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KEASBEY & MATTISON COMPANY

MANUFACTURERS OF ASBESTOS AND MAGNESIA PRODUCTS SINCE 1873

AMBLER, PENNSYLVANIA

EXECUTIVE OFFICES

December 30, 1940

HB

K&M No. 2059

head. pt. 1 report

W. W. F. Shepherd, Esq.
Turner & Newall Ltd.
Spotland, Rochdale

Dear Mr. Shepherd:

On January 18, 1940, with my letter K&M No. 1722, I sent you copies of Dr. Leroy U. Gardner's report covering his research work on asbestosis carried out at the Saranac Laboratory.

I now hand you herewith a copy of Dr. Gardner's further progress report dated November 30, 1940 on Experimental Asbestosis, and also copy of his Supplementary Discussion on Experimental Asbestosis.

The interesting point in these reports is that Dr. Gardner suggests that possibly through further research on his part a method of treatment for asbestosis may be developed. As you know, during the past three or four years the industry has financed this research work, and we are now considering the question of whether or not we will subscribe a further $1,000 as our share for carrying Dr. Gardner's experimental work through 1941.

I would appreciate receiving any comments which you or any of the others in T&N Ltd. would care to make concerning the progress made by Dr. Gardner.

I am also sending a copy of this report to Mr. O. C. Smith.

Yours very sincerely,

KEASBEY & MATTISON COMPANY

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Att.
FOLLOW COPY

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PLAINTIFF'S EXHIBIT D1202.01

PLAINTIFF'S EXHIBIT WV-000377

Progress Report on Experimental Asbestosis at

the Saranac Laboratory. November 30, 1940.

The experimental study of asbestosis still continues to sustain the tentative conclusions reported a year ago. Since the proposed hypothesis of mechanical injury by inhaled asbestos is new and not generally accepted much time and effort have been devoted to criticism and verification of our own work. The loan of an x-ray diffraction apparatus by the General Electric Co. last summer has permitted more accurate analyses of raw materials and the air-borne dusts to which animals have been exposed. Chemical and microscopic methods on which we were previously forced to rely were inadequate for mixtures of minerals containing serpentine and chrysotile. The x-ray has disclosed that air-borne dusts of both the long and the short fibre asbestos with which we have worked contained much less chrysotile than we had supposed. This does not vitiate the value of previous conclusions but merely demonstrates that a comparatively small concentration of long fibres in the air is capable of causing asbestosis. Our quantitative data have a definite bearing on standards of safe concentration for asbestos dust.

Considerable information has accumulated on the behavior of fine asbestos dust which is new, at least to industrial hygienists. Progress has been made in understanding the nature of the injury resulting from inhaled asbestos. We seem on the way to reconciling the undeniable evidence of chemical activity manifested in the formation of the asbestosis body with the hypothesis of injury by mechanical trauma. If our present theories are sustained it is even conceivable that a method of treatment might be evolved.

In view of the progress that has been made I am hoping that the sponsors of this research may be disposed to continue their appropriation of $5000 for another year.

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In this period we should be able to complete the work still in progress and the projected collateral experiments that are discussed in the appended supplement. We could then make a final report with well tested conclusions as to the mechanism of injury from inhaled asbestos fibre, the significance of the asbestosis body, the non-progressive nature of asbestosis. We shall be in a position to contribute evidence for the establishment of safe concentrations of asbestos dust in industrial plants. We may still be able to demonstrate whether, in the absence of infection, inhaled long fibre dust produces pulmonary changes whose shadows on an x-ray film resemble those in the human subject. We might even develop a method of treatment that would be applicable to human beings.

(SGD) LEROY U. GARDNER

Leroy U. Gardner, M. D., Director
Saranac Laboratory

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SUPPLEMENTARY DISCUSSION OF EXPERIMENTAL ASBESTOSIS

The following discussion is presented for the information of anyone interested in the details of the program of research at the Saranac Laboratory. Even here it is impossible to consider individually the 33 different experiments which constitute the basis of this work. It will be more informative to comment on their significance and bearing on the problem as a whole.

A summary of our difficulties in attempting to maintain high atmospheric concentrations of very short chrysotile fibre is presented not only because it explains the delays and pitfalls in such experimentation but because it demonstrates peculiarities in the behavior of dust of this type. It will be recalled that we had proposed to use a dust of fine asbestos rather than one of longer fibres to produce advanced reaction in the shortest possible time. This procedure seemed advisable on the supposition that the injury was chemical and consequently the smaller particles would present a greater surface contact between irritant mineral and body fluids - a train of circumstances which had been proved for quartz. After examining several samples of fine asbestos dust from an industrial plant one was finally discovered which contained a very considerable proportion of fibrous elements. It was obtained by screening the settlings from a collector system on a carding operation. Petrographic and chemical analysis indicated that the coarser components, large enough to be identified by these methods consisted of chrysotile, serpentine and accessory silicates, magnetite and carbonate minerals. Although there was much beside chrysotile in the mixture, the same materials would have been inhaled by men employed in the plant so that we were not much concerned. As the fibrous components of this material were still quite large it was decided to regrind it in a steel mill. Chemical

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analyses and x-ray diffraction patterns, which we then had to have made in an outside laboratory, satisfied us that the milling had merely reduced the particle size of the mixture without altering its composition. Accordingly we continued to grind screened collector settlings in quantities sufficient to maintain a supply in the dust room. The maximum particle size, with occasional exceptions, was 2 or 3 microns.

When the extremely fine material was placed in one of the hoppers ordinarily used for generating dust clouds, difficulties were encountered. At customary paddle speeds the dust was so light that all of it was immediately thrown out of the hopper; at slower speeds "pilling" occurred, much of the material being rolled in firm spheres from 0.75 to 1 mm. in diameter. Throughout the first experiment, as previously reported, this difficulty was overcome by mixing approximately 20 per cent of unground material with the ball-milled product and maintaining routine paddle speeds. Study of the atmospheric dust generated from this mixture showed what were then considered negligible quantities of long fibres in the atmosphere. It was therefore assumed that the smooth paddle would continue to break up very little of the long asbestos. This procedure was followed for 30 months with the essentially negative results reported to you on December 13, 1939.

However, as mentioned then, appreciable numbers of longer asbestosis bodies were beginning to accumulate in the lungs of exposed animals. Just after making the report one animal sacrificed revealed evidence of early reaction in the pulmonary framework. These tissue changes were still of microscopic proportions but their appearance raised a question. Was this reaction due to the small number of long fibres or was it a delayed effect of the much more abundant fine material? Since an unproven hypothesis was involved we had no choice but to start a new exposure without the possible contamination from unground dust.

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Accordingly this was started in January 19, 1940 using 100 guinea pigs. For the first 7 months we attempted to compensate for the pilling process by adding freshly ground dust to the spherules in the hopper each day. Impinger dust counts revealed atmospheric concentrations averaging approximately 100 million particles per cubic foot of air which were maintained for 8 hours each day. Most of this dust was so fine that the microscope failed to differentiate between fibrous and particulate elements. Chemical analysis demonstrated apparently adequate quantities of magnesium silicate although it was impossible to be certain whether in the form of chrysotile or serpentine. However, the x-ray diffraction method became available shortly and it was used to determine the proportion of chrysotile in the dust. The precaution was taken to collect the samples from the atmosphere with an electric precipitator as there has been some doubt as to the efficacy of the more usual impinger in sampling dusts of a fibrous nature. The x-ray disclosed that the air-borne dust contained not much more than 5 per cent of chrysotile; most of the fibrous elements in the parent material had gone into the formation of the spherules that remained in the hopper. About 95 per cent of the dust in the air was serpentine, magnetite and carbonate minerals. However, the lungs of the exposed animals had accumulated large numbers of short chrysotile fibres in their 7 months of exposure. Inside of phagocytes were many minute asbestosis bodies. As in the previous experiment there was not even a suggestion of early fibrosis.

In order to disperse all of the chrysotile in the ground material as air-borne dust it was necessary to experiment again. Finally it was found that a hopper equipped with steel wire brushes, like those used for the long fibre asbestos, prevented pilling and would produce high concentrations of atmospheric dust.

Since this change was inaugurated on August 30 of this year the average concentration of dust inside the animals' cages has been 170 million particles per

cubic foot of air. Its content of fibrous chrysotile is about 7 to 8 per cent, or approximately 75 per cent of the free fibres in the raw material. (In analysis of the ground material only the effective fibrous chrysotile is considered as such. Any masses still not separated into individual fibres are classified with the serpentine.)

Twenty-three pigs, sacrificed after exposures up to 11 months (7 months at the lower concentration and 4 after installing the brush hopper) have shown no gross evidence of any pulmonary reaction. With the microscope great numbers of minute asbestosis bodies are visible. None of them is long enough to project beyond the borders of the phagocyte in which it lies and hence there can be no mechanical injury of the pulmonary tissues. Thirty-five more guinea pigs, 40 white rats and 25 white mice are still alive and being exposed. We hope they can be continued in the dust house for another year. At the end of this period they should constitute an adequate check on our first experiment.

The contrast between the absence of reaction to such fine dust and that to the long fibre is striking. After one year's exposure to the latter there is gross evidence of fibrosis. The microscope shows collars of fibrosis about the bronchioles which are as well developed as observed after twice the exposure to the Kings Floats asbestos employed for the experiment originally reported.

The differences in the two groups become all the more striking when one compares the dust concentrations and particularly the concentrations of the fibrous elements in the two experiments. For the inert short fibre dust the average total concentration of particles of all kinds was 118 million and for the active long fibre dust, only 48 million particles per cubic foot. By computation the corresponding concentrations of fibrous chrysotile in the two exposures were 9.571 million and 5.905 million particles per cubic foot respectively. In other words, only about 6 million long fibres per cubic foot of air were necessary to

produce asbestosis at a rate probably more rapid than occurs in human subjects, whereas 1.6 times this concentration of the short fibre had essentially no effect.

These figures on concentrations indicate the difficulties of maintaining fibrous dusts in atmospheric suspensions, an observation borne out by the low dust counts reported in all surveys in the asbestos industry. Compared with those in other dusty trades they appear low, a result which some observers have attributed to inadequacy of the impinger for fibrous dusts. However, the results of our experiment with long fibrous material emphasize the possible hazard from apparently low atmospheric concentrations. They also indicate that the composition as well as the concentration of the dust should be considered before deciding that a hazard exists.

One further check of the effect of grinding a mixture containing chrysotile fibres, magnetite, serpentine and carbonates still has to be made before we shall be satisfied that we have proved our point on the effect of particle size. This becomes necessary in view of our recent discovery that on dry grinding quartz with the inert mineral hematite, the usual toxic action of the quartz is completely neutralized. It is not anticipated that any of the contaminants in the asbestos mixture will be mechanically deposited upon the surface of the active chrysotile as has occurred in the case of the quartz and iron oxide. However, we must eliminate this possibility before we can be satisfied with our results. We have accordingly milled pure chrysotile to the same particle size for injection into the lungs of guinea pigs. If this proves to be as inert as the impure asbestos the test would prove that only reduced particle size is responsible for there can be no protective coating in the hardened steel mills that we are employing.

One other test should be made to demonstrate whether the formation of asbestosis bodies is a protective mechanism that prevents further mechanical injury from inhaled asbestos fibres. Injection of a considerable quantity of these

bodies into the lungs of guinea pigs should demonstrate whether they are still capable of provoking fibrosis. We have at last succeeded in developing a method of recovering asbestosis bodies from human lungs without appreciable alteration in composition and as soon as enough of them can be collected we expect to make this test. A negative result will of course constitute reliable evidence for believing that asbestosis is not a progressive disease. Our theory, based on other observations, suggests that only the freshly inhaled fibres which have not yet been coated with body fluids and iron are irritating to the lungs. As such coating is acquired after a few months contact with lung tissue, no new fibrosis should develop in men whose exposure has ceased.

When these tests are completed and when the current inhalation experiments have been continued for another year, I shall be satisfied that we have thoroughly tested the validity of the hypothesis that the irritation from asbestos is basically mechanical in nature.

As indicated in the last report, we were at a loss to reconcile the obviously chemical process of forming asbestosis bodies with the mechanical hypothesis. Further observation has suggested an answer. It will be recalled that unlike the free forms of silica, the asbestos minerals as a group cause no reaction in any organs but the lungs and even in their lungs all species of animals do not respond in the same manner. In those locations where the injected asbestos (not only chrysotile but crocidolite, amosite, anthophyllite and a sodium-iron tremolite) failed to cause fibrosis, there were no asbestosis bodies and within a few weeks we could find no trace of the injected fibres. We are now using x-ray diffraction to determine whether any of the minerals actually remain. As far as this work has progressed the analyses demonstrate that the fibres have dissolved and disappeared. Where solution occurs no fibre would be left to cause mechanical irritation.

We have attempted to discover why asbestos should dissolve in some tissues and not in others. No definite answer can be given at the present time but it seems

that slight variations in acidity may be responsible. These cannot be measured in the living animal as any known method of procedure is itself sufficient to alter the pH of the tissues. However, it is known that there are slight but definite variations in the CO_2 tension of the air inside the lungs of the several species of animals with which we have worked and this would of course be associated with some changes in acidity. Qualitative experiments in vitro have demonstrated that in water or in human lung juice saturated with CO_2, chrysotile fibres undergo partial solution. The experiments must now be repeated on a quantitative basis to discover the optimum concentration of CO_2 at which solution occurs. We must also find out whether any other organic acid that might be concerned will dissolve asbestos. By so doing we might demonstrate the mechanism responsible for the complete disappearance of inhaled asbestos and absence of reaction in the rabbits' and dogs' lungs, the development of both asbestosis bodies and fibrosis in the lungs of guinea pigs and human beings and the variable intermediate findings in cats, white mice and rats. This knowledge might also lead to a comprehension of individual susceptibility and could conceivably be applied in treatment of human disease.

The subject of x-ray appearances has been temporarily deferred until we could produce an advanced type of asbestosis in some animal large enough to permit adequate films to be made. Recent autopsies on some of the cats being exposed to long fibre suggest that they may fill this need. We shall have chest films from time to time as their exposure continues.