the two samples of atmospheric dust, which were derived from the same parent material, may have been due to the day-to-day variation in humidity inside the dust room.

III. REVIEW OF PREVIOUS REPORTS

During the course of the investigation with Kaylo dust five interim reports were issued.

The first report, dated May 13, 1946, revealed that in guinea pigs

exposed for 14 months to Kaylo dust the tissue reaction consisted only of microscopic focal collections of dust cells. The associated tuberculous infection had also been absorbed [illegible] to be of significance.

In the second report, dated October 30, 1947, it was noted that there was evidence suggesting that Kaylo dust when inhaled into the lungs produces pulmonary fibrosis in rats exposed for 18 months or in guinea pigs exposed for 20 months. These findings seemed to show Kaylo dust to be a biologically inert material. As the experiments dealing with the effect of the dust on a tuberculous infection the results were inconclusive, indicating that the experiment should be repeated.

The third report, dated October 30, 1948, presented the final observations on the effects of inhaled Kaylo dust on normal uninfected guinea pigs. Contrary to previous tentative impressions, based upon an exposure of 20 months, which suggested Kaylo dust to be inert, the study of animals exposed for 34 months indicated that the material is not inert but is capable of prolonged inhalation, of producing asbestosis in guinea pigs. However, neither silicosis nor the diffuse fibrosis which is caused by inhaled tuberculous [illegible] developed in the exposed animals.

The fourth report, dated April 30, 1949, reviewed the results of the first 3 reports of a new experiment in which the effect of inhaled Kaylo dust on a tuberculous infection in guinea pigs was studied. No definitely adverse effect of the dust on the infection during this 8-months period was noted.

The fifth report, dated January 1, 1950, supplemented the information given in the fourth report by extending the observations to infected animals.

that had been exposed to Kaylo dust for periods up to 14 months. The findings at that time suggested that Kaylo dust had a slightly adverse influence on the bounce of the pulmonary infection in guinea pigs but that the effect was by no means as pronounced as that of quartz dust.

[illegible] (July 1958)

As a continuation of the previous interim reports and as a summary for this final report, a review of the entire program of study is reported.

In the inhalation experiment (Saranac Laboratory No. 1012, 1100, 1104) groups of guinea pigs, rats, and hamsters were placed in a cubical dust room, 3 feet in dimension, in which an atmospheric suspension of Kaylo dust was maintained. The room was operated for more than five years, from February 1948 to June 1953. About 450 animals were used in the experiment and some of them lived in the dust room for as long as 3 years.

Conditions of exposure

The atmospheric suspension of Kaylo dust was created by the action of a paddle that rotated inside a hopper, located in a corner of the dust room, which contained the finely-divided Kaylo product. The dust cloud generated in this manner floated out into the room where it was maintained for 8 hours on five days of the week and for 4 hours on Saturdays. At regular intervals during the experiment a few animals were killed and the tissues examined grossly and microscopically to determine the nature and the extent of the dust reaction. The tissue was also analyzed chemically to estimate the amount of Kaylo dust retained in the lungs of animals exposed for definite periods of time.

Dust counts of atmospheric samples collected in the dust room with the midget impinger were made regularly. The concentration of dusts used to infect the animals was determined periodically within the range of 101 to 186 mil. The particle size data of the mid the overall average was 115 million. In the experiments with infected animals the concentration was higher, the average being 213 million.

D. Exposure of uninfected animals

Three species - guinea pig, rat, hamster - were employed in this phase of the investigation. A summary of the findings is given in table 2.

(1) Guinea pigs. At the beginning of the experiment 100 uninfected guinea pigs were placed in the dust room and 6 months later 25 more were added to replace animals that had died in an epidemic of acute pneumonia. Since this disease is occurred at this time also in animals exposed to small [illegible] quartz room, the unfortunate epidemic was [illegible] would result. [illegible] of this kind, which occurs occasionally in experiments of this type, it must be controlled. Groups of guinea pigs, numbered [illegible] were killed at 2, 4, 6, 8, 12, 16, 21, 24, 27, 30, 36, and 42 months after the beginning of their exposure to dust. [illegible] and the [illegible] of the pathology findings would be followed.

In guinea pigs exposed for periods up to 42 months there was only a mild tissue response to the dust and in this case the condition was limited to the accumulation of dust [illegible] in alveolar macrophages in groups of adjoining air spaces [illegible]. The interalveolar alveolar walls were only slightly thickened by accumulations of mononuclear [illegible] cells and multinucleated

giant cells were visible but there was no excessive proliferation of tissue histiocytes or deposition of connective tissue. A few asbestosis bodies were seen (fig. 4). Microscopic study of the tracheobronchial lymph nodes, which became enlarged but remained soft, revealed clusters of inactive dust cells similar to those in the lungs but without asbestosis bodies. It is pertinent to point out here that animals exposed to asbestos dust for a similar 30-months period exhibit a severe tissue reaction with the production of fibrosis (fig. 5). For comparison, a lung section of a normal guinea pig is shown (fig. 6).

The 9 animals exposed to Kaylo dust for more than 30 months (3 animals for 33 months and 3 animals for 36 months) showed not only the lesions like those of the 30-months animals but also exhibited a true fibrosis of a type characteristic of the response of guinea pigs to inhaled asbestos fibers. This reaction is a rather diffuse type of fibrosis which forms principally about the bronchioles, the small ducts from which the terminal air spaces, or alveoli, arise. A comparison of fig. 7 and fig. 5 reveals the similarity of the tissue reaction produced in the lungs by Kaylo dust and by asbestos dust. The lesions in the tracheobronchial lymph nodes showed no change between 30 months and 36 months.

(2) Rats. This species was employed because typical nodular fibrosis produced by inhaled quartz dust develops more rapidly in rats than in animals of other species. Forty rats were used and some of them were exposed to Kaylo dust for as long as 18 months. Pneumonia was not a problem during the first year of the experiment but among the rats exposed for 13 to 18 months 13 animals died with terminal bronchiolitis and lobular

pneumonia. Since laboratory [illegible] older than one year, even those not exposed to dust, are normally subject to this type of lesion, the high mortality rate is not considered significant. In order to follow the progression of the tissue reaction to the inhaled Kaylo dust rats were killed in groups of 4 after 6, 9, 12, 15, and 18 months of exposure. It was revealed (Fig. 8) that throughout the experiment the reaction to the dust consisted of focal collections, in the alveoli, of macrophages which contained particles and spicules of dust. The only change observed as the exposure period became longer was an increase in the number of the alveolar foci. Similar dust-filled macrophages were seen in the tracheobronchial lymph nodes. In no animal was there any tissue reaction typical of silicosis. The peribronchiolar fibrosis of asbestosis was not discovered, though occasional asbestosis bodies were observed. In view of other experiments with pure long-fibre asbestos dust, typical peribronchiolar fibrosis would not be expected in 18 months exposure to Kaylo dust.

(3) Hamsters. Twenty hamsters were placed in the dust room and after 3, 6, 12, and 18 months of exposure 5 animals were killed at each period for study; at the 6 months period 6 animals that died from other causes were examined. Histologic examination revealed that the Kaylo dust accumulated very slowly in the lungs. No fibrosis was seen except in one hamster, which had been exposed for 18 months. In that animal there was a trace of peribronchiolar fibrosis so slight that it could be definitely recognized only at high magnification. Asbestosis bodies in small numbers and at the usual sites were present.

3. Exposure of tuberculous animals

There are three types of experiments which are valuable for determining the effect of inhaled dusts on the course of tuberculosis in experimental animals. In the superimposition experiment normal animals are infected with tubercle bacilli by the inhalation method and then are immediately transferred to the dust room. Thus, the tuberculous disease and the injection by inhalation of dust will develop simultaneously. In the postexposure experiment the animals, after having inhaled with the tubercle bacilli, are allowed to live in a clean atmosphere for several months before being exposed to dust. During this period the tuberculous disease generally regresses and scar tissue takes place. Following exposure of the animals to some dusts the lesions may continue to regress or, with other dusts, the tuberculous process may become active and spread. The predisposition experiment is one in which animals are exposed to dust for several months, are then infected, and are immediately returned to the dust room, where their exposure to dust is continued. In this way the effect of a previous dust exposure on the early course of a tuberculous infection can be studied.

For investigating the effect of inhaled kaolin dust on the course of tuberculous infection a particular attenuated strain of human-type tubercle bacilli, known as the R_1 strain, was employed. This strain has a low degree of virulence for guinea pigs and, in the normal animal, produces a self-limited disease which will progress for 4 to 6 months and subsequently heal. In an animal which has inhaled quartz dust or certain other toxic dusts, however, the disease usually progresses continuously and ultimately causes the death of the animal. Since experience has indicated that tubercle

bacilli of the H_1 strain have about the same degree of virulence for the guinea pig as tubercle bacilli of the human strain have for man, it is possible to obtain some information upon the influence of various dusts on the H_1 tuberculous infection in guinea pigs and the effect of these dusts on the tuberculous disease in the animal members.

For inducing the animals with tubercle bacilli an inhalation chamber was used. A glass tube was fitted over the animal's nose and into this tube a suspension containing a known number of bacilli of the H_1 strain was sprayed with a Wolfhügel nebulizer. As the animal breathed, it inhaled the aerosphered suspension of bacilli into the lungs, where they became established.

(1) Simultaneous initial exposure of guinea pigs to the tuberculous organism and to dusts by inhalation started. In the first experiment in which animals were infected with tubercle bacilli at the time that their exposure to dusts was started (Table 3), 25 guinea pigs were used but an epidemic of pneumonia during the first 10 months reduced to 16 the number of animals available for study. Two of these died at 14 months, apparently from progressive tuberculosis, and 2 others died from undetermined causes, but not from tuberculosis. In the remaining 12 animals the course of the tuberculous disease was followed by killing 1 or 2 animals at 1, 3, 6, 12, 15, 18, and 24 months after infection. In 11 of the 12 animals the lesions were isolated, encapsulated, and regressing; in the remaining animal, which was killed at 15 months, the lesions were widespread throughout the lung but fibrosis had been produced, which indicated a tendency to heal. In an attempt to develop a strain of guinea pig resistant to the infection that had caused the pneumonia, some of the animals were used for breeding during

tubercle bacilli, whether the infection is combined with dust exposure or not, those animals must be excluded in assaying the effect of an inhaled dust upon a tuberculous infection. It is believed that "sports" are animals whose native resistance to the attenuated R_1 organism is unusually low. Support for this belief is given by experience with quartz dust, a definitely hazardous material, which reactivates an inhalation infection produced by attenuated R_1 bacilli but ordinarily is not associated with tuberculous extension to organs other than the lungs and tracheobronchial lymph nodes.

The control non-dusted group (table 3) of guinea pigs for this experiment was infected at the same time as the experimental group of animals subsequently dusted. The same culture of organisms was used for all animals. The tuberculous infection followed its usual course in the control group and resolved in all of the animals except one, a "sport", in which the disease spread.

Although a progressive tuberculous disease was noted in 4 guinea pigs of the second experiment, the degree of extension of the disease in them was slight. The remaining 23 animals, 8 of which died of intercurrent pneumonia, showed no spread and the infection followed the natural course of progression and healing as in the non-dusted control animals. It is believed, therefore, that the inhaled Kaylo dust had no significantly adverse effect on the tuberculosis.

(2) Reactivation infection: guinea pigs, after being infected, lived in clean air for several months before being exposed to Kaylo dust.

In the reactivation experiment (table 4) 26 guinea pigs were infected with the attenuated bacilli and allowed to live in a clean atmosphere. Animals

of this group were transferred to the dust room at 2 months (10 animals), 4 months (8 animals), and 6 months (7 animals) after infection. In order to follow the course of the disease further a pair of animals of the first sub-group (2 months in clean air) was killed after only 2 months of dust exposure and, in addition, animals from all groups were killed in pairs after 4, 8, and 12 months of exposure to the dust. Examination of the tissues of the dusted animals failed to reveal a significant reactivation of the tuberculous disease by the inhaled Kaylo dust. Only one animal showed evidence of spreading pulmonary tuberculosis, minimal in extent (Fig. 10). That animal was 1 of 3 that had lived in clean air for 2 months after infection and then had been exposed to the dust for 12 months.

In the control group (table 1) the tuberculous disease behaved in the normal manner and healed, with the exception that one animal (a "spert") developed a spreading disease and died from tuberculosis 6 months after infection.

(3) Predisposition infection: guinea pigs were infected 3 months after their exposure to Kaylo dust was started. An experiment of this type is a severe test because a dust that is only very slightly toxic may produce tissue changes which, though minor in character, may be sufficient to alter profoundly the development of a fresh tuberculous infection. In this experiment (table 5), which was designed to study the effect of Kaylo dust accumulated in the lung upon a newly-developing tuberculous disease, 50 guinea pigs were exposed to the dust for 3 months and then were infected with attenuated tubercle bacilli. The dust exposure was immediately resumed and carried on for another 21 months.

During the course of this experiment 5 animals were killed at the end of the preliminary 6 months' dusting period. They showed only an occasional deposit of dust particles in the alveolar spaces. Of the dusted and uninfected animals, 1 died from intercurrent pneumonia, which eliminates them for purposes of analysis; 1 animal died at 14 months after infection from spreading tuberculosis; and the remaining 17 animals were killed in pairs at 5, 6, 7, 8, 10, 12, and 18 months and 3 were killed at 21 months after infection. Of the latter group of 17 animals, 1 showed many spreading tubercles, 10 revealed both dead spreading tubercles and 6 exhibited healed tubercles. These findings indicate that a tuberculous infection in guinea pigs that originates several months after a prolonged exposure of the animals to flyle dust are initiated may be unfavorably influenced by the inhaled dust. This influence, however, is minimal in degree.

The tuberculous infection in the control animals (table 5) in general progressed and healed. Of the control animals there was, as usual, 1 "spare animal", killed 20 months after infection, which revealed a few scattered isolated tubercles that were of the spreading type.

5. Analysis of tissue of exposed animals

Chemical analysis of the lungs of uninfected guinea pigs that had inhaled flyle dust for periods up to 33 months yielded the data recorded in table 6. It will be noted that as the period of exposure became longer the ash values gradually increased, thus showing that mineral matter was accumulating in the lungs. There was a pronounced increase in the silica component up to about 20 months and then a slight decrease. The reason for

this condition, which has been observed in experiments with other dusts. ... not entirely clear but it seems to be due to dilution of the whole ... with the deposition of fibrosis as a result of the increase ... to silicosis which developed, as already mentioned, in the guinea pigs ... exposure to silica dusts. Since only 2 animals ... for each exposure period, individual values occasionally ... out of line but the general trend is clearly indicated.

V. REVIEW OF EXPERIMENTAL FINDINGS

The findings derived from the various inhalation experiments will be reviewed briefly and some points of significance mentioned.

A. Findings for normal animals inhaling Kaylo dust

The results of the inhalation experiment prove that Kaylo dust, when inhaled into the lungs of guinea pigs for a prolonged period (60 to 1... months) is capable of producing the peribronchiolar fibrosis characteristic of the early silicosis. No fibrosis was formed by the inhaled dust in mice or in hamsters, with the exception that fibrosis was barely recognizable in a single hamster, exposed for 18 months. In animals exposed for 60 months or more the lungs showed no fibrosis but certain aspects of the lesions, although masked by the reaction to the inert components in Kaylo dust, were compatible with an early stage in the development of pneumoconiosis, a disease in which there is a predilection for the silicon to localize in the terminal bronchioles. This selection is a result of particulate material, which is ordinarily deposited chiefly in the alveoli rather than in the bronchi of

calcium silicate which is the major constituent of Kaylo it may be said that although there is no scientific information about the effect of that compound on pulmonary tissue, there is much clinical and experimental evidence to suggest that it is biologically inert. Furthermore, in the inhalation experiments with Kaylo dust there was no deleterious effect noted which could be attributed to the calcium silicate component of the inhaled material. This observation is supported by our studies concerning similar calcium silicates in cement.

3. Findings for tuberculous animals inhaling Kaylo dust

The inhalation experiments in which tuberculous guinea pigs were exposed to Kaylo dust indicate that when the animals were infected with attenuated tubercle bacilli at the time exposure to the dust was started, i.e. were infected prior to that time, the inhaled Kaylo dust had little or no unfavorable effect of significance on the tuberculous infection. In most of the exposed animals the tuberculous disease healed in a manner similar to that in the few animals that exhibited a spreading type of lesion. The aggravation of the disease by the dust was minimal.

When the animals inhaled Kaylo dust for several months before being infected, the subsequent accumulation of the dusts in the lungs seemed to have a slightly unfavorable influence on the usual course of the tuberculous disease.

VI. SUMMARY

1. Kaylo dust, when inhaled for a prolonged period, is capable of producing

in the lungs of guinea pigs, but not of rats, the peribronchiolar fibrosis typical of asbestosis.

3. The inhalation of Keylo dust will not cause in guinea pigs, rats, or hamsters either silicosis or the diffuse fibrosis which sometimes follows the inhalation of diatomaceous earth.

4. The inhalation of Keylo dust does not significantly influence the usual course of tuberculosis in guinea pigs infected with attenuated tubercle bacilli, provided the infection is given to the animals before they are first exposed to the dust. In guinea pigs that have inhaled Keylo dust for several months before being infected, a continuation of the exposure appears to have a slightly unfavorable effect on the disease.

[illegible]

[illegible]

[illegible]	[illegible]
[illegible]	[illegible].09
[illegible]	[illegible].07
[illegible]	0.22
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	[illegible]
[illegible]	0.37
[illegible]	[illegible]
[illegible]	[illegible].82
[illegible]	[illegible]
	[illegible].4

[illegible] diffraction [illegible]

[illegible] principally of clay-like masses [illegible] produced a [illegible] X-ray diffraction pattern, presumably [illegible] hydrous calcium silicates. Quartz particles up to [illegible] were present, but they were not numerous and by weight probably made up less than 1 per cent of the sample. [illegible] 5 per cent of the material [illegible] calcite and approximately 10 to [illegible] chrysotile [illegible]. [illegible] was largely fibrous. The fibers and bundles present [illegible] several millimeters in length and were seldom [illegible] than 0.5 millimeter.

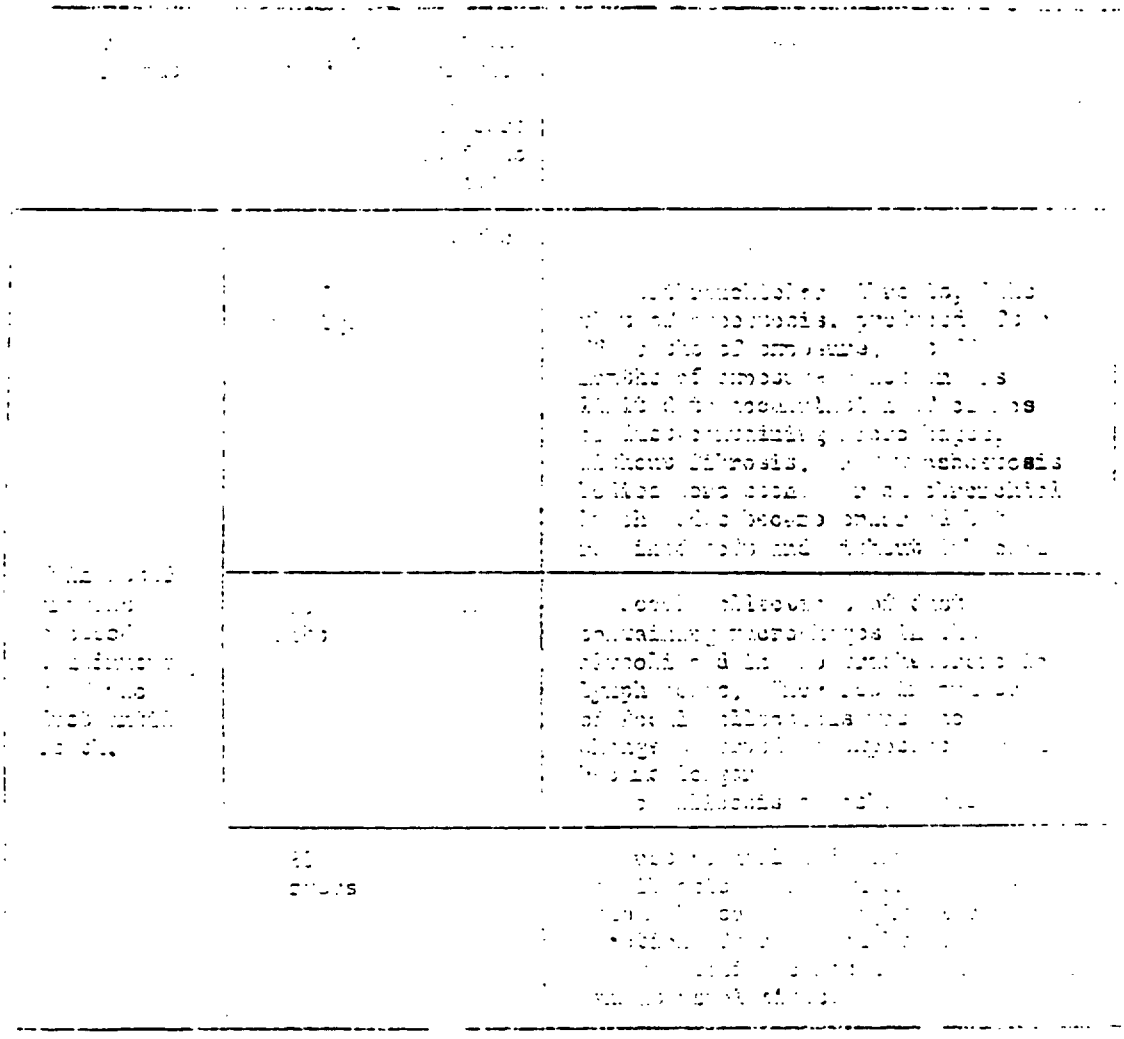

Table [illegible]

[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible] ... other 5 exposed animals were [illegible]"
[illegible] ion; n. [illegible]	34 [illegible]	[illegible]	[illegible]

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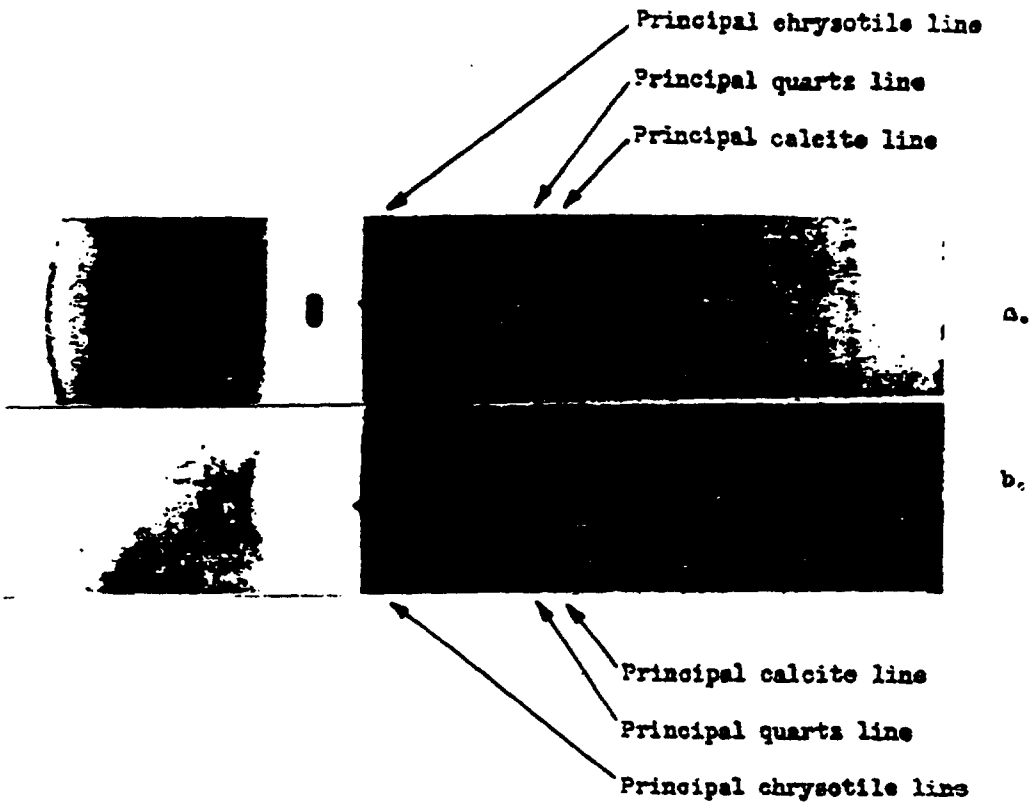

Fig. 1

X-RAY DIFFRACTION PATTERN OF KAYLO

a. Kaylo dust received in January 1946.

b. Kaylo dust received in January 1949.

Both patterns contain lines which represent a moderate amount of chrysotile and of calcite and a small amount of quartz. Faint lines representing what is probably the hydrous calcium silicate component of Kaylo are also present in both patterns. In addition, the original film of pattern b contains a very weak line corresponding to amosite but the line is too faint to appear in the reproduced pattern.

The quartz content indicated by pattern a is less than 1 per cent and by pattern b, about 4 per cent.

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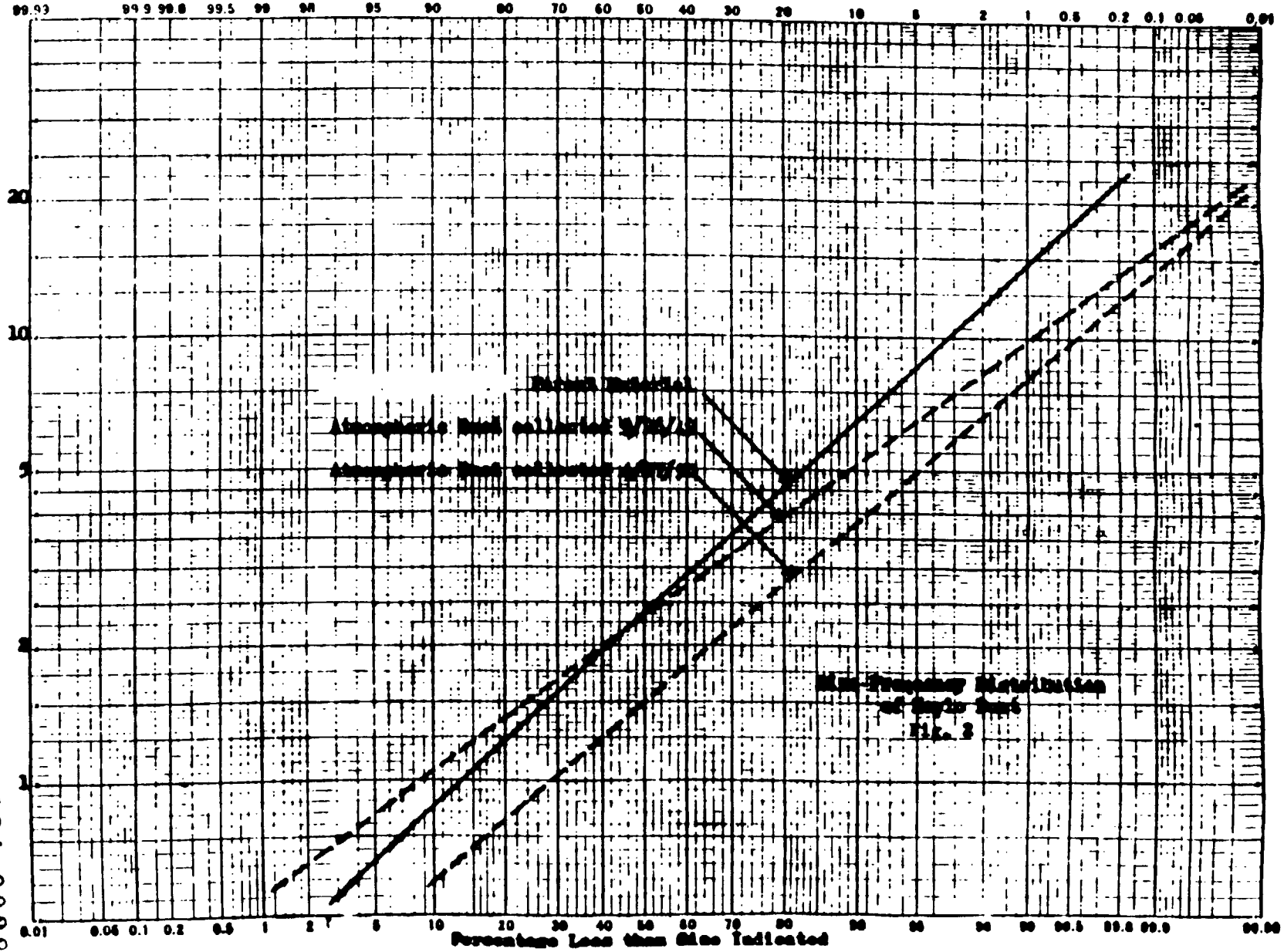

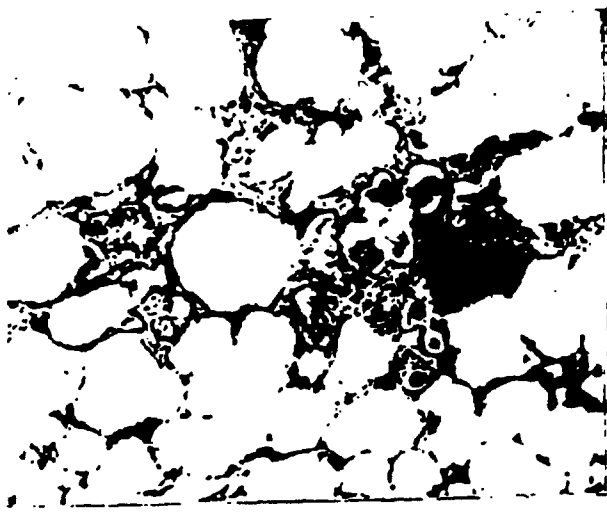

Fig. 3

Fig. 4

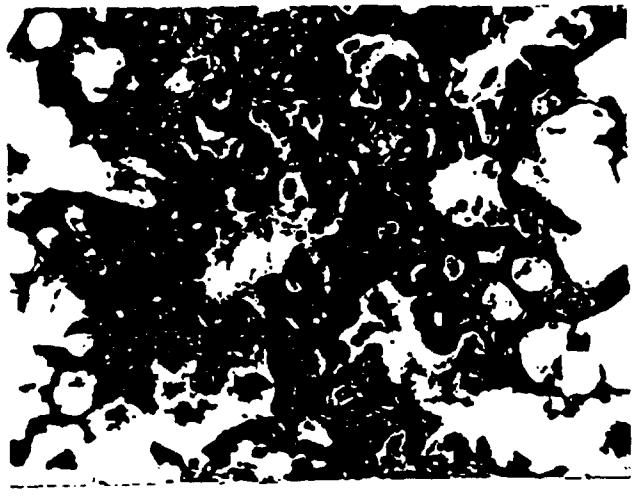

Fig. 5

Fig. 3. Lung tissue of a guinea pig exposed for 30 months to Kaylo dust by inhalation and then killed. A cross section of a bronchiole is shown just above and slightly to the left of center of the figure. The other spaces are alveoli. Note the dark masses within some of the smaller spaces, especially to the right of the bronchiole. These masses are macrophages and ruptured-nucleated giant cells. Note the thinness of the wall of the bronchiole; it is virtually normal, as is apparent on comparison with the tissue section of a normal guinea pig (fig. 5). An asbestosis body is present in this field and is revealed in fig. 4 at higher magnification. (200 X)

Fig. 4. High magnification of the tissue section shown in fig. 3. This higher magnification of part of the field of fig. 3 reveals a typical form of asbestosis body, the dark curved elongated structure to the right of center. (1200 X)

Fig. 5. Lung tissue of a guinea pig exposed for 30 months to Kings Mountain asbestos dust by inhalation and then killed. The bronchiole in this [illegible] micrograph is [illegible]

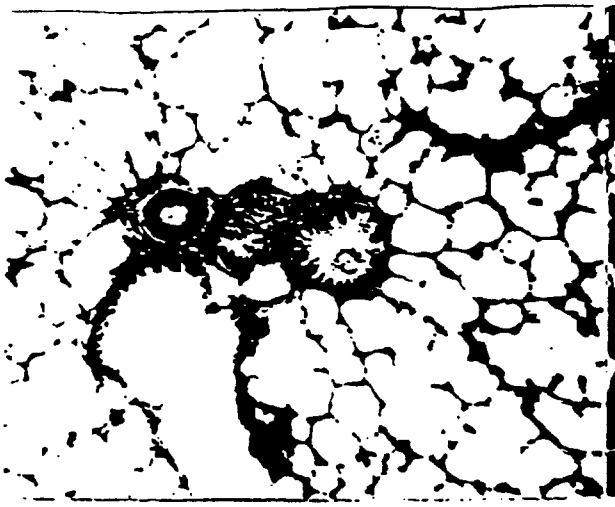

Fig. 6

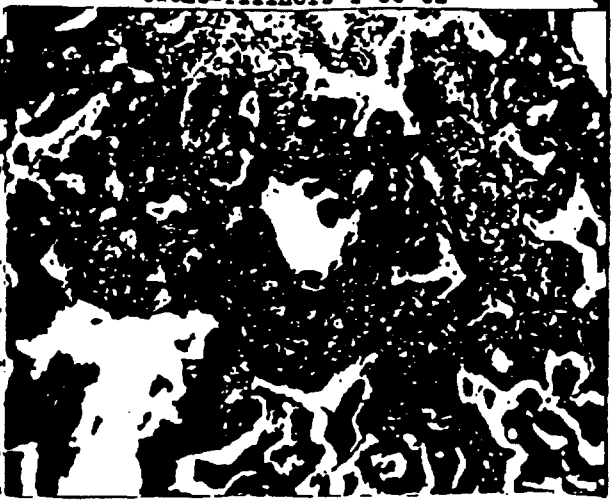

Fig. 7

Fig. 8

Fig. 6. Lung tissue of a normal guinea pig. This field shows two bronchioles, one in cross section at the right of center and the other in longitudinal section. The small associated blood vessel is visible above the bronchiole in longitudinal section. Compare the thickness of the wall of these bronchioles with the thickness of wall of the bronchioles in figs. 3, 5, and 7. Note also the empty alveoli and the thin alveolar walls in the normal animal. (200 X)

Fig. 7. Lung tissue of a guinea pig exposed for 36 months to Kaylo dust by inhalation and then killed. In this photomicrograph a bronchiole is just above and to the right of center. Note the thickness of the tissue between the lumen of the bronchiole and the lumen of the adjacent alveoli in comparison with the thin bronchiolar walls in figs. 3 and 6. Note also that the greatly thickened bronchiolar walls of the animal exposed to asbestos dust for 30 months (fig. 5) are similar to those of this animal, exposed to Kaylo dust for 36 months. Fine strands of fibrous tissue are visible near the bronchiole in this photomicrograph but they are more apparent, because they are less dense, in the area at the right of the field where fibrosis has extended to adjacent alveolar walls. (200 X)

Fig. 8. Lung tissue of a rat exposed for 18 months to Kaylo dust by inhalation and then killed. The photomicrograph reveals simple accumulation of cells in alveoli. The cytoplasm of the cells is packed with particles of dust. Note that the alveolar septa, even those of spaces containing numerous dust cells, are thin and delicate. (200 X)

Fig. 9

Fig. 10

Fig. 11

Fig. 9. Lung tissue of a guinea pig infected with attenuated tubercle bacilli and immediately exposed to Kaylo dust by inhalation for 24 months, and then killed. The figure is a slightly magnified photograph of the routine histologic preparation of the lungs, including both lungs from apex to base. The cluster of dark foci of irregular outline in the lower center (median lobe) and at the right (left caudal lobe) are foci of active spreading tuberculosis. The widely-distributed minute dark foci are merely lymphoid cell clusters and are unrelated to the infection. The extent of the tuberculous activity is seen to be exceedingly small. (1.5 X)

Fig. 10. Lung tissue of a guinea pig infected with attenuated tubercle bacilli and kept in clean air for 2 months, then exposed for 12 months to Kaylo dust by inhalation, and killed. The dark zone, irregular in outline, in the left upper quadrant (right cephalic lobe) is an area of active spreading tuberculosis. A smaller but similar focus is visible at the lower margin of the left cephalic lobe. Again, as in fig. 9, the extent of the tuberculous process is very small. (1.5 X)

Fig. 11. Lung tissue of a guinea pig exposed to Kaylo dust by inhalation for 3 months, then infected with attenuated tubercle bacilli and exposed to the dust for an additional 16 months, and killed. The numerous poorly-defined dark zones, irregular in outline, are all sites of active, spreading tuberculous disease. The tuberculous involvement exhibited in this photograph is the most extensive noted in any animal killed during the experiment. The involvement is relatively slight in comparison with the progression which occurs in animals exposed to quartz dust under similar conditions; in fact, all of the animals exposed to quartz dust would have died within 12 months after infection because of almost complete loss of functioning pulmonary tissue. (1.5 X)