INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

MELLON INSTITUTE, 4400 FIFTH AVENUE

PITTSBURGH, PA 15213

PROGRESS REPORT NO. 2

on

Fibrous Dust Studies

for

Johns-Manville Corporation
PPG Industries
Pittsburgh Corning Corporation
Owens-Corning Fiberglas Corporation

by

Paul Gross, M.D.
Director of Research Laboratory

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

June 1967

INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

MELLON INSTITUTE ◆ 4400 FIFTH AVENUE

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PROGRESS REPORT NO. 2

on

FIBROUS DUST STUDIES

for

PITTSBURGH CORNING CORPORATION

JUNE 1967

1. Concerning the specificity of ferruginous bodies, in the first stage of this investigation, it has been found that ferruginous bodies, indistinguishable from asbestos bodies, are formed in the lungs of hamsters in response to respirable filamentous particles of such non-asbestos materials as ceramic aluminum silicate, silicon carbide, and glass. The importance of these findings may be judged from the attached correspondence with th editor of the AMA Archives of Pathology. Accordingly, Dr. Paul Gross has prepared a letter, transmitting a manuscript based on findings in the F undation's laboratory for consideration for publication in the same journal. The letter is dated July 19, and the manuscript will be forwarded that day if no objections are received. We believe that the best interests of the sponsors will be served by its publication in the most expeditious manner possible, but transmittal may easily be delayed temporarily if questions arise or if it seems desirable to do so.

II. With regard to the pathogenicity of respirable fibrous dusts of different composition, results reported below are based only upon a study f accrued mortality in each animal exposure group (either due to pneum nia or repeated intratracheal injections of dust). As such, the findings are very preliminary and require substantiation based on observations of animals still on test.

1. Glass

a. Glass (uncoated). In hamsters, this dust evoked f cal macrophage reaction with associated ferruginous bodies. No fibrosis was

observed. In rats, no alveolar mural changes were noted. However, in several scattered bronchioles, there were obstructing polypoid structures of inflammatory fibrous tissue that enclosed numerous glass particles. This bronchiolar inflammation is attributed to the entrapment (at the site) of large aggregates of interlaced glass fibers during the intratracheal injection.

b. Glass (coated with phenol-formaldehyde resin). As with the uncoated glass, this dust produced no discernible alveolar mural lesion; but, because of the impaction of aggregates in bronchiolar lumens, there were lesions in these regions of impaction comparable to those described above.

c. Glass (coated with textile binder). Still in preparation. No progress to report at this time.

2. Ceramic aluminum silicate. The pulmonary reaction to this dust in hamsters was similar to that observed with glass dust except that ferruginous bodies were more plentiful. No fibrosis was demonstrable. In rats, there was an occasional bronchiolar polyp of inflammatory tissue enclosing refractile fibrous dust particles. Occasional small collections of alveolar macrophages were also seen. There was no evidence of alveolar wall fibrosis.

3. Organic fibers. This material was either rapidly removed or underwent resorption because considerable difficulty was encountered

in recognizing evidence of dust injection. Few small collections of dust-containing alveolar macrophages were observed in hamsters and rats. There was no alveolar fibrosis. No ferruginous bodies were found in the lungs of hamsters.

4. Attapulgite. Aside from scattered small collections of alveolar macrophages, no other significant abnormality was observed in the lungs of hamsters or rats. No ferruginous bodies were found.

5. Natural chrysotile. In hamsters the pulmonary reaction to this dust consisted of a diffuse proliferation of alveolar cells and macrophage reactions. Many asbestos bodies were present among these cells in the air spaces at nine months. In rats, the reaction was multifocal and consisted of mural fibrosis involving respiratory bronchioles, alveolar ducts, and their evaginating alveoli.

6. Synthetic chrysotile (Grandquist). In hamsters this dust provoked a moderate macrophage reaction. No ferruginous bodies were found. In rats, there were initially only slight focal alveolar cell proliferations associated with collections of macrophages. Nine months after the intratracheal injection of the synthetic chrysotile, there was questionable thickening of the wall of some respiratory bronchioles. Th re was no active inflammation and no evidence of fibrosis.

7. Synthetic chrysotile (Grandquist) plus adsorbed nickel phosphate. The pulmonary response to this dust in rats was characterized

by a moderately intense multifocal inflammatory reaction centered in the respiratory bronchioles. The inflammatory reaction at the nine-month period included the proliferation of fibrous tissue which obliterated the lumens of the air spaces. This reaction greatly resembled that produced by natural chrysotile. No ferruginous bodies were found.

III. A supplemental study was designed to explore the etiologic role of various components of chrysotile asbestos in the production of lung fibr sis and/or lung tumors. For this purpose, the following series of rats have been injected intratracheally with suspensions of the following materials (all of them of respirable size):

1. Chrysotile dust known to be carcinogenic
2. Synthetic chrysotile
3. Synthetic chrysotile plus nickel
4. Synthetic chrysotile plus chrome
5. Synthetic chrysotile plus nickel, chrome, and benzopyrene
6. Nickel with carbon as carrier
7. Chrome with carbon as carrier
8. Benzopyrene with carbon as carrier
9. Filamentous glass with phenol-formaldehyde coating
10. Filamentous glass with textile binder coating
11. Filamentous glass, uncoated.

As mentioned in II above, concerning results of the preceding phase, data are available only from a relatively few spontaneous deaths which have occurred and such tentative findings as have been observed, and their interpretation, are included in the above discussion. It appears at this point that the trace metals, injected as particulates into the lungs, will probably not be biologically active. It will probably be necessary or advisable to supplement these series by injecting rats intratracheally with synthetic chrysotile to which the trace metals have been adsorbed in a manner similar to that used for adsorbed nickel phosphate.

Comment on Findings to Date

The appended manuscript furnishes irrefutable evidence that ferruginous bodies indistinguishable from asbestos bodies may be produced in lungs from certain non-asbestos filamentous particles of respirable size.

Data so far collected shows that such dusts as aluminum silicate, silicon carbide, and glass, all previously shown to be "biologically inert," will produce ferruginous bodies when injected into the lungs in filamentous form and also confirms their lack of fibrogenic potential. Therefore, there is no reason whatsoever to equilibrate production of ferruginous bodies and pathogenesis. Further data are needed to extend these observations to include lack of cancerogenic potential, however.

Letters to the Editor

TODAY'S PRESSING QUESTION—HOW SAFE IS URBAN AMBIENT AIR?

To the Editor.—Professor J. G. Thomson made a notable contribution to pathology when he announced the discovery of "asbestos" bodies in the juice of lungs taken from nonoccupationally exposed urban population of Capetown, South Africa.[1] Unfortunately, the far-reaching conclusions he has derived since, resting upon little or no evidence, tend to detract from the value of this finding.

In the present paper (*Arch Path* 81:458, 1966), professor Thomson has shown an awareness of—but dismissed too lightly—the obvious objection to his thesis, "the suspicion that asbestos fibers are now a hazard of urban living is confirmed more amply than expected."

This thesis appears to be based on Dr. Thomson's premise that asbestos bodies are specific and do not form in response to other materials. As pointed out by Thomson there are, in addition to the "curious" bodies, also so-called pseudo-asbestos bodies. The latter, he rightly differentiates from true asbestos bodies by the opaque, irregular, central cores.

The pressing question today is the following one: Are there materials other than asbestos, that are of filamentous character and manufactured today, that are part of ambient urban air, and that will stimulate alveolar phagocytes to produce asbestos bodies?[2] These materials could probably be classed mostly as plastics and would, most likely, have one important feature in common, namely, a biologic "inertness." As a possible example, one might consider that filamentous plastic dust has been produced in homes from carpets woven of synthetic yarns. The use of vacuum sweepers equipped with high-speed beaters would tend to reduce some of the fibers to a respirable particle size. It is a curious fact that no publication has appeared describing the pulmonary reaction to such dust.

There is, of course, no answer to this question at the present time. Yet, far from accepting Dr. Thomson's assumption that asbestos bodies are specific for asbestos fibers, the US Public Health Service has recently authorized and funded work in several laboratories in the United States to investigate this question (as well as others) to the tune of over $600,000.

A number of other statements in Dr. Thomson's paper deserve comment. His declaration, "There are statements in the literature on asbestos, mainly by people other than pathologists, that the asbestos body is nonspecific. These opinions are not held by histopathologists today . . . ." is not necessarily true. I, for one, Dr. Arthur J. Vorwald,[3] Dr. John M. G. Davis,[4] of Cambridge, England, and Dr. A. Collet[5] in Dr. Policard's laboratory near Paris have open minds on this problem.

Another statement requiring correction, based apparently on inadequate information, is that, "Man and the guinea pig seem to be the only animals in which asbestos fibers are regularly and rapidly converted into asbestos bodies." Wagner[6] found asbestos bodies in the lungs of rabbits and monkeys exposed to asbestos dust. We have found abundant asbestos bodies in the lungs of hamsters exposed to chrysotile asbestos dust.[7]

Because of the present uncertainty regarding the specificity of the asbestos body, the term "ferritin" body was suggested. This term was criticized because the composition of ferritin has not been adequately characterized. Perhaps the use of the term "ferruginous" body will serve the purpose until it can be shown that these structures are specific for asbestos fibers.

Dr. Thomson declared that, "Many of the very thin and sharp asbestos fibers move downward toward the lung bases owing to lung movement, cardiac action, and gravity." In the presence of "dry" lungs such transport of asbestos fibers and ferruginous bodies would necessarily (at least in the lower lobes) have to go counter to the mucociliary escalator—a feat which is difficult to imagine. A more reasonable explanation of the observation that ferruginous bodies are more abundant in the basal portions of the lungs is that in many people dying of natural causes, this is where fluid tends to accumulate terminally. Under the latter conditions, the opposing action of the escalator mechanism is overcome by the sheer volume of fluid rolling over the mucous blanket like tidal waves with every inspiration. According to this concept, the concentration of ferruginous bodies in the basal portions of the lungs would have no clinical implication except that of a terminal event, similar to, if not identical with, terminal hypostatic congestion and edema of the lungs.

Part. Gross, MD
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REFERENCES

1. Thomson, J.G., et al.: Asbestos as Modern Urban Hazard, *S Afr Med J* 37:77-81, 1963.
2. Davis, J.M.G.: Electron-Microscope Studies of Asbestosis in Man and Animals, *Ann NY Acad Sci* 132:98-111, 1965.
3. Vorwald, A.J.: Personal communication to the author, May 20, 1966.
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5. Collet, A.: Personal communication to the author, May, 1966.
6. Wagner, J.C.: Asbestosis in Experimental Animals, *Brit J Industr Med* 20:1-12, 1963.
7. Gross, P., and deTreville, R.T.P.: Progression of Asbestosis, to be published.

To the Editor—The criticisms in the letter of Dr. Gross which call for a reply are concerned

with the specificity of asbestos bodies and with the movements of asbestos fibers in the human. Dr. Gross agrees with me that the pseudoasbestos bodies can be differentiated from the genuine asbestos bodies by the nature of their central cores, but instead of concluding, as I do, that true asbestos bodies are acceptable markers of asbestos inhalation, he postulates that synthetic fibers are present in urban air and might lead to the production of asbestos bodies. I do not know of any evidence to that effect. He goes on to discuss in particular filamentous dust from carpets woven from synthetic yarns, and expresses surprise that no publication has appeared on the pulmonary reaction to such dust. I am not surprised, as these synthetic fibers are elastic and not of the type that produces fine dust, but if such a publication does appear I shall be more surprised than Dr. Gross if it includes a description of asbestos bodies, as the man-made fibers in carpets are much thicker than the fiber in the center of an asbestos body. Further, to get fragments as short as asbestos bodies, averaging 40μ to 50μ from synthetic fibers would imply brittle characteristics which these plastic fibers do not possess, and would require something more than a vacuum sweeper for their production, if they could be produced at all without the use of a microtome or other cutting tool. Unless one can suggest an inhaled material with the features of an asbestos fiber inside an asbestos body with a length of 5μ to 130μ and a thickness of 1μ or less, as Dr. Gross has failed to do, it would seem more logical and practical to regard asbestos bodies as markers of asbestos inhalation, however unwelcome or inconvenient to some that conclusion may be.

Dr. Gross suggests that my statement that man and the guinea pig appear to be the only animals in which asbestos fibers are regularly and rapidly converted into asbestos bodies is incorrect, and as support mentions that asbestos bodies have been found in the lungs of rabbits, monkeys, and hamsters exposed to asbestos dust. He could also have added that one author on one occasion saw one asbestos body in the lung of a rat exposed to asbestos dust; it is equally irrelevant. I was discussing the animal species that *regularly and rapidly* formed asbestos bodies, not those in which they would be *found*.

This matter is not an unimportant one, and it would seem desirable in experimental asbestosis to use not rats or rabbits, but to use the guinea pig, the animal that consistently shows a pulmonary response to asbestos fibers similar to that in man, with the production of pulmonary fibrosis as well as of asbestos bodies.

Most important perhaps is his last paragraph concerning the movement of asbestos fibers. Dr. Gross omits the first part of the quoted sentence and that which follows it, in which I stress that while the needle-like asbestos fibers can move downwards, the asbestos body with its sharp points blunted by the protein and iron encrustation can not. He, however, discusses the impossibility of the downward descent of asbestos fibers and asbestos bodies on an equal basis, puts forward the idea of the only possible mechanism of this, and thinks very little of his own suggestion. On this we are in complete agreement, but he does not comment on the obvious mechanism in the article.

The evidence that asbestos fibers before they become asbestos bodies move downwards and laterally from lung movements and gravity is inferential, but does explain some of the unusual features of asbestosis, which are otherwise inexplicable. The main objection to it as far as I can see is that it introduces a mode of transport not present in other varieties of pneumoconiosis, but other pneumoconioses are not due to thin sharp fibers. The lung containing the needle-like sharp fibers of asbestos could be regarded as a shaking machine, and one which is always in action as the lung is never at rest. The fibers we are discussing are often too long to be phagocytosed by dust cells, and would tend to move downwards in the erect posture occupied by most human beings for two thirds of the day and laterally for the remaining third during sleep. This explains why asbestosis is more marked at the base unlike other pneumoconioses such as silicosis, which is more marked in the apical portions of the upper lobes; why pleural plaques, calcified or not, now accepted by most as resulting from inhalation of asbestos, are present posteriorly and laterally in the parietal and not the visceral pleura; why they are more common inferiorly than superiorly and are not seen anteriorly, as adults rarely sleep in the prone position. The movement of these asbestos fibers outwards from the lungs explains why such pleural plaques are initially seen over the unyielding ribs and not over the soft easily penetrated intercostal regions, and for the same reason are found in the diaphragm over the tendinous portion, and not the muscular portions. It is probably the reason why these pleural plaques are seen more frequently in cases with little or no pulmonary asbestosis, as there is no pulmonary fibrosis to block their outward passage, and this may well be the explanation of the apparent paradox that malignant mesotheliomas of pleura are seen more often with a mild or trifling asbestosis than with a severe classical asbestosis. It is a rational explanation why these mild cases of asbestosis may be associated with a malignant mesothelioma of the peritoneum. It is surely significant that bare asbestos fibers, but not immobile asbestos bodies, have been demonstrated in all these extrapulmonary lesions.

To conclude, perhaps it would be easier to appreciate the basic differences between other pneumoconioses and asbestosis and its complications if we stopped talking of asbestos dust, and used instead the term employed in the German literature—asbestos uroilen.

J. G. Thomson, M.D.
Medical School
Cape Town, South Africa

Letters to the Editor

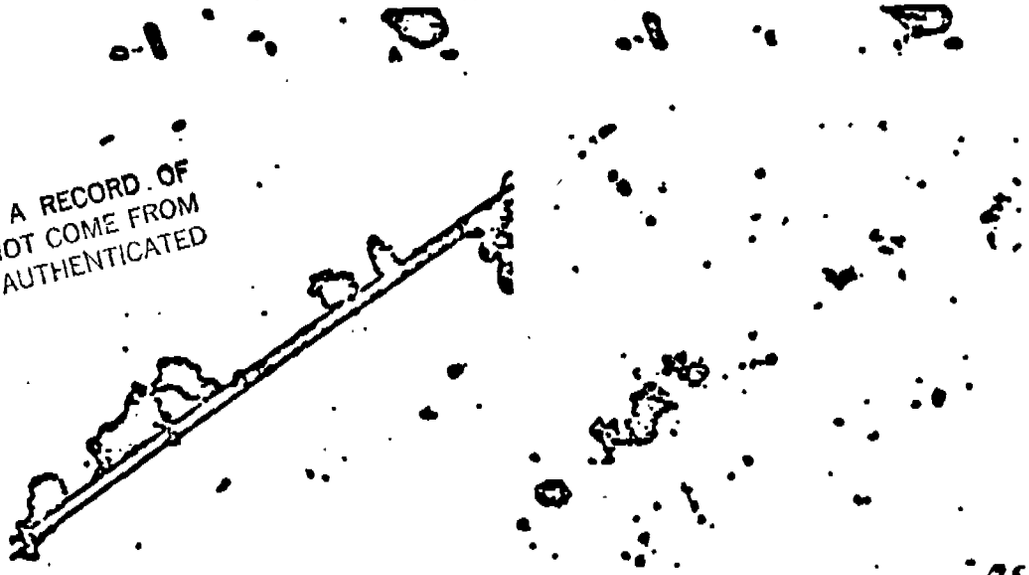
REPLY TO DR. THOMSON

To the Editor.—In view of his skepticism, Am. Rev. of Pathology 82:195-196 (Aug.) 1966, concerning Dr. Gross' suggestion that nonmineral, filamentous dust particles may be present in the ambient air, comparable in size to that of asbestos fibers that have caused the development of asbestos bodies, Dr. Thomson will find the attached photomicrographs of interest (Fig 1 and 2). Numerous such fibers were found in ordinary house dust and their disappearance on microincineration proves that they are not asbestos. Dr. Thomson's opinion that nonmineral fibers in ambient air are not sufficiently fine to form the cores of ferruginous bodies is thus definitely open to question.

At present, Dr. Gross is attempting to develop factual information concerning penetration of ferruginous bodies from a variety of fibrous dusts. Dr. Thomson is not in a position to speak for

Fig 1.—*Left*. Fibrous dust particle of 3μ diameter and approximately 40μ in length before microincineration. *Right*. Same after microincineration. The particle has disappeared.

Fig 2.—*Left*. Fibrous dust particle 3.4μ in diameter and more than 180μ long before microincineration. *Right*. It, too, has disappeared in the process of microincineration.



all histopathologists—certainly not for Dr. Gross nor for the other experts from the United States, Great Britain, and France listed in Dr. Gross' letter—on the matter of specificity of ferruginous bodies as being caused only by asbestos. In his rebuttal of Dr. Gross' letter, Dr. Thomson again appears to attempt to speak for the profession when he says that pleural plaques now are "accepted by most" as resulting from inhalation of asbestos.

In a recent monumental study involving 438 consecutive autopsy cases, Meurman[1] concludes (p 83):

"The frequency of cases with plaques was about the same in two of the three hospital districts investigated in different parts of Finland, whilst in the third it was lower. Plaques proved to be an equally common finding in a district in Southwest Finland with no asbestos deposits and no particular asbestos industries, as in a district in East Finland with an asbestos mine and mill and extensive anthophyllite asbestos deposits near its eastern border. Plaques were encountered in 32.2% of the urban population and 31.8% of the rural population."

The purposeful publication of erroneous assumptions, which have no apparent basis in fact and have primary emotional appeal was criticized by the late Dr. Frank Princi[2] in his Chairman's Address (Medical Perspective in Atmospheric Hygiene) before the AMA Scientific Session on Preventive Medicine in 1962 as being far too common. He called for adherence to the scientific method on the part of scientists, indicating their responsibilities to the public as well as to science in such matters. Those who have not done so should review Dr. Princi's article in light of the present disagreement and be guided accordingly.

In the present state of knowledge, Dr. Thomson's insistence on the specificity of ferruginous bodies and pleural plaques for asbestos fibers is not justified scientifically.

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References

1. Meurman, L.: Asbestos Bodies and Pleural Plaques in a Finnish Series of Autopsy Cases. *Acta Path Microbiol Scand* (suppl) 181:1966.
2. Princi, F.: Medical Perspective in Atmospheric Hygiene. *JAMA* 182:650-655 (Nov 10) 1962.

RAPID HISTOLOGICAL DIAGNOSIS

To the Editor.—The supravital technique for making fast tissue diagnoses at the time of surgery was simplified twenty years ago.[1-3] Since then, the method has continued to yield its rewards in a few places but it has not gained many new adherents. This situation would appear to have been caused by the increasing popularity of the more cumbersome "frozen-section" technique which provides more familiar patterns of more entrained preparations.

Our experience with these two contrasting prototypes of examination is being recorded in an effort to verify quantitatively for the many what may have seemed obvious only to the few.

The data (the Table) show a very small improvement from 2.3% overall error in the period when only the supravital rapid-section (R-S) technique was employed (1958-1962) to 1.9%[4] in the later period when cryostat microtome frozen-section methods were added. This may be attributable to an increased breadth of experience and improved judgement over the years, rather than to methodological differences. Either figure compares favorably with the 3% overall inaccuracy cited by other investigators.[5,6]

In the later period (1963-1964), where the desirability of employing an added (frozen-section) technique was determined by the difficulties of each case, it is paradoxical that the only false positive errors occurred in settings where the added effort was not made, and may be an expression of an irreducible minimum of failure of performance.

More important than numerical data are the

Data Showing Contrast Between Frozen-Section and R-S Techniques

			False Positive		False Negative		False Pos + Neg		Index		Cancel		Partial or Defer	
		Total	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
1958-1962	R-S only	3,149	3	0.3	22	2.0	25	2.3	26	2.3	902	86.4	136	13.6
1963-1964		730	3	0.4	11	1.5	14	1.9	37	5.3	665	88.7	86	11.3
	R-S only	416	3	0.7	5	1.2	8	1.9	2	0.5	380	93.7	36	8.3
	Frozen + RS	314	0	0.0	6	1.8	6	1.8	15	4.5	278	82.4	50	17.6

APPENDIX C

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Dear Dr. deTreville:

The enclosed copy of a letter to the Editor from Dr. Thomson. Since I did not forward (probably an error) your lette: to him, I believe his letter should be published.

I believe this interchange should now be terminated. I trust this will be agreeable to you.

Sincerely yours,

D. Murray Angevine

D. Murray Angevine, M.D.
Chief Editor
Archives of Pathology

DMA:cg

LETTERS TO THE EDITOR

Reply to Dr. de Treville's letter.

To the Editor, - In my reply to Dr. Cross' suggestion that non-mineral filamentous dust particles could form the centre of asbestos-like bodies, my comment was that "unless one can suggest an inhaled material with the features of an asbestos fibre inside an asbestos body with a length of 5μ to 150μ and a thickness of 1μ or less, as Dr. Cross has failed to do, it would seem more logical and practical to regard asbestos bodies as markers of asbestos inhalation, however unwelcome or inconvenient to some that conclusion may be."

Dr. de Treville, Archives of Pathology 62: 496 - 497 (Nov 1960), in reply to this, produces photomicrographs of non-asbestos fibres with thicknesses of 1μ and 3.6μ, and on this concludes that my opinion that "non-mineral fibres in ambient air are not sufficiently fine to form the cores of ferruginous bodies (asbestos bodies)" is thus open to question. My opinion, of course, is still open to question, but the average thickness of the asbestos fibre in the centre of the asbestos body is 0.5μ, without considering the miniature asbestos bodies demonstrated by the electron microscope, and all Dr. de Treville has done is to fail to find any non-asbestos fibres in household dust as thin as those in the centre of asbestos bodies.

Dr. de Treville next accuses me of attempting to speak for the profession when I say that pleural plaques are now "accepted by most" as resulting from the inhalation of asbestos. His only support for this is to quote a paragraph from the monograph by Meurman stating that pleural plaques were about as frequent in a district in Finland with no asbestos deposits and no particular asbestos industries, as in a district with an asbestos mine and mill. This is preceded by a statement that "Meurman concludes", but the quotation is from a summary of his findings (page 83) and not from his conclusions which are given later (pages 97 - 99) under the heading of General Summary. Dr. Meurman naturally discusses the evidence for and against the relationship between asbestos inhalation and pleural plaques, and it is an easy matter to select from this discussion (pages 87 - 96) opinions against that association. Meurman's opinion on the relationship between asbestos bodies and pleural plaques is very clearly stated in his summary. "Plaques were observed in 52.2% of the urban population and in 31.0% of the rural population. In the rural districts cases with bilateral plaques were more frequent than plaque-free cases only in the asbestos mining commune and in one of its neighbouring communes." "Asbestos bodies in the lungs and pleural plaques occurred more often in conjunction than separately, the difference being very highly significant". "The present results seem to indicate that pleural plaque formation, in particular when it is bilateral, and the occurrence of asbestos bodies in the lungs, have some aetiological factor in common. The dust that induces the formation of asbestos bodies does not, however, seem to be the

acic cause of plaque f rmation".

Readers of this correspond nce may judge for themselves whether Dr. de Treville's quotation from Neurman gives a correct or incorrect impression of Dr. Neurma.'s opinion on the relationship between asbestos inhalation and asbestos plaques.

J.G. Thomson

J.G. THOMSON, M.D.
Medical School
Cape Town, South Africa.

Note on copy of Transactions: APPENDIX D
Dr. Angevine —
Please see p. 111 for a picture of a ferruginous body produced by Dr. Gross.
RTP deT.

March 8, 1967

Dr. D. Murray Angevine
Chief Editor, Archives of Pathology
Department of Pathology
University of Wisconsin
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470 North Charter Street
Madison, Wisconsin 53706

NOTE: THIS
NOT CO[illegible] FILES

Dear Dr. Angevine:

Regarding Dr. Thomson's reply, by way of review, it should be recalled that the following two basic assumptions in his paper (Arch. Path. 81:458, 1966) were challenged:

1. that histopathologists today do not believe that the asbestos body may be nonspecific, and

2. that it is now accepted by most that pleural plaques result from inhalation of asbestos.

In a paper given in October,[1] Dr. Paul Gross reported early findings of his research[2] on production of ferruginous bodies with non-asbestos filamentous fibers of respirable size. Scientific questions are properly settled by consideration of such data, not by opinions. The very existence of Dr. Gross research is adequate proof that Dr. Thomson does not speak for all histopathologists today concerning specificity of so-called asbestos bodies for asbestos inhalation.

Mourman's findings, mentioned by Dr. Thomson, are in accord with those published earlier[3] by Dr. Kenneth Smith, who said, "If inhalation of the asbestos fiber alone could cause pleural plaques, one would expect to find plaques wherever the fiber is used." Mourman's conclusion that "the dust that induces the formation of asbestos bodies does not, however, seem to be the sole cause of plaque formation" does not appear to be consistent with the second assumption of Dr. Thomson.

Further work is certainly needed to shed light on this important area, as the occurrence of ferruginous (so-called asbestos bodies) has been found

in almost half (48%) of the individuals studied at autopsy in Montreal by Thurlbeck.[4] Fortunately, plans for such are being made through cooperative efforts involving industry, government, universities and private institutions, as was pointed out in a recent meeting held by Industrial Hygiene Foundation (IHF) and reported in IHF Medical Series Bulletin No. 11 entitled "Asbestos Bioeffects Research for Industry." A limited number of copies of this publication will be made available to readers of Archives of Pathology upon request without charge while the supply lasts.

Sincerely yours,

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

deT:sje
cc: Dr. Paul Gross
bcc: Mr. E. K. Davison
Mr. Hugh Jackson

Enclosure: All four references were sent to Dr. Angevine.

1. Transactions of Industrial Hygiene Foundation 31st Annual Meeting, 1966.

2. Industrial Hygiene Foundation Medical Series Bulletin No. 11, "Asbestos Bioeffects Research for Industry," 1966.

3. The Pneumoconioses. A.J. Lanza, Editor. Grune & Stratton, Inc., New York, 1963.

4. The Incidence of Asbestos Bodies in the Lungs at Random Necropsies in Montreal. Lily Anjilvel and W. M. Thurlbeck. Can. Med. Assn. J. 95, 1179-1182, Dec. 3, 1966.

APPENDIX E

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April 4, 1967

Robert T. P. deTreville, M.D.
Managing Director
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Dear Dr. deTreville:

I wish to thank you for your letter of March 8 together with enclosures. After careful consideration, I do not believe it advisable to publish further correspondence on this matter in the Archives of Pathology. It would seem that after the initial exchange of opinions in print that further discussion should be by correspondence of participating parties.

I assure you that this is not a deliberate attempt to curtail debate but rather than a continuation of it may not be of large reader interest.

Sincerely yours,

D Murray Angevine

D. Murray Angevine, M.D.
Chief Editor
Archives of Pathology

DMA:cg

APPENDIX F

INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

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July 19, 1967

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Dr. D. Murray Angevine
Chief Editor
Dept. of Pathology
University of Wisconsin Medical School
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Madison, Wisconsin 53706

Dear Murray:

I am enclosing an original and two copies of our manuscript, "Pulmonary Ferruginous Bodies: (1) Their Development in Response to Filamentous Dusts, (2) A Method of Isolating and Concentrating Them," together with two sets of illustrations for your consideration for publication in the AMA Archives of Pathology.

The work reported in this paper is a logical follow-up of the correspondence between Dr. J. G. Thomson and our laboratory that was published in the Archives of Pathology, Vol. 82, in August and November, 1966.

With best regards.

Sincerely,

Paul Gross, M.D.
Director of Research Laboratory

PG:ejd
Enclosure

4904

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APPENDIX C

INDUSTRIAL HYGIENE FOUNDATION OF AMERICA, INC.

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PULMONARY FERRUGINOUS BODIES:

1. Their Development in Response to Filamentous Dusts
2. A Method of Isolating and Concentrating Them

by

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ABSTRACT

Formation of ferruginous bodies should not be confused with pathogenicity. Failure to understand this differentiation may result in the erroneous generalization that all fibrous dusts share the ability of asbestos to produce lung damage.

Such materials as fibrous aluminum silicate, silicon carbide whiskers, cosmetic talc, and glass fibers produce ferruginous bodies experimentally which are indistinguishable from those produced by asbestos fibers.

A method of isolation and concentration of ferruginous bodies from lungs of animals and humans is described. Ferruginous bodies from asbestos fibers are much more pleomorphic than has been described (except by Gloyne and Merewether, International Labour Office, Occupation and Health Supplement, Asbestos, January, 1938, page 7), casting further doubt on morphological distinctions used in the past in separating so-called asbestos bodies from pseudo-asbestos bodies.

Introduction

Worldwide attention was refocused on ferruginous bodies by the publication of Thomson,[1] who found this phenomenon in the lungs of more than 30% of unselected autopsied adult hospital patients in Capetown. A similar percentage was noted in Miami, Florida,[2] 43% in Pittsburgh, Pennsylvania,[3] and 48% in Montreal, Canada.[4] The higher percentag s reported in Pittsburgh and Montreal are possibly inherent in the more intensive searches carried out in these cities. These bodies are similar to asbestos bodies though the nature of the central fibers have not been identified.

Asbestos bodies are golden-brown, ferro-coated formations found in the lungs of persons who have inhaled asbestos dust. They are generally described as symmetrical, segmented structures usually with clubb d ends, 3 to 5 microns in diameter and 20 to 50 microns long. The core of these bodies is composed of a transparent colorless asbestos fiber, although this fiber is not always demonstrable.

Pseudo-asbestos bodies are similar to asbestos bodies, but are formed in the lungs in response to inhaled non-asbestos fibrous materials. Apparently the only difference between an asbestos body and a pseudo-asbestos body is that in the former, the central fiber is composed of asbestos and in the latter, of material other than asbestos.

Since asbestos-like bodies can form in response to respirable, transparent, colorless fibers deposited in the lungs and composed of materials other than asbestos and since classifying these structures based upon identification of the central fiber presents difficulties, a generic term, "ferruginous" body, has been proposed for all bodies formed in response to the presence (in body tissues) of a broad spectrum of fibers, including asbestos. Davis[5] and Collet[6] demonstrated by electron microscopic studies of macrophages that ferruginous bodies are formed intracellularly by granules of ferritin or a ferritin-like protein that are precipitated upon and around some foreign materials.

As asbestos body, therefore, is only one kind of ferruginous body, one in which the central filament is an asbestos fiber. As will be seen later, the appearance of these bodies and their dimensions are so varied as to defy the reasonably short description usually employed.

The problem now confronting investigators concerns the significance of the widespread finding of ferruginous bodies in the lungs of urban p pulation groups. The solution of the problem is, of course, linked to the identity of the central fiber about which the ferruginous body forms and which is at present unknown. It is hoped that recent analytical advances, such as lectron diffraction and microprobe will provide techniques for definitive identification of the central fiber.

Up to this point, the identification of ferruginous bodies in the lungs of unselected autopsied hospital patients as asbestos bodies[1] has been based on the hypothesis that transparent fibers of respirable size composed f materials other than asbestos either are not encountered in industrial and community environments, are not deposited in the lungs, or do not result in the formation of ferruginous bodies when inhaled.

Respirable fibers, however, are apparently ubiquitous.[7] They may be mineral, animal and vegetable in nature and from both natural and synthetic origin. They are disseminated through industrial processing, community activities, personal habits, and the action of natural forces. Also, we recently reported that a ceramic fiber of respirable size, composed of aluminum silicate, resulted in the formation of ferruginous bodies.[8] The latter were indistinguishable from some of the asbestos bodies isolated from an asbestotic lung of a known asbestos worker. (Fig. 1) Although non-segmented, they were golden-yellow, symmetrical, clubbed bodies, staining deep blue with Perls' test and exhibiting a central transparent filament.

This paper discusses our further findings as follows:

a. Ferruginous bodies are developed in the lungs of hamsters in response to the presence of "biologically inert" filamentous aluminum silicate, glass, and silicon carbide particles.

b. A simple method is made available for isolating ferruginous bodies and bare fibers (inclusive of asbestos bodies) from lungs. The method is given in detail and the results obtained described briefly.

The Production of Ferruginous Bodies

Groups of 12 hamsters each were injected intratracheally with 3.5 mg fibers contained in 0.5 ml of aqueous suspensions. This was done under light ether anesthesia with the aid of an illuminated, self-retaining speculum that made the vocal chords visible and allowed the insertion of a long 18-gauge needle between the vocal chords under direct observation. All of the following were injected:

1. Ceramic aluminum silicate fibers. This is an uncoated ceramic fiber with a median diameter of 2.0 μ. Fifty percent of the fibers were under 75 μ in length and many filaments were shorter than 15 μ. No free silica was detected in the fibers.

2. Silicon carbide whiskers. These were 99.5+ percent SiC. They had a range of fiber diameter from 0.5 to 3.0 μ, with a fiber length that ranged from 100 to 750 μ.

3. Glass fibers, uncoated. The fibers had a mean diameter of 0.4 μ and a mean length of 4.4 μ.

4. Cosmetic talc. Fifty percent of the fibrous material in the talc was under 0.2 μ in diameter and 1.0 μ in length.

5. Attapulgite. Fifty percent of the fibers were under 0.1 μ in diameter and 1.0 μ in length.

6. Chrysotile. Most of the fibers were of ultramicroscopic dimensions.

Isolation and Concentration of Ferruginous Bodies

Samples of lung tissue cut into thin strips three to four mm thick or fragments about 0.5 cc in volume, are placed in clean glass or plastic containers. To the tissue is added about 20 times the tissue volume f commercial 5% sodium hypochlorite solution. This is allowed to stand undisturbed at room temperature for several hours until all chemical action has ceased. More hypochlorite solution is then added at frequent intervals until the tissue has been digested.

For small lungs, such as those of rats and guinea pigs, the frequency of addition of fresh hypochlorite solution and the amount should be such that all lung tissue is digested in approximately 24 hours. For human lungs, unless quantitative recovery of ferruginous bodies is desired, complete digestion is not necessary.

In the case of human lungs, the ferruginous bodies and bare fibers are often associated with a sticky lipidic film adherent to the bottom of the container. The stickiness allows one to pour off all the fluid and undigested lung tissue without loss of the bodies and fibers. Because of the presence

of anthracotic pigment, the film usually has a dirty gray color. The film is dissolved by vigorously washing it with a mixture composed of one volume chloroform and two volumes of approximately 50% ethyl alcohol; the total volume should be the minimal necessary to remove all the film. The wash fluid is centrifuged for about five minutes. Because of their high specific gravity, the ferruginous bodies and the insoluble mineral particles settle to the bottom of the tube. On the other hand, most of the carbonaceous material collects at the interphase between the chloroform and the aqueous alcohol. If too much alcohol is used, the carbonaceous material will lose some of the water that lowers its specific gravity. As a result, there will be no separation between the anthracotic material and the ferruginous bodies. In such cases, rehydration with water followed by the addition of chloroform will usually effect a good separation.

All of the fluid and solid material above the sediment at the bottom of the tube are discarded, and the walls of the tube are cleaned of the adherent anthracotic material. The sediment is washed several times with water to remove all hypochlorite and other water-soluble materials. It is then stored in an aqueous or alcoholic medium.

When smears are made of the suspensions, it may be advisable to dehydrate the smear and use a mounting medium to render much of the mineral dust associated with the ferruginous bodies less conspicuous. The naked fibers remain visible.

In the case of small animal lungs, chloroform and the supernatant fluid were poured into centrifuge tubes in a proportion of 1:2. After centrifuging, the supernatant fluid was carefully removed and discarded except for about 1 ml left undisturbed on the bottom. The film on the bottom of the original container in which the lung tissue was digested, was then removed as in the case of human lungs. This fluid was added to a pool of whatever sediment was obtained from the supernatant fluid. The subsequent procedure was the same as with human lungs.

We have worked with formalin-fixed tissue only, but there appears to be no reason why this method should not work equally well with fresh lung tissue.

Results

Paraffin Sections

Initially the ferruginous bodies were sought only in paraffin sections that had been stained with hematoxylin, eosin, or Perls' test for iron. Because of the paucity and small size of these bodies in the sections, the hematoxylin made the search more difficult. Subsequently, replicate sections that were given the Perls' test only, or also lightly counterstained with eosin and cleared, proved to be satisfactory.

The injected fibers generally were confined to the air spaces where they were associated with free macrophages. Some of the filaments passed

through the bodies of one to three, and even four, macrophages so that these cells appeared to be impaled as though upon a spit (Fig. 3C). When the sections had been stained for iron, the dust-containing areas, under low magnification, were usually marked by a granular deep blue coloration.

In sections of lungs of hamsters killed one month after an intratracheal injection of aluminum silicate and glass fibers, occasional ferruginous bodies were found. These were non-segmented, light yellow, structures with bipolar clubbing and a transparent central filament (Figs. 2A, 3A). These, subsequent to the Perls' test, took on a deep blue color that often obscured the central filament. Very similar non-segmented bodies were seen in suspensions of isolated and concentrated human asbestos bodies derived from an asbestotic lung of a worker known to have been exposed to chrysotile asbestos dust for 30 years (Fig. 1).

The ferruginous bodies that formed in response to chrysotile asbestos were smaller than those that formed in response to aluminum silicate and glass and also different from the latter two in being segmented (Fig. 4C). The ferruginous bodies were more readily found in the lung sections of hamsters injected with aluminum silicate filaments than in lung sections of animals injected with filamentous glass or chrysotile dust. No ferruginous bodies were found in the lung sections of hamsters injected with silicon carbide filaments at this time (one month post-injection).

Examination of lung sections of hamsters killed six months after the intratracheal injection of the filamentous dusts revealed no more ferruginous bodies than those encountered five months earlier. No segmented forms were found except in association with chrysotile dust. No ferruginous bodies were seen in lung sections of hamsters injected with silicon carbide. Dust-containing alveoli found in sections of lung from a hamster injected with talc were easily identified because of the blue coloration caused by the presence of iron; however, ferruginous bodies could not be identified. Similarly, no ferruginous bodies were found in lung sections from hamsters injected intratracheally with attapulgite.

Lung Digests

The smears of the sediment derived from the digestion of the lungs from hamsters injected six months previously with aluminum silicate, glass, and chrysotile, respectively, consisted largely of naked filaments, but many ferruginous bodies were also seen. Although most of the ferruginous bodies that had formed in response to aluminum silicate and glass fibers were non-segmented, a number of segmented forms were also found (Figs. 2B, C, D; 3B, C, D). A more prolonged search of the sediment from lungs of hamsters injected with silicon carbide was necessary before several ferruginous bodies could be found. This search was facilitated by applying Perls' test for iron to the smear. The bodies were mostly nonsegmented, and except for the clubbed ends, the coating on the filaments was thin. One silicon carbide fiber was found with a club-shaped coating at one end, a fusiform coating near

the other end, and a very slight thickening near the middle (Fig. 4A). Two segmented ferruginous bodies that had formed around silicon carbide fibers were observed. Unfortunately, the diffusion of the blue pigment of the body rendered its outline fuzzy (Fig. 4B).

The sediment from a lung from a hamster injected with talc was composed largely of crystalline plates; but upon careful search, a number of n n-segmented ferruginous bodies were also found. These too had a transparent central filament. (Fig. 2A, 3A) Because the Prussian blue reaction for iron had also been used in this smear, the outlines of these bodies were fuzzy because of the diffusion of the pigment (Fig. 4C).

Unexpectedly, ferruginous bodies were more difficult to find in lung sections after chrysotile, than after aluminum silicate injections. The same finding was observed with the concentration method. Although few in number, all asbestos bodies were segmented (Fig. 4D).

One of the most interesting observations was that, when stain d for iron, filaments that passed through the bodies of one or more macrophages showed a coating of ferritin or ferritin-like material only on the intracellular portions of the filament (Fig. 3C).

The sediments from the lungs of hamsters injected with attapulgite revealed no ferruginous bodies. The failure to find ferruginous bodies in these sediments may be interpreted as a negative control to indicate that our positive findings were not attributable to the accidental inhalation of fibers in the ambient laboratory air.

The sediment from the human asbestotic lung was a rusty, red-brown color; in the smear, a wide variety of asbestos bodies were seen in addition to innumerable naked fibers. As previously indicated, a large number of the asbestos bodies were pale, thin, and nonsegmented. Also of interest, was the fact that many of the largest bodies did not have smooth surfaces, but were spiculated. The spicules were often coarse and had squared-off ends. A few of the bodies lacked symmetry. Some pear-shaped bodies without a central filament were also seen. Although most of the bodies were more or less rectilinear, many curvilinear forms were also present. Some of the latter appeared to measure between 180 to 270 degrees of arc. In the larger spiculated forms, the central fiber was often obscured by the thick, dense, red-brown coating. Some of the very long thin fibers (50 to 100 μ) often had segments of ferro-protein at either end with relatively long stretches of naked fiber in between.

In an attempt to free asbestos bodies from adherent fine carbon particles present in an otherwise "clean" suspension, it was subjected t ultrasonic vibrations for a few seconds. Unexpectedly, only naked fibers remained, and no asbestos bodies could be found in the suspending fluid.

Comments

Because bodies similar to, or identical with, asbestos bodies have been found in human lungs about which definitive knowledge of the identity

of the central fiber is lacking, the generic designation of ferruginous body has been proposed to cover both asbestos and so-called pseudo-asbestos bodies.[8] The distinction heretofore made between asbestos bodies and pseudo-asbestos bodies may have been based in part on what the observer believed to be an appearance consistent or inconsistent with that of asbestos bodies. More often, however, this distinction was based on the observer's knowledge that the host had or had not been exposed to respirable asbestos fibers. Consequently, it would probably be correct to say that the crucial point of difference between a diagnosis of an asbestos body and one of a pseudo-asbestos body is the observer's knowledge, from the case history, of whether the central fiber could be an asbestos fiber or not.

Regardless of the nature of the central fiber, the bodies that result in response to the presence of filamentous dust in the lung have as a common feature a coating of iron-containing protein (ferritin or ferritin-like). Furthermore, it appears probable from a study of the pleomorphism of human asbestos bodies, which was so well illustrated by Gloyne and Merewether,[9] that differences in size, segmentation, or other morphologic features of the ferruginous coating would not serve to distinguish between ferruginous bodies of asbestotic origin and those of non-asbestotic origin.

Thomson has proposed to differentiate ferruginous bodies into asbestotic and non-asbestotic ones on the basis of the transparency or opacity

of the central fiber.[2] This proposal seems inappropriate inasmuch as we have demonstrated that a number of transparent fibers of respirable size other than asbestos are capable of producing ferruginous bodies that are indistinguishable from those produced by asbestos.

At any rate, it is obvious from the production of ferruginous bodies in hamsters in response to respirable, colorless, transparent filaments of aluminum silicate, glass, and silicon carbide, that such bodies represent a general reaction to filamentous particles and are not a specific reaction to asbestos fibers. To what extent our findings may have application to the ferruginous bodies that are being found with increasing prevalence in human lungs [1-4] remains to be determined. The applicability depends, of course, upon the identity of the central fiber in the ferruginous bodies. The method of isolation and concentration of uncoated fibers and ferruginous bodies from human lungs described in this paper may help in the study of the nature, identity and prevalence of inhaled filamentous particles and associated pulmonary ferruginous bodies.

It is highly probable that the composition of the ferruginous body is altered by the method used for isolating them, since it is not likely that with the destruction of proteins leading to the liquefaction of all tissue elements in the lung, the protein in the ferruginous bodies should be spared. In all likelihood, the protein constituent of the bodies is destroyed and only the iron

and other inorganic components remain to retain and maintain the form of the bodies. The fragility of this chemically altered ferruginous coating is indicated by the ease with which it is removed when subjected to ultrasonic vibrations, thereby rendering the central fiber naked. This may further facilitate the identification of these fibers.

There appears an increasing tendency to consider all filamentous dusts in the same category as asbestos with regard to their pathogenic potential. This reasoning is probably based on a mechanistic concept of the pathogenicity of fibrous dust in general and asbestos dust in particular. Such a mechanistic concept holds that the pulmonary fibrosis in asbestosis is the tissue response to mechanical trauma produced when pulmonary cells are perforated or impaled by the fine points of the asbestos fibers.

It need only be recalled that a similar mechanistic concept of th pathogenicity of crystalline silica was abandoned many years ago because of overwhelming evidence against its validity. Just as the proven biologic "inertness" of diamond dust was the coup de grace for the mechanistic pathogenetic concept of silicosis,[10] so should the proven biologic "inertness" of filamentous aluminum silicate[11] have done the same for the mechanistic pathogenetic concept of asbestosis.

Extremely thin flakes of glass may also be considered to have sharp cutting edges; yet, this has also been found biologically "inert" when inhaled or injected into the lungs of animals. Silicon carbide, noted for its hardness

as well as sharp edges and points that make it such an ideal abrasive, when inhaled as a fine dust or injected intratracheally, has resulted in a pulmonary response likewise classified as biologically "inert."[12-13]

Gaining increased attention is a newer concept that the potential of extraneous trace metals and other materials associated with fibrous minerals can cause the injury previously attributed to fibers. The respirable fibers may provide a transport mechanism for dosing tissues with injurious materials associated with the fibers. Cralley et al.,[7] have shown that asbestos textile workers in the past have been exposed to appreciable concentrations of nickel, chromium and manganese associated with the fibrous mineral and abraded from the alloy metal in asbestos processing equipment. They state further that there is evidence that this phenomenon exists in relation to a number of other fibrous minerals. There is also some indication that the biological response in the formation of ferruginous bodies may be related to the nature and extent of the layer of metal solute surrounding the fiber. Additional research needed in these areas is currently underway.

Unless the above facts are kept in mind, the finding that ferruginous bodies are formed in response to aluminum silicate, silicon carbide, and glass filaments in the lungs, may be used as still another reason for erron ously classifying these dusts with asbestos in their ability to produce lung damage.

Summary

The mechanistic theory of pathogenicity of dusts, which in the case of silicosis long ago proved groundless, nevertheless has again been raised with regard to fibrous dusts such as asbestos. Reasons are given why the formation of ferruginous bodies should not be confused with pathogenicity. Failure to understand this differentiation has resulted in some instances in the erroneous generalization that all fibrous dusts share the ability of asbestos to produce lung damage.

Such inert materials as fibrous aluminum silicate, silicon carbide whiskers, and fibrous glass produce ferruginous bodies experimentally which are indistinguishable from those produced by asbestos fibers.

Details of a method of isolation and concentration of ferruginous bodies from lungs of animals and humans are described. With this new technique, much more extensive studies of ferruginous bodies found in the lungs of asbestos workers with definite asbestosis (fibrosis of the lungs) have been made possible. Ferruginous bodies from asbestos fibers are much more pleomorphic than has been described, casting further doubt on morphological distinctions used in the past in separating so-called asbestos bodies from pseudoasbestos bodies. Attempts to identify central cores of ferruginous bodies by analytical means such as electron diffraction and microprobe techniques are underway.

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Fig. 1

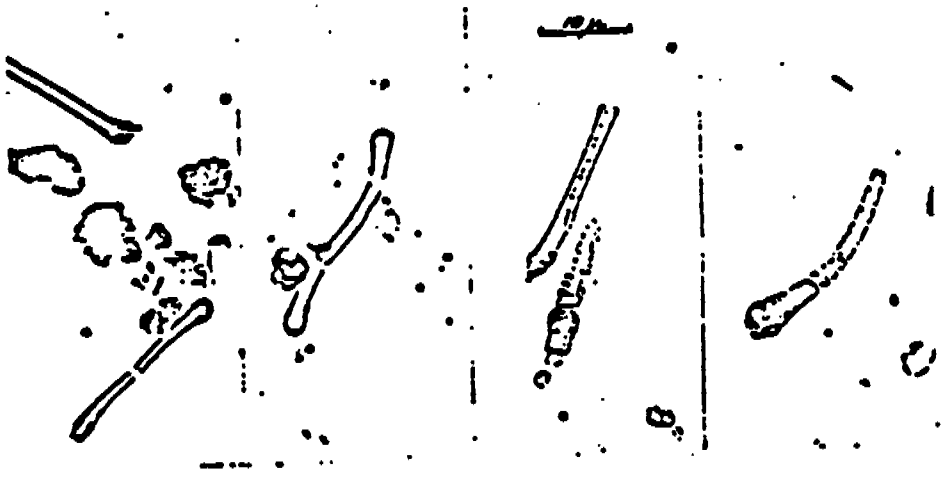

Fig. 2

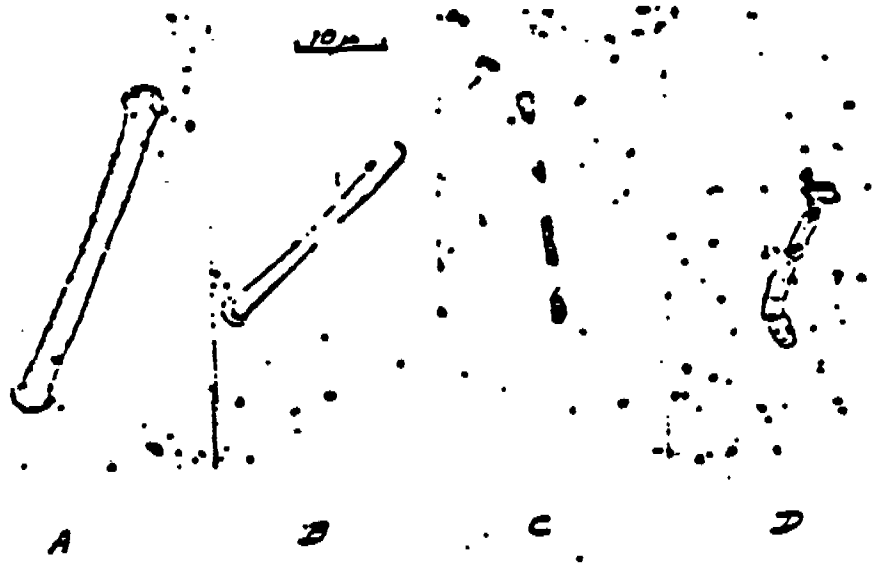

Fig. 3

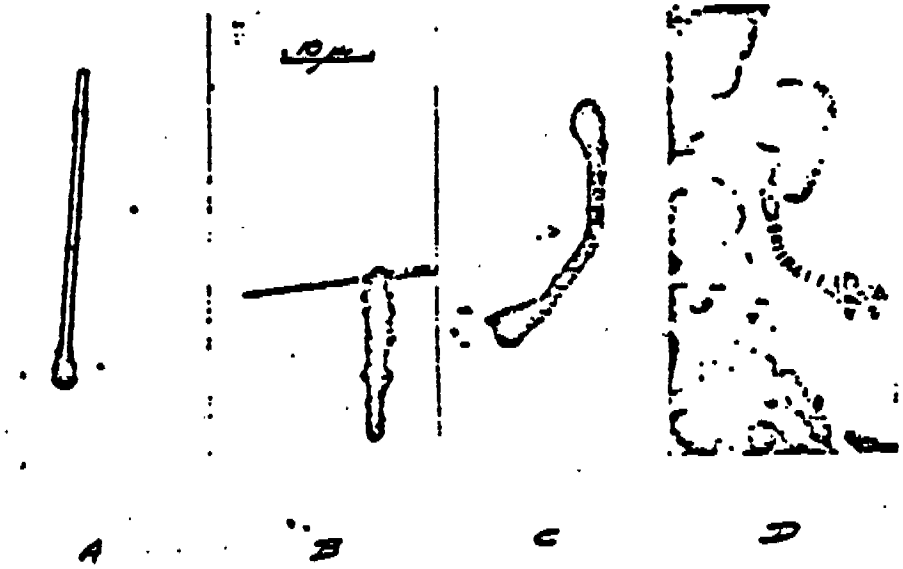

Fig. 4

Legends of Illustrations

Fig. 1 Asbestos bodies from the lung of an asbestos worker to illustrate some of the more simple forms that may be found. In addition to some apparently naked fibers, there are pale, nonsegmented, rodlike bodies with bipolar clubbing. The dust was probably chrysotile. Concentration method. Smear. Unstained. X 1100

Fig. 2 Ferruginous bodies formed in response to the intrapulmonary presence of aluminum silicate filaments in a hamster killed five months after an intratracheal injection of 3.5 mg. of the dust. These are pale yellow to golden in color and transparent. The central filament is visualized with difficulty because the index of refraction of the mounting medium on the slide is close to that of the filament. This can be appreciated in D where a naked filament about 1 μ in diameter traverses the approximate middle of the field, and a 3-μ thick fiber cuts across the right lower corner. Concentration method. Unstained smear. X 1100

Fig. 3 Ferruginous bodies formed in response to the presence of filamentous glass dust in a hamster killed five months after an intratracheal injection of 3.5 mg. of such dust. These bodies appear to be very similar to the more simple asbestos

bodies pictured in Fig. 1. Bodies in A, B, and D are unstained and are found in a smear of sediment btained by the concentration method. The ferruginous body in C is from a section of lung from the same animal. The section was stained for iron, but is otherwise unstained. Four macrophages are faintly outlines. Their cytoplasm incorporates portions of a glass filament. Only the intracellu portions of the filament are coated with iron. X 1100

Fig. 4 Ferruginous bodies formed in response to other filamentous dusts in the lungs of hamsters. A, B, and C are from smears of sediment obtained by the concentration meth d and stained for iron (Perls' test). The central fiber in A and B is silicon carbide; and in C, tremolite (talc). The body in A shows a clublike thick coating of iron at the lower end, a fusiform coating near the upper end, and a slight swelling near the middle. A blue coloration of the surface of the fiber extends throughout its entire length. The body in B is segmented, but is fuzzy because of diffusion f the Prussian blue color. The other two fibers in B are uncoated. A similar fuzziness is seen in the tremolite ferruginous body in C for the same reason. The ferruginous body in D has a chrysotile fiber in its center. This is from a stained secti n of hamster lung. X 1100