

THE TRUDEAU FOUNDATION
FOR
THE CLINICAL AND EXPERIMENTAL STUDY OF PULMONARY DISEASE

AT SARANAC LAKE, N. Y.
THE SARANAC LABORATORY
THE TRUDEAU FOUNDATION
THE TRUDEAU SCHOOL

AT TRUDEAU, N. Y.
THE DEPARTMENT OF PHYSIOLOGY
THE DEPARTMENT OF BIOCHEMISTRY
THE DEPARTMENT OF RADIOLOGY
THE TRUDEAU LABORATORY

November 16, 1948

Mr. U. E. Bowes
Owens-Illinois Glass Company
Toledo 1, Ohio

Dear Mr. Bowes:

Enclosed you will find three copies of a report on the results of animal experiments with Kaylo dust. As is our custom, we have summarized briefly material previously presented, including our interim report dated October 30, 1947, and have given detailed discussion only of subsequent developments. When all experiments have been completed, we expect to prepare a final report which will include details of each phase so that all data will be available in one place. However, the experimental study of the effects of inhaled Kaylo dust on normal uninfected animals is now finished and conclusions expressed on that subject are final rather than tentative.

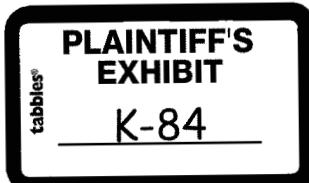
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"In consequence of the experimental studies with guinea pigs to determine the biological activity of Kaylo, it may be tentatively concluded that Kaylo alone fails to produce significant pulmonary damage when inhaled into the lung."

During the 30 to 36 months period, however, definite indication of tissue reaction appeared in the lungs of animals inhaling Kaylo dust and therefore, I regret to say, our tentative conclusion quoted above must be altered. In all animals sacrificed after more than 30 months of exposure to Kaylo dust unmistakable evidence of asbestosis has developed, showing that Kaylo on inhalation is capable of producing asbestosis and must be regarded as a potentially-hazardous material. It should be noted that since neither silicosis nor the diffuse pulmonary fibrosis caused by inhaled diatomaceous earth was observed, the quartz and diatomaceous earth components of the dust apparently do not produce their typical lesions.

In order to present more information on the subject asbestosis, certain evidence derived from our experimental work with asbestos dust has been discussed. As these findings have not yet been released for publication, I request that, while using them as required in formulating a safety program, you regard them as confidential.

OTIS HISTORICAL ARCHIVES
NATIONAL MUSEUM OF HEALTH AND MEDICINE
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At this time may I review briefly the financial arrangement for conducting the investigation with Kaylo? The research program up to this year was carried on under a contract, initiated in 1945, by which the experiments would be subsidized with a grant of \$5,000. per year. As pointed out in my letter of March 3, 1948, the contract terminated officially on February 15, 1948, but the investigation would be continued without charge until June because the original experiments were started late. Since a check was received which took care of the subsidy up to November 15, 1947, there is due on the old contract the sum of \$1,250. for the final quarter of the contract (from November 15, 1947 to February 15, 1948). We have delayed sending an invoice for the final quarter until all work could be finished and a final report submitted. Following the termination of the experiment in June, it has required several months to do the histological work, study the tissue sections, collate the data and prepare the report which accompanies this letter.

We are including in the report a brief review of the new experiments in which the effect of inhaled Kaylo dust on tuberculous infection is being studied. Your purchase order #170 authorizing this experiment at \$5,000. for one year is dated February 3, 1948, but owing to a shortage of animals and other unavoidable delays the actual experimental work did not get under way until May. Hence we have concluded that financial support for this new program should be dated from May 1, 1948. For support outlined in my letter of March 3, I suggested a two-year contract at \$7,000. per year. Your letter of March 31 acknowledged this but failed to confirm the extra amount of \$2,000. involved. Nevertheless, we have proceeded at the old rate and are endeavoring to absorb the increased cost from our Foundation reserve.

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	\$3,750.

PLAINTIFF'S
EXHIBIT

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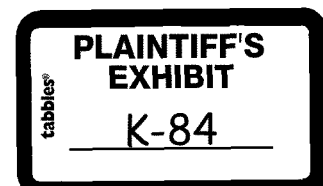
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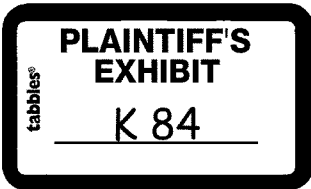
Sincerely yours,

Arthur J. Vorwald, M.D.
Director

LJV:LB
Encs. (3)

OTIS HISTORICAL ARCHIVES
NATIONAL MUSEUM OF HEALTH AND MEDICINE
ARMED FORCES INSTITUTE OF PATHOLOGY





A F F I D A V I T

WASHINGTON DISTRICT OF COLUMBIA)
) ss.
~~COUNTY OF~~ _____)

BEFORE ME, the undersigned Notary Public, personally came and appeared MIKE RHODE, a person of the full age of majority, being of sound mind and body, who, after being first duly sworn by me, did depose and say:

I MIKE RHODE, am the custodian of the originals of the documents attached hereto as Exhibit A, pages 1 through 18. I hereby certify that the documents attached hereto are true, correct and authentic copies of documents authorized by law to be filed and actually on file with the Armed Forces Institute of Pathology.

Michael Rhode
MIKE RHODE, AFFIANT

SWORN TO AND SUBSCRIBED before me, the undersigned Notary Public, on this the 24th day of February, 1989.

Sheila R. Betasso
NOTARY PUBLIC

My Commission Expires:

SHEILA R. BETASSO
NOTARY PUBLIC DISTRICT OF COLUMBIA
My Commission Expires November 14, 1991

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Arthur J. Vorwald, M.D.
Director

AJV:LB
Encs. (3)

INTERIM REPORT
REGARDING THE BIOLOGICAL ACTIVITY
OF KAYLO DUST

to the
OWENS-ILLINOIS GLASS COMPANY
TOLEDO, OHIO

by
THE SARINAC LABORATORY
SARINAC LAKE, NEW YORK

OCTOBER 30, 1948

Submitted by:

Arthur J. Vorwald, M. S., Director
The Edward L. Trudeau Foundation

In cooperation with:

Philip C. Pratt, M. S.
Thomas H. Dertan, M. S.
Anthony B. DeLahart

INTRODUCTION

One year ago, on October 30, 1947, an interim report was submitted, covering the progress of certain animal experiments with Kaylo over a total period of 30 months. It was necessary at that time to recommend further experiments concerning certain phases of the problem. The present report deals with the final phases of the experiment then in progress and with the early observations made in the new series of experiments.

The original experiment has now been completed and the conclusions drawn are based upon the results of a full three years' exposure to an atmospheric suspension of Kaylo dust. Previous experience has shown that this is the required period over which exposures to a dust of doubtful biological activity must be continued before final conclusions are warranted. This experiment, in fact, constitutes an example of the importance of such prolonged study for, as is to be shown below, the findings at three years were strikingly different from those at two and one-half years and the tentative conclusion reached at that time must now be altered. Thus, at the time of the previous report, the evidence indicated that Kaylo acted as an inert dust in normal rats and guinea pigs; resulting only in the formation of clumps of dust cells, without fibrosis. However, it will be shown below that Kaylo is capable, on prolonged inhalation, of producing asbestosis in the lungs of guinea pigs, and that it should be handled industrially as a hazardous dust.

This report will be presented in four sections as follows:

- A. Final observations, dust inhalation in normal guinea pigs.
- B. Discussion.
- C. Conclusions.
- D. Progress report on new series of experiments.

A. Final observations, dust inhalation in normal guinea pigs.

Reference to the Interim Report of October 30, 1947, will reveal that two groups of normal guinea pigs were placed in the dust rooms one group in February 1945 and the second in August 1945. The animals were exposed to atmospheric suspensions of Kayle dust for eight hours daily, five and one-half days a week throughout the experiment. The dust concentration, which varied somewhat from time to time, has averaged 116 million particles per cubic foot of air over the entire course of the experiment to date.

A brief review of the observations described on page 4 of the previous report will reveal that up to thirty months the reaction in guinea pigs was limited to the accumulation of clumps of macrophages, containing dust particles, in groups of adjacent air spaces. While occasional multinucleated giant cells were seen, there was no undue proliferation of tissue histiocytes and fibrosis was absent. A few unmistakable asbestos bodies were identified. In general, the accumulation of cells of the types described above and their persistence as such over a full three year period, without the development of fibrosis, has been found to indicate that the agent responsible for them is not capable of producing fibrosis. Such agents are now considered to be "biologically inert," since the mere cellular accumulation has not been shown to affect pulmonary function or resistance to disease.

However, of nine animals sacrificed subsequent to thirty months in the present experiment, all have shown not only the above lesions but also have developed true fibrosis of a type characteristic of the response of guinea pigs to asbestos. This is a rather diffuse type of fibrosis which forms chiefly about the small air ducts, known as bronchioles, from which the air spaces, or alveoli, of the lung arise. The appended photomicrographs show the nature of the lesions being discussed. This condition is identical with asbestosis as can be seen by comparing

Figure 2 with Figure 3.

The lesions in the tracheobronchial lymph nodes showed no change between thirty months and three years.

Chemical analysis of the lungs of guinea pigs that had inhaled Kaylo dust for periods up to 36 months yielded the data given in Table 1. It will be noted that as the period of exposure became longer the ash value gradually increased, indicating an accumulation of mineral matter in the lungs. There was a pronounced increase in the silica component up to about 30 months and then a slight decrease. The reason for this condition, which has been observed in experiments with other dusts, is not entirely clear. Since only two animals were analyzed for each exposure period, individual values were occasionally out of line but the general trend was clearly indicated.

B. Discussion.

The final observations in this experiment with Kaylo inhalation in normal guinea pigs, reported above and illustrated in the figures, prove that Kaylo is capable of producing the characteristic reaction, asbestosis. It is evident, therefore, that a considerable portion of the asbestos component in Kaylo remains unchanged during the manufacturing process or, if it is changed, that the altered product maintains its capacity to cause fibrosis. While the lesions up to 30 months showed no fibrosis, certain aspects of them were compatible with a preliminary stage in the development of asbestosis. These aspects were masked by the inert type of reaction to the materials other than asbestos in the dust. The characteristic early stage of the reaction to asbestos is the predilection of the fibers to localize in the lumen and wall of the small air ducts, known as terminal bronchioles. This is in contrast to particulate materials, which localize chiefly

in the actual air spaces, or alveoli. In the present experiment the greatest portion of the inhaled dust, being particulate, lodged in the alveoli and masked the peribronchiolar deposition of some of the fibrous component. In retrospect, it is possible to discern that there is more evidence of dust cell activity in the region of the bronchioles than is characteristic of the reaction to an inert particulate dust. Little significance was attached to this at the time of the previous report because there was no evidence of the development of fibrosis.

The differences between the early reaction to Kayle and that to asbestos may be interpreted as a modification of the lesions by the particulate components of Kayle. "Modification" of silicosis is well recognized when lesions of that disease develop following inhalation of a mixed dust containing quartz together with materials of an inert nature, such as iron oxide.

It is of importance to note that while the peribronchiolar reactions observed incriminate Kayle as capable of producing asbestosis, they exclude the possibility that it may cause silicosis, since, over a full three year period, there is no animal eye focus of hyaline nodular fibrosis characteristic of the reaction to quartz. Furthermore, it may be added that the animals show no evidence of the type of diffuse fibrosis which has been observed in this laboratory to follow inhalation of diatomaceous earth dust. In regard to hydrated mono-calcium silicate, a major constituent of Kayle, it may be said that while there is no pointed evidence as to its effect on pulmonary tissue, there is such evidence to show that a variety of silicates, including some forms of calcium silicate, are biologically inert. It seems likely that the calcium silicate in Kayle should conform with this previous experience.

Thus, the possibility expressed by Doctor Gardner in his early consideration of this problem, that Kayle might produce two pneumoconioses, asbestosis and silicosis, with the resultant safety hazards, has been adequately studied, and concern over