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INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

MELLON INSTITUTE, 4400 FIFTH AVENUE

PITTSBURGH, PA. 15213

Report on

PRELIMINARY STUDY OF BRAKE-DRUM DUST: COMPARATIVE PATHOGENICITY

for

JOHNS-MANVILLE CORPORATION

by

Paul Gross, M.D.
Director of Research Laboratory

February 14, 1967

Robert T. P. deTreville, M.D.
Managing Director

Introduction

As an explanation for the occurrence of ferruginous ("asbestos") bodies in the lungs of 30 to 40% of the general population in large cities, Thomson[1] has indicated that urban populations are being exposed to asbestos dust and that a likely source of this dust was from the wearing down of automobile brakes.

Details of Preliminary Study

At the request of Dr. Kenneth W. Smith, Medical Director, Johns-Manville Corporation, a preliminary study of the pathogenicity of "brake-drum dust" was done. This dust, free of iron, was suspended in water and 1 ml containing 3.5 mg was injected intratracheally into rats and hamsters. Some of the rats were killed four days later. The lungs were examined microscopically and the changes compared with the four-day lesions seen in the lungs of rats injected intratracheally with the dusts of (a.) crystalline silica, (b.) chrysotile, and (c.) kaolin, respectively. The chrysotile had been similarly suspended in water and given in the same dosage.

Results

The results were as follows: crystalline silica and chrysotile caused a severe inflammation best described as an obliterative bronchiolitis that could not be differentiated one from the other. Whereas, the reactions caused by both, kaolin and brake-drum dust, were also similar to one another and were of the so-called "biologically inert" type. This reaction consisted essentially of the accumulation within scattered alveoli of scavenger cells filled with the respective

dusts. There was no significant development of the connective tissue that, in the case of silica and chrysotile, tended to obliterate the air spaces and ducts.

Tentatively, therefore, the brake-drum dust tested should be categorized as "biologically inert."

Recommendations for Further Studies

A proposal for further investigation of the pathogenicity of brake-drum dust has been prepared at the request of Johns-Manville Corporation. Analytical laboratories at Johns-Manville Corporation have reportedly been unsuccessful in identifying asbestos fibers in brake-drum dust and the Industrial Hygiene Foundation's preliminary studies have shown that the dust behaves differently than chrysotile asbestos, with effects on lungs which closely resemble those produced by inert dusts, such as kaolin. If these findings should be borne out by further studies, their publication would help prove that Thomson's assumption was erroneous.

Essential to publication would be the development of data from inhalation of brake-drum dust by adequate numbers of several species of laboratory animals. Tentatively, it is suggested that of 40 animals in each of four species (guinea pigs, rats, hamsters and mice) 30 be exposed over most of their life span (two years in all except mice, which have a shorter life span and require only one year) to a concentration of about 100 mg/m^3, the other 10 serving as controls. This concentration would be produced in an 8' x 8' x 8' chamber by means of Wright dust-feed dispersion equipment. Frequent quantitation of the chamber atmosphere, close

observation and care of the animals and extensive histopathological observations would be necessary over a three-year period of research. The cost would be $200,000: $50,000 the first two years and $100,000 the third. Histological sections will receive special staining and microscopic examination by research pathologists, who will take thousands of photomicrographs of their findings and use some of these to document their report, which will be suitable for publication.

As a means of developing additional information which cannot take the place of the inhalation study but will give earlier indication of lung changes, it is recommended that a similar study be done by intratracheal injection technique, giving 80 animals (20 of each species listed above) a single injection of near maximal dose tolerated without death. These animals would be pastured for one year, killed and examined by the same research pathological techniques. The two-year study would cost $75,000: $25,000 the first year and $50,000 the second (the second year including the histopathological studies and preparation of a report). Although not considered adequate for publication alone, the results by injection would be incorporated with the inhalation study findings and be a valuable supplement to it.

Costs of the combined studies will be $275,000: $75,000 the first year, and $100,000 on each of the two successive years.

References

1. Thomson, J.G., et al. Asbestos as Modern Urban Hazard. S. Afr. Med. J. 37:77-81, 1963.

Tentative Outline of Brake-Drum Dust Investigation

A. Intratracheal Injection ($75,000)

a. 20 Guinea Pigs
b. 20 Rats
c. 20 Hamsters
d. 20 Mice

} Single injection of near-maximal dose tolerated without death.

Pastured for one year and killed.

B. Inhalation ($200,000)

a. 40 Guinea Pigs
b. 40 Rats
c. 40 Hamsters
d. 40 Mice

} 8' x 8' x 8' chamber Wright dust-feed dispersion (at least two needed).

Two-year exposure. Concentration ~ 100 mg/m^3.

One-year exposure for mice because of shorter life expectancy.

Two-year exposure for others.

Six-month holding period.

Six months for processing and writing report.

Total: Three-Year Study

Cost: $275,000

INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

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PITTSBURGH, PA. 15213

PRELIMINARY INVESTIGATION

of the

PULMONARY HAZARD CREATED BY BRAKE-DRUM DUST

for

JOHNS-MANVILLE CORPORATION

by

PAUL GROSS, M.D.
Director of Research Laboratory

May 1967

Iron-free brake-drum dust (a little less than 1 gm) was obtained from Dr. Kenneth W. Smith. Portions of this dust were suspended in water so that 1 ml contained 3.5 mg.

The investigation is divided into two components, a short-term study and one of longer duration.

I. Short-Term Study: The purpose of this study was to compare the pulmonary lesions produced by this dust in rats with those produced in rats by other dusts whose pathogenic potential is well known or is documented. These dusts included chrysotile, quartz, aluminum silicate, and silicon carbide. The different dust lesions were all produced by the same intratracheal dosage and were all of the same age (4 days).

Groups of four rats each were injected intratracheally with 3.5 mg of the above dusts respectively, including the brake-drum dust.

Results: As can be seen in Figs. 1 and 2, the pulmonary reaction to brake-drum dust is essentially limited to a few of the alveoli evaginating off respiratory bronchioles and adjoining alveolar ducts. This reaction consists of cellular proliferation with a concommitant elaboration of supporting argyophilic stroma, thereby causing some mural thickening and the obliteration of a few scattered alveoli. In contrast to the lesions produced by chrysotile[1] and quartz dusts,[2] the inflammatory tissue did not extend into the lumen of the alveolar ducts or bronchioles, nor were more than a few of the evaginating alveoli affected. Indeed, the pulmonary reaction caused by brake-drum dust at this time more closely resembles that produced by aluminum silicate and silicon carbide, both of which have been demonstrated to belong in the non-fibrogenic category.[3,4]

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II. Longer-Term Study: The purpose of this study was to determine (a) if ferruginous bodies were formed in response to the presence of this dust and (b) if the character of the pulmonary response would continue to be as mild as seems to have been indicated by the four-day lesion.

For these purposes, both rats and hamsters were employed. Twelve hamsters were injected intratracheally on three different occasions with 3.5 mg of brake-drum dust. Three of these were killed for sampling 7 1/2 months after the injection. Lung washings were obtained from these animals using a modified LaBelle and Brieger technique. The sediments from two were smeared on glass slides and the sediment of the third animal was processed for electron microscopy and electron diffraction study. The lungs were processed for microscopic study.

Ten rats were also injected intratracheally with 3.5 mg of brake-drum dust from Johns-Manville, and held for additional injections and longer survival.

Results: Smears of the sediment from the lung washings of the hamsters showed large numbers of ferruginous bodies, many of them segmented, and all indistinguishable from asbestos bodies.

Sections of the lungs of hamsters, killed 7 1/2 months after the initial intratracheal injection, show minimal involvement of the parenchyma. The changes are limited to scattered respiratory bronchioles. These show focal cellular thickening of their walls and occlusion of a few of their evaginating alveoli by prolifereted cells, macrophages, and occasionally also, by a foreign-body-type giant cell. In an occasional involved alveolus black pigment is present.

There is no evidence of collagen formation and, significantly, the lumens of the affected respiratory bronchioles are widely patent. Furthermore, it should

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be emphasized that except for a few of the alveoli evaginating off some of the respiratory bronchioles, the alveolar tissue appears normal.

This minimal degree of involvement encountered in hamsters injected intratracheally with brake-drum dust stands in striking contrast to the diffuse, severe, and fatal pneumonitis caused by chrysotile dust in the same animal species.(1) The lesions encountered in the lungs of hamsters more than seven months after the initial intratracheal injection of brake-drum dust, which are minimal, tend to substantiate the short-term findings in the lungs of rats injected with the same dust.

Further data on the pathogenic potential of brake-drum dust will be forthcoming when the rats presently on test will be killed and their lungs studied microscopically.

Comment: The data obtained from this preliminary study indicate that Thomson was probably correct in his surmise that brake-drum dust was a source for the ferruginous bodies found in the lungs of urban dwellers.(5) It is questionable, however, that Thomson's designation of them as "asbestos" bodies was proper; during the process of production of the brake linings and dust, the amount of heat to which the asbestos fibers were subjected is thought to have been such that they lost the water of hydration characteristic of the chrysotile molecule.

Regardless of what name is given to the ferruginous bodies induced in lungs by the presence of brake-drum dust, they are morphologically indistinguishable from asbestos bodies. Because of this fact, brake-drum dust would be suspect as having the same pathogenic potential as asbestos. The preliminary information developed in this study would, however, tend to lessen the justification

for this suspicion. Nevertheless, the existence of this suspicion makes a more extensive and thorough investigation highly advisable in the interest of the industry. Testing the hypothesis based on the preliminary findings described in this report appears mandatory. Results, if substantiated, will certainly merit consideration for publication in the professional literature.

References

1. Gross, P. and deTreville, R.T.P.: Experimental Asbestosis - Studies on the Progressiveness of the Pulmonary Fibrosis Caused by Chrysotile Dust. Arch. Env. Health. To be published.

2. Gross, P. and Brieger, H., Silicotic Bronchiolitis Obliterans: A Focal Clearance failure. Arch. Env. Health, 12, 5-9 (1966)

3. Gross, P. et al: The Effects of a Synthetic Ceramic Fiber Dust Upon the Lungs of Rats. Arch. Ind. Health, 13, 161-166 (1956)

4. Gross, P. et al: Experimental Tuberculopneumoconiosis, A.M.A. Arch. Ind. Health, 19, 320-334 (1959)

5. Thomson, J. G. et al: Asbestos as Modern Urban Hazard, S. Afr. Med. J. 37, 77 (1963)

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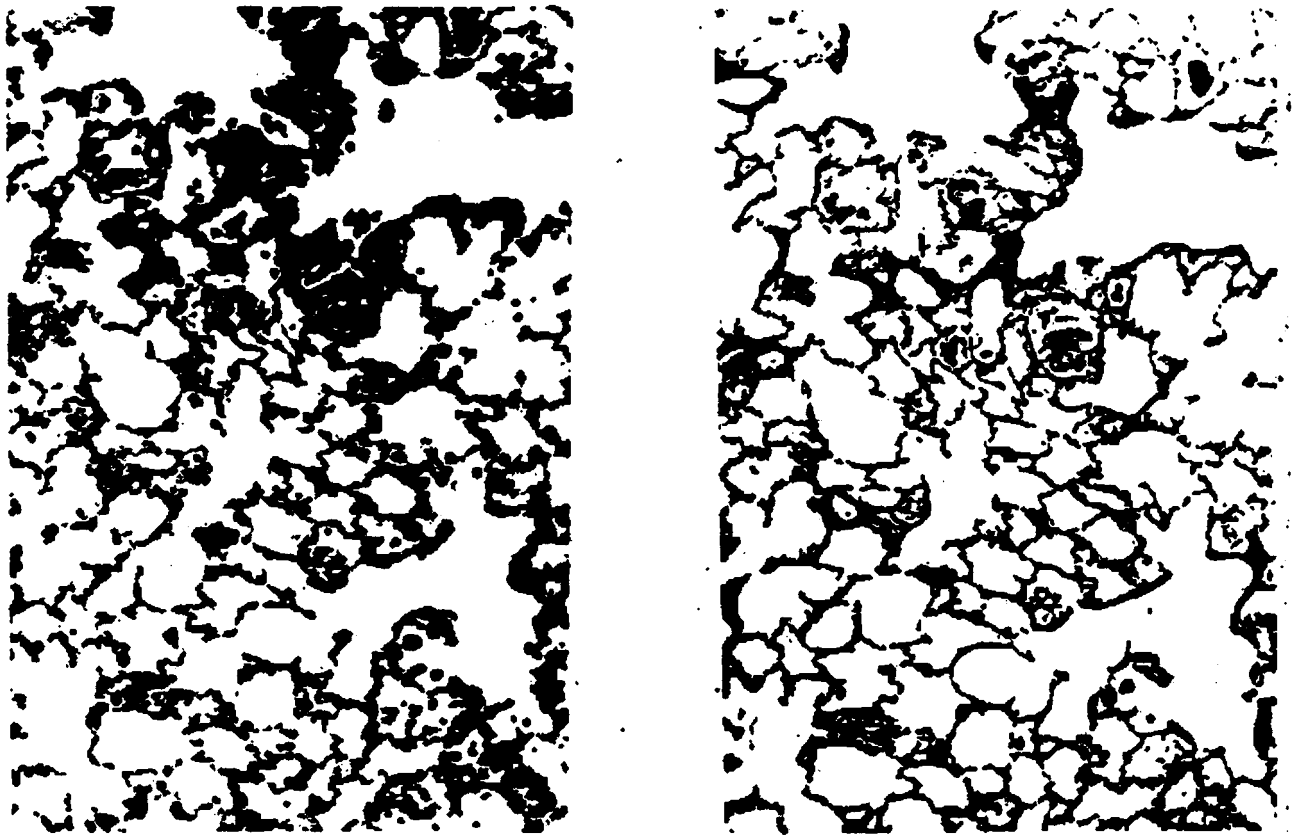

Fig. 1 <u>left:</u> At the top of the picture there are portions of two alveolar ducts that show cellular thickening of the walls with involvement of scattered alveoli. Alveolar involvement is strictly limited; it consists solely of proliferated cells filling alveolar lumens. Of additional significance is the fact that elsewhere the lung tissue appears essentially normal although an unusually large number of free alveolar macrophages are present. From a rat killed 4 days after an intratracheal injection of 35 mg brake drum dust. H. & E. x150

<u>right:</u> The same field as on the left, after the section had been decolorized and impregnated with silver, shows stromal proliferation that parallels the cellular proliferation and is strictly limited to the involved alveoli. x150

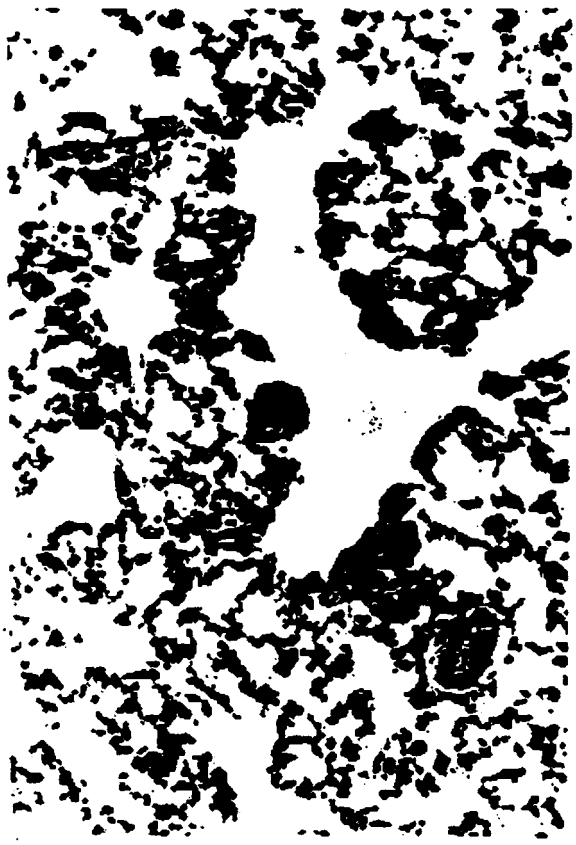

Fig. 2 left: This field shows a respiratory bronchiole dividing into two alveolar ducts. There is focal cellular mural thickening that extends into a few evaginating alveoli. There is some increased cellularity of surrounding alveoli with an increase in the number of free macrophages. H. & E. x150

right: The same field as on the left, after the section had been decolorized and impregnated with silver, shows occlusive stromal proliferation involving only a few alveoli. There is also arborescence of the argyrophilic mural stroma related to increased cellularity of the alveolar walls, which past experience has shown to be completely reversible. x150

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INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

MELLON INSTITUTE, 4400 FIFTH AVENUE

PITTSBURGH, PA. 15213

MEMO TO: Dr. Robert T. P. deTreville

FROM: Dr. Paul Gross

DATE: June 1, 1967

RE: Preliminary Study on Brake-Drum Dust

A report submitted to Johns-Manville Corporation of a "Preliminary Study of Brake-Drum Dust: Comparative Pathogenicity" dated February 14, 1967, indicated that brake-drum dust caused an early reaction of lung tissue of the kind provoked by dusts that are classified as biologically "inert."

The present report confirms the findings of the previous one and also covers important observations on extensions of this study.

Of primary interest to the asbestos industry is the finding that inhaled brake-drum dust is indeed capable of causing the lung to produce ferruginous bodies that are (with the optical microscope) indistinguishable from asbestos bodies; and, in spite of this fact, the dust does not have the fibrogenic potential of asbestos dust as judged by the lung's response to the dust as long as seven and one-half months after its introduction into the lung.

The asbestos industry should be interested to know whether this lack of fibrogenic potential of brake-drum dust can be substantiated. A more comprehensive study would be required, which will involve several species of animals and the introduction of the dust into the lungs not only by intratracheal injection, but also by inhalation.

It is probably of equal, if not greater, importance to the industry to know if the brake-drum dust has the cancerogenic potential that has been associated with asbestos dust.

In the report of February 14, 1967, there is an outline of "Recommendations for Future Studies." These recommendations require modification

because they were based on the assumption that iron-free brake-drum dust would be available in practically unlimited supply. We have since been informed to the contrary.

With the amount of available brake-drum dust very limited, the inhalation technique requires redesigning in order to allow recirculation of the dust with minimal loss.

PG:sjc

JOHNS-MANVILLE
RESEARCH & ENGINEERING CENTER
P.O. BOX 159 • MANVILLE, NEW JERSEY • TELEPHONE: (201) RANDOLPH 2-9000

April 12, 1967

Dr. Paul Gross
Director of Research Laboratory
Industrial Hygiene Foundation of America, Inc.
Mellon Institute
4400 Fifth Avenue
Pittsburgh, Pennsylvania 15213

Dear Dr. Gross:

I am sending, under separate cover, two samples of synthetic chrysotile for use in your research. These samples were prepared by Dr. Julie Yang of our laboratory. The sample labeled "Synthetic Chrysotile" is the purest material we have been able to synthesize. The impurities which are present (see attached table of properties) were probably contaminants in the magnesium hydroxide used as a raw material. It is unfortunate that we were not able to grow longer fibrils, but this requires the use of a mineralizer which would introduce unwanted impurities into the system.

The sample labeled "Ni-containing Synthetic Chrysotile" contains 2.2 per cent nickel. The nickel is most probably in the divalent form and substituted for the magnesium in the chrysotile lattice. Electron micrographs of both samples are attached.

Very truly yours,

James Leineweber

James P. Leineweber, Chief
Basic Chemistry Research Section

mac

Attachment

ATTACHMENT

	Synthetic Chrysotile	Synthetic Ni-Chrysotile
X-ray Diffraction	Chrysotile	Chrysotile
Electron Micrographs		
A. Morphology	Fibrous	Fibrous
B. Size	Up to 5 microns	Up to 2 microns
Ignition Loss @ 1800F	13.2%	12.7%
Impurities* by Emission Spectrograph		
Al	0.018%	0.02
Ca	0.18%	0.14
Fe	0.017%	0.06
Cr	--	0.06
Cu	--	0.10
Ni	--	2.2

*Concentrations reported as element, not oxides

June 2, 1967

Mr. Hugh M. Jackson, Director
Industrial Relations & Management
Development
Johns-Manville Corporation
22 East 40th Street
New York, New York 10016

Dear Hugh:

Per your telephone instructions yesterday, enclosed are reports on the Coalinga and Brake-Drum Dust Studies. Final reports on both studies will be made in about a year, following death and histopathological studies of the animals still under observation. No further charges are anticipated by Dr. Gross with regard to these preliminary investigations. An invoice in the full amount for the Coalinga Study is enclosed. A statement for the Brake-Drum Dust Study is also attached.

Obtaining support from industry for the more comprehensive study of brake-drum dust is now our most important concern as Dr. Gross is prepared to go ahead as soon as such a commitment is received. He would like to start injections intratracheally at once, and redesign of our inhalation technique to conserve available dust should also begin without delay.

Dr. Gross hopes to report his preliminary findings at the Antigua Meeting in November, if Johns-Manville has no objection. It will be mutually advantageous to be able to indicate the follow-up studies are well under way by then, and whether they seem to substantiate the earlier findings regarding inertness.

Please call if there should be any questions.

As mentioned, your participation in the meeting of the Foundation's Board of Trustees was most helpful and was appreciated by all of us. I look forward to our continued association in the work of the Foundation.

Sincerely yours,

Robert T. P. deTreville, M.D.
Managing Director

deT:sjc
Enclosures
cc: Dr. Paul Gross
Mr. C. L. Sheckler

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Research and Engineering Center
June 30, 1967

File 259

H. M. Jackson - DHQ

Industrial Hygiene Foundation of America, Inc.
Fibrous Dust Study

Attached are comments from Sid Speil and Jim Leineweber on the Industrial Hygiene Foundation prospectus for "An Investigation of: a. The specificity of Asbestos Bodies and b. The Biologic Effects of Trace Substances Associated with Chrysotile Asbestos", dated June 1, 1966. Perhaps we can discuss some of these July 6 when Paul Gross visits the laboratory.

F. L. Pundsack/ae

F. L. Pundsack

ae
Enc.

cc: S. Speil
J. P. Leineweber
E. M. Fenner -Enc.
Att: C. L. Sheckler (received a copy of the prospectus)