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PNEUMOCONIOSIS

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PULMONARY FERRUGINOUS BODIES STUDIES ON THEIR ORIGIN

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Since the discovery by Thomson *et al.*[1] of structures indistinguishable from asbestos bodies in lungs of urban dwellers of Cape Town more than 6 years ago, his findings have been amply confirmed by investigators in large cities as well as some smaller communities in Europe and from North America.[2-7] Although it has long been known that filamentous dust particles of diverse composition, when deposited in lungs, may cause the formation of bodies similar to asbestos bodies,[8] these could generally be differentiated from asbestos bodies by their usually opaque and, at times, irregular contour of the central core, and they were then called pseudo-asbestos bodies. However, with the advent of industrial production of transparent, thin fibers approximating in size and optical microscopic appearance to some of the respirable asbestos fibers, the possibility arose that these man-made fibers could also cause the production of pseudo-asbestos bodies when inhaled. Recently it was demonstrated that these man-made fibers, when injected intratracheally into hamsters and guinea pigs, actually did cause the production of structures indistinguishable from asbestos bodies. With proof at hand that these golden to red-brown, elongated, bipolar-clubbed, but not necessarily segmented, iron-containing structures are not specific indications of the presence of asbestos fibers, these structures were given the generic name of 'ferruginous' bodies, reserving the term 'asbestos' body for those ferruginous bodies in which the central core is known to be an asbestos fiber.[9]

As Thomson has pointed out, the presence of ferruginous bodies in the lungs of urban dwellers suggest contamination of urban air with a filamentous dust resembling asbestos. Whether or not this dust actually is asbestos has not been established.

Because, at one time, the pathogenicity of asbestos dust was believed to be linked with the production of innumerable traumatic punctures of tissue by the pointed ends of the dust fibers, in the minds of some all fibrous dusts were assumed to be endowed with a similarly high pathogenic potential. However, more than 10 years ago, a dust composed of filamentous ceramic aluminium silicate was shown to belong in that category of dusts designated as biologically 'inert'.[10] This type of dust produces a pulmonary response having the following characteristics:

1. Collagenization is absent or insignificant;
2. The anatomic integrity of the air spaces is preserved;
3. The changes are potentially reversible.

This finding, of itself, should have laid the mechanical theory of the pathogenesis of asbestos dust to rest just as the biologic 'inertness' of diamond dust laid the mechanical theory of the pathogenesis of quartz dust to rest. Nonetheless, the dust of filamentous glass has become suspected of being fibrogenic, apparently on the basis of assumed mechanical trauma. Yet, glass dust derived from flakes of gossamer-thin glass, possessing sharp cutting edges, when deposited in air spaces, has been shown to be biologically 'inert'.[11]

Rats and hamsters were exposed to 3 kinds of fibrous glass dusts; uncoated, coated with a phenol-formaldehyde type of resin, and coated with a starch binder. The concentration of the dusts in the inhalation chambers averaged 100 mg./m.^{3}. About 60% of the dust particles were fibrous and their average diameter was 1 μ. After one year of exposure to this heavy concentration of all 3 types of dust, the pulmonary reaction consisted merely of focal accumulations of dust-filled macrophages localized largely to alveoli in the proximal portion of primary lobules. The reactive stroma associated with these cells consisted of a few delicate argyrophilic fibers. There was no destruction of alveoli and no

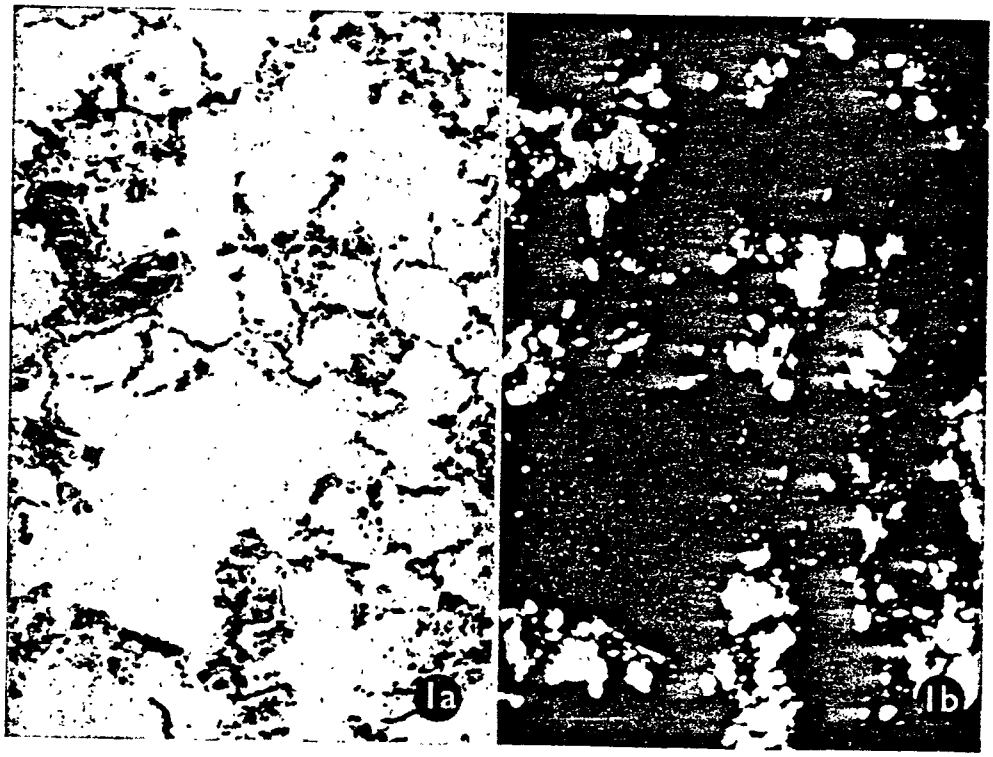


Fig. 1. The pulmonary response to inhaled fibrous glass dust consists only of macrophages which are filled with this dust. The macrophages are well preserved and show no evidence of degeneration. There is no fibrosis and alveolar walls are thin. From a rat exposed to fibrous glass dust for twelve months at 100 mg/m³. Hematoxylin and eosin. ×110.

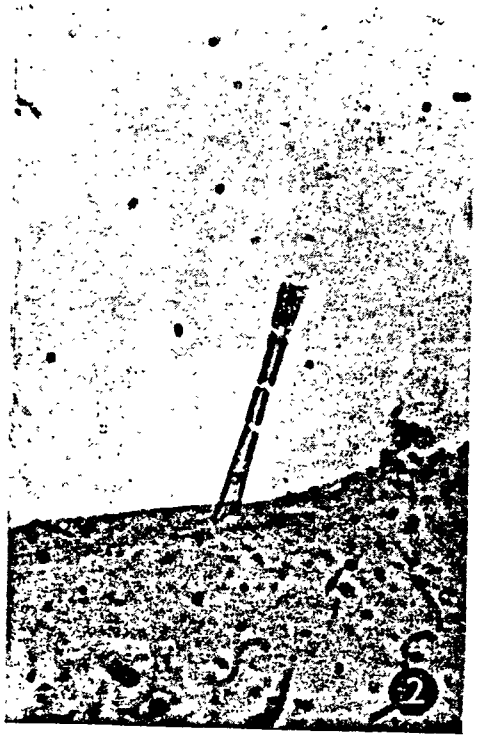


Fig. 2. Ferruginous body washed from the lungs of a hamster exposed to fibrous glass dust for twelve months at 100 mg/m³ concentration. The ferruginous material appears as though fractured. Nevertheless, the central glass core appears to be continuous. Unstained. × 960.

collagen formation (Fig. 1). Abundant ferruginous bodies were found in the hamster lungs (Fig. 2). No differences in the reaction to the 3 different kinds of glass dust could be detected.

It has been suggested that one source of the ferruginous bodies in urban dwellers could very well be the asbestos that is comminuted by the friction of the asbestos-containing brake lining against the steel brake drum of automobiles.[1] This possibility could be evaluated by animal experiments and was considered worthy of a pilot study before proceeding with a full-scale investigation.

Brake drum dust consists mainly of iron, a phenol-formaldehyde type resin, and forsterite. The latter is a mineral which is formed when chrysotile is heated so that it loses its water of crystallization. Brake drum dust was rendered iron-free by magnetic separation. Although it contains a few scattered transparent fibers 50 to 75 μ long and about 1 μ in thickness, the X-ray diffraction pattern was negative for chrysotile. The dust is essentially non-fibrous. As this was intended to be a preliminary type study, only a few rats and hamsters were employed (10 of each). These animals were injected intratracheally with acqueous suspensions of the dust. The dosage was 2 × 10 mg. for rats and 3 × 3.5 mg. for hamsters. The animals tolerated the dust well and they were killed one year later. The tissue reaction to this dust was very similar to that seen in the animals injected with fibrous glass, consisting of collections of dust-filled macrophages situated in alveoli clustered in the proximal portion of primary lobules. There was no

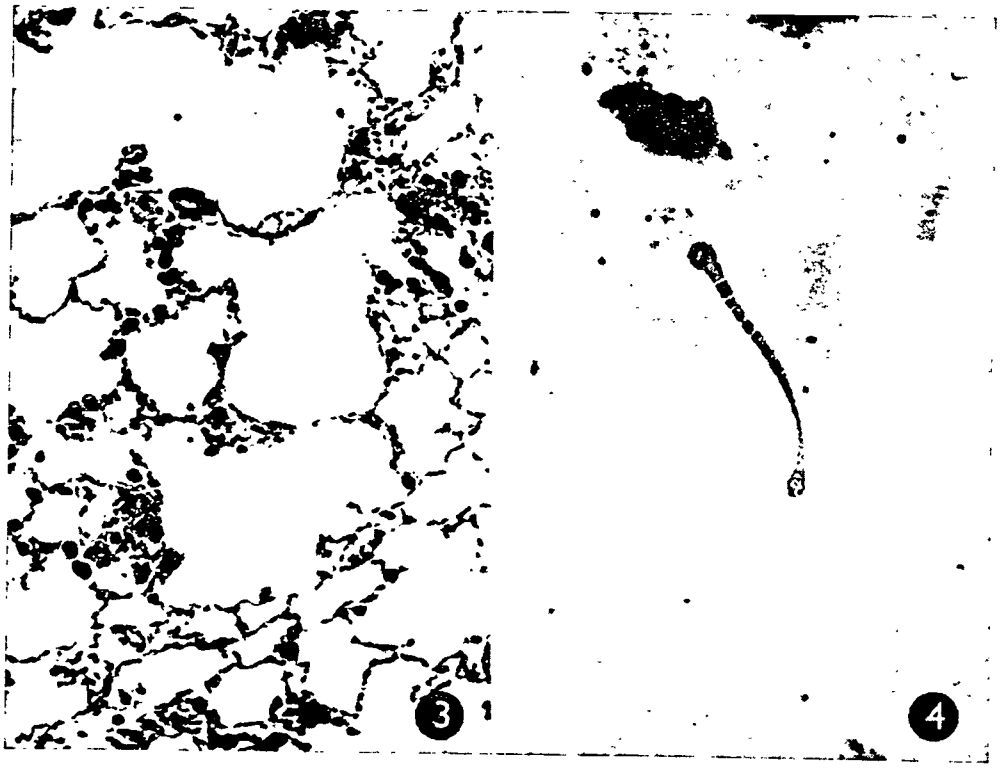


Fig. 3. This rat was injected intratracheally with 20 mg. of iron-free brake-drum dust and killed one year later. Similar to the reaction to fibrous glass, there is no fibrosis and alveolar walls remain normal. Air spaces contain collections of macrophages which stain darkly because of the ingested dust. Hematoxylin and eosin. ×110.

Fig. 4. Ferruginous body from the lung of a hamster injected with brake-drum dust and killed 6 months later. This ferruginous body is an asbestos body. It was found in a smear of the sediment from saline injected into the lung. Perl's stain. ×960.

indication of collagenous fibrosis (Fig. 3). The hamster lungs contained many ferruginous bodies (Fig. 4).

In order to determine the nature of the dust causing the production of ferruginous bodies in the lungs of urban dwellers, it has become necessary to identify the material constituting the central core of the ferruginous bodies isolated from the lungs of these people. The method of isolation has been published[12] and involves the digestion of small pieces of lung tissue (about 300 gm. wet weight) with 5% sodium hypochlorite (household bleach) for 24 hours, removal of the remaining undigested lung tissue, and resuspension of the centrifuged sediment in a mixture of 50% alcohol and chloroform. Ferruginous bodies, because of their high iron content, have a high specific gravity and will be found in the sediment at the bottom of the tube. Carbonaceous material, if not dehydrated by excessive strength of alcohol, will be found at the interphase between the chloroform and the aqueous alcohol. The sediment containing the ferruginous bodies is washed and resuspended in water. Ferruginous bodies are transferred to electron microscope grids from such suspensions by means of micro-manipulators. It may be of interest to observe that the sediment from the lungs consists mostly of angulated colorless, glass-like particles and often contains many more naked fibers of different sizes than ferruginous bodies. Some of these naked fibers are obviously man-made, since the ends show evidence of heat-softening as indicated by the formation of loops, shepherd crooks, or merely bulbous enlargement.

Twenty-eight ferruginous bodies from as many lungs of city dwellers from Pittsburgh that had been transferred individually to electron microscope (E-M) grids were examined by electron diffraction at the Mellon Institute (Carnegie-Mellon University), along with 6 ferruginous bodies similarly isolated from lungs of hamsters injected intratracheally with iron-free brake drum dust and then transferred to E-M grids.[12]

Inasmuch as the iron encrustation in the ferruginous body interferes with the production of a satisfactory electron diffraction pattern, the central filament had to be scanned from end to end to find a region, at least 500 × 500 Å, which was free of iron deposits. Such an area was found on each of the ferruginous bodies examined and provided a satisfactory electron diffraction pattern.

Chrysotile, which constitutes about 90-95% of all asbestos used in the United States, is different from other types of asbestos in that it is composed of tubular crystals which give it a unique electron diffraction pattern. The other types of asbestos, composed of solid filaments, require more exact orientation of the fiber in order to obtain the same electron diffraction pattern as that of a standard sample.

Not one of the consecutive 28 ferruginous bodies isolated and analyzed yielded an electron diffraction pattern which could be identified as that of chrysotile (Fig. 5). On the other hand, of the 6 ferruginous bodies isolated from hamster lungs injected with brake drum dust, all gave an electron diffraction pattern characteristic of chrysotile (Figs. 6 and 7); 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. These 6 ferruginous bodies were, therefore, asbestos bodies.

Since the ferruginous bodies from the human lungs failed to give the electron diffraction pattern of chrysotile, the latter can be excluded as the central fiber in all bodies examined to date. However, because a diffraction pattern was demonstrated, the fibers must necessarily have a crystalline structure. This excludes such vitreous materials as glass, mineral or rock wool, and other ceramic fibers. At the same time, the diffraction pattern is not sufficiently similar to patterns of known samples of amosite or crocidolite to allow positive identification of either, but neither is it possible to exclude these or possibly some of the other forms of asbestotic minerals.

A recent report of an analysis of ferruginous bodies isolated from the lungs of shipyard workers in Flushing, Netherlands, has shown that these were indeed asbestos bodies, inasmuch as the central cores consisted of amphibole asbestos.[13] Such findings were to have been expected since shipyard workers are exposed to amosite and crocidolite asbestos. It should be noted, however, that the above results do not necessarily apply to the ferruginous bodies of urban dwellers who are not occupationally exposed to asbestos.

Since 90-95% of the asbestos used in the United States is chrysotile, one would expect chrysotile to constitute the central core of at least some of the ferruginous bodies isolated from the lungs of city dwellers, i.e. if these people were actually exposed to asbestos dust.

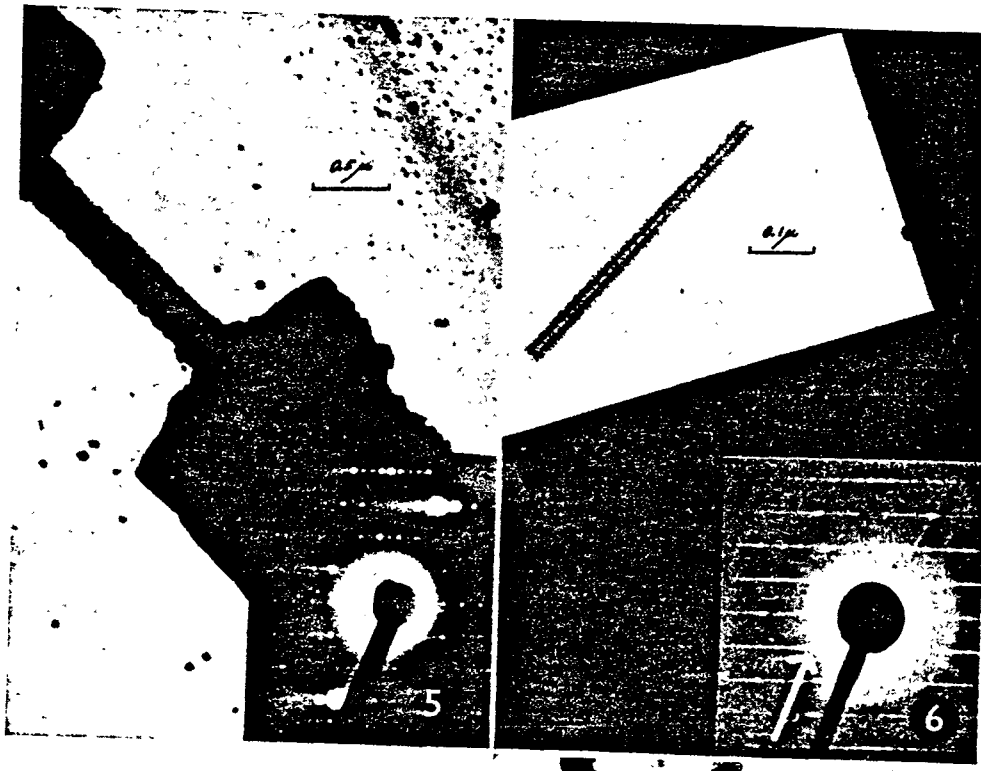
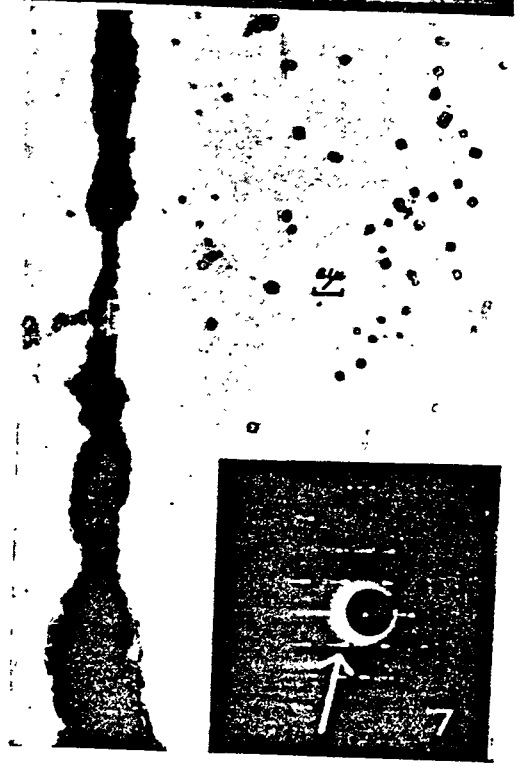


Fig. 5. Electron photomicrograph of a portion of a ferruginous body from a human lung. The region photographed was selected because it is not covered by ferruginous material. It measures about 0.3 × 1.6μ and is from where the electron diffraction pattern was obtained (lower right corner). This pattern is unlike that obtained with chrysotile (compared with Fig. 6).

Fig. 6. Electron photomicrograph to show the central cavity of a tubular crystal of chrysotile. The electron diffraction pattern of chrysotile is shown in lower right corner. The characteristic and unique feature of this electron diffraction pattern is the exclamation-mark or tear-drop shape of the pips on the layer lines (arrow).

Fig. 7. Portion of a ferruginous body, as seen under an electron microscope, from the lung of a hamster injected with brake-drum dust intratracheally and killed one year later. The naked portion of the central core measures about 0.06 × 0.3μ. The electron diffraction pattern from this region of the core (lower right corner) resembles that of chrysotile (compared with Fig. 6). This ferruginous body is, therefore, an asbestos body.



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, 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.

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