PROCEEDINGS

FIBROUS DUST SEMINAR

November 22, 1968

Medical Series
Bulletin No.
16-70

INDUSTRIAL HYGIENE FOUNDATION OF AMERICA

5231 CENTRE AVENUE PITTSBURGH, PA. 15232

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Mellon Institute of
Carnegie-Mellon University
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Industrial Hygiene Foundation of America, Inc.
5231 Centre Avenue
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PREFACE

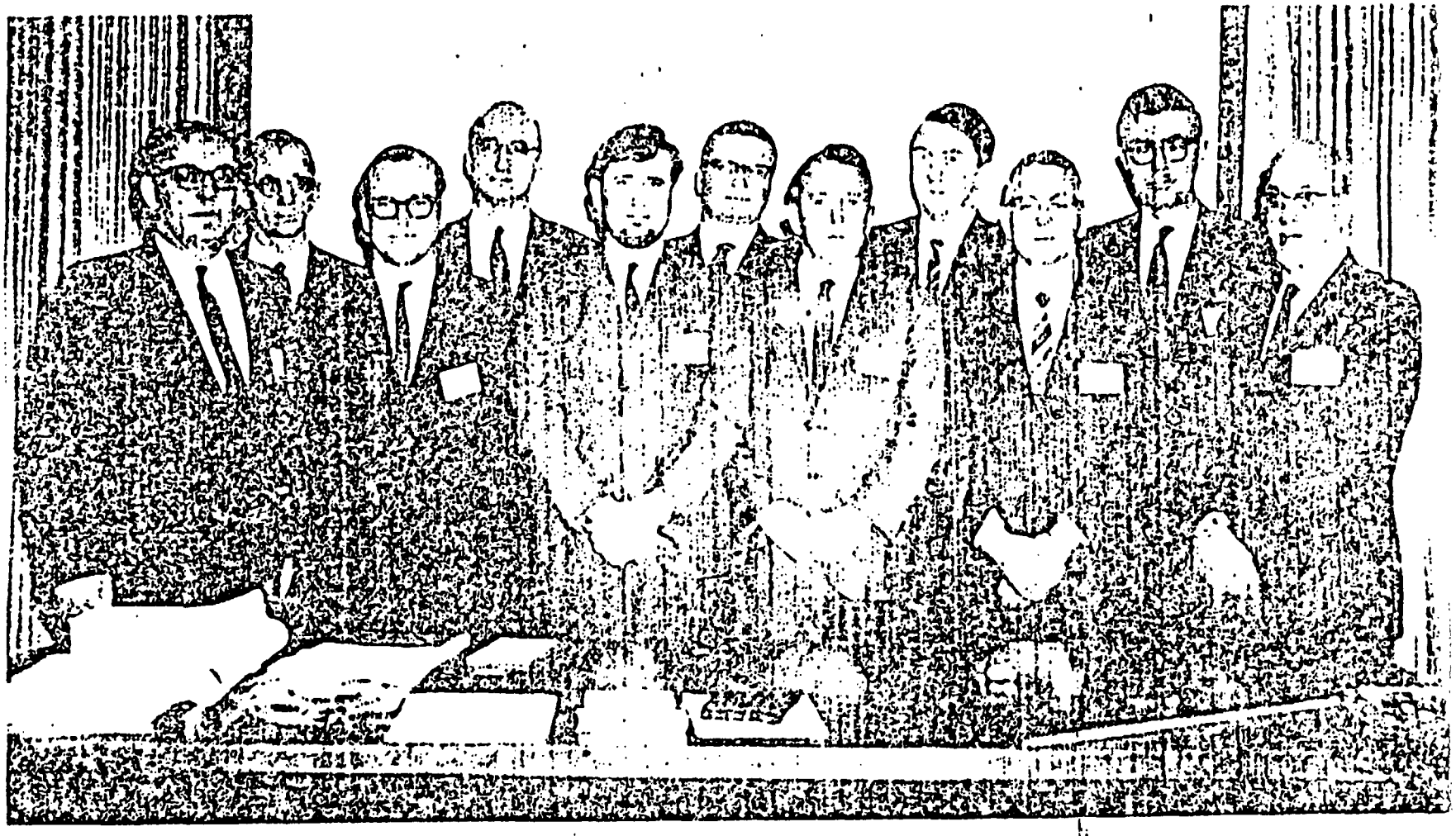
This Fibrous Dust Seminar represents an important step towards fulfillment of the first goal in which direction industry should be moving according to Dr. Theodore Hatch, IHF Trustee Emeritus, in Industrial Hygiene Highlights - Vol. 1—i. e., protection of employee health.

These proceedings exemplify industry's attempts with IHF's help to advance scientific progress by use of epidemiological and biostatistical studies, in plant as well as in the experimental research laboratory.

Studies on fibrous glass, which appears to have no demonstrable pathogenic effects, provide an effective control over those investigations on asbestos bioeffects reported herein, all of which have been performed in or for IHF. It can be seen that studies designed to investigate pathogenic effect become highly sophisticated in an attempt to prove the "null hypothesis." These studies of fibrous dusts are still under way and further progress will be reported as it developes in an effort to keep our members and the interested scientific and professional communities advised.

The use of fibrous dusts is so widespread today that all those responsible for employee health should find this bulletin interesting and useful.

Robert T. P. deTreville, M. D., Sc. D.
President



FIBROUS DUST SEMINAR SPEAKERS

Left to right: Dr. Joseph L. Goodman, Martin N. Haller, Dr. Benjamin J. Lambiotte, Dr. Robert T. P. deTreville, Dr. H. Michael D. Utidjian, Dr. Jon L. Konzen, Dr. W. Clark Cooper, Dr. John M. G. Davis, Dr. Lewis J. Cralley, Dr. Philip E. Enterline, Dr. Paul Gross

Morning Session

FIBROUS GLASS HEALTH RESEARCH IN THE UNITED STATES

Moderator: W. Clark Cooper, M.D.
School of Public Health, University of California

WELCOME

Robert T. P. deTreville, M. D., Sc. D. *

As there are only a few people here not representing companies already in the Foundation's membership, or agencies familiar with the Foundation, I will take only a minute to talk about IHF. I would like to call your attention first to the Foundation's new book, Volume I in our new Industrial Hygiene Highlights series; it is a valuable technical reference and we would like for everybody here to know about it. It has some information on IHF in its preface and foreword; however, for individuals who may want to know more about the Foundation's plans, I have brought along copies of the CONSAD Report "National Needs, Goals, and Resources in Planning for the Long-Range Future in Occupational Health," and I have some other descriptive information, all of which is available upon request.

Before launching into the first of the two sessions of this meeting, I would like to call on Dr. G. Arthur Webb, Associate Director of Mellon Institute of Carnegie-Mellon University, and Chairman of the Foundation's Board of Trustees, to say a few words of welcome: Dr. Webb.

DR. G. ARTHUR WEBB: Thank you, Bob. It is traditional for somebody to open a meeting, and that is my purpose. I am very pleased to see you all here, and I hope that you will find it possible to tour and enjoy the facilities of the Institute during the course of the meeting. The program, as I have read it, appears very interesting, and as you have much to cover today, I will not prolong my remarks.

DR. deTREVILLE: Thank you, Dr. Webb. While IHF's headquarters is now located elsewhere, the work of IHF Fellows within Mellon Institute was directly responsible for this meeting.

Several years ago, when Dr. Paul Gross, Director of the Foundation's Research Laboratory, first expressed interest in extending his studies from the experimental pathology laboratory to include use of some of the higher resolution instrumentation fields, I talked with Drs. Webb, Harrison Davies, Robert Rice, Larry Vassamillet, and several other scientists on Mellon Institute's staff about the possibility of using some of the equipment here in the Institute. This was necessary to pursue the exploratory studies which will be described later. It was possible for us to use the electron probe, a $130,000 piece of equipment, as well as several of Mellon Institute's electron microscopes, including the Phillips 200.

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*President, Industrial Hygiene Foundation of America, Inc., 5231 Centre Avenue, Pittsburgh, Pa. 15232.

By way of "seed money," it was possible for us to receive funds from Mellon Institute's General Research Grant (funded by the National Institutes of Health) to supplement an existing research contract from the Public Health Service, Division of Occupational Health covering part of our Fibrous Dust Study. As a result, we have launched into a fairly comprehensive study so that it is possible for us, at this meeting today, to bring some new data, new information, to you. By receiving and sharing such information, we should contribute towards scientific progress and advance knowledge concerning fibrous dusts, their bioeffects, and the control of any hazards that may be associated with these dusts.

The first, or morning, session on "Fibrous ~~Glass Health~~ Research in the United States" will be moderated by Dr. W. Clark Cooper. Dr. Cooper is known to all of you, I feel sure, from his past long and productive career in the Public Health Service. His last assignment there was: Head of the Division of Occupational Health. Upon retirement, he went to the University of California, School of Public Health at Berkeley to become a Professor of Occupational Health. I should add that Dr. Cooper is associated with a colleague at Berkeley, Dr. Irving Tabershaw, Professor of Occupational Medicine, School of Public Health, in Tabershaw-Cooper Associates. In this capacity, Dr. Cooper is consultant to the West Coast Association of Contractors and Asbestos Workers that have put together funds from both labor and industry to study what environmental health problems exist and how to control them in insulation work. Dr. Cooper, therefore, is very well grounded, both in training and experience to moderate this session this morning, and I am delighted to have my old friend, Clark Cooper, here to help us with this part of the program: Clark.

OPENING REMARKS

W. Clark Cooper, M.D.*

Thank you, Bob, for the opportunity to take part in this interesting session. It is unusual in occupational health that instead of worrying about a medical problem, a suspected disease, we are devoting our morning to a subject where studies in animals, our knowledge of fiber size and respirability, and observations in man do not point to a serious problem.

Nevertheless, the meeting is appropriate and timely; the technology of fiber glass is changing. We are increasingly aware of deficiencies in our knowledge of the behavior of fibrous minerals. The time is upon us when the earliest workers exposed in this relatively new industry might be expected to show evidences of damage, if the potential is there. It is necesessary that we look in order to be sure.

*Professor in Residence, Occupational Health, School of Public Health University of California, Berkeley, Calif. 94720

So without any more talk on my own part, I think we should proceed with the program which is starting somewhat in reverse, I guess. We are talking about the medical findings without proceeding with a description of what glass is, what it does in animals. We are jumping right into the problem in terms of what do we know in regard to the people who have been exposed, and we will be starting with a discussion of studies which have been carried out in a plant which, I am advised is the oldest and largest plant in the United States where fibrous glass has been made. It is a study which reflects some of the design and thinking of Drs. Ciocco, Enterline and deTreville, and of the gentleman who will be presenting the paper for us today, who is the first Industrial Hygiene Fellow in Occupational Medicine in the Foundation, who comes to Pittsburgh from a medical education in London, internship in Highlands General Hospital, service in the Royal Army Medical Corps, service in the Middle East with the Iraq Petroleum Company, several years with the Slough Industrial Health Service, in Trinidad, West Indies (for the last, I believe, three or four years) and who has been in Pittsburgh since June 1, 1967, when he was made a Mellon Institute Fellow assigned to the Industrial Hygiene Foundation. He will discuss some of the Foundation's Statistical Studies of Health of Fibrous Glass Workers, and I am glad to introduce Dr. H. Michael Utidjian, who two months ago, accepted the position on the faculty at the University of Pittsburgh in the department of Epidemiology, which he now holds, as Assistant Professor.

IHF STATISTICAL STUDIES OF HEALTH OF FIBROUS GLASS WORKERS

H. Michael D. Utidjian, M.D.

At the request of Dr. deTreville of IHF in 1967, Dr. Antonio Ciocco, Professor and Chairman of the Department of Biostatistics at the Graduate School of Public Health, University of Pittsburgh, planned a cross-sectional study of the employees of the Owens-Corning Fiberglas plant at Newark, Ohio, to determine whether or not prolonged exposure to a "working environment" containing airborne dust from the manufacture and processing of fibrous glass, is associated with any recognizable abnormality of the respiratory system, detectable from respiratory illness history, lung function, and chest X-rays. This study was undertaken by IHF at the request of the manufacturers of fibrous glass on the recommendation of Dr. George W. Wright, Head, Medical Research Department, St. Luke's Hospital, Cleveland, to supplement the survey of chest x-rays on approximately half the work force at the same plant.

*Assistant Professor, Dept. of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pa. 15213

The previous study was conducted by Dr. Wright in 1963. The results, which were published in the January 1968 issue of the AMA Archives of Environmental Health, were reported by Dr. Wright to be negative, from a strictly radiological standpoint.

SELECTION OF THE SAMPLE

The management of the Owens-Corning Fiberglas plant at Newark, Ohio, furnished the following through IHF:

1. A list of names, ages and badge numbers of the total current male payroll of the plant including the office workers.

2. An estimate of time-integrated exposure to process dust for every employee. Based on these estimates, employees were classified into highest, intermediate and lowest exposure categories. The management had exclusive access to:

(a) The employment histories (many of which were interrupted by World War II and by voluntary resignations and re-employment);

(b) The details of the changing plant locations of employees, and specific occupations throughout their employment history, and

(c) The history of estimated dust levels at different plant locations since the beginning of plant operations some 30 years ago. For these reasons the plant's management was considered to be the best arbiter of this important question.

The total payroll was also subdivided into three current age groups namely — under 30, 30-49 and 50 and over. These two threefold classifications create nine 'age x exposure' groups. It was then decided, in consideration of a desirable total sample size in terms of practicability, and of minimum numbers for statistical significance, to attempt to provide at least 30 male employees in the highest 'age x exposure' group or "cell". (See Table I)

It was then found that the total number of employees available in the "youngest least-exposed" group (top left-hand corner in three-fold square) was only 21. As this was the only deficient cell in terms of hypothetical availability of employees, and as this was considered to be the least significant cell, the modified sample plan for 261 of the 2,400 odd employees, was proposed. (See Table I.)

The eight remaining "cells" were filled by a selection of employees within each 'age x exposure' group, by the use of random numbers. The proposed sample would therefore be classified as a stratified random sample.

As there was some time lapse between the statistical planning and the field survey, by the time of the first working expedition to the plant in August, 1968, some of the original selection had been lost, chiefly by resignations and drafting for military service. There had also been one death from causes other than pulmonary disease. Lastly, although altogether three field trips were made to the plant in August, September and October, a further number of selected employees was not accessible by reason of vacations and current sickness. Finally 232 of the originally possible sample of 261 were investigated, and their distribution among the "cells" is shown in the third part of Table I. Note, however, that the greatest deficit is in the youngest age group and that the highest exposure/oldest "cell" is intact with the full thirty. An investigation was made of the reasons for non-availability of employees, and as in no case was the absence found to be due to illness referable to the respiratory system, it was decided to proceed with this reduced sample rather than incur the possible statistical bias introduced by substitution.

THE QUESTIONNAIRE

All 232 employees examined were subjected to a questionnaire, blank copies of which have been circulated among you. This is based upon a modification of the British Medical Research Council "Bronchitis" questionnaire, now in use in a major study of Canadian asbestos miners.

Sections 1 and 2 were completed by the personnel and medical departments from company records, and section 3 by the work supervisor. All parts of Section 4 were administered at interview conducted by two IHF staff physicians assisted by Dr. J. Konzen, Owens-Corning Fiberglas, Corporate Medical Director, to whom none of the employees nor their medical histories were previously known. The appraisal and scoring of all the completed questionnaires and the organization of the data into tables acceptable to the biostatisticians, was performed by one of the three physicians involved in the interviewing. Following completion of the questionnaire each employee was weighed and his height measured by the plant nursing staff and spirometry was then performed by Dr. Ben Lambiotte of the Foundation's staff (who will be speaking later in the program), using a standard Collins' type spirometer. Two acceptable forced expiration tracings were obtained from each subject. While it will be possible later to calculate the $F.E.V._{1.0}$ and Maximum Mid-expiratory Flow Rates from these tracings, at this time only the total vital capacity (untimed) will be presented.

Lastly, the chests of all subjects had been X-rayed recently by well trained technicians in the plant clinic, and the films read by fully qualified radiologists in the community. Drs. Konzen and deTreville reviewed these 14 x 17 films, and Dr. Konzen will discuss the radiological findings later in the program. I shall largely confine myself to the results of the questionnaire and will refer only very briefly to the results of spirometry and radiography.

INTERPRETATION OF RESULTS OF QUESTIONNAIRE

The questionnaire focuses upon the history of respiratory and chest illness, lifelong and recent, as recalled by the subject. Every attempt was made by the interviewing physicians to elicit true information, as far as possible without the use of leading questions. Obviously the answers to some of the more objective questions are more reliable than those to the subjective questions. Very little reliance can be placed on the numerical estimates in smoking histories, for example. However, by definition, symptoms are entirely subjective and I believe that much useful and valid information lies in this area. As will be appreciated from the approximate estimates of exposure category, as outlined, the immediate object of this survey is to try to discern gross relationships, if any exist, between exposure and effects on the respiratory system. It is expected that these studies will be followed in the near future by a more detailed investigation in a smaller group. It is proposed to subject half of age group 3 with the lowest exposure and half of the same age group with the highest exposure, to CO diffusion studies in a well equipped Cardiopulmonary Laboratory of a nearby hospital. Subjects will receive a general medical evaluation and any further additional studies which may be indicated by clinical findings.

THE RESULTS

It may be stated in general that so far in this survey, no clear relationships have emerged between degree of exposure as herein defined, and any of the disease parameters studied. Advancing age alone does appear to be related to chest illness, or symptoms, and impairment of ventilatory capacity, which is, of course, entirely anticipated. These statements are perhaps best illustrated by showing several tables of the distribution of symptoms of respiratory illness among the 9 age/exposure groups. In all cases the figures shown are percentages rather than absolute numbers, in view of the inequality of the populations in the cells. Table 2 shows the distribution pattern of significant cough. If you follow the percentage figures from left to right you will see a fairly consistent progression with advancing age. However, if you follow them vertically there is little evidence of progression with increasing exposure, except in the 30-49 year column. This may be offset by columns 1 and 3.

TABLE I

THE ORIGINAL SAMPLE PLAN

EXPOSURE	AGE <30	30 - 49	50+	TOTALS
1 (least)	30	30	30	90
2 (medium)	30	30	30	90
3 (highest)	30	30	30	90
	90	90	90	270

THE MODIFIED SAMPLE PLAN

EXPOSURE	AGE <30	30 - 49	50+	TOTALS
1 (least)	21	30	30	81
2 (medium)	30	30	30	90
3 (highest)	30	30	30	90
	81	90	90	261

FINAL DISTRIBUTION OF SUBJECTS INVESTIGATED

EXPOSURE	AGE <30	30 - 49	50+	TOTALS
1 (least)	19	26	28	73
2 (medium)	26	28	27	81
3 (highest)	20	28	30	78
	65	82	85	232

(QUESTIONNAIRE DATA)

COUGH

EXPOSURE GROUP	AGE <30	30 - 49	50+
1	26%	15%	32%
2	27%	14%	44%
3	10%	25%	27%

TABLE 3

(QUESTIONNAIRE DATA)

"BRONCHITIS"

EXPOSURE GROUP	<30	30 - 49	50+
1	5%	8%	4%
2	12%	11%	11%
3	15%	18%	13%

TABLE 4

(QUESTIONNAIRE DATA).

"DYSPNEA OF EFFORT"

EXPOSURE GROUP	AGE <30	30 - 49	50+
1	21%	23%	36%
2	23%	18%	41%
3	15%	32%	27%

TABLE 5

(QUESTIONNAIRE DATA)

"WHEEZING"

EXPOSURE GROUP	AGE <30	30-- 49	50+
1	37%	19%	29%
2	23%	18%	22%
3	5%	11%	33%

TABLE 6

(QUESTIONNAIRE DATA)

History of Chest Illness Within Past 3 Years

EXPOSURE GROUP	AGE <30	30 - 49	50+
1	5%	12%	4%
2	4%	0	11%
3	5%	4%	10%

TABLE 7

(QUESTIONNAIRE DATA)

Total History of Chest Illnesses

EXPOSURE GROUP	AGE <30	30 - 49	50+
1	37%	42%	50%
2	38%	36%	52%
3	20%	39%	57%

(QUESTIONNAIRE DATA)

Total Chest Illness Score (History & Symptoms) vs. Exposure

Age Group 1

Score		Exposure 1	2	3
(<5)	1	63%	69%	90%
(5 - 9)	2	21%	15%	10%
(10 - 14)	3	11%	12%	0
(15+)	4	5%	4%	0

Age Group 2

Score Group	Exposure 1	2	3
1	65%	71%	64%
2	23%	21%	29%
3	8%	7%	7%
4	4%	0.	0

Age Group 3

Score Group	Exposure 1	2	3
1	50%	44%	63%
2	25%	33%	17%
3	21%	19%	10%
4	4%	4%	10%

TABLE 9

(SURVEY MEASUREMENT DATA)

SPIROGRAPHY - VITAL CAPACITY

DEVIATION FROM PREDICTED V.C. vs. EXPOSURE

Age Group 1

	V.C. DEVIATION	Exposure 1	2	3
1	(> + 1.00 liters)	0	4%	0
2	(+ 0.5 to 1.00 liters)	11%	4%	5%
3	(0 to + 0.5 liters)	16%	12%	35%
4	(- 0.5 to 0 liters)	37%	50%	35%
5	(- 0.99 to - 0.5 liters)	37	12	25
6	(- 1.00 or more liters)	0	19	0

Age Group 2

V.C. DEVIATION	Exposure 1	2	3
1	4%	4%	0
2	19%	0	11%
3	15%	21%	14%
4	31%	39%	39%
5	19%	29%	25%
6	8%	4%	11%
UNKNOWN	4%	4%	0

TABLE 10

(SURVEY MEASUREMENT DATA)

SPIROGRAPHY - VITAL CAPACITY

DEVIATION FROM PREDICTED V.C. vs. EXPOSURE

Age Group 3

V.C. DEVIATION	Exposure 1	2	3
1	4%	0	0
2	7%	4%	3%
3	18%	15%	13%
4	14%	26%	40%
5	36%	41%	27%
6	18%	15%	13%
UNKNOWN	4%	0	3%

DISCUSSION

FROM THE AUDIENCE: How do you explain what almost looked like a favorable effect of heavy exposure in several of these groups which might suggest that people who tended to have cough or tended to have certain symptoms would be selectively taken out of dusty jobs, and to what extent can you control for the movement of people who are developing symptoms out of dusty jobs in a study like this?

DR. UTIDJIAN: I think this is a very good point and I entirely agree with you. I think this is the only possible explanation for this apparent beneficial effect of exposure, and I think the only way to eliminate this is by a longitudinal cohort study.

DR. deTREVILLE: Dr. Ciocco introduced one longitudinal control into the experimental design. He was concerned that individuals who were working in clerical non-dusty jobs today might have been moved there within the recent past as a result of symptoms and signs developed in their work; so the degree of exposure shown is an integrated estimate based on their total experience at Owens-Corning Fiberglas and not just on their present assignment.

DR. CHARLES S. BISHOP (Owens-Corning Fiberglas): I have been the plant physician of the plant in question for many many years and am very familiar with these test subjects, many of them on an individual basis. I think the thing that you are struck with when you first examine work histories of these employees is the number of jobs, and the different ones they have held at Owens-Corning Fiberglas. It is not unusual at all for the man to have held 30, 35, and even 40 different jobs during the time that he has been there. Many of the people who are now in supervisory, clerical positions, served in the ranks many years ago, when work was first started at the Newark plant. People who are in one or another of these so-called "high exposure" jobs now, however, tend not to move because it is a responsibility which pays better.

When Dr. George Wright (Cleveland) came down to do the x-ray study he has subsequently reported, we had nothing formal to offer him. We decided quite arbitrarily that the exposure periods, would be that if a man had worked as little as two years in a "high exposure" area and perhaps five years in the plant, he would classify as "high". However, many of them actually worked in "high exposure" for many many years.

FROM THE AUDIENCE: The diffusion studies are anticipated to take half of the least exposed people in the oldest age group and half of the most exposed in the oldest age group, is that right?

DR. UTIDJIAN: Yes.

FROM THE AUDIENCE: One question for Dr. Bishop. In this "high exposure" group that is shown here, are they wearing personal protective equipment all the time?

DR. BISHOP: No sir. The only personal protective equipment that is needed in work in the plant is when they work in the "batch house"; this is quite a different thing, involving potential free silica hazard.

DR. COOPER:

I know there are a lot of other important questions that could arise as to the types of fibers to which these individuals were exposed 20 years ago and 10 years ago, but we have still an important paper before the break, so I would move on to our next study of a group of workers exposed to fibrous glass. In this case, it is a study based upon social security records, which we once called Old Age Survivors Disability Insurance (and I think they are now the Bureau of Retirement Survivors Insurance records) and also some of the environmental studies that are being done by the Public Health Service.

I will save time on the introduction here by not going extensively into the background of our speaker, whom I am sure all of you know as having been identified with the industrial hygiene work of the Public Health Service for the last 25 or 30 years, who has been very much involved in the studies of the effects of fibrous dusts with the Public Health Service. He is now Associate Chief of the Occupational Health Program for Field and Epidemiologic Studies. If he can tell you the name of his organization's current incarnation, I would be happy to hear it again, because I am sure it has a different name from the name it had two weeks ago, and probably may well be a different one two weeks from now. I introduce Dr. Lewis Cralley who will briefly outline the study he has underway.

RECORDS STUDIES OF HEALTH OF FIBROUS GLASS WORKERS

Lewis J. Cralley, Ph. D. *

The National Insulation Manufacturers Association (NIMA) during the past several years has been bringing together and evaluating available information on the health of workers manufacturing and using fibrous glass. Recognizing that the fibrous glass manufacturing industry is a relatively old one with a stable work force, NIMA requested that the Bureau of Occupational Safety and Health explore the possibility of obtaining additional information on the health profile of workers in the fibrous glass industry. It was believed that data on specific causes of death and life expectancy patterns on this group would be important information in assessing any health problem associated with exposure to fibrous glass. This data would supplement that of other studies which have been reported this morning which related to a more intense study of smaller groups of workers.

* Scientist Director, Associate Chief, Occupational Health Program, Field Studies, U. S. Dept. Health, Education & Welfare, Public Health Service, Consumer Protection & Environmental Health, Environmental Control Administration, Bureau of Occupational Safety & Health, 1014 Broadway, Cincinnati, Ohio 45202.

Mortality information of this nature would be more meaningful if complete information were made available on the work history of each worker in the study.

On reviewing the history of the fibrous glass manufacturing industry, the Bureau of Occupational Safety and Health believed that useful data would result from a records study as covered above, of the workers in this industry. We have already duplicated over 20,000 records of employees in the fibrous glass insulation and textile manufacturing industry. A large number of the workers have been in the industry 25 years and longer. To back this up, we are doing limited environmental studies within each of these plants to get a parameter of the nature and the extent of exposure to fibrous glass, and are characterizing the fibers as to physical dimensions of diameter and length.

We feel that for the most useful data we must extend this type of a study to include also workers manufacturing fibrous glass textile materials.

We would also like to extend the study to the manufacture of microfibers if we can get a large enough group to study.

DISCUSSION

FROM THE AUDIENCE: Would you say a few words about microfibers as relates to insulation vs. weaving applications?

DR. KONZEN: For textile fibers, the average range is about 14 hundred thousandths of an inch which is four microns. The diameter ranges from about 12 to 18 hundred thousandths of an inch (by dividing by 4 you can come into microns). This technical data is reported in Dr. Eldred P. Heisel's study in the November, 1968 issue of the Archives. We have to make a differentiation here between textile and wool fiber. Further you have to break it down as to how much is produced in each category of fiber. The vast majority of wool fibers (that used for insulation) are 6 to 6 1/2 microns or more in diameter.

FROM THE AUDIENCE: Can we make any statement as to the chronology of the introduction of these different sizes of fibers? It seems to me this is important in the study, such as what Dr. Cooper was talking about; what was going on 25 years ago, 10 years ago, 5 years ago.

DR. CRALLEY: We are getting that information as part of our environmental study. This is going to be a retrospective—and then converted into a longitudinal—cohort study, and we expect along the line that some smaller diameter fibers will be introduced into processing.

FROM THE AUDIENCE: Are you going to be able to differentiate individuals whose predominant exposures were outside respirable range?

DR. KONZEN: The majority of wool fibers will still be greater in diameter than can be respired. In other words, we are lowering diameter from the range of broomstraws to something less than broomstraws.

FROM THE AUDIENCE: What kind of curve of distribution do you expect if you have a hundred million fibers? I get concerned with mediums and averages as compared to distribution.

DR. CRALLEY: This ties into what Paul Gross is going to be talking about a little later on. We have a cohort of people under study and as workers for any reason come to autopsy, Dr. Gross will get lungs for study of the nature of the fibers present. Having the background (i. e., work history and studies of the environment), we will be able to develop a broader picture than any one parameter alone would give.

FROM THE AUDIENCE: Is this a mortality study or a disability study or what?

DR. CRALLEY: Right now, it is a mortality study. This retrospective approach, turning into a longitudinal one, with an environmental study tied onto it, will fit into other studies already underway.

FROM THE AUDIENCE: Is there any potential of getting useful data as to disability from the Bureau of Old Age and Survivors Insurance?

DR. CRALLEY: We plan to check into that but have not done so yet.

CLIFFORD SHECKLER (Johns-Manville Corporation): I think the term microfibers is misleading because we are talking about—and I am just guessing—perhaps one percent of the total fibrous material manufactured; so, I think that when we talk microfibers we ought to talk "specialties," and when we talk "insulation" fibers we ought to talk "insulation" fibers.

FROM THE AUDIENCE: But they all come under the generic term fibrous glass, which is the subject of our conference today.

SIDNEY SPIEL (Johns-Manville Corporation): In this regard, I feel there is a point that ought to be brought up here. We talk about glass fibers, beta fibers, textile fibers, etc. There is a standard terminology, using letters; in other words, a C fiber is around 5 or 6μ; a B fiber (whether it is a beta fiber textile drawn, or whether it is B fiber insulation) is around 4μ. There is an A fiber around 2μ. Double A (which Johns-Manville makes) ranges from between three-quarters of a micron and one and a

half all the way down to five hundredths of a micron. So there are a whole series of these fibers. The microfibers, as has been mentioned, are a very small part of this (less than 1%), but in any study of people who are exposed to fibers, if you don't separate the generic terms of microfibers from "textile" fibers, and from the not "broomstraws," from the "broom-handles," that used to be made years ago (i.e., 10 to 20μ in diameter), the validity of studies would need to be questioned. You are talking about two different types of exposures completely. I think that in any mention of glass fibers, you have got to tie the fiber diameter in.

DR. CRALLEY: We are going to do environmental characterization of the fibers being processed versus those in the air.

DR. KONZEN: I agree completely that the type of exposure should be more precisely defined in order to relate the ultimate data properly; but I think that we also have to recognize that in environments where, normally, the fibers are large, there are still some fibers of respirable sizes found, so in reality, all sizes can be tied together in an industrial exposure.

CLIFFORD SHECKLER: The point is really this: in textile fibers where you are "pulling" fibers under controlled conditions, you do have a very small range. In other words, if there are 5μ fibers, it will go say from 4 to 7 or something like that. Insulation fibers spread all over. Numberwise you have a lot of "fines"; weightwise, of course, these make up an insignificant fraction of the total. How do you measure; what do you measure? Weight? Numbers? The important point is that in insulation you do have a spread and it ties in with the age of the production equipment and many other factors.

DR. KONZEN: And it has over the years. The spread has become narrower. Normal or average diameter was formerly much larger, but if you look at some of this "old stuff," there were fibers well down into the respirable range; so our production workers from the first have been exposed to relatively large quantities of small diameter fibers. I have a sneaking suspicion, just from comments made about the "old process" by old timers in my company that they must have had significant exposure to microfibers.

FELIX STEIN (University of Pittsburgh): We have been talking to Dr. Gross about a phase of this study and as I listen to the discussion, I am inclined to think it takes on greater and greater significance. He has asked us if we could analyze post-mortem lung residues for size distribution. Now certainly in considering post-mortem findings, one must take into consideration the intervening clearance processes in the lung;

but we could, I think, break down what is left in the lung from the point of view of microfibers, broomhandles, or anything else. Then, the key point would be to try to relate this to a really good assessment of the health status of all individuals so studied. I think the lung residue analysis is going to take on much more weight without having any other good measure of retrospective environmental assessment.

DR. deTREVILLE: In the original design of this study, you can see some of the really difficult types of problems that we had to deal with. We did not have a recognized pathological endpoint to aim at, as there is in the case of asbestos. We did not have good means of estimating the environmental exposures, and we were sure that there had been some variation in this, because there had been, ten or more years ago, a considerable improvement in housekeeping and engineering controls of dustiness. But for the purpose of this epidemiological, biostatistical evaluation, Dr. Ciocco said it would be sufficient to choose three levels of approximation under the general terms: "heaviest dustiness" (by visible dustiness or by any other criteria that the plant would like to use) versus a "control" group (which would be the sheltered group in clerical work) and an "intermediate" group. With these very broad, very poorly defined environmental estimates, we would see what could be developed by history, by clinical findings, and by using any laboratory aids that we might be able to use, such as pulmonary function studies or x-rays.

Dr. Ciocco said that, as a beginning, pulmonary function "screening" would be sufficient; for example, in helping to get the gross estimates needed here, it might actually suffice if we knew whether the man concerned could blow out a candle or not, or whether he could blow a whistle. In other words, we should avoid getting too sophisticated until we could find out more about the general nature of any observable changes in pulmonary function or health status. Dr. Ciocco, because of circumstances beyond his control, is not able to be with us this morning. I invited Dr. Thomas Mancuso, Professor of Epidemiology from the University of Pittsburgh, to attend and as I see he is here, I would like to call on him to say a few words.

DR. THOMAS MANCUSO (University of Pittsburgh): This is unexpected, but I do have a few comments. I think what is happening here is really a reflection of all of the difficulties associated with doing an epidemiological study retrospectively and then prospectively. Under the circumstances, you need to do exactly what you are doing. I would encourage you to move forward in this direction. Dr. Cralley's approach is fine. I think that we are all in agreement here as to what industry will really need to know, and frankly, there will not be any better information available, because you have the primary source of the data. I am hopeful that the prospective study, using the successive cohort technique, will probably answer some of your questions. As each manufacturing process changes (or even

as the working environment changes, if you compared each cohort, that is each series of new employees who entered into the working environment at a given point in time with each other), you will pick up these differences. So, it is possible and feasible to derive very meaningful results from what you are doing, despite all the difficulties associated with it. There is the question, of course, of being able to define the populations, which fortunately you can do from the company records which are not available from any other source. I think if you follow the populations long enough, making sure that each succeeding cohort is followed for the same latent period, (they all have to be followed for the same latent period because otherwise the observations have no meaning) then the researcher would be sure that the observation period is long enough for whatever biological effect which may be concerned. From the study that Dr. Cralley is doing, it will be possible to say that in a series of successive cohorts, each observed for a latent interval period of, say 20 years, that there has been no discernible effect of this; and then the same cohort population that he has identified could be run through each succeeding five years from now, over as many decades as desired. So that then you could say that after 25 years there is no effect, after 30 years there is no effect, after 35, after 40. What you are doing is a very fundamental piece of work, and I certainly think that the industry is very wise to do this, and I think the approach is very sound.

DR. COOPER: We have time for one more question and that is going to be mine. Has anyone found ferruginous bodies in the sputum of a man exposed only to fibrous glass, that is, "asbestos bodies," so-called?

DR. GROSS: No. The probability exists that they could occur, as we have produced them experimentally in hamsters, as you know; but have not studied sputum of workmen for such bodies. Dr. Utidjian later in the meeting will describe ferruginous bodies of unknown origin found at autopsy in individuals not known to have been exposed to fibers occupationally.

DR. COOPER:

Our next speaker, Dr. Paul Gross, needs no introduction to this audience or to anyone considering the potential biological effects of inhaled materials. So we will proceed to the next talk on IHF's Pathological Studies of Respirable Fibrous Glass Dust. These studies are becoming increasingly important with the increasing likelihood of exposure to fibrous glass in size ranges that we formerly did not ordinarily encounter.

A COMPARISON OF THE EFFECTS IN EXPERIMENTAL ANIMALS OF CERTAIN FIBROUS DUSTS

Paul Gross, M. D.*

FIBROUS GLASS:

The pulmonary response, in both rats and hamsters, to the presence of fibrous glass dust, is characterized by relatively small macrophage accumulations without significant stromal change. Whether the fibrous glass dust used was coated (either with a phenol-formaldehyde-type resin or with a textile-type binder) or not, there was no demonstrable difference in reaction. This biological "inertness" of fibrous glass dust persisted in spite of an extremely high total exposure—24 months to dust concentrations which averaged somewhat in excess of 100 mg/m^3.

So far as the amount of glass is concerned, the inhalation animals have a much larger amount of glass in the lungs than do the intratracheally injected animals. Although the exposure was very high, it was often very difficult to identify any reaction to the presence of the inhaled glass dust. This occurred because most of these animals that were allowed to live two years ultimately died of spontaneous pulmonary disease, which overshadowed the reaction to the glass dust. As can be seen, this reaction to the glass dust is so minimal that it is very easily masked by the spontaneous disease. The only proof that these animals did indeed inhale or did have an intratracheal injection of glass dust was obtained by demonstrating the glass dust in the ash of lung sections after microincineration.

Inasmuch as we have demonstrated that as a result of exposure of animals to high concentrations of filamentous glass dust for as long as one year, no fibrogenic lung changes develop, it seems reasonable to exclude the filamentous shape of the asbestos dust particle as being a significant factor in its pathogenicity.

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ASBESTOS (Natural and Synthetic):

On the other hand, Harington[1] found carcinogenic aromatic hydrocarbons associated with crocidolite, and work in our laboratory demonstrated an incidence of lung cancer in excess of 40% in rats exposed to chrysotile dust that was found to be associated with an increased amount of nickel and chromium. These findings suggested that the asbestos mineral per se may not be the pathogenic component of the dust but may be merely the carrier of such pathogenic component.

In order to test this hypothesis, we have obtained synthetic chrysotile from two sources: Dr. William T. Granquist, Senior Fellow, Mellon Institute, and Dr. Frederick L. Pundsack, Director of Corporate Research and Development, Johns-Manville Corporation. We do not know the trace metal content of these materials at the present time, but Dr. Lewis J. Cralley's laboratory (U. S. Public Health Service, National Center for Urban and Industrial Health) is now analyzing these materials.

These dusts were injected intratracheally into rats with conflicting results.

Attempts to modify the pathogenicity of natural asbestos (as judged by the fibrous tissue reaction) have so far been unsuccessful.

EDITOR'S NOTE: In a paper by Gross, deTreville and Cralley, "Studies on the Carcinogenic Effects of Asbestos Dust," to be published in the Proceedings of the Johannesburg Pneumoconiosis Conference (held at Johannesburg, South Africa, April 23-May 2, 1969), the following pertinent information is abstracted:

"The possibility that trace-metals bound to our chrysotile dust were the carcinogenic agent responsible for the lung cancers seemed attractive because of the disparity in the lung cancer prevalence that was found among British asbestos textile workers exposed prior to 1933[2] and that found among Canadian chrysotile asbestos miners who were exposed from 1950 to 1956.[3] In the former, the prevalence of lung cancer was found ten times greater than that of the general population, whereas no increased risk of lung cancer was found among the Canadian asbestos workers. We would like to think that the reason for this difference may be that the dust to which the Canadian workers had been exposed had had less contact with steel alloys and, therefore, had a lower trace-metal content than the dust of the asbestos textile workers.

"Another finding which made the trace-metal concept attractive as the explanation for the asbestotic lung cancers was the biologically 'inert' pulmonary reaction which has been obtained following intratracheal injections of synthetic chrysotile. This would seem to indicate that the relatively pure, tubular, crystal of hydrated magnesium silicate, the basic unit of chrysotile, is, of itself, not carcinogenic.

"For the experimental investigation of the elutable trace-metal concept of asbestotic carcinogenesis, we added synthetic chrysotile to solutions of various metallic salts such as nickel chloride, chromic chloride, cobaltic chloride, and potassium permanganate. During constant stirring, a proper reagent was added to each of these solutions in turn so as to precipitate an insoluble compound of each of these metals. The sediment, consisting of amorphous precipitate and of the insoluble metallic compound bound to the synthetic chrysotile, was washed free of unreacted chemicals. Standardized suspensions of these materials were injected intratracheally into rats.

"Other rats were injected intratracheally with oxides of nickel, chromium, manganese, and cobalt, alone and in combination, with and without added benzopyrene. Added groups of rats were similarly injected with suspensions of talc with a naturally high nickel content and talc with a naturally low nickel content, respectively. All of these animals were allowed to live out their lives but no lung cancer developed in any of them.

"In retrospect, we believe that the main reasons for the negative results were the insolubility of the metallic additives, as well as insufficient dosage. We are continuing this study, using finely divided pure metals and more soluble compounds of these metals.

"Following intrapleural injections of chrysotile dust into hamsters, we obtained several undifferentiated cellular tumors without glandular components. These tumors were classified as undifferentiated sarcomas.

"Intra-abdominal injections of chrysotile dust into rats resulted in the formation of generalized, highly vascular granulations from which extensive bleeding occurred and many animals died of intra-abdominal hemorrhage. Many of the peritoneal bleeding granulations proved to be acellular, fibrous tumor tissue very similar to that comprising the subcutaneous fibrosarcomas so common to this animal species. Because of this similarity and the absence of any epithelial tissue components, these tumors were classified as fibrosarcomas. In one of these tumors, extensive bone formation was present.

"It seems, therefore, that although much work has been done attempting to explain the mechanism of experimental asbestotic carcinogenesis, no definitive results can be reported at this time."

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FROM THE AUDIENCE: Dr. Gross, you mentioned that your analysis of the dust showed that about 40 per cent was non-fibrous and that 60 per cent was fibrous. Could you tell from your slides whether or not the dust that was actually retained in the lungs was primarily fibrous or the reticulate dust?

DR. GROSS: From the ash you can see that most of the dust is tightly packed in the lung; but there are regions where the dust is more discrete, and you can see a number of fibers. How much of the packed dust is fibrous and how much is non-fibrous, I do not know at the present time. We shall know better when we digest the lung and subject the mineral residue to analysis.

FROM THE AUDIENCE: Do you know if there are any studies that have been done anywhere that would indicate that glass fibers are not inert? Please say if there are any contradictory studies; and, if so, how would you explain them?

DR. GROSS: Unfortunately, no definitive work has been done on the biological effects in animals of filamentous glass; that by Schepers was not with glass alone, but with a combination of fibrous glass, fillers, and binders. Also, as I recall, he made no reference to use of controls. He did not attempt to differentiate observed changes from those which are seen from endemic pulmonary disease; hence, his reported findings must be considered inconclusive.

DR. CRALLEY: Regarding pathogenicity of fibrous dusts, it appears that the effects of asbestos are due not to the shape of the asbestos fibers themselves, but to other factors that are introduced concurrently.

DR. GROSS: In this regard, more than ten years ago, we performed an investigation of another fibrous dust, produced by the Carborundum Corporation: ceramic aluminum silicate. This dust, which was of respirable size, was injected and inhaled by animals and it produced in the lungs findings very close to those demonstrated today in regard to glass, indicating that the fibrous shape of the dust particles play no significant role per se in producing pulmonary reaction.

FROM THE AUDIENCE: How do the results of this study compare with a similar experiment conducted with asbestos?

DR. GROSS: With inhalation of asbestos, in a two-year study using somewhat lower than average exposure levels, we obtained a high rate of pulmonary collagen formation in rats and guinea pigs within six months; and by one year, the fibrosis was well developed. Also, after sixteen months, we began getting cancers.

FROM THE AUDIENCE: Going back to fibrous glass, what is the range of sizes of the glass fibers?

DR. GROSS: Five to 10 microns in length, and one-half micron in diameter.

DR. COOPER:

The next paper on our program, which will relate to some of the "Physiological Studies of the Health of Fibrous Glass Workers," will be presented by another of the Mellon Institute Fellows. A physician who received his degree from the University of Oklahoma, spent five years in Saudi, Arabia with the Arabian American Oil Company, and after he returned to the United States, was Medical Director for Mack Trucks in Hagerstown, Maryland. Dr. Benjamin J. Lambiotte began graduate training at the University of Pittsburgh in 1966 where he received his Master of Public Health degree, and is now in his third year of residency program for Occupational Medicine Board Certification: Dr. Lambiotte.

PHYSIOLOGICAL STUDIES OF HEALTH OF FIBROUS GLASS WORKERS

Benjamin J. Lambiotte, M.D.*

In our efforts to define and measure the effects of industrial processes, products and wastes on health, it is necessary to make certain hypotheses within a framework of known and accepted pathologic entities. In this case, pneumoconiosis is defined as "a diagnosable disease of the lungs produced by the inhalation of dusts."[1]

In this study, our concern is with the dusts that result from the processes and products of the fibrous glass industry.

Dr. Utidjian has presented the initial study of these workers. Further detailed study of pulmonary function on a segment of that population is planned. The hypothesis of this planned study simply stated is: inhalation of fibrous glass dusts will cause demonstrable changes in the pulmonary function of exposed workers.

If this hypothesis is true, then the tests that measure these functions will show greater degradation in the highly exposed, older workers with long service than in the lesser exposed workers of the same age group with long service.

If the hypothesis is not true, then there should be no difference in the pulmonary function of the two groups.

The appropriate selection of tests of pulmonary function that will give evidence to prove or disprove the hypothesis is based upon what we know about the behavior of, and lung reactions to, dusts of similar physical characteristics as fibrous glass.

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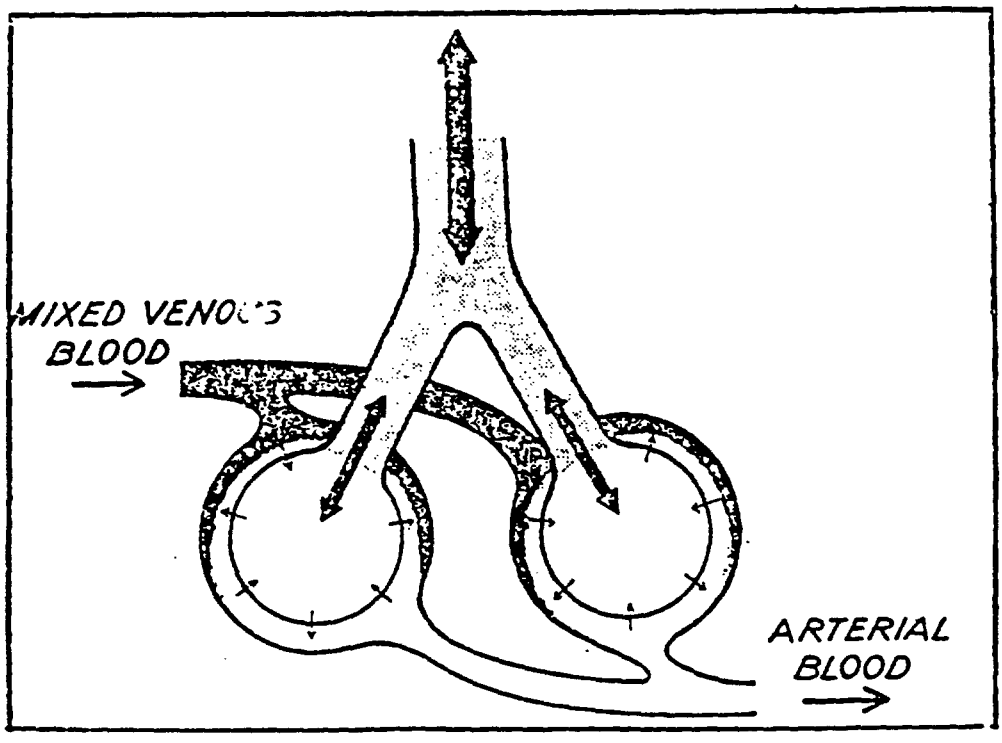
This knowledge clearly indicates that the point of our attack should be the alveolar membrane, its blood supply, and the mechanical functions of respiration.

In order to clearly understand how, and how well, these tests measure the pulmonary functions in question, it is necessary to indicate on a model the areas of concern.

Figure 1[2]



The mechanical functions to be measured are concerned with the area indicated on Figure 1: the movement of air in and out of the trachea and large bronchi via:

1. The active muscles of inspiration.
2. The recoil of the stretched elastic tissues of the lungs and the thorax due to the potential energy stored in them at inspiration.
3. The resistance to air flow in the conducting airway system.

This indicates the area of alveolar ventilation, i.e., the area where gaseous exchange takes place. The fine arrows indicate this exchange.

The two elements influencing diffusion are:

1. The condition of the membrane
2. The condition of the capillary bed, i.e., the alveolar blood flow.

Equipment used for examining the mechanical factors of respiration is a Collins 13-1/2 liter spirometer. This device consists of a bell in a water seal, the movement of which is recorded on a paper chart. The subject is asked to inspire maximally from the bell, then to expire as fully and as rapidly as he can.

Figure 2[2]

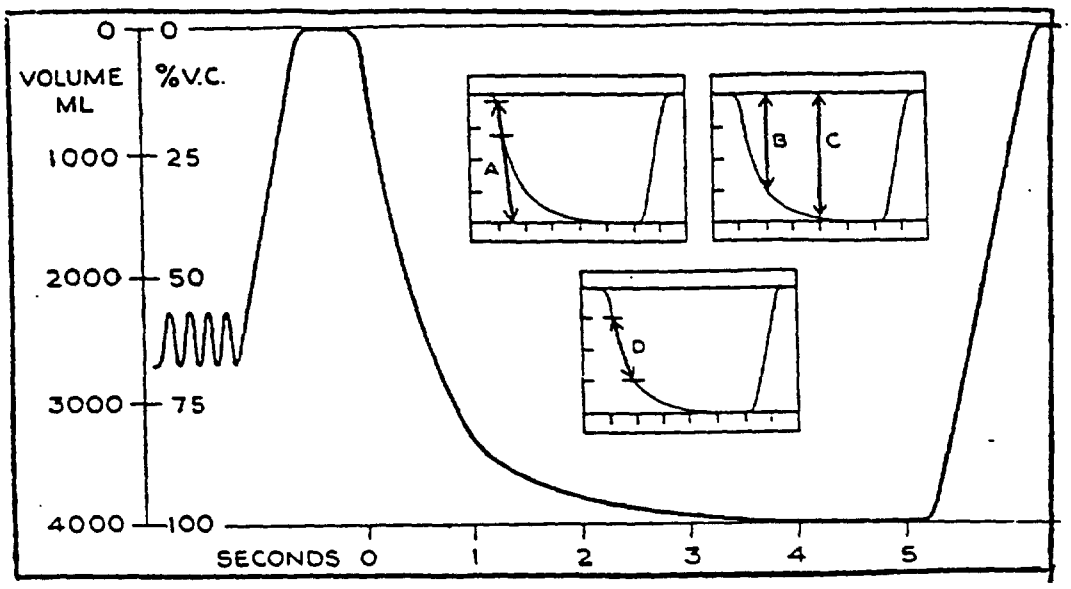


Figure 2 shows a typical normal curve illustrating the parameters that measure the performance of the mechanical functions of the lung.

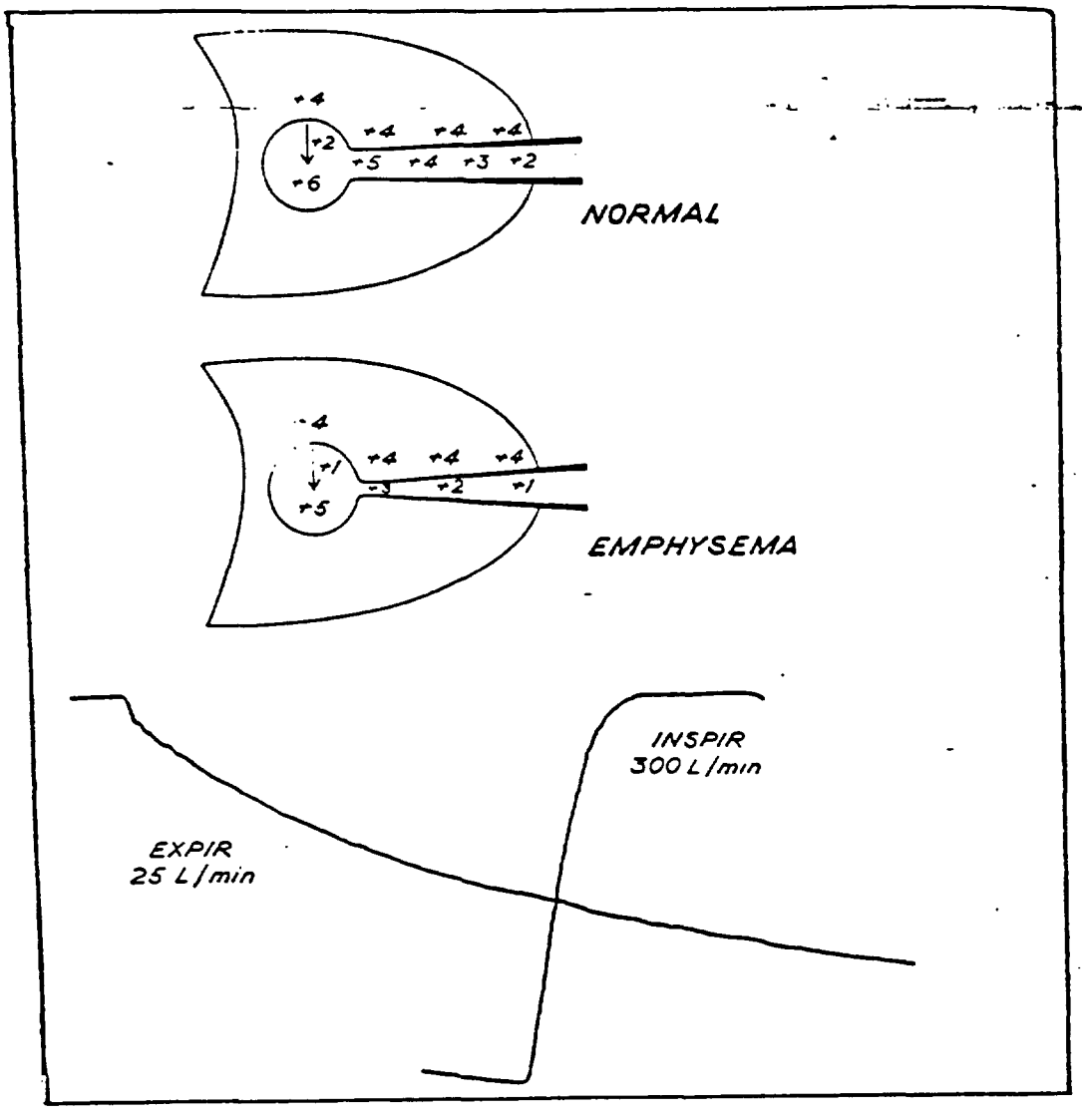
A illustrates the maximum expiratory flow rate measured in l/m for the first liter of expired gas (after a lag of 200 ml caused by inertia in the system).

B and C are the forced expiratory volumes expired in one second and at three seconds. (Usually expressed in per cent of the total.)

D is the maximal mid-expiratory flow rate in l/m during the middle 50% at the expired volume.

In order to grasp just what these parameters measure, Figure 3 shows the slopes of the curves in a case of emphysema, characterized by reduced recoil and increased resistance to flow. Note that the slope of this curve is made more shallow than in the previous illustration but the slope of the inspiratory curve is similar to the inspiratory curve in the normal.

Figure 3[2]



The models illustrate this phenomenon. Thus, we see the "check value" effect, open in inspiration, closed in expiration—a complicated series of events with the net result, air trapping, characteristic of the disease emphysema.

In order to ascertain the condition of the alveolar membrane and its blood supply, the rate of diffusion of gases across the membrane must be measured. These measurements are made by taking advantage of the

[illegible] characteristics of carbon monoxide. A single breath or one to two minutes breathing of a concentration of 0.3% is not dangerous.

Carbon monoxide has a remarkably high affinity for hemoglobin, so that the greater the diffusing capacity of the alveolar membrane, the greater amount of carbon monoxide will enter the blood stream and be bound to hemoglobin per unit of time.

Thus, in a thickened membrane with poor capillary flow, there will be less carbon monoxide uptake than with a normally functioning membrane with normal blood flow.

Obviously, a decrease in the carbon monoxide uptake can result from a combination of events:

1. Disease associated with thickening and separation of the capillary and alveolar wall.
2. Disease associated with decreased surface area due to destruction of alveolar and capillary beds.
3. Diseases associated with total loss of blood flow, e.g., occlusion of blood vessels.
4. Diseases that cause accumulation of fluid in the alveolar space causing reduced diffusion.

The reverse may also occur, i.e., greater carbon monoxide uptake due to disease in which the pulmonary capillary blood volume is increased.

Figure 4[2]

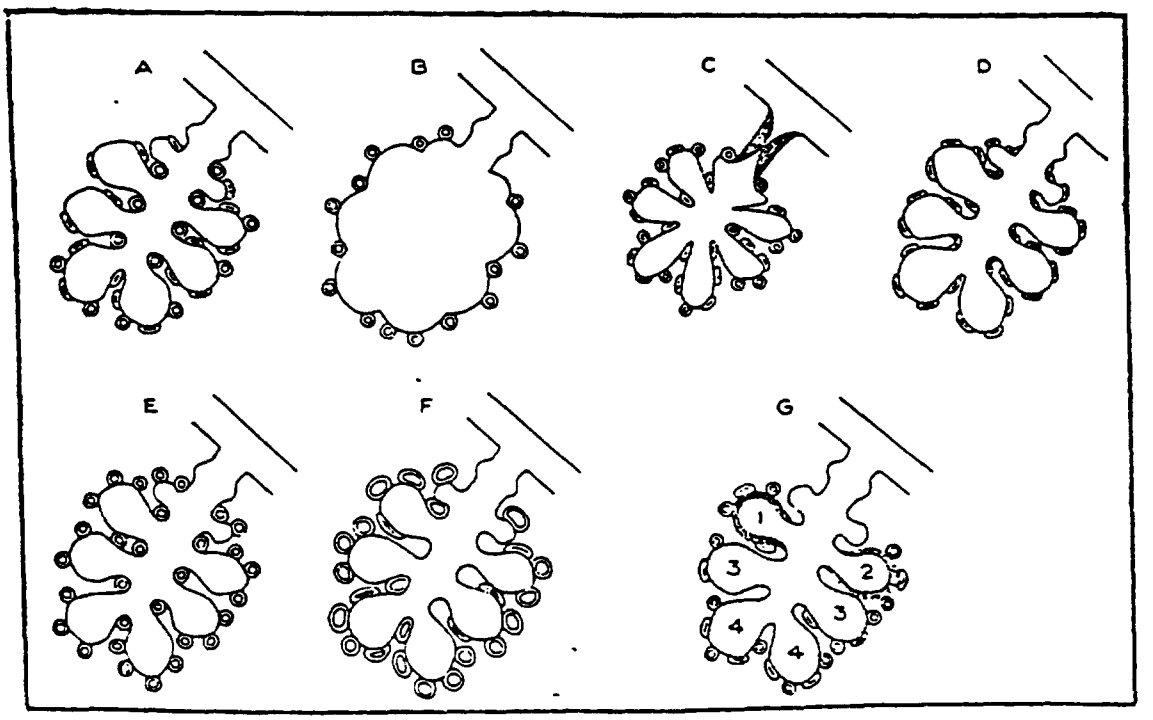


Figure 4 illustrates some of these conditions:

A is normal.
B is destruction of the wall plus reduced capillary bed.
C is obstructed air flow.
D is obstructed blood flow.
E and F illustrates condition where carbon monoxide uptake might be increased, i.e., increased number of capillaries and increased size of capillaries.
G illustrates a variety of interferences due to change in the condition of the membrane: thickening, tissue separation, beginning pulmonary edema, non-ventilated alveoli filled with exudate or fluid.

This brief discussion indicates that by using a combination of tests of pulmonary functions, such as:

1. Spirogram: forced expiratory volume, one, two, or three seconds; forced mid-expiratory flow; maximum flow rate; total vital capacity.
2. Diffusion capacity,* resting and with exercise: measured by the steady state carbon monoxide uptake method (based on recommendations of Dr. George Wright, St. Luke's Hospital, Cleveland, Ohio; Advisory Fellow of IHF).
3. Calculation of:

Total lung capacity; functional residual capacity; residual volume, and by comparing meaningful deviations from "normal" of these parameters in these two populations, i.e., the older, highly exposed groups versus the older, lower exposed groups, these objective measurements would quantify any significant effects of fibrous glass dusts exposure on the function of the lungs, provided no other explanation can be found for these differences.

Obviously, failure to demonstrate such differences would help document the null hypothesis.

Either event would be useful in furthering our efforts to measure and obtain information about the effects of industrial processes, products, and wastes on health.

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* The December 1968 issue of the Industrial Hygiene Digest of the Industrial Hygiene Foundation contains a discussion, in a book review, of the relative merits of the various carbon monoxide uptake methods.

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DISCUSSION

DR. COOPER: Are there any questions or comments on Dr. Lambiotte's outline of some of the things that ought to be in the contemplated studies?

DR. LEE B. GRANT, PPG Industries: This was a general discussion of the pulmonary function studies intimating that from these studies there will be selected certain studies that will be utilized with your approval. Are you prepared to say what those particular studies will be?

DR. LAMBIOTTE: At this moment, we plan, in a general way, to measure the mechanical function of the lung and the diffusion capacity. This will be done using a steady state CO diffusion and the usual parameters, as I outlined, to measure the mechanical function. This will be done on the selected groups, half of the oldest, highest exposed workers, and half of the oldest, least exposed workers.

FROM THE AUDIENCE: Can you give a time relationship as to when, possibly, these studies may be initiated?

DR. deTREVILLE: We have heard from the physiologist at Newark's Licking County Hospital that the equipment has been selected, and as soon as the administrative details of getting the equipment there and getting things lined up can be worked out, the studies will be performed. Hopefully, some of this information will be available to guide the standard setting Threshold Limit Committee of the American Conference of Governmental Industrial Hygienists as they prepare their recommendations for 1969.

Introduction

Many of us had the good fortune to hear our next speaker give a general discussion of some of these problems we are discussing today at the 33rd Annual Meeting of the Industrial Hygiene Foundation. Today, I think he will be adding new information on one particular portion of IHF's studies with which he has assisted. During his military service, this speaker saw the career advantages of industrial hygiene and occupational health; he had the good fortune to go to another excellent site of occupational health graduate training—Harold Magnuson's Institute in Ann Arbor—where he had a distinguished record. After his third (in plant) residency year at Ford Motor Company, Dr. Jon L. Konzen joined Owens-Corning Fiberglas Corporation as corporate Medical Director. He will now describe his company's Radiological Studies of Fibrous Glass Workers.

RADIOLOGICAL STUDIES OF HEALTH OF FIBROUS GLASS WORKERS

Jon L. Konzen, M.D.*

The Owens-Corning Fiberglas Company began performing preplacement and periodic chest x-rays on its employees about the time that manufacture of fiber glass was begun on a plant scale. The newspapers were then full of "silicosis" and the company's management then began anticipating that a question would be raised concerning a relative hazard to health of exposure to fiberglas dust. While the x-rays taken were intended chiefly for occupational health service use in hiring and placement operations, Dr. Charles Bishop, Plant Physician, recognized from the beginning that such records would have value for research purposes some day, and all such records were preserved, except for a few which were damaged in a flood. A comprehensive review has been made of these records with the assistance of Dr. George Wright of Cleveland, noted authority on occupational diseases of the chest. Dr. Wright published his findings (AMA Arch. Environ. Health, Jan., 1968).

In planning the epidemiological study on which /Dr. Utidjian has already given a preliminary report, the question was raised by Dr. Ciocco, Research Advisor to the Foundation, whether it would not be possible to develop data to supplement Dr. Wright's report. Dr. Wright's report dealt with 1500 employees of the total plant population of approximately 2400, on whom there were x-rays dating back to 1963 or earlier. Our present study is a random sample of approximately 10% of the plant population. For this sample we have x-rays on every individual, hence, Dr. Ciocco felt radiological examinations for a representative sample was important as this was not possible in Dr. Wright's study.

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At the time of our plant epidemiological survey, Dr. deTreville and I reviewed the chest x-rays on every employee examined. It must be recognized before proceeding to the results of our study that these individuals are all working and that if there had been significant evidence of active disease or any abnormal finding, they would have been screened out for further study. Notation was made of all findings of significance from the earlier review of the Board Certified Radiologists who had initially reviewed the films. We were not as interested in incidental findings such as "healed ghon tubercle" as we were in attempting to detect any evidence either of "dust patterns" or suggestion of micronodulation. Admittedly, we were not looking at these films, therefore, as qualified radiologists, but as scientists attempting to find a measurable radiological end point to include in our total epidemiological research protocol. Therefore, while we have for research purposes identified the films as "positive" and "negative", it is to be understood that these terms have no connotation of diseases in the context of our study. The results of our observations were entered in the nine boxed research square which Dr. Utidjian has described earlier. With the three categories of age and estimated exposure shown, it will be seen in Figure 1 that there was no tendency for individuals with the highest exposure for the longest number of years to have any greater frequency of "abnormals" than individuals with shorter, lower levels of exposure. Interestingly enough, there was a tendency for smokers to have a greater incidence of "positives". I think this is all we can say about this aspect of the Industrial Hygiene Foundation study at this time.

Figure 1

CHEST RADIOGRAPHS
% IDENTIFIED AS POSSIBLE DUST PATTERNS
(exaggerated linear markings)

Age \ Exposure	1	2	3
I	16%	8%	30%
II	15%	11%	14%
III	14%	15%	10%

DR. deTREVILLE: It might also be of interest to add at this point that, according to Dr. Utidjian, there was no history of bronchitis (cough and sputum) in any non-smoker in the individuals identified as "positives", so these findings are consistent with the recognized relationship between smoking and bronchitis.

DR. THOMAS F. MANCUSO (University of Pittsburgh): I should like to caution you in regard to your interpretation of the presumably negative findings and to remind everyone, if I understand the study properly, that this was an x-ray study of a population at a given point in time, which represented a cross-section of the population working at that point in time; and, therefore, represents what we call a survivor group. It is really a selective group—those individuals who are healthy enough to work. It does not include individuals who have been employed many years prior to that time, who have left because of illness. We find this is very true in industry that over various points in time, depending upon the economic conditions or production and so forth, that there is remarkable variability in the individuals who are sick, who leave, either of their own accord or in relationship to some policy. So, I do not think really that this particular study, other than providing you with some particular type of lead for your own purposes, should have much attention given to it; and I would not add the additional refinements that you are doing to it, because basically it is a survivor population. I am interested, however, in the comment in regard to what Dr. Wright did, as I am not acquainted with that particular study. But if his x-ray study which you referred to, again was a cross-sectional study of the population, then we are in the same situation. If, however, he has combined this type of study with, say x-rays from pre-employment examinations at a given point in time, say 1945 versus examinations 20 years later, 5, 10, 15, 20 years later, then he had a longitudinal progressive change of x-ray. In such a study you are more apt to be on safer ground, provided, of course, that the x-ray measurements were done the same way, the film was processed the same way, etc. On the face of it, therefore, I cannot see that the Industrial Hygiene Foundation study, as conceived and reported here, will add anything to Dr. Wright's study.

DR. E. A. GAENSLER (Boston University School of Medicine): I don't quite understand: First you said that you had 33 "abnormal" x-rays of the 226. Then you said all of these had been read by a radiologist and had been considered as 'normal.' Then you said that this was not the sort of thing that would prevent any individual from being employed in the pre-employment examination, and then you refer to 'micro-nodulation.' Well, it seems to me there needs to be better definition.

[illegible] that Dr. Gaensler has said is a just criticism. We went into this recognizing that we were working in the dark. There was no micro-nodulation of the type that you would see in the ILO standard films. None of these would have been considered "positive" for early fibrosis. What we were seeking was any evidence of the type of dust pattern described by Gardner (quoted in Johnstone's Occupational Medicine and Industrial Hygiene. C. V. Mosby Co., St. Louis, 1948, p. 339):

> "The mere aggregation of particles themselves...increases the density of the delicate connective tissues about the vessels ...(which may be observed in such cases to be)...heavier than normal. As a great many kinds of dust produce such changes, exaggerated linear markings are common findings in persons employed in industry. There is nothing specific about such a pattern to indicate its cause and it is rarely associated with clinical findings...."

DR. PHILIP ENTERLINE (University of Pittsburgh): I would like to both agree and disagree with Dr. Mancuso's comment. First, I agree that any working population is a selected group of individuals, and there are many hazards in drawing conclusions. On the other hand, this picture is different from the picture you would find if you examined a group of people working with asbestos, or groups of coal miners, or dozens of other studies of working populations which have these same selective biases operating. This study of fiber glass workers does not appear to show any significant disease. I do not see how 226 people could have such normal lungs unless they are really pretty healthy—more healthy than workers in some other industries where similar studies have been done.

DR. deTREVILLE: Let me say that there are diagnoses that the radiologists have put on here and we have classified these and sent these into Dr. Ciocco. We have not yet worked these up. These are the things that Dr. Wright looked for—abnormalities of any type from the standpoint of healed tuberculosis and that sort of thing.

FROM THE AUDIENCE: Those did occur in this as you would expect in any study of the general population?

DR deTREVILLE: Oh yes, these did occur.

DR. LEE B. GRANT (PPG Industries, Inc.): My concern is about the reporting of such a study. The literature is already confused enough.

DR deTREVILLE: I think the important thing here is that Dr. Ciocco asked a question about the published study on the employees studied by Dr. Wright, in that there appeared to be the same thing that had been pointed out earlier: the employees in some of the dustier areas seem

to have actually less abnormal findings than those working in the clerical, less dusty areas. The question was: "Is there anything that would suggest bias here in removing from the work area those individuals who for one reason or another cannot work?" This is simply an attempt to look from a different vantage point at the same group of employees randomly selected. Whether or not anything will be done on this will be a result of men like Dr. Ciocco and Dr. Wright looking at all of this together and seeing whether it means anything or not. Over a period of the last two to three years, we have been trying to come up with methods of studying a population of this type that has had the longest exposure in industry to a material of unknown toxicity, and we have to start somewhere. One of the hardest things, as I mentioned, has been getting started on the pulmonary function studies. We have been discussing it for a matter of one or two years. So, if there is a little confusion in this, I hope you will bear with us. We are actually pioneering and pushing the frontiers forward in this, and meetings of this type are most helpful to us.

DR. ENTERLINE: I think the only comment that I would like to make at this time is that if there were a serious problem here I think it would show up. We have had problems in other industries that did show up. It is true that there might be something very subtle here that is being missed but, if so, I think this problem is of a different dimension than some of the ones we are more familiar with. I wondered if the readers of these x-rays knew what the exposure levels were?

DR. deTREVILLE: No, not until after our review

DR. ENTERLINE: Did you know the ages of the people?

DR. KONZEN: No, but you can guess that.

DR. deTREVILLE: Yes, some of the packages of x-rays were thick, and some films went back over 20 years.

DR. MANCUSO: You can guess just by looking at other characteristics of the film. So you cannot disguise the age of a man entirely in a study of this kind. To speak of Dr. Gaensler's very good point, I would still like to say that I think some films are more normal than others and there are things that worry you in a film, but you are still not prepared to call anything definite. I think Dr. Grant's point is if you start calling it something you are already in trouble. On the other hand, in very multiple readings of film, if you have five readers, three readers, or ten readers reading films, you will get some films upon which they will all agree every time they read them. You will get another film that one man will call doubtful this time, and another man will call positive. You begin to get the feeling that the second film is in some way a different category from the one on which everybody agrees.

DR. deTREVILLE: According to Dr. Eugene Pendergrass of Philadelphia, recently it has been shown that "bronchovascular markings", which had been read previously by radiologists relate to dynamics in the cardiovascular circulation, i.e., whether the heart is in "systole" or "diastole". So some things that may very well be observable, may very well be completely without meaning from the standpoint of pneumoconiosis.

DR. BISHOP: I would like to clear up a point. The radiologists who review our films have the entire file of films and the history of the individual. Further, if they have any questions about technique, e.g., full inspiration at the time of taking the film, or anything like that, another film is taken at their request.

DR. ENTERLINE: I just want to add something. I think the study is alright, as long as we are thinking about the fibrotic types of diseases that we talked about this morning. When we did a study of working uranium miners, we were looking for silicosis and we could never have detected from that study that we had a cancer problem. Cancer was a different kind of disease than we were really looking for, and could exist only briefly in a working man. The kind of diseases that you are looking for is an important factor in the design of epidemiological research.

MODERATOR'S SUMMARIZATION

(Morning Session)

W. Clark Cooper, M.D.

Summarizing this session is an easy and pleasant assignment. Much of what we have heard is negative or is a promise of studies to come. The important thing to emphasize is that serious work of this nature is underway, and a year or two from now we should have even more substantial evidence. The probable growth potential of the fibrous glass industry makes it imperative to keep on top of this from a health standpoint. All of the speakers are to be congratulated on their clear and succinct presentations which made the work of the moderator so painless.

Several points brought up in the discussion deserve emphasis: (1) Dr. Spiel's caution to us that fibrous glass is a generic term and that in our reports and studies we must clearly differentiate fiber classifications and sizes; (2) Mr. Stein's reminder that the lungs of workers exposed in the past should be studied to determine the amounts and size distribution of glass fibers that may be present, as sizes have not been so narrowly controlled to ensure non-respirability; and (3) Dr. Mancuso's valuable suggestion that successive cohorts should be studied to get maximum epidemiologic return on the relatively small populations of exposed workers.

I want to thank the Industrial Hygiene Foundation for providing this forum for discussion and applaud the enlightened cooperation of those in the industry who are working together to supply much needed documentation of exposures and responses to fibrous glass in its various forms.

Afternoon Session

BIOEFFECTS RESEARCH FOR UNITED STATES ASBESTOS INDUSTRY

Moderator: Lewis J. Cralley, Ph.D.
U. S. Public Health Service

OPENING REMARKS

Lewis J. Cralley, Ph. D. *

The types of asbestos of commercial interest in the United States, that is, amosite, crocidolite and chrysotile differ among themselves, and also each class will differ greatly according to chemical and physical properties. Such differences include such factors as the harshness, the dimensions of the fibers or fibrils themselves, the chemical composition, the extraneous materials that may be associated with them, either as a mineral and/or as they are extracted and processed, the amount of free silica, oils, and many other parameters. Also, some forms of asbestos have a physical property of being able to pick up contamination from the processing itself.

Another important factor, I think, is that there is well established animal and human experience of the biological effects of exposure to asbestos, which has not been associated with fibrous glass. We have a different type of an industry, in a way, a different type of exposure. Although it is fibrous material, the parameters are quite different.

I believe that as we look backwards we are getting away from the narrow type of research and reporting as has been done so much in the past (which was essential) of the biological effects of human exposures using very limited parameters; whether it was either of measuring the exposures or the resultant health profile.

We are getting now more into the causes and meaning of these interrelationships and of how to use an essential material safely.

With this very brief background, I would like to get into this afternoon's discussion, because it is going to be a full afternoon.

The first speaker, Dr. Joseph L. Goodman, is going to talk about Asbestos Exposure in the United States Textile Industry during quite a span of its history. Dr. Goodman is on the visiting faculty of the Medical University of South Carolina. He is chairman of the Committee on Industrial Medicine of the State of South Carolina and of the Carolinas. He is a member of the American Academy of General Practice and chairman of its Occupational Medicine Committee, and is a member of the Industrial Medical Association. I have known Dr. Goodman personally for a number of years, and am impressed with his knowledge and the practical approach he has to resolving health problems encountered in the asbestos textile industry in North and South Carolina. With this background, and in order not to take further time away from his important subject, I will turn the podium over to Dr. Joseph Goodman.

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* See p. 16.

ASBESTOS EXPOSURE IN THE U.S. TEXTILE INDUSTRY
- 1930 TO DATE -

Joseph L. Goodman, M.D.*

I have been asked today to present a paper on the differences in asbestos exposure in several textile factories in various parts of the United States since 1930, and the clinical importance of the improvements in industrial hygiene which have been implemented. The term "asbestos" covers all forms of mineral fibrous crystals. When various forms of asbestos are fiberized, the resultant fibers differ physically and chemically. The three types of asbestos which are commercially important are chrysotile (white), crocidolite (blue), and amosite (gray). Anthophyllite is reportedly the first asbestos used by man, when it was applied as a reinforcement for earthenware pots 6,000 years ago in Finland. Chrysotile is used predominently in U.S. Asbestos Textile factories. In our factory in North Charleston, South Carolina, for example, we have eliminated crocidolite altogether. Although use of asbestos goes back 6,000 years, the history of its use in this country spans little more than 60 years. Murray[1] reported in 1907 the case of an asbestos worker who had died of "typical pulmonary fibrosis", and this biological effect of asbestos, i.e., asbestosis, is generally well known.

The soft pliable nature of chrysotile fibers makes them ideal for textile weaving applications. Asbestos has many uses, such as brake linings, tiles, flooring compound, fireproofing (even in Apollo capsules). Subsequent to reports of the fibrogenic effects of asbestos fiber, cases were reported of bronchogenic cancer in an asbestotic worker; the first such case came from Dr. Kenneth Lynch[2], on one of our own employees in 1935. More recently has come the discovery of an association between non-occupational asbestos exposure and long delayed pleural and peritoneal cancer, by Wagner[3], but the relationship is anything but clean-cut as pointed out by Sluis-Cremer[4]. Finally, Thomson's[5] discovery of "asbestos bodies" in a significant percent of the lungs of the general population in South Africa and Miami, Florida, created much concern which has been considerably reduced by the work of Industrial Hygiene Foundation's Dr. Paul Gross and others on "Ferruginous Bodies" and their non-specificity.[6,7]

By way of historical background, in the 1920's there were several textile plants that had very crude systems for the removal of dust. Dust was often exhausted straight through the roof into the atmosphere, a cyclone type of elimination.

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Figure 1 shows work practices in the early 1930's. It barely shows the man at the next machine as visibility was limited to about 20 or 30 feet. Notice the employee assigned to wipe off the electric bulbs so that people could see better. Obviously, it was extremely dusty. In this plant in 1921 and 1922, dust was exhausted through the ceiling, as mentioned and this was a fairly general practice. The next approach, shown in Figure 2, was downdraft ventilation, in which a hole was drilled in the floor, lined with sheet metal ducting, and equipped with a fan at the other end. All but a few windows were nailed up, leaving sufficient air flow so that the workers would not be in a vacuum. This reduced the dust level in the atmosphere to the point that one could see the employee at the next machine. The dust so removed was emptied into what was called the "dust room" shown in Figure 3. It was about 150 feet long and had burlap sacks nailed to 2 x 4's. Dust from the pipes emptied into these sacks. The routine way that they cleaned up this area was to send a man through with a "beater" as shown. He whipped the sacks in order to loosen the material and get it to settle to the bottom. In addition an individual used to have to go in with a shovel periodically to empty the sacks; usually this ranged from weekly to monthly. As shown in Figure 4, other individuals had to crawl through the ventilating system to rake out asbestos dust which had collected in the pipes. You can imagine that the exposure of the individual during this particular operation must have been maximal.

Figure 5 pictures the modern situation, showing a "wheelabrator" composed of approximately 1140 large canvas sacks. The dusty air enters from the bottom. It has a cutoff valve at the bottom which decreases the flow of air, and the large fibers which are trapped drop into carts that sit at the bottom of a sheet metal bin. The fiber dust so collected is reintroduced into the system. We have two of these large collection systems in our plant. One modern dust system conducts 53,000 and the other 90,000 cubic feet of air per minute.

The above-mentioned cutoff can be seen in Figure 5. The large fibers fall to the bottom, and the fine dust is blown up into these sacks, which need to be emptied only twice a year. The air which goes through these canvas bags is not recirculated. So our preventive engineering methods have effectively reduced dust from carded material. A sufficient capture velocity is maintained to keep dust out of the atmosphere.

Some operators also need to wear respiratory protection with the hood in operation.

Even where bulk raw materials are prepared and held waiting to go into the "card room", the atmosphere is so relatively free of dust that there is no longer any reduction in visibility whatsoever looking across the plant's interior.

Fig. 1

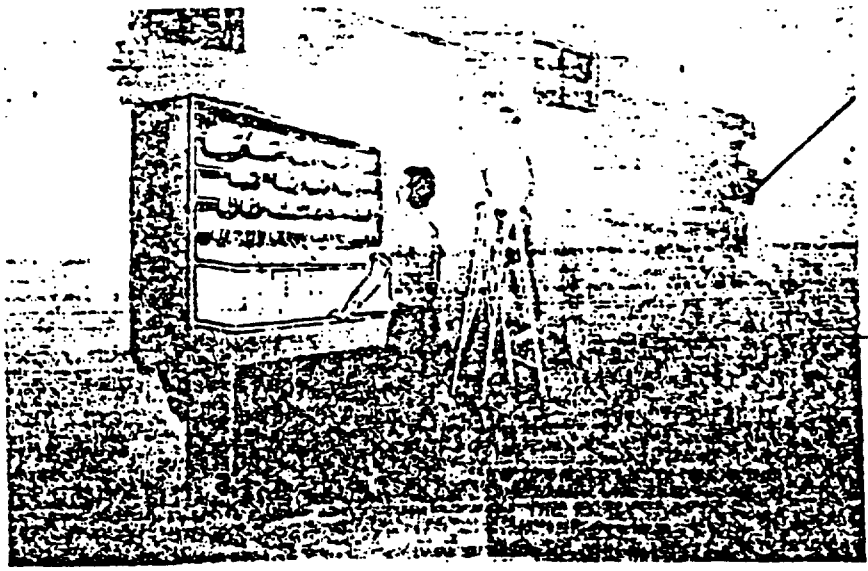


Fig. 2

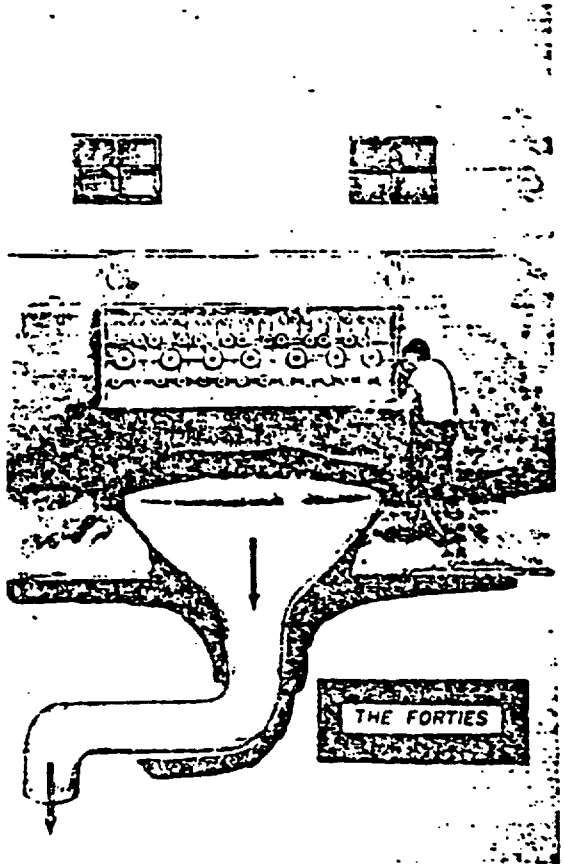


Fig. 3

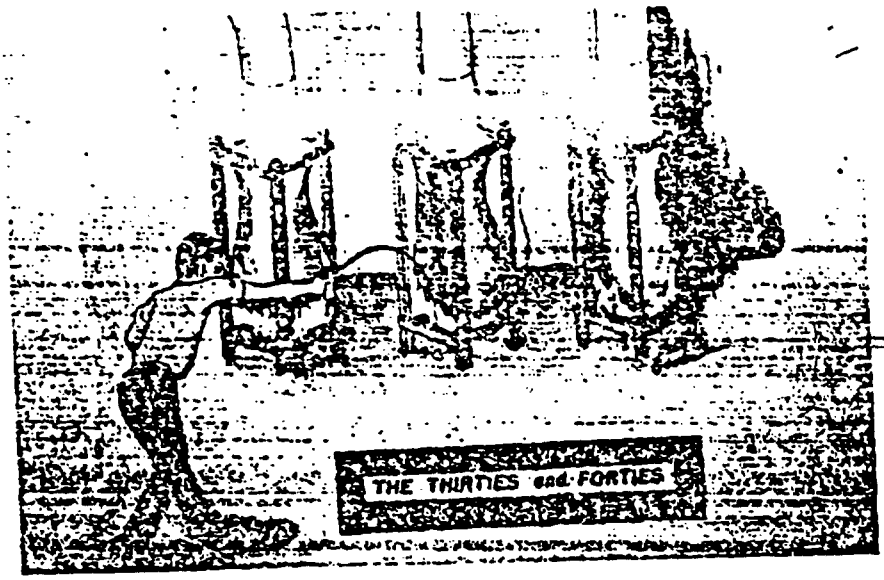


Fig. 4

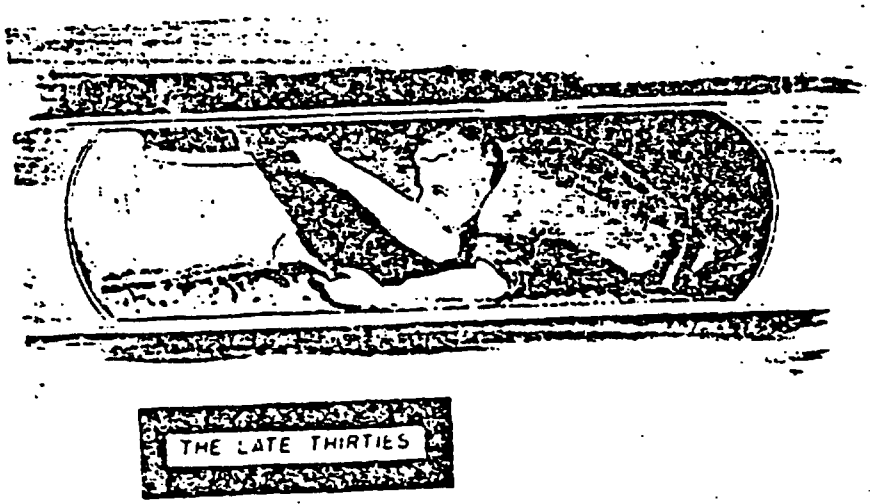
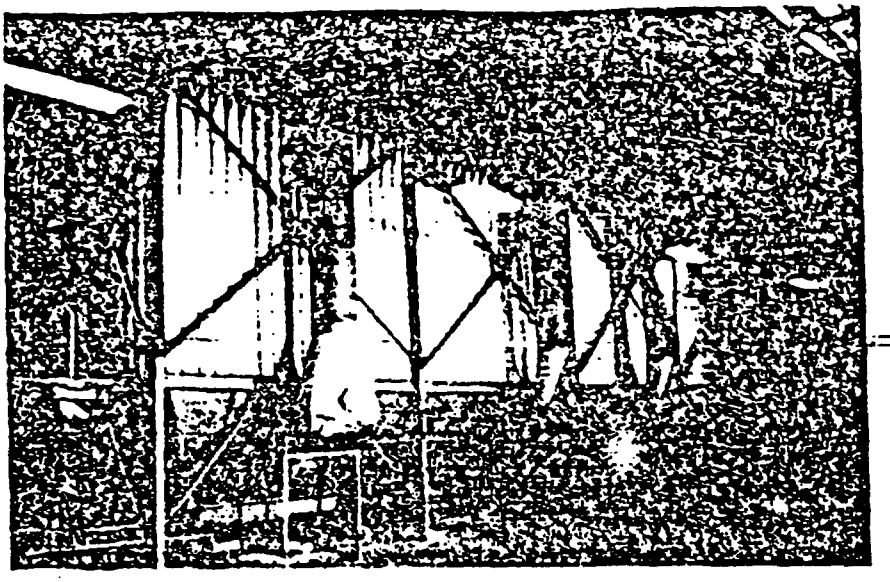


Fig. 5



At the other end of the "card room" there is an assembly of duct systems and cycloning equipment that ventilate the atmosphere around the machines.

One machine takes the mixture of cotton and asbestos over the "camel back". After traversing the full length of the machine, the exhausted air runs into a large duct having a flow rate of about 3,000 cubic feet.

Three 30-inch ducts clean out the weave room and the card room. There are 300 feet between the weave room, card room and the dust-collecting wheelabrator shown in Figure 5.

We are in the process of providing dust controls for the few individuals who now have to wear respirators. A few places have to be cleaned out every day, because the long fibers (or "fly" as they are also called) become trapped and accumulate, and these maintenance operations are still not well enough controlled that need for respirators has been eliminated.

In spinning and weaving the equipment (especially the spindles which rest in funnels) goes at a terrific rate of motion. This process is enclosed all the way until it enters into a large duct which carries the exhausted air to the collection point.

A free hanging apron helps prevent escape of dust. This is a relatively clean operation, although the machine is rather old. The apron also provides safety protection when spindles, which move at a terrific rate of speed, have to be moved for maintenance or other operations. Exhaust ducts rise in between the rows of spindles and run along the top of the spinning apparatus.

The weaving process, which is our dustiest area, has a stiff sheet metal duct, and also flexible apparatus on both sides that are moved with the machine operator, as he works along.

I might add that it has been difficult to get people to wear respiratory equipment continuously, even for their own protection; hence the attempt has been made to control dustiness adequately to make their use unnecessary, except for brief maintenance-type operations.

In addition, at the suggestion of the Asbestos Textile Institute at our last meeting, a "wet weaving" process has been instituted on a trial basis to help control dustiness. The area concerned appears to be relatively "dust-free" and the method may thus offer promise.

We also humidify the atmosphere in the spinning area; at the ceiling, jets of steam are released and the high moisture level causes asbestos fibers to agglomerate and drop to the floor.

Figure 6 summarizes dust counts taken since 1942 in asbestos textile plant atmospheres. The data, which are not entirely ours, give a cross-section of several plants in different areas of the United States. It can be seen that the levels measured since 1952 have been within the existing Threshold Limit of 5 mppcf set by the American Conference of Governmental Industrial Hygienists. Some of these data have been collected by the U. S. Public Health Service.

You see, back into 1942 in this particular factory, dust counts peaked as high as 35 mppcf in places where the sacks were opened, and "picking" was done, and there was a sudden drop as they cleaned up the operation in 1943. You can also see counts for carding, spinning, and weaving. In carding, they stroke the asbestos fiber, to get it in line, and this has been one of the dustiest operations, and most difficult to control.

Figure 7 relates deaths due to asbestosis to dust levels in the period 1930-65, showing a peak in deaths in 1955. A corresponding peak in the carcinoma deaths occurred in 1959, as shown in Figure 8. Note that the cancer death peak in 1959 is apparently entirely due to lung carcinoma. Incidentally, we did include mesothelioma; we had two mesotheliomas and one sarcoma of the lung (in a lady). Since 1959 we

Fig. 6

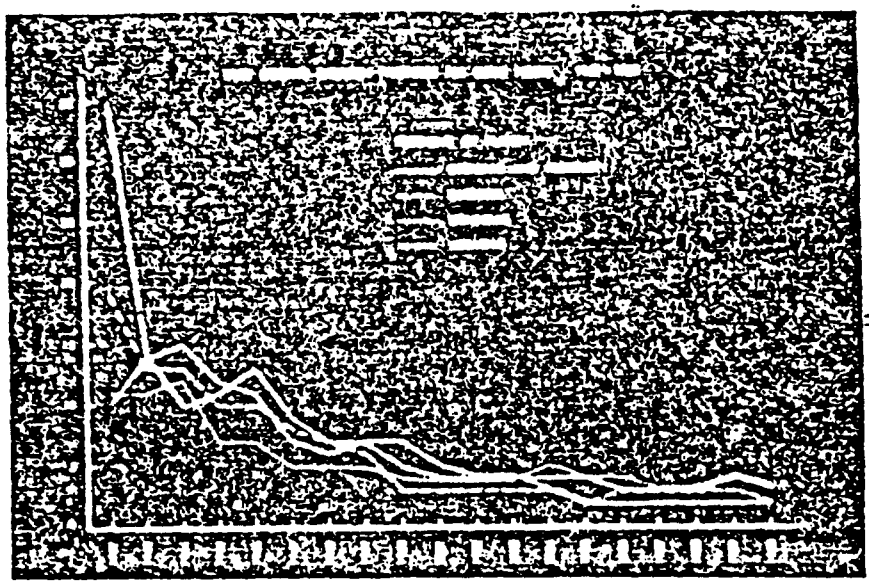


Fig. 7

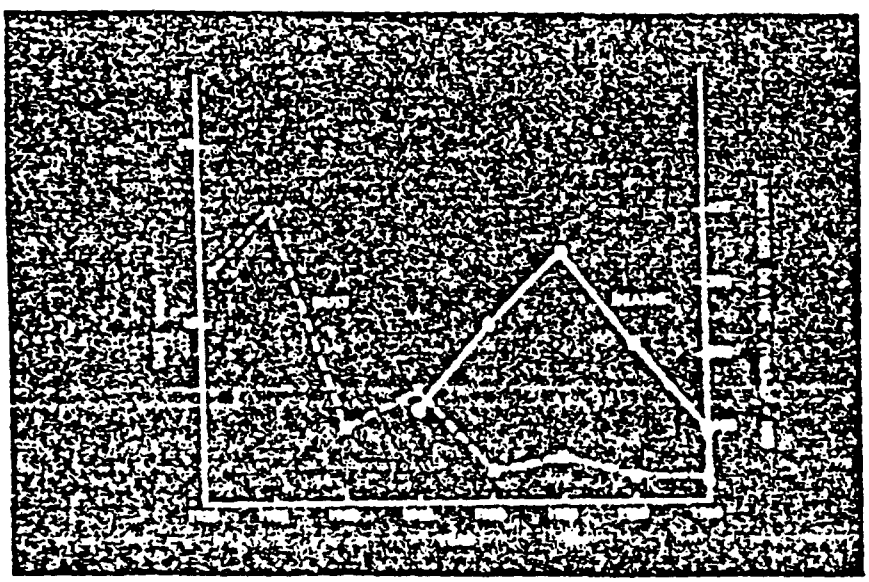
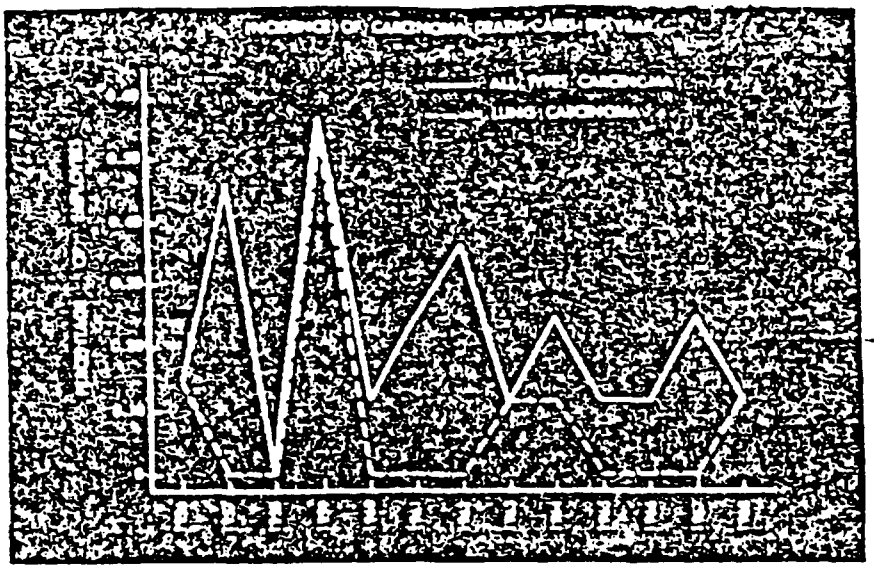


Fig. 8



have noticed a drop in the bronchogenic carcinoma, which is shown and which is not according to the national average. This drop appears to be related to the cleaning up of the plant and the resulting reduction in dust exposure which I have described; and our experience is thus supportive to that of Turner Bros. in England, as reported by Knox[8].

In summary, there is a considerable amount of information on the mortality and morbidity of Asbestos Textile Workers in the United States, and we are cooperating with the U. S. Public Health Service and the Industrial Hygiene Foundation in every possible way to develop more and better data on such experience and its relation to environmental exposures. This should, therefore, be considered a preliminary report.

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DISCUSSION

FROM THE AUDIENCE: I assume the dust counts have been collected with impinger, and microscopically counted?

DR. GOODMAN: We have used a new Bausch & Lomb electronic instrument. We have tried to correlate the Bausch & Lomb with the impinger method, but there seemed to be difficulty. The accuracy of the impinger method is only 10 to 15 percent plus or minus, with two people doing the counting; whereas the Bausch & Lomb instrument gives more consistent results by eliminating the human element.

FROM THE AUDIENCE: The dust count is much higher with the Bausch & Lomb; is there a correlation?

DR. CRALLEY: The correlation is made on the same type of dust evaluation that was made in the early 1930's so it did have an internal comparative value, though we do not know what the counts mean precisely. An interesting side comment: this is one of the plants that

is participating in the U. S. Public Health Service study we are doing now. We went there and they said, "Do you see this room? This is the room that Greenburg, Bloomfield and the others used over 30 years ago to do their dust counts when they did their first studies on asbestos." The plant had gone to the trouble to move out the work that was in progress there, and to reconstruct the facility, with a bit of nostalgia, and present it to us in continuation of work which had been started by the U. S. Public Health Service over 30 years ago.

FROM THE AUDIENCE: What was the size of the employee group at Dr. Goodman's plant?

DR. GOODMAN: It has varied from as low as 367 employees in 1932, during the "Great Depression", to a high of 1605 in 1965. The latest figure I have is about 1527 for the year 1967.

Our next presentation is on the Statistical Studies of the U. S. Asbestos Textile Workers.

I have known Phil Enterline for some time and have traveled a lot with him. He is a dynamic person and dynamic situations usually developed when he and Dr. Roy Gibson (now Regional Medical Director with Gulf Oil Corporation) were around, and I had the privilege of traveling with them. I learned to expect the unexpected. When Dr. Enterline was in the Public Health Service he was assigned to our Occupational Program and we gave him "the basics". He got his best training, no doubt, while he was with us for a number of years; then McGill stole him away from us. He made a number of contributions there, and subsequently the University of Pittsburgh has gained by his presence. You have to know Phil personally to appreciate his capabilities and enthusiasm: and how he puts himself into every project in which he works.

STATISTICAL STUDIES OF U. S. ASBESTOS PRODUCTS WORKERS

Philip E. Enterline, Ph. D. *

This is a report on the mortality experience of selected groups of workers in the asbestos products industries in the United States. Data presented were obtained from records maintained by the U. S. Social Security Administration and from death certificates filed with State Departments of Health. The focus of this report is on lung cancer deaths and on asbestosis deaths which occur in asbestos products workers, and on the relationship of these two diseases to levels of asbestos dust exposure, duration of exposure, and time since first exposure. Details of the methods employed are contained in earlier papers.[1,2]

Some Earlier Results

In a previous report, an attempt was made to answer the question whether a given dose of asbestos dust would in the long run produce more lung cancer or more asbestosis in human populations.[3] This is an important question from the standpoint of relating asbestos dust level standards for the prevention of asbestosis to the prevention of lung cancer. During the follow-up period studies, it appeared that the dose-response relationship for asbestos dust and lung cancer was quite different from the relationship for asbestos dust and asbestosis, and that small doses produce about as much lung cancer as asbestosis while large doses produce considerably more asbestosis than lung cancer. Moreover, it

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appeared that the time required for the production of lung cancer following exposure was considerably greater than the time required for the production of asbestosis.

Tables 1 and 2 summarize some of the results reported earlier. Table 1 represents the results of following 21,755 white males for a period up to 15 1/2 years with work experience in one of three groups of asbestos products industries. Environmental data for these industries indicate that average asbestos dust exposures range from modest in the asbestos building products industry to fairly high in the asbestos textile products industry. Table 1 shows that both "asbestos lung cancer" deaths (defined as the absolute excess in lung cancer deaths over an expected number of deaths based upon experience of white males in the entire United States) and asbestosis deaths are related to levels of exposure in industry. It appears that this relationship is considerably stronger for asbestosis than for lung cancer, with modest levels of exposure producing about as much lung cancer as asbestosis while high levels produce considerably more asbestosis than lung cancer.

Table 1

U. S. ASBESTOS PRODUCTS WORKERS EMPLOYED
AT SOME TIME DURING 1948-1951,
SHOWING PERSON YEARS LIVED AND DEATHS
AT AGES 15-64 DURING THE PERIOD 1948-JUNE 1963
THREE ASBESTOS PRODUCTS INDUSTRIES

	BUILDING PRODUCTS	FRICTION MATERIALS	TEXTILE PRODUCTS
PERSON YEARS	171,199	99,604	24,415
"ASBESTOS LUNG CANCER"			
NO. OF DEATHS	15	10	7
RATE PER 100,000	8.8	10.0	28.6
ASBESTOSIS			
NO. OF DEATHS	19	23	16
RATE PER 100,000	11.1	23.1	65.5

Table 2 combines the three industries and compares deaths in three time periods. Of interest here is the fact that the "asbestos lung cancer" deaths did not start showing up in the cohorts in the study until the latter part of the follow-up period, whereas asbestosis deaths occurred more uniformly throughout the period. This is probably a reflection of a longer latent period for lung cancer, although from this table one cannot determine whether it might not also be a reflection of a longer duration of exposure and thus a greater total exposure. Table 2 also suggests that were a longer follow-up period possible, more lung cancer might have been observed, relative to asbestosis, so that the death rates shown in Table 1 for "asbestos lung cancer" may be understated relative to the death rates for asbestosis. Doubling the numbers of lung cancer deaths in Table 1, for example, would make the gradients for lung cancer closer to those for asbestosis.

Table 2

U. S. ASBESTOS PRODUCTS WORKERS EMPLOYED AT SOME TIME DURING 1948-1951 SHOWING PERSON YEARS LIVED AND DEATHS AT AGES 15-64 DURING THREE TIME PERIODS

	1948-1952	1953-1957	1958-1963
PERSON YEARS	87,792	102,441	104,985
"ASBESTOS LUNG CANCER"			
NO. OF DEATHS	0	12	20
RATE PER 100,000	0.0	11.7	19.1
ASBESTOSIS			
NO. OF DEATHS	13	21	24
RATE PER 100,000	14.8	20.5	22.9

Additional Data

In addition to the cohort of 21,755 men upon which Tables 1 and 2 are based, some data are now available on a cohort of 1,151 white males who were working in three asbestos textile plants during the period 1938-41, or some ten years earlier than the cohort previously reported on. This provides an additional period of follow-up for workers in an environment where asbestos dust exposures were probably fairly heavy.

Data on this cohort also provide some evidence regarding the importance of duration of exposure as compared with the latent period or time since first exposure.

Table 3 shows the age distribution of this new cohort as of the year 1940; the mortality experience as of December 31, 1947, and, for those surviving, whether they were still employed in asbestos textile plants as of January 1, 1948. As Table 3 shows, 50 deaths occurred before January 1, 1948 at all ages. The bulk of the cohort left the asbestos textile industry with only roughly 10 percent remaining as of the beginning of 1948. Those who remained tended to be somewhat older than those who left, and this is consistent with data available from other sources on labor turnover.

Table 3

STATUS OF 1,151 WHITE MALES WORKING IN ASBESTOS TEXTILE PLANTS IN 1938-41, AS OF JANUARY 1, 1948, BY AGE IN 1940

Age in 1940	Beginning Population	Died before Jan. 1, 1948	Alive Jan. 1, 1948: Still employed in Industry	Alive Jan. 1, 1948: Not employed in Industry
15-24	266	3	17	246
25-34	473	8	38	427
35-44	212	11	23	178
45-54	126	13	18	95
55-64	60	10	8	42
65-74	13	5	2	6
75-84	1			1
Total	1,151	50	106	995
Mean age in 1940	33.8	46.8	37.0	32.8

Table 4 shows deaths which occurred at ages 15-64 among the 1,137 men who were under the age of 65 when they entered the cohort. As in Tables 1 and 2, the main reason for confining the table to the age group 15-64 was that the few deaths eliminated tended to be among men who were quite old at the time the cohort was picked up. The mortality of older men actively at work appeared from this and from other studies to be quite unusual and their experience is difficult to compare with other populations from which an expected rate could be calculated.

Table 4 shows that deaths went up with time, as one might expect in groups of men who are growing older. Deaths due to lung cancer started to appear in the period 1953-57 when they constituted about eight percent of the total deaths and in 1958-63 when they constituted 15 percent. Deaths due to asbestosis were more uniformly distributed throughout the follow-up period, as was the case in Table 2. An expected number of deaths has not been calculated here as it was in Tables 1 and 2, so that "asbestos lung cancer" is not shown. It is of help in evaluating Table 4, however, to know that for white males in the United States at ages comparable to those in the cohort studied here, the proportions of total deaths that would be expected to be due to lung cancer for the period 1948-52, 1953-57 and 1958-63 are 3.2 %, 4.1% and 5.5% respectively. Thus, the proportions observed considerably exceed the proportions expected.

Table 4

DEATHS AT AGES 15-64 IN A COHORT OF 1137 WHITE MALES WORKING IN ASBESTOS TEXTILE PLANTS IN 1938-41

PERIOD OF DEATH	TOTAL DEATHS	DEATHS DUE TO: LUNG CANCER	ASBESTOSIS
1938-42	9	0	0
1943-47	30	1	1
1948-52	43	0	1
1953-57	37	3	4
1958-63	59	9	5
TOTAL	178	13	11

It would be useful to know if the occurrence of lung cancer and asbestosis was related to whether or not men were still employed in asbestos textile plants as of January 1, 1948. This is shown in Table 5 for 1,042 men at ages under 65 who were still alive on January 1, 1948. As shown in Table 3, 106 of these were still employed in asbestos textile plants while 995 had left that employment. For those still employed on January 1, 1948, 17 or 16% died during the next 15 1/2 years, while for the 995 not still employed, but apparently alive on January 1, 1948, 122 or 12% died within the next 15 1/2 years. Part of the difference in mortality relates to age differences as shown in Table 3. However, this does not account for all the mortality difference.

For those still employed a large number of asbestosis deaths occurred and it is, in fact, striking that in the period 1958-63 over half of the deaths (6 out of 11) were due to either lung cancer or asbestosis, with 2 out of 11 or 18% due to lung cancer. Recalling that lung cancer accounts for only about one out of every twenty deaths in the general population of males, and that asbestosis deaths are extremely rare, the importance of long-term exposure to high doses of asbestos is clearly demonstrated.

Among the group of men who left the asbestos products industry prior to January 1, 1948 and who may have had only brief exposure to high levels of asbestos dust, there is definitely an excess of lung cancer deaths some twenty years after these men were first observed, with seven out of 48 deaths or 15% due to lung cancer during the period 1958-63. On the other hand, there was only one death due to asbestosis in this cohort during this period.

From Table 5 it can be concluded that large doses of asbestos dust over fairly short periods of time are important in producing lung cancer but do not produce much asbestosis. Large doses over extended periods of time produce a great deal of asbestosis but with no appreciable increment in lung cancer. Men who left employment in an asbestos textile plant experienced an excess in lung cancer (15% of total deaths) some twenty years after the first exposure not much different from those who stayed (18% of total deaths). By contrast, men who left employment had relatively little asbestosis (3 out of a total of 122 deaths) as compared with those who stayed (7 out of a total of 17 deaths).

Table 5

DEATHS AT AGES 15-64 IN A COHORT OF 1,042 WHITE MALES WORKING IN ASBESTOS TEXTILE PLANTS IN 1938-41 AND ALIVE JAN. 1, 1948 BY EMPLOYMENT STATUS

Period of [illegible]	Total Deaths	Still employed in Asbestos Textile Plants Jan. 1, 1948			Not employed in Asbestos Textile Plants Jan. 1, 1948		
		Total Deaths	Lung Cancer	Asbestosis	Total Deaths	Lung Cancer	Asbestosis
[illegible]-52	43	2	0	0	41	0	1
[illegible]-57	37	4	0	3	33	3	1
[illegible]-63	59	11	2	4	48	7	1
[illegible]	139	17	2	7	122	10	3

DISCUSSION

Data presented here are consistent with those reported by Newhouse [illegible] showed little difference in lung cancer deaths between men with short, as compared with long, periods of asbestos dust exposure.[4] One reservation that needs to be made in interpreting data presented here is whether those persons who died of asbestosis would not have ultimately developed lung cancer, particularly in view of the apparently differing latent periods for these two diseases. The men who developed asbestosis among the group who remained in the industry may have, in fact, been protected from lung cancer by their long exposure and total dose.

Previous studies of the health effects of asbestos dust have no doubt been over simplified. Specific human responses must depend upon an interaction among the intensity of exposure, the duration of exposure and the time since significant exposure first occurred. Effective control standards cannot be developed until these relationships are better understood.

SUMMARY

1. A previous report on the relationship between asbestos dust and the development of two diseases, lung cancer and asbestosis, showed that the dose-response relationship differed for these two diseases. Small doses of asbestos dust appeared to produce about as much lung cancer as asbestosis while large doses appeared to produce more asbestosis than lung cancer.

2. Additional data are presented on the relative importance of duration of exposure as compared with the time since first exposure for these two diseases using a group of men whose level of exposure was probably fairly high.

3. 1,151 white males working in asbestos textile plants around 1940 were followed for deaths through June, 1963. This cohort was divided into two groups: those still working in asbestos textile plants in early 1948 and those who had left, but were still living in early 1948.

4. During the period 1948 to June, 1963 both groups experienced an increased mortality from lung cancer whereas deaths from asbestosis were confined almost entirely to men who remained in the plants.

5. It was concluded that large doses of asbestos dust over relatively short time periods are important in producing lung cancer but do not produce much asbestosis. On the other hand, large doses over longer periods of time do not cause much additional lung cancer, but a considerable increase in asbestosis.

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3. Enterline, P. E., Asbestos Dust Increments and Mortality from Two Diseases, Presented at the Second International Conference on the Biological Effects of Asbestos, Dresden, April 22-25, 1968.

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DISCUSSION

DR. COOPER: It is very interesting to see the extent to which Dr. Enterline's findings agree with the data presented by Dr. Molly Newhouse in Dresden.

DR. CRALLEY:

The next presentation will be by Dr. Paul Gross on the Studies on the Pathogenicity of Brake Drum Dust. We all know Paul Gross, personally. He has been introduced before, so without any further ado, Paul.

STUDIES ON THE PATHOGENICITY OF BRAKE DRUM DUST

Paul Gross, M. D. *

Thomson[1] of South Africa, in an effort to attach clinical significance to his finding of ferruginous bodies in the lungs of non-occupationally exposed urban dwellers, suggested that the presence of occasional small foci of mild interstitial pulmonary fibrosis in the lung bases of some of these people represents minimal asbestosis that developed in response to the inhalation of brake drum dust, a common pollutant in urban atmosphere. There is little doubt but that brake linings do get worn down in the stop-and-go traffic of large urban centers and inasmuch as these centers have large numbers of automotive vehicles, a large amount of brake drum dust may be generated.

However, it is incorrect to assume that the fibrous material embedded in the plastic of the brakeband is asbestos. As a result of the amount of heat to which the chrysotile had been subjected during embedding in plastic as well as during the friction against the steel brakedrum, the mineral lost its water of hydration and was converted into an anhydrous material called forsterite. This material no longer gives the x-ray diffraction pattern which identifies the crystals of chrysotile.

Although the brake drum dust contained no chrysotile, but rather forsterite, there were two questions which demanded answers:

1. Is the brake drum dust (minus its iron content) fibrogenic even though it no longer contained chrysotile?

2. Are the fibers of forsterite in the brake drum dust capable of producing ferruginous bodies?

We attempted to answer these questions by injecting this dust intra-tracheally into rats and hamsters.

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* See p. 22.

EDITOR'S NOTE: From a paper by Gross, deTreville, and Haller "Studies on the Origin of Pulmonary Ferruginous Bodies," in the Proceedings of the Johannesburg Pneumoconiosis Conference, Johannesburg, South Africa, April 23 - May 2, 1969, the following pertinent observation is added:

> "Of six ferruginous bodies isolated from hamster lungs injected with brake drum dust, all gave an electron diffraction pattern characteristic of chrysotile; this, in spite of the relative paucity of fibers in the dust by optical microscopy and the negative x-ray diffraction pattern of the powder. The six ferruginous bodies were, therefore, asbestos bodies... since 90-95% of the asbestos used in the United States is chrysotile, one would expect at least some of the bodies isolated from lungs of city dwellers to be chrysotile if these people were actually exposed to asbestos dust.
>
> "It is, of course, possible that in continuing this investigation and isolating ferruginous bodies from the lungs of many more people—and examining more than one body per lung—that asbestos fibers may be identified in their cores. Nevertheless, the failure to find a chrysotile core in any of the 28 consecutive ferruginous bodies examined is considered significant."

Also of interest is the following abstract of a paper by Gross, deTreville, and Haller, "Asbestos Versus Non-Asbestos Fibers, Ultramicroscopic Criteria," scheduled for publication in the AMA Archives of Environmental Health:

> "To classify usefully fibrous dusts inhaled by urban populations, it is suggested that they be categorized initially as asbestos or nonasbestos fibers. This would supply information sufficient for statistical significance and reduce analytical requirements, saving time and money.
>
> "The ultramicroscopic criteria of asbestos fibers are: ends which have profiles characterized by step-like interruptions up or down from each other, as seen at a magnification of 20,000 or 25,000 X under the electron microscope; a surface view (scanning electron microscope at the same magnification) characterized by parallel longitudinal lines that delineate the fibrils.
>
> "The ultramicroscopic criteria of nonasbestos fibers viewed at 20,000 or 25,000 X magnification are: ends which have uninterrupted linear profiles; a surface view devoid of longitudinal parallel lines.

"This differentiation of inhaled fibers is a screening procedure not free of error, particularly for fibers substantially thinner than 1μ in diameter. However, the error may be reduced by increasing magnification correspondingly."

Although identification of the central fiber of ferruginous bodies and of naked fibers has been accomplished by electron diffraction[2] and electron microprobe analysis,[3] these techniques are laborious and time consuming processes. Furthermore, for a large-scale investigation such as becomes necessary to obtain statistically reliable data, the extensive use of the above techniques could prove enormously expensive since it would tend to monopolize the costly equipment involved and the time of trained technicians.

Also, the need has existed for a method which would (1) facilitate acquisition of the necessary data, and (2) do so rapidly and economically. The purpose of this communication is to suggest a means for satisfying these needs.

To test the validity of these concepts, electron photomicrographs were made of the ends of several chrysotile, amosite, and crocidolite fibers as well as the ends of a similar number of glass, ceramic aluminum silicate, and silicon carbide fibers, all of which had diameters within the range of 0.1μ to 2.0μ. Without the observer's knowing the identity of the fibers on the photographs, the latter could be sorted easily, quickly, and correctly into asbestos and non-asbestos categories on the basis of the above concepts. A magnification of X 20,000 or X 25,000 appeared to be optimal for this purpose.

If a fiber is classified as asbestos, it may be desirable not only to confirm this, but also to determine whether it is of industrial origin (i.e., chrysotile, amosite, or crocidolite) or non-industrial origin (i.e., tremolite or actinolite). In such cases, use of electron diffraction and/or microprobe techniques would be required, but for a much smaller number of examinations, in all probability.

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DR. CRALLEY:

Speaking of ferruginous bodies and asbestos bodies, our first presentation, which will be on Methodology, will be given by Dr. Michael Utidjian. We met Dr. Utidjian earlier this morning, so I will turn the program right over to him.

PATHOLOGICAL STUDIES OF FERRUGINOUS BODIES:

METHODOLOGY

H. Michael D. Utidjian, M.D.*

Looking for ferruginous bodies with the light microscope, in thick sections of human lung, is literally like looking for the proverbial needle in a haystack. Examining smears of lung juice obtained by squeezing or scraping fresh post-mortem material is only a little more sensitive a method.

Ideally, if one could discover a solvent which dissolved all lung tissue, blood clot and exudate, and left only the ferruginous bodies intact (inevitably together with any other insoluble mineral matter, inorganic carbon, etc.) it would be possible to rapidly extract all the ferruginous bodies that a lung might contain.

Domestic bleach, the active constituent of which is 5% sodium hypochlorite, while not the ideal solvent, certainly approaches it. It has been known for many years that a solution of sodium hypochlorite will digest and liquefy blood clot and many tissue proteins. Fortunately it attacks the ferritin or ferritin-like protein coating of ferruginous bodies only very slowly. Also fortunately it digests the denatured proteins of formalin-fixed lung tissue only a little more slowly than fresh lung. This is the basis of the technique of extracting and concentrating ferruginous bodies from human post-mortem lungs, described in full detail in my paper[1], of which reprints have been distributed to you this afternoon.

Thin slices of formalin-fixed lungs are floated on undiluted domestic bleach for approximately 24 hours. The finer structures of the lung are preferentially digested, leaving a shrivelled skeleton of the interlobular fibrous septa, arterioles and larger blood vessels. Any inorganic matter and any ferruginous bodies present in the lung fall out and form a sediment on the bottom of the container. This sediment is invariably a mixture of all the retained inhaled inorganic materials present in the lung at death, including any ferruginous bodies which may be present. These inorganic materials typically include carbon or carbonaceous material, amorphous mineral matter, naked inorganic

* See p. 3.

fibers—both natural and man-made, and a varying abundance of ferruginous bodies. A good separation of the carbon from all the other denser materials is quite simply achieved by emulsification suspension in an alcohol-water-chloroform medium, followed by centrifugation.

Chloroform having a specific gravity of 1.5 and being almost immiscible with water forms a very distinct lower layer, at the bottom of which a small solid deposit of denser inorganic matter, including any ferruginous bodies present, but very little free carbon, is formed. This deposit has only to be resuspended in water, smeared on a slide, and examined unstained under the light microscope at medium power, and any ferruginous bodies are very easily seen—in all their pristine beauty.

Once seen, the ferruginous bodies can, with skill and patience, be aspirated into a glass micropipette, under direct vision microscopy, with the use of a conventional micro-manipulator. Thence they can be transferred individually onto a suitably coated copper grid, for electron microscopy. We found that the ferruginous bodies were remarkably robust and would stand a fair amount of micro-manipulation without visible structural damage.

The possibility of quantitative estimation of the total number of ferruginous bodies in a human lung, by the application of this general technique, was explored. It would take a very long time to totally digest an entire human lung, fresh or formalin-fixed by this method, and moreover there is strong evidence to suggest that if ferruginous bodies are exposed to the action of the bleach for more than 24 hours they themselves will be attacked, and their coating destroyed. An attempt was made to prepare a homogenate of lungs, both fresh and fixed, by a Waring blender, and then to digest an aliquot portion of this homogenate by the same technique. However, it became obvious that no ferruginous bodies were surviving the severe mechanical vibratory forces imposed by the blender, so this approach was abandoned also. However, a thin full longitudinal slice from each lung from apex to base, can be weighed wet, and the combined weight of the two slices related to the original wet weight of the intact lungs. A longitudinal slice should contain a fairly representative concentration of ferruginous bodies, as compared to the whole lung. Such a slice, if no more than 2-3 mm. thick, and if turned over as it floats on the surface of the bleach, from time to time, so that both cut surfaces are attacked, should yield practically all the ferruginous bodies it contains, in the space of 24 hours. A visual count may then be made, under medium power, of the total number of bodies present in smears prepared from an aliquot portion of the total suspension. Although there are obvious sources of error, and approximations, in this method, it is thought to be the best means of quantitative estimation available at this time.

In our study of last year, in Pittsburgh, a constant wet weight of fixed lung tissue was processed from each lung specimen obtained. The volume of the final suspension was kept constant, and one standard drop of the well-shaken suspension was used to prepare each smear, and five smears from each subject were examined and counted. Three "abundance categories" were arbitrarily defined, for comparative purposes. These were: (1) No more than one body in the five smears; (2) Two to five bodies in any one smear; and (3) More than five bodies in any one smear.

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DISCUSSION

DR. deTREVILLE: To me, the most striking observation arising out of the use of the method described by Dr. Utidjian, which is described in detail in the publication to which he has referred, is that, given sufficient lung tissue for digestion, it should be possible to find at least one ferruginous body in everyone who comes to autopsy.

DR. CRALLEY:

Our next presentation is on Instrumentation by Martin N. Haller of Mellon Institute. He has a little different background than the speakers who have appeared up until now.

Mr. Haller received a B.S. in Physics from the University of Pittsburgh in 1951. After graduation, he spent ten years on an Air Force Cambridge Research and Development Program for High Temperature Electronic Circuitry. In 1961 he joined the staff of the Mellon Institute of Carnegie-Mellon University working on research services; and since that time has provided electron microscopy services to the Institute and done research in this area. He will report now on some of the research he has done.

PATHOLOGICAL STUDIES OF FERRUGINOUS BODIES: INSTRUMENTATION

Martin N. Haller*

Fibers obtained from the lungs of twenty-eight general population autopsies, male and female, were examined by electron microscopy and electron diffraction techniques in an attempt to identify the fiber core material. Since these bodies were typical "asbestos" bodies in shape (dumbbell shaped), it was thought that they were probably chrysotile, amosite, or crocidolite, with the first named mineral most likely to be that present (it is used in 90% of all American asbestos manufactured products).[1] Because chrysotile fibers appear to be hollow in the electron microscope,[2] they are easily identified by inspection. None of the samples examined in this study appeared to be hollow, although all possessed areas free of extraneous material such as ferritin, and could, therefore, be examined for this feature. The other common forms of asbestos are opaque to electrons, so it was concluded that the fibers examined here were one of these. The fibers were next manipulated in such a way as to yield their characteristic electron diffraction patterns, so that measurements of interplanar crystal lattice spacings could be made. This technique offers unique advantages for these fibers, since selected small areas (down to 0.01 square micron) can easily be obtained in modern electron microscopes. Work with known "standard" samples of chrysotile, amosite, and crocidolite showed that useful diffraction patterns could be obtained from fiber areas as small as 500 by 500 A, and as large as 5000 by 5000 A. In addition, for the three minerals of interest here, typical "layer line" diffraction patterns are obtained if the fiber axis is perpendicular to the electron beam. Measurements of the diffraction patterns obtained (to an accuracy of $\pm$ 1%) showed that none of the fibers examined

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were identifiable as one of the three forms of asbestos mineral cited above. In particular, none was chrysotile, since this mineral, due to its hollow structure, has a unique and readily identifiable diffraction pattern.[3] Considering the wide range of chemical composition found in the other fibrous minerals, it was concluded that positive identification of these fibers required a certain minimum knowledge of their chemical composition (possibly by electron microprobe measurements), and further electron diffraction information to allow construction of probable unit cells. The results of this work can thus be stated as:

1. The fibers were crystalline (i.e., probably mineral).
2. The fibers were long chain silicates.
3. The fibers examined here were not crysotile asbestos.

EDITOR'S NOTE: The abstract of a paper by Gross, deTreville, and Haller, "Pulmonary Ferruginous Bodies in City Dwellers, A Study of Their Central Fiber," which appeared in the AMA Archives of Environmental Health 19: 186-188, August, 1969, and which effectively summarizes the significance of Mr. Haller's observations, follows:

> "Chrysotile, which comprises more than 90% of the asbestos used in this country, has a characteristic electron diffraction pattern because of its unique, hollow, tubular, crystalline structure, as seen under the electron microscope.
>
> "On the basis of the electron diffraction pattern, chrysotile was decisively excluded as a constituent of the cores of all 28 ferruginous bodies isolated from lungs of urban dwellers not occupationally exposed to asbestos.
>
> "This exclusion is considered highly significant because if the ferruginous bodies in the above city dwellers had been caused by the inhalation of asbestos dusts, then some of the cores should logically be composed of chrysotile."

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DISCUSSION

FROM THE AUDIENCE: Have any ferruginous body central cores that have been obtained from any of Dr. Gross' animals been studied to see if their patterns have been altered?

DR. GROSS: Yes, we have identified chrysotile as the central core of ferruginous bodies experimentally produced in hamsters from brake drum dust.

FROM THE AUDIENCE: As far as the fibers that had been converted to amorphous form, would they not give this pattern?

MR. HALLER: No, they would not give a diffraction pattern at all, nor would the cores of ferruginous bodies formed from filamentous glass.

FROM THE AUDIENCE: You said that you might have to use the electron microprobe. Looking at your electron diffraction patterns, which are quite good, I wonder what microprobe analysis might add?

MR. HALLER: The microprobe, by determining qualitatively and quantitatively the atomic composition, can help identify unknown fibers. The resolution depends upon the type or model of microprobe used. These fibers are not large to begin with; so they must be located, and the probe resolution must be adequately high.

DR. J. P. LEINEWEBER (Johns-Manville Research Center): The bare regions of the central core were a half micron by a micron. That would be good enough for microprobe.

MR. HALLER: Let me say that the philosophy behind the initial effort here was to do this as simply as possible in an effort to find a technique that would quickly and positively identify the core of any of the ferruginous fibers.

DR. COOPER: The one thing that you definitely have shown is that they are not chrysotile. I think that is obvious.

MR. HALLER: I think that is absolutely true, without question. I might add that by electron diffraction, it has not been possible, with our existing equipment, to distinguish among the various asbestotic minerals, other than chrysotile, because they are all so similar. We shall probably have to rely on chemical analysis; and hence, on the microprobe, in carrying forward our studies in the future.

DR. CRALLEY:

Our next speaker is going to talk about some of the Basic Considerations in the Pathological Studies of Ferruginous Bodies. Many of us know Dr. John Davis. Just a couple of interesting sidelights: he is an associate of Dr. John Beatty, who many of us know and deeply respect. Another interesting sidelight: he broke the equivalent of the sound barrier in Cambridge, he was the first person to receive a fellowship paid by an industrial supported group, which is the Asbestos Research Council, if I am not mistaken. This is quite an accomplishment and an attest to the esteem to which they hold him. It is indeed a pleasure to have Dr. Davis discuss our next subject.

PATHOLOGICAL STUDIES OF FERRUGINOUS BODIES: - BASIC CONSIDERATIONS

John M. G. Davis, Ph.D.*

Before the advent of electron microscope studies comparatively little was known about the structure and methods of formation of asbestos bodies. These structures were first observed by Fahr and Feigel in 1914,[1] but they were not immediately associated with asbestos exposure. They were later described by other workers including Cooke in 1924[2] and Stewart and Haddow in 1929.[3] Gloyne in 1932[4] gave detailed descriptions of the very pleomorphic gross anatomy of asbestos bodies, and also demonstrated that each body contained a central core of asbestos dust surrounded by a coating containing both iron and protein material. Electron microscope studies, commenced in 1962 (Davis 1965),[5] and still in progress, have given a great deal of new information which is best summarized as follows:

1. Asbestos body formation is an intracellular process and the bodies are formed mainly in giant cells, although single macrophages and fibroblasts may be involved.

2. The body coating consists largely of small dense granules approximately 60A° in diameter which are believed to be Ferritin.

3. The coating is usually laid down as a single layer, but sometimes there are several layers of varying thickness and density.

4. The outer layers of a few bodies consist of fine filaments about 60A° in diameter that appear to be Apatite Crystals.

5. Only a small proportion of asbestos fibers ever become coated.

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6. Only fairly long fibers form true bodies, i.e., fibers of 5 microns and up. Very small dust particles rarely become associated with Ferritin granules.

7. A body can form in a cell while other fibers in the same cell remain uncoated.

8. The body is often separated from the cell cytoplasm by a membrane but this is not always present.

From this point it was decided to look for new information about the chemistry of asbestos body formation in two directions. It was planned to examine old tissues in which bodies had been formed for a long time, and tissues of young animals that had contained dust for a few days only and might be expected to show the earliest stages of body formation. The early electron microscope studies of asbestos body formation were done with guinea pig lung tissue that had been dusted by inhalation. Although many bodies formed in the lung tissue during the first 6-8 weeks they were widely scattered and it was difficult to find many of them for electron microscope study. It was decided, therefore, to use the technique of intrapleural injection in subsequent studies. When asbestos dust is injected into the pleural cavity of guinea pigs, a large granuloma is produced within a few days which consists largely of giant cells. Large numbers of asbestos bodies form in these cells and can be recognized as little as two weeks after dust injection. Their numbers increase up until about six weeks after which they apparently remain constant. The granuloma shows little further structural change until about a year after dust injection, although after this time the giant cells are gradually replaced by fibrous tissue which ages until by eighteen months after injection the granuloma is replaced by a mass of almost acellular collagen. When this happens the asbestos bodies are left behind among the collagen fibrils and so are all uncoated particles of asbestos dust. Eventually many of the fibrous masses begin to calcify, and calcified pleural plaques are produced which are very similar to those found in cases of human asbestosis.

When calcification occurs in the old guinea pig lesions a very strange picture is seen with the light microscope. The collagen fibers become interlaced with a network of strands, about 2-3μ in diameter, which stain densely with hematoxylin. Among these strands, apart from genuine asbestos bodies, a number of quite large laminated spheres can be seen which are up to 30-40μ in diameter, and a Perl's stain reveals that some of these contain a little iron.

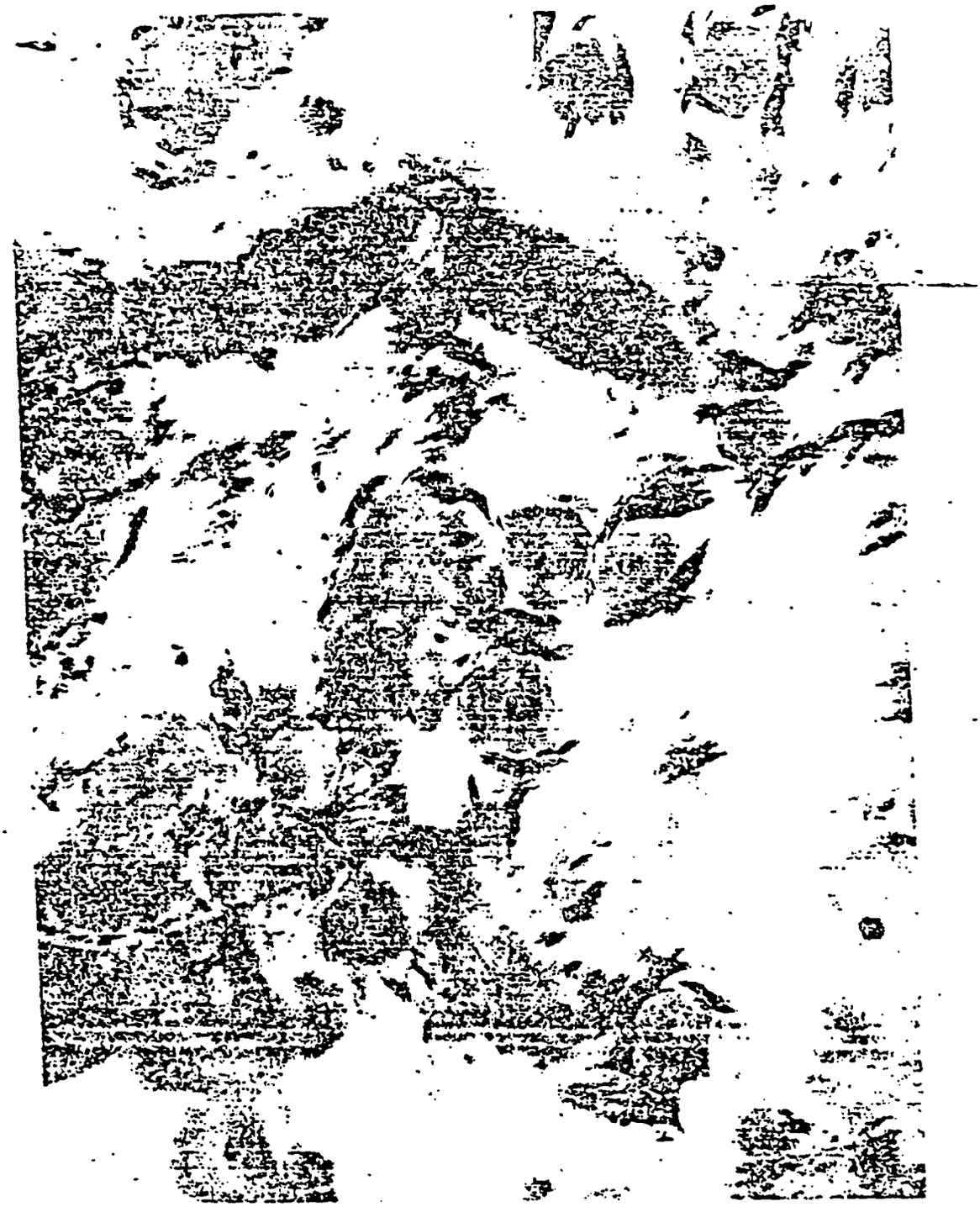
In the electron microscope it was found that large amounts of asbestos dust still remained in the old fibrous lesion, and that the hematoxyphil network was produced by all this dust becoming coated with a thick layer of material that appeared to consist of small granules 40-50A

in diameter, but which were of much lower density than the ferritin granules of normal asbestos bodies (Figures 1 and 2). In some cases, especially in the laminated spheres, some ferritin granules were present, mixed with the lower density granules, when the contrast between the two was quite apparent. When calcification occurred the apatite crystals were first seen around the periphery of the coated asbestos fibers, but eventually they were found throughout the entire tissue.

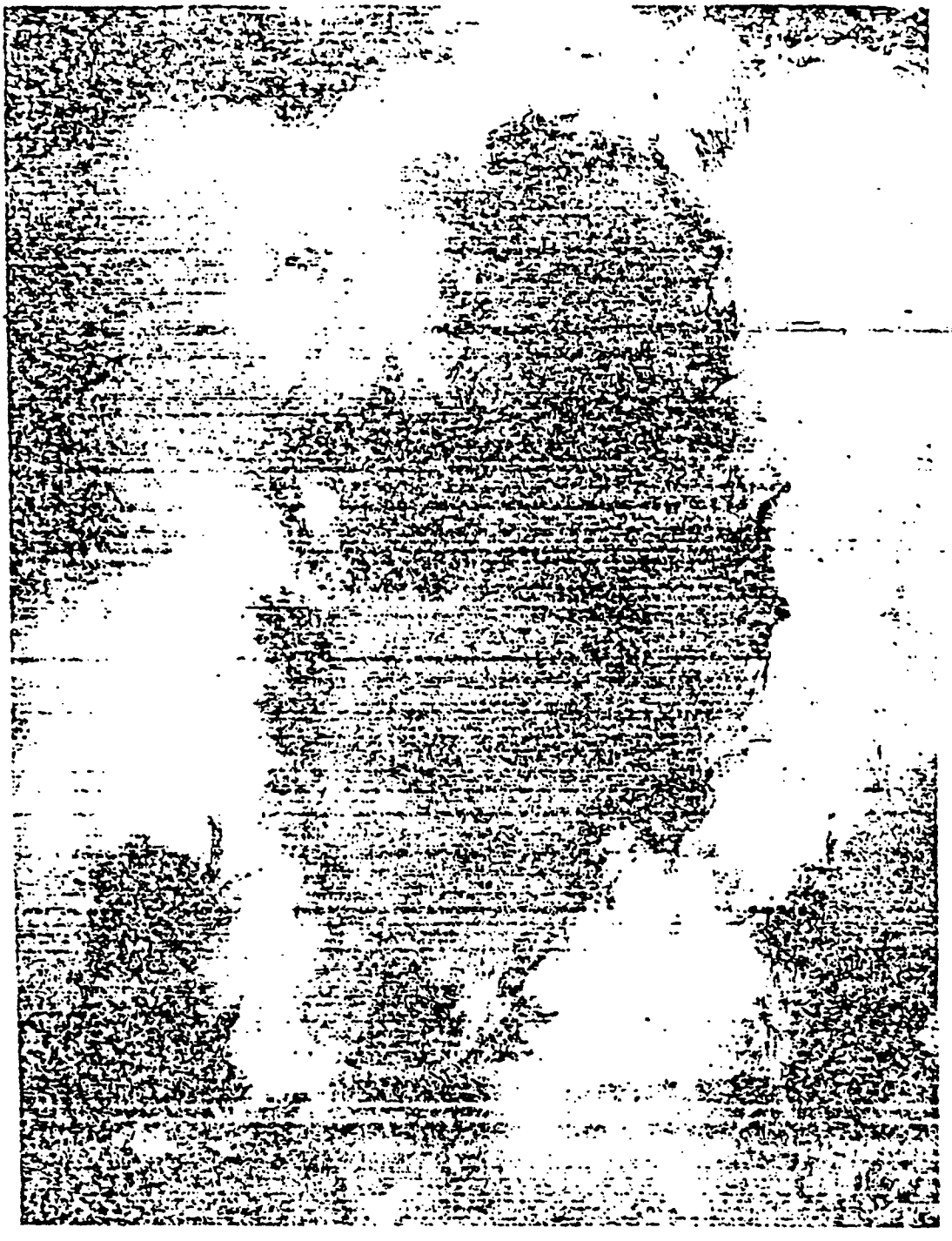
These findings are important from two points of view. First, when it was realized that only a small percentage of dust ever became coated to form asbestos bodies, it was difficult to decide if this was due to a few fibers having a different chemical composition than the rest, or whether only a few fibers found themselves in a suitable chemical environment for coating to occur. The finding that all dust fibers become coated with something in early calcification certainly suggests that it is the environment that is important. Moreover, the fact that the coated dust in these areas is really quite like genuine asbestos bodies, may indicate that the important elements of the localized environment needed for asbestos body formation and the generalized environment of calcifying tissues, may be very similar. A great deal of information is certainly available on the chemistry of tissue calcification and although some of this is contradictory most workers appear agreed that one important factor in tissues about to calcify is that there is a great increase in acid mucopolysaccharides. It seemed likely, therefore, that the material coating of the asbestos dust in the calcifying lesions might be acid mucopolysaccharide, and this was confirmed by histochemical staining. The material proved to be P.A.S. positive, showed metachromasia with toluidine blue, and actively took up colloidal iron in Hale's staining technique. This last method is not only the most specific of the three for acid mucopolysaccharides, but it may indicate the method of formation of asbestos bodies. If the dust were coated first with acid mucopolysaccharide, this material would automatically become impregnated by any colloidal iron in the area, and the most abundant source of this material would be ferritin. In cellular tissues the supply of ferritin would be good, but in areas of acellular avascular collagen the supply would probably be very small and this could account for the fact that the dust coating found in the calcifying tissues contained little iron.

If this suggestion were correct, then at the start of the experiment it should be possible to demonstrate dust fibers coated only with mucopolysaccharide before iron impregnation has begun. Present studies involve the examination of dust granulomas during the first few days after dust injection and it has indeed been possible to find several asbestos fibers coated with a thick layer of low density material in which ferritin impregnation has only just begun (Figure 3). These studies are being continued.

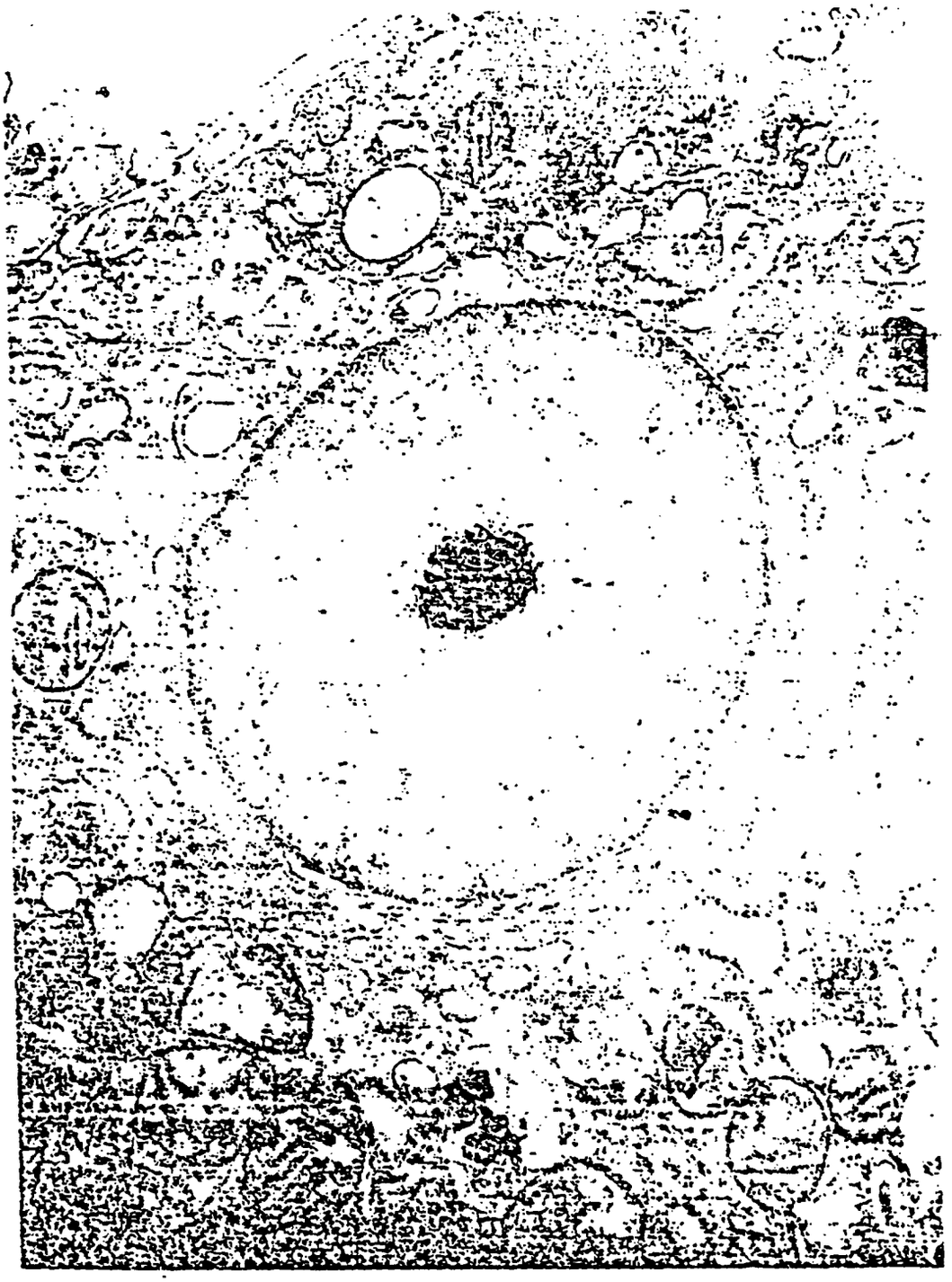
Fig. 1



An area of old fibrous tissue from a guinea pig pleural cavity. The fibrous tissue contains much chrysotile asbestos dust which has all become coated with a thick layer of acid mucopolysaccharide. The area is just beginning to calcify and small masses of apatite crystals can be seen around the coated dust. --Magnification X 25,000



A high magnification picture from the same area as Fig. 1. A fine granular structure can be seen in the acid mucopolysaccharide material that surrounds the chrysotile dust. It can be seen that when apatite crystals are first deposited in the earliest stages of calcification, they appear in close contact with the surface of the mucopolysaccharide. -- Magnification X70,000



Part of a giant cell produced in a guinea pig pleural cavity in response to an injection of chrysotile asbestos dust ten days previously. The cell cytoplasm contains a bundle of chrysotile crystals surrounded by a thick layer of low density material. This material is just beginning to be impregnated by small dense granules which probably represent ferritin material. -- Magnification X 36,000

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