Reprinted from the Archives of Environmental Health
August 1969, Volume 19

K-28126-((132) R

REPRINT CHEMT

Pulmonary Ferruginous Bodies in City Dwellers

A Study of Their Central Fiber

Paul Gross, MD;
Robert T. P. deTreville, MD, D Sc;
and Martin N. Haller, Pittsburgh

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.

IT has recently been suggested that the prevalence of ferruginous ("asbestos") bodies in the lungs of city dwellers not occupationally exposed to asbestos was largely dependent upon the method and diligence employed in searching for the ferruginous bodies.[1]

The reported prevalence of the positive cases was represented to range from 30% to 70% of the hospital deaths investigated; whereas, by digesting some of the lung tissue, a 97% prevalence of lungs positive for ferruginous bodies was found among randomly selected autopsied hospital patients in Pittsburgh.[1]

Ferruginous bodies, which are indistinguishable from those produced by asbestos dust, were recently demonstrated in lungs of hamsters injected intratracheally with

Submitted for publication Feb 29, 1969; accepted March 17.

From the Industrial Hygiene Foundation of America, Inc (Drs. Gross and deTreville), and the Mellon Institute (Mr. Haller), Pittsburgh.

Reprint requests to Industrial Hygiene Foundation of America, Inc., 5231 Centre Ave, Pittsburgh 15232 (Dr. deTreville).

fibrous dusts other than those of asbestos.[2] In view of this demonstration, it would seem proper to ask whether the "asbestos" bodies found in city dwellers have been evoked by the inhalation of asbestos dust or the inhalation of fibrous dust of other compositions.[3]

Based on the assumption that there is a substantial contamination of urban air by asbestos dust, it has been suggested that the source of such dust is from the brake lining of automobiles, the weathering of asbestos cement products (shingles and tiles), as well as from insulation used in the building construction industry.[4] Inasmuch as 90% or more of the asbestos used in the United States is chrysotile,[5] and since very little of other types of asbestos is used in the above-named products, the major component of the asbestos dust that is assumed to contaminate urban air would logically be chrysotile. Since there are no grounds for believing that asbestos bodies develop with greater difficulty around chrysotile fibers than around the fibers of other types of asbestos that may be inhaled, it would be reasonable to expect the vast majority of ferruginous bodies in the lungs of nonoccupationally exposed city people to have a central core of chrysotile—if the ferruginous bodies are indeed asbestos bodies.

Inasmuch as chrysotile fibers appear to be hollow in the electron microscope,[6] these may sometimes be identified by inspection. Furthermore, because of its hollow structure, chrysotile has a unique and readily identifiable diffraction pattern.[7] Because chrysotile lends itself so readily to positive identification by electron microscopy, we undertook a study of the central cores of ferruginous bodies derived from lungs of people of Pittsburgh not occupationally exposed to asbestos. We are here reporting the results of our study.

Methods and Materials

Ferruginous bodies isolated from the lungs of 28 people[1] were placed upon electron microscope grids by means of a micromanipulator. In the electron microscope, it became necessary to find a suitable fiber area on the ferruginous body that was free of electron-opaque encrustation (possibly ferritin) which would have interfered with the study of the core. Work with "standard" samples of chrysotile, amosite, and crocidolite showed that useful diffraction patterns could be obtained from fiber areas as small as 500 × 500 Angstrom, and as large as 5,000 × 5,000 A. All bodies examined had fiber areas suitable for such study. The bodies had to be manipulated in such a way as to yield their characteristic electron diffraction patterns, so that measurements of interplanar crystal lattice spacings could be made. Typical "layer line" diffraction patterns are obtained if the fiber axis is perpendicular to the electron beam. Ferruginous bodies isolated from the lungs of hamsters killed 12 months after an intratracheal injection of 25 mg of brake-drum dust (iron-free) were similarly placed upon electron microscope grids, and electron diffraction patterns were obtained of the central filaments.

Results

None of the cores of the 28 ferruginous bodies showed the hollow, tubular structure characteristic of chrysotile. Measurements of the diffraction patterns obtained (to an accuracy of ± 1%) on each of the cores of these bodies from human lungs showed that none of the fibers examined were identifiable as one of the three forms of asbestos cited above. In particular, chrysotile could be excluded as being involved in the formation of the ferruginous bodies. On the other hand, the central filament of the ferruginous bodies isolated from hamster lungs injected with brake-drum dust yielded electron diffraction patterns characteristic of chrysotile.

Comment

Although we have failed to identify the fibers that caused the population of ferruginous bodies in people not occupationally exposed to asbestos, we have decisively excluded chrysotile. This exclusion is highly significant in view of the fact that if asbestos dust were the contaminant in urban air responsible for the formation of these bodies, chrysotile would be the most prominent constituent of the cores and should be identifiable in some of the ferruginous bodies recovered from the lungs of these people, particularly since we have demonstrated that the cores of ferruginous bodies resulting from intratracheal injections of brake-drum dust were composed of chrysotile.

From the fact that the central fibers of the ferruginous bodies examined demonstrate an electron diffraction pattern, it must be concluded that the fiber is crystalline, but identification must await further electron diffraction information and possibly electron microprobe measurements. Its crystalline diffraction pattern effectively rules out fibrous glass, glass wool, and other vitreous materials in this sample which have been shown experimentally to be capable of producing ferruginous bodies.[8]

A recent analysis, utilizing an electron microscope, of the central fiber of asbestos bodies removed from lungs of people who had worked in a Flushing (Netherlands) shipyard, led to the conclusion that these cores were composed of amphibole asbestos.[9] This might have been expected since crocidolite and amosite have long been the predominant types of asbestos used in the shipbuilding industry. However, the relevance, if any, of this finding to the ferruginous bodies found in the lungs of urban dwellers, not occupationally exposed to asbestos, would appear to be doubtful.

This investigation was supported in part by Public Health Service research grant PH86-66-156, National Center for Urban and Industrial Health, and grant FR 05580 from the National Institute of Health.

Michael D. Utidjian, MD, Department of Epidemiology, University of Pittsburgh Graduate School of Public Health, isolated the ferruginous bodies and transferred them to electron microscope grids.

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ST001579

Printed and Published in the United States of America

K-28126

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ppm CPFA (as Sterculia foetida oil) together with 4 ppb aflatoxin B₁ for 15 months than in those fed 3-methylcoumarin (50 ppb), gossypol (250 ppm) or polymerized vegetable oil (0.5%) in addition to aflatoxin. Moreover, tumours developed earlier and liver damage was more severe.

Nutritional value of processed fats

Finally there is the problem of the nutritional value of processed fats. As we have already reported (BIBRA Bull. 1965, 3, 123), there is no evidence that the partial hydrogenation of vegetable oils in the manufacture of margarine and shortenings has any harmful nutritional effects, although this leads to the formation of small amounts of *trans* isomers of polyunsaturated FA, and decreases somewhat the content of essential FA.

Sucroglycerides, produced by the transesterification of triglycerides with sucrose, are also innocuous except after prolonged ingestion of large amounts (*ibid* 1966, 5, 452). Even when sucroglycerides (lard-sucrose sucroglyceride and palm oil-xylitol xyloglyceride) were fed to rats (for 200 and 100 days, respectively) at dietary levels as high as 25%, liver and serum lipid concentrations were unaltered (Tudisco, Arzneimittel-Forsch. 1967, 17, 550). And apart from slight unspecific changes in the liver, attributable to the high fat content of the diet, no other organ was damaged.

Interesterification of fats has also been introduced within the last few years to produce solid fats with a high linoleic acid content. In this process, non-hydrogenated vegetable oils are mixed with small amounts of highly hydrogenated fats and then interesterified, in the presence of a catalyst, to rearrange the FA radicals on the triglyceride molecule. Measurements of digestibility, the biological activity of the contained linoleic acid, tissue cholesterol levels, growth, reproduction and longevity, together with histological examination of various tissues, show that these interesterified fats (82.5% unhydrogenated and 17.5% fully hydrogenated cottonseed oil) have no deleterious effects when fed to rats at a dietary level of 15% (Alfin-Slater *et al.* J. Am. Oil Chem. Soc. 1966, 43, 110; Nutrition Reviews 1966, 24, 201). And their nutritive value is at least as good as that of unhydrogenated cottonseed oil and other edible fats with similar contents of essential FA.

GETTING TO GRIPS WITH ASBESTOS

The widespread use of asbestos has magnified its occupational and environmental hazard to health. The risk, formerly confined to workers engaged in its manufacture, now extends to those involved in its many industrial applications and to a lesser extent to the public at large (BIBRA Bull. 1966, 5, 626). Asbestosis, the lung fibrosis caused by inhalation of asbestos particles, has been recognized for 40 yr. A more sinister result of asbestos exposure, which has come to light in the last few years, is the development of mesothelial tumours of the pleura and peritoneum. This sudden discovery called for an immediate assessment of the magnitude of the hazard and although several questions still remain unanswered, measurable progress has been achieved.

Source of carcinogenic hazard

Asbestos is commercially available in various forms, namely chrysotile (white asbestos), crocidolite (blue asbestos), amosite, anthophyllite, tremolite and actinolite. Chrysotile accounts for 82% of the UK market, amosite 13% and crocidolite 5%. According to a UK Advisory Panel ("Problems Arising from the Use of Asbestos: Memorandum of the Senior Medical Inspector's Advisory Panel." HM Factory Inspectorate. HMSO, London, 1967), epidemiological evidence points to crocidolite as the form mainly responsible for the carcinogenic hazard. However, animal experiments indicate that other forms of asbestos are carcinogenic. Amosite and crocidolite but not chrysotile were found to produce cancer in rats when injected subcutaneously (Roe et al. Rep. Br. Emp. Cancer Campn 1966, no.44, Part II, p.7), but a positive result with inhaled chrysotile was achieved in rats by Gross et al. (Archs envir. Hlth 1967, 15, 343). These three forms and anthophyllite have each produced experimental asbestosis in guinea-pigs (Holt et al. J. Path. Bact. 1966, 92, 185), but since the relevance of asbestosis in the aetiology of lung tumours is still obscure, this experiment throws no light on the carcinogenic potential of the four forms. As discussed by Hourihane & McCaughey (Post-grad. med. J. 1966, 42, 613), mechanical as well as chemical factors contribute to the production of fibrosis and may be involved in the carcinogenic process, and the possible participation of contaminants, e.g. oils, iron, nickel and chromium, cannot be excluded.

Control of use of asbestos

Various authors have emphasized the gravity of the asbestos hazard and the need for stringent controls (Gould, New Scient. 1967, 33, 453; Cooper, Archs envir. Hlth 1967, 15, 285; Lancet 1967, i, 1311; British Medical Journal 1967, 3, 62). Gould (loc.cit.) puts the problem in perspective by pointing out that a total of only 500 cases of mesothelioma has so far been reported throughout the world compared with 25,000 cases of lung cancer diagnosed each year in the UK alone. The Lancet (loc.cit.) welcomes the 1967 draft UK regulations, which will eventually supersede those of 1931, but hopes that certain deficiencies will be overcome before the draft becomes law. For example, to exclude completely the emission of asbestos dust from the workshop is not a practical proposition and instead a maximum allowable concentration should be imposed. Unless legislation is enforceable it tends to be neglected, argues the Lancet (loc.cit.). Meanwhile, as has been mentioned earlier (BIBRA Bull. 1967, 6, 474), the UK Advisory Panel (loc.cit.) recommends the substitution of crocidolite by other forms of asbestos wherever possible.

Occupational and environmental exposure

It has now become established that asbestos is an important atmospheric contaminant. More curious is the fact that asbestos finds its way into beer and other drinks as a result of its presence in pads used for filtration (Biles & Emerson, Nature, Lond. 1968, 219, 93). One pint of beer yields about 5000 asbestos fibres but their size is such that all 5000 laid end to end are estimated to measure less than 0.1 in. No doubt other environmental sources have yet to be discovered, but the important question to be answered is what level of exposure constitutes a hazard. Some headway has been made in resolving this problem. Asbestos particles deposit themselves in the lungs and after a process of phagocytosis are

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transformed into asbestos bodies. These bodies are to be found both in workers occupationally exposed to asbestos and in people living in urban regions. In 100 consecutive hospital autopsies of people living near Glasgow, 25 of the cases exhibited asbestos bodies but, surprisingly, none were found in any of the 58 women examined (Roberts, J. clin. Path. 1967, 20, 570). Across the Atlantic in Montreal, a different situation was observed in a similar random group at autopsy, 52 men (57%) and 16 women (34%) showing asbestos bodies (Anjilvel & Thurlbeck, Can. med. Ass. J. 1966, 95, 1179). Neither study pointed to an association between the occurrence of asbestos bodies and malignancy but a higher prevalence of asbestos bodies is usually found in cases of mesothelioma.

The formation of asbestos bodies is part of the process leading to the development of asbestosis. Whether lung cancer is a complication of asbestosis or is produced in the absence of this condition, thus being a hazard in its own right, has still to be decided. In 68 workers with asbestosis, 15 presented lung cancer (Lieben, Archs envir. Hlth 1966, 13, 619). Borow et al. (J. Am. med. Ass. 1967, 201, 587) consider that the increase in the incidence of mesothelioma and asbestosis is a reflection of the diversification in asbestos usage and report that of 17 cases of mesothelioma examined, two had no history of occupational exposure. Lieben & Pistawka (Archs envir. Hlth 1967, 14, 559) documented 42 cases of mesothelioma. Occupational exposure accounted for ten of these, environmental exposure in the vicinity of an asbestos plant for eight and home contact with asbestos workers for three. Of the rest, significant exposure was questionable but probable in ten cases, but no history of exposure could be obtained in 11 cases. The UK Advisory Panel (loc.cit.) claims that in its experience and despite tentative evidence to the contrary, there has been no excess of lung cancer among asbestos workers in the absence of demonstrable asbestosis. Prospective studies are needed to ensure that the hazard of excess bronchial cancer has been removed by recent improvements in factory conditions.

Based on a study of mortality data covering a 16.5-yr period on over 21,000 asbestos workers and over 6000 workers not exposed to asbestos, Enterline & Kendrick (Archs envir. Hlth 1967, 15, 181) found that the increased mortality rate (21% above normal) in heavily exposed workers was due partly to cancer of the respiratory system. Less heavily exposed workers showed a slightly raised death rate from respiratory cancer and a high death rate from asbestosis. In another mortality study by Kleinfeld et al. (ibid 1967, 15, 177) on 46 asbestos-insulator workers, the incidence of lung cancer was nine times that among average US citizens. Although both these studies showed an increased incidence of cancer of the gastro-intestinal tract among asbestos workers, the UK Advisory Panel (loc.cit.) is sceptical about such claims. Graham & Graham (Envir. Res. 1967, 1, 115) suggest that asbestos may be an aetiological factor in ovarian cancer. Asbestos-induced changes in the guinea-pig and rabbit ovary were histologically similar to those occurring in the early stages of human ovarian cancer. On the available evidence, however, only the lungs can be named as a confirmed site of malignancy.

Asbestos workers are obviously advised to undergo routine medical examinations. Any improvement in the prognosis of asbestosis must depend on its early diagnosis so that no further exposure contributes to the progression of the disease. Kennedy & Routledge (Br. J. ind. Med. 1967, 24, 232) carried out clinical, radiological and lung-function investigations in workers exposed to different atmospheric concentrations of asbestos. High-level exposure in two workers produced minor radiological changes and abnormal pulmonary function. Only two of ten less exposed workers suffered a similar fate. Of the lung-function indices studied, a reduction in inspiratory capacity was found to be the most sensitive indicator of early asbestosis. Apart from the need for an early warning system for asbestosis, it is essential that universal agreement is reached on the clinical, physiological and radiological criteria used for diagnosing this disease. Otherwise, the full value of the epidemiological studies currently being undertaken will not be realized.

Asbestos bodies

In cases of mesothelioma and asbestosis, asbestos bodies are to be found in abundance in lung tissue. Other fibrous materials when inhaled form similar bodies in the lungs and it is important that in reporting the presence of asbestos bodies, positive identification of asbestos should be made (Lewinsohn, Br. med. J. 1963, 2, 120; Gross et al. Am. ind. Hyg. Ass. J. 1967, 28, 541; deTreville, J. Am. med. Ass. 1968, [illegible], 1142). Investigators should not rely on morphological diagnosis alone and unless asbestos fibres can be demonstrated the bodies should be called "ferruginous bodies". Asbestos can be detected in biological material by a method involving ultrasonic disintegration followed by examination of heat resistance, water insolubility and optical properties (Peacock, Lancet 1968, i, 1155). The formation of asbestos bodies in guinea-pigs' lungs has been studied by Holt & Young (J. Path. Bact. 1967, 93, 696) and by Davis (Br. J. exp. Path. 1967, 48, 379). It appears that the asbestos fibres are swallowed up by the macrophages to form phagosomes. Cytoplasmic proteins are adsorbed into the asbestos fibre resulting in a contraction of the phagosome to form residual asbestos bodies having a beaded or corrugated structure. Once the asbestos fibres reach the pleural cavity, they are unlikely to be transported to other sites of the body to any significant extent. Using radiolabelled asbestos, Holmes & Morgan (UKAEA Research Group Report AERE-R 5289, HMSO, London, 1967) found that less than 10% of an intrapleural dose had vacated the chest region even after 50 days.

Conclusion

Keane & Zavon (Archs envir. Hlth 1966, 13, 171) have concluded that of the materials encountered by pipe insulators, asbestos alone presents a serious health hazard, and it is likely that in other industries, too, asbestos provides the major hazard. The asbestos problem presents a formidable challenge which is being met conscientiously by the responsible parties. While there is little room for complacency, there is even less for the exaggerated claims of danger made by the Rachel Carsons of our society.