DISTRIBUTION OF MINERAL PARTICLES AND FIBERS IN THE LUNG AFTER EXPOSURE TO ASBESTOS DUST

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AS THE result of experimental work on the production of asbestosis in animals, Vorwald and associates [1] concluded that typical peribronchiolar fibrosis was produced when the particle length of the inhaled asbestos dust lay between 20 and 50 μ. The asbestos caused fibrosis by the mechanical action of the fiber on the lung tissue. When the animals were withdrawn from the dusty atmosphere, the lesions did not progress but rather tended to regress. Asbestosis bodies, formed around inhaled asbestos fibers, were found to be inert as fibrogenic agents when they were injected into the trachea. The length of exposure to dust necessary to induce typical fibrosis by inhalation was between one and two years.

In the series of cases which we have studied and reported on before (Knox and Beattie [2]), we noted that the time interval between the first exposure to asbestos dust and the appearance of asbestosis in autopsy specimens was not less than 12 years. It appeared to us that the long interval between first exposure and the appearance of typical fibrotic changes indicated that the mechanism for the production of human asbestosis differed from that responsible for the experimental type. If the mere presence of asbestos particles within a critical size range was the essential factor in the production of human asbestosis, it would be difficult to explain why so many persons escape any asbestotic change even when exposed for more than 30 years. It is generally agreed that soon after inhalation the majority of the asbestos fibers become included in the asbestosis bodies. The experiments of Vorwald and his co-workers suggested that these structures are inert but the bodies do not remain as intact structures indefinitely. With the passage of years they become "weathered," eroded, segmented, and finally fragmented (Cooke,[3] McDonald,[4] Gloyne,[5] Beger,[6] Gloyne [7]). It was thus possible that in man the fibrotic changes in the lung might be related to this process of disintegration of the asbestosis body.

We have noted already that the degree of asbestosis appeared to be correlated more closely to the sum of the years of exposure to dust and the years of survival after the last exposure than to the total mineral content of the lung parenchyma (Knox and Beattie [2]). This finding suggested that, if disintegration of the

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asbestosis bodies was an essential factor in the production of fibrotic change, then there ought to be a change in particle-size distribution in the direction of a fall in the numbers of the larger particles as survival time increased. The formation of large numbers of smaller sized particles, however, might not be apparent in the counts, if the rate at which such particles were removed from the lungs kept pace with their rate of production. On the other hand, if the rate of production were greater than the rate of removal, then it might be possible to determine if fibrotic change were correlated with a rise in the small particle-size counts.

MATERIAL AND METHODS

The series of cases studied was the same as that reported in our paper on mineral content of the lungs (Knox and Beattie[2]). There were 27 workers, 21 men and 6 women. The duration of exposure to asbestos dust varied between 5 and 33 years, and the length of time from the last exposure to death ranged from less than 1 year to 21 years. The cases have been arranged in order of increasing survival time. The exposure and survival times are given to the nearest year. Asbestosis has been graded into three degrees according to the pathological reports based on the histological appearances found in the lung parenchyma.

Particle-size distributions were determined on the incombustible and acid-insoluble residues of lung parenchyma prepared by the method of King and Nagelschmidt.[8] Pooled samples of these residues were made from each lung and, after mixing, small aliquots were taken. After being moistened with a wetting agent, the aliquots were suspended in an appropriate volume of water, care being taken to prevent flocculation and the inclusion of air bubbles. A drop of the suspension was then placed on a microscope slide and a drop of polyvinyl alcohol added to the suspension. Fluid was then dried off on an electric hot plate. Five slides were prepared from each aliquot and four aliquots prepared from each pooled sample. The slides were placed in a microprojection apparatus and the image of the particles projected on a sheet of paper at a magnification of × 1,000. Light-field illumination was used. Fifty fields were counted on each slide. Care was taken to obtain a suspension sufficiently dilute to ensure accurate counting. The number of particles in each of the following size ranges was counted:

Less than 5 μ	Between 26 and 35 μ
Between 5 and 15 μ	Between 36 and 45 μ
Between 16 and 25 μ	Over 45 μ

Light-field illumination was chosen to facilitate counting of large numbers of fields. It was realized that with this method very small particles would not be counted, and consequently the values given for counts in the smallest size range would be less than the true values.

To facilitate comparison of the different particle-size distributions, the number of particles in each size range is expressed as a percentage of the number of particles found in the size range 16 to 25 μ in each lung specimen.

OBSERVATIONS

The particle-size distributions in the residues from the lungs of the 27 cases are given in the Table. As the residues from which the distributions were determined were pooled samples from different areas of the lung parenchyma, it was possible that such pooling might introduce considerable errors if the particle-size distribution varied significantly from area to area. It was found from a study of particle-size distributions from samples representing different areas of the lungs from four cases that particle-size distributions did not vary significantly from area to area within the same lung. The mean distributions given in the Table are therefore representative of the distribution within the whole lung.

Particle-Size Distributions Expressed as Percentages of Count in the 16 to 25 μ Range

Case No.	Sex	Total Exposure Time, Yr.	Survival Time, Yr.	Asbestosis, − +	Mean Particle Counts: Less Than 5 μ	5-15 μ	16-25 μ	26-35 μ	36-45 μ	Over 45 μ
3	M	26	0	++	364	193	100	36	21	0
23	M	28	0	+	458	217	100	42	0	0
26	M	20	0	+	510	290	100	51	15	6
9	M	11	0	−	612	389	100	62	18	12
17	M	12	0	+	394	281	100	79	9	2
25	M	8	0	−	627	329	100	38	17	21
12	F	32	1	−	501	257	100	48	0	17
2	M	27	2	+++	689	387	100	33	0	9
5	M	28	2	+	433	225	100	50	17	5
21	F	33	2	−	573	381	100	14	2	6
4	F	14	2	+	627	296	100	62	20	5
19	F	8	2	+	522	359	100	41	8	7
6	M	22	3	+	421	325	100	51	25	17
10	M	9	3	−	510	322	100	50	20	6
14	M	27	4	+	517	281	100	46	18	2
22	M	7	6	−	486	369	100	31	12	0
1	M	23	7	+++	610	487	100	0	0	0
27	M	21	8	+++	786	521	100	22	2	0
20	M	25	8	+++	829	644	100	11	4	0
8	F	27	8	+++	898	591	100	4	1	1
13	M	27	8	+	496	321	100	0	0	0
7	F	6	9	+	611	418	100	0	2	0
28	M	5	11	−	587	292	100	0	0	0
11	M	22	14	+++	720	599	100	0	0	0
24	M	19	14	+++	1,006	707	100	0	0	0
15	M	14	17	−	529	386	100	2	0	0
16	M	10	21	+	647	411	100	9	0	0

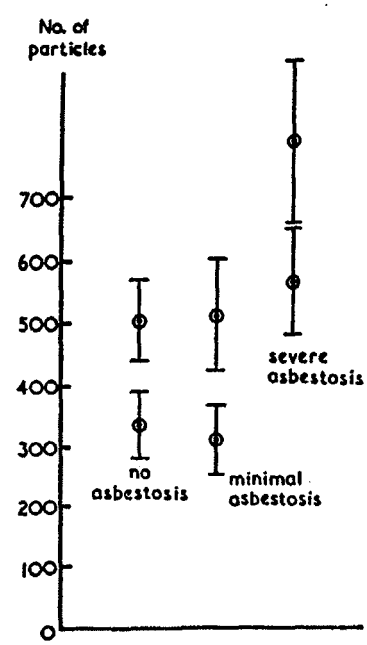

Chart 1.—Mean particle counts in the less than 5 μ and the 5 to 15 μ ranges in cases with no asbestosis and in those with minimal and severe asbestosis. The standard deviation for each mean value is given by the verticle line through this value. These counts were made on the incombustible and acid-insoluble residue of lung parenchyma.

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'article Counts			
25 μ	26-35 μ	36-45 μ	Over 45 μ
90	36	21	0
00	42	0	0
30	51	15	6
00	62	18	11
00	79	9	2
00	38	17	21
00	48	0	17
100	33	0	9
100	50	17	8
100	14	2	6
100	62	20	5
100	41	8	7
100	51	25	17
100	50	20	0
100	46	18	2
100	31	12	0
100	0	0	0
100	22	2	0
100	11	4	0
100	4	1	1
100	0	0	0
100	0	2	0
100	0	0	0
100	0	0	0
100	0	0	0
100	2	0	0
100	9	0	0

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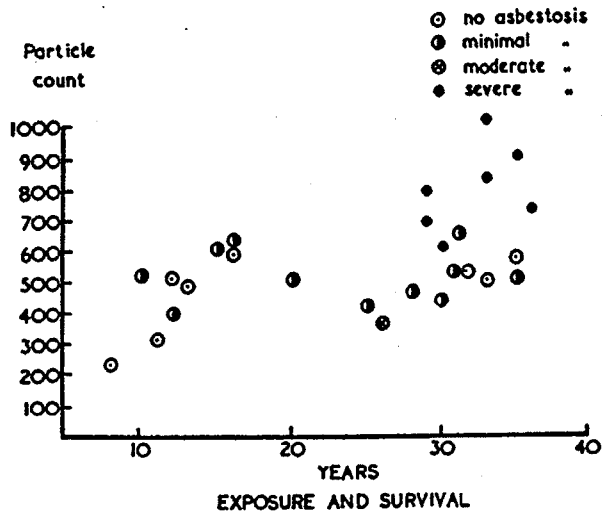
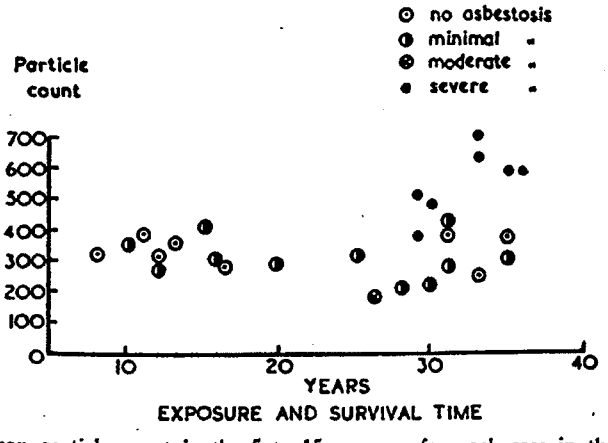
5 to 15 μ ranges in cases with no standard deviation for each mean its were made on the incombust-

Relation of Particle Size to Degree of Asbestosis.—In those cases which showed severe asbestotic changes in the lung parenchyma, the mean number of particles less than 5 μ in length was 791 (S. D. ± 134, S. E. ± 55). In the size range 5 to 15 μ the mean count was 562 (S. D. ± 106, S. E. ± 43). Cases with minimal



art 2.—Mean particle count in the less than 5 μ range for each case in the series plotted the sum of the exposure and survival times.



art 3.—Mean particle count in the 5 to 15 μ range for each case in the series plotted the sum of the exposure and survival times.

sis gave a mean count of 512 (S. D. ± 85, S. E. ± 26) in the less than 5 μ and 311 (S. D. ± 57, S. E. ± 17) in the 5 to 15 μ range. Cases with no sis gave corresponding counts, as follows: less than 5 μ, 503 (S. D. ± 66, 23) and from 5 to 15 μ, 332 (S. D. ± 45, S. E. ± 16). The results are graphically in Chart 1.

conclusive evidence that this is so, other than the fact that in these cases, as we have shown already, both the hilar and pleural and subpleural tissues contain much mineral material (Knox and Beattie [2]).

The association of high counts in the small particle ranges with severe asbestosis and the absence in three of these cases of any fibers with a greatest length in excess of 26 μ suggest that human asbestosis, at least of the severe type, is not due to the mere presence within the lung of particles with greatest lengths within a critical size range of 20 to 50 μ. The high counts of such critical size fibers in many of the cases with no asbestosis or minimal fibrosis and with long exposure and short survival times would suggest that the mechanism for the production of clinically recognizable asbestosis differs from that which induces peribronchiolar fibrosis in experimental animals.

Our findings thus indicate that a rise in the numbers of small mineral particles derived presumably from the breakdown of asbestosis bodies is associated with severe fibrotic changes in the lung parenchyma. This implies that either these particles or some other product of the breakdown of the bodies can exert a fibrogenic effect on lung tissue. If these products are removed as rapidly as they are formed, then either no asbestosis develops or a minimal degree of change occurs. It is suggested above that a reduced rate of removal of these products may be due to partial blockage of the drainage routes from the lung, i. e., either toward the lung hilus or toward the pleural surface. It is conceivable that any pathological process which would cause any inflammatory change in the hilum or in the lymph nodes into which the pleural lymphatics drain might cause a further reduction in the drainage rate and might precipitate the onset of severe fibrotic changes. Cardiac decompensation too might be a factor in the precipitation of these changes.

SUMMARY

The particle-size distributions in the incombustible and acid-insoluble residues from the lungs of 27 persons who had been exposed to asbestos dust were determined.

The number of particles with greatest lengths in excess of 26 μ was considerable up to the eighth year after the last exposure to asbestos dust and then sharply fell.

The number of particles within the size ranges of 5 μ and less and between 5 and 15 μ remained constant over a very long period in those cases which showed no sign of asbestosis or minimal fibrotic change. The cases of severe asbestosis showed a significant rise in the numbers of such particles.

It is considered that the mechanism which is concerned with the production of human asbestosis is not the same as that which is responsible for the production of asbestotic changes in experimental animals exposed to high concentrations of asbestos dust. The appearance of such changes appears to be related to the breakdown of asbestosis bodies which may liberate some fibrogenic agent.

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micronodules. A number of shadows indicated emphysematous lesions with enlarged heart. Hilar shadows suggestive of anthracosilicosis were lacking. Signs of old healed tuberculosis were found in 2 of the 100 miners.

The conclusion is that breathing dusty air in the mines of the lignite field of Provence may at worst set up after many years a slight diffuse fibrosis of no significance.

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AXIAL TOMOGRAPHY IN THE STUDY OF ADVANCED SILICOSIS. G. BONTE, E. BALGAIRIES, G. TRINEZ, and G. DECLERQ, Rev. méd. min. **6**:36-48, 1953.

The authors describe how during the past five or six years tomography of the chest has been found of value in locating pulmonary lesions. Now they state that by moving the subject in relation to the direction in which the x-rays are falling so as to travel through the chest to the film a three-dimensional view of any lesion may be obtained. The exact way in which these movements of the subject in relation to the x-rays can be carried out is described and illustrated in detail. This form of tomography is named stratigraphy, or axial-transverse tomography. In cases of advanced massive silicosis, a better picture is obtained of the exact size of the lesion and of its location with regard to the large blood vessels and the heart. This procedure allows a much better definition of the opacities seen. It may, of course, be equally useful when examining abdominal lesions.

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PRESENCE OF ASBESTOS FIBERS IN URINE OF WORKERS EXPOSED TO ASBESTOS HAZARD. V. WYSS, Rass. med. indust. **22**:55-56, 1953.

In urinary sediment of two asbestos workers asbestos fibers were seen; the same finding was detected in urine of two female patients, suffering from asbestosis, who had left their work seven years before.

BIOL. ABST. [INDUST. HYG. DIGEST].

DERMATITIS FROM PHENOLIC-CRESOLIC RESINS. R. LUVONI, Rass. med. indust. **22**:333-336, 1953.

The effect of contact of foundry workers with phenolic-cresolic resins was investigated. Eczematous dermatitis accompanied by painful itch and formation of blisters was recognized in several workers who handled the resin-sand mixture used to make molds for molten metal. Removal of the affected persons from the resin handling resulted in the disappearance of the skin affections. Since only half of the persons working in the foundry presented similar skin conditions, a form of allergy is thought to have been responsible.

CHEM. ABST. [Indust. Hyg. Digest].

Industrial Toxicology

STUDIES ON PATIENTS SUFFERING FROM ACUTE EXPOSURE TO VAPORS OF NICKEL CARBONYL. F. WILLIAM SUNDERMAN and JOHN F. KINCAID, J. A. M. A. **155**:889-894 (July 3) 1954.

Clinical observations are reported on 36 persons accidentally exposed to the vapors of nickel carbonyl. Two patients died, and many of the others were critically ill. The concentrations of nickel in urine and blood were determined in samples obtained from exposed persons. The authors' studies indicate that the nickel concentrations in urine and blood are increased many-fold above normal after exposure. Increase in the concentration of nickel in urine may be correlated with the severity of exposure. Dimercaprol (BAL) was administered to 32 exposed persons, 31 of whom survived. Insofar as the authors are aware, this is the first report of the use of dimercaprol in the treatment of nickel carbonyl poisoning. The administration was attended by an increased excretion of nickel in urine and a marked decrease in the concentration of nickel in blood. It is the authors' considered opinion that the administration of dimercaprol was beneficial in practically all cases and may have been lifesaving in several.

FROM THE AUTHORS' SUMMARY.