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EXPERIMENTAL ASBESTOSIS IN GUINEA PIGS

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A description of changes in the lungs of rats which had inhaled very fine chrysotile asbestos dust has been published (Holt, Mills and Young, 1963). Severe lesions developed a few weeks after the dust was inhaled, yet few particles of asbestos were visible in sections. By dark ground illumination, areas were visible in these sections where dust particles that were too small to be observed by transmitted light were aggregated.

In human asbestosis, the lungs contain many asbestos fibres up to 40μ and some even longer, and also asbestos bodies, which are fibres coated with protein. Few fibres and no bodies were visible when the sections of rat lungs were viewed in the optical microscope. Apparently the respiratory passages of the rat are capable of removing from the air nearly all particles of dust larger than about a micron, and this may account for the difference between asbestosis as seen in the rat and in the human lung.

This paper reports experiments on guinea-pigs which had been caused to inhale fine particles of asbestos. A dense dust cloud was established by using a modification (Holt, Mills and Young, 1964) of an apparatus previously described (Holt and Young, 1960). The dust contained many particles less than 1 μ long.

The same damage was observed as in the lungs of rats, but the guinea-pig lungs have numerous particles of asbestos which are longer than a micron and also typical beaded and non-beaded asbestos bodies. Early sections are characterized by large mononuclear macrophages which are filled with dust particles and multinuclear giant cells lying in a reticulin mesh. Groups of macrophages become enclosed by a delicate collagen capsule and later collagen replaces reticulin in the substance of the nodule. The giant cells which are so obvious in the early sections, become less frequent after a few months. In one experiment guinea-pigs were exposed to a dense dust cloud over a period of only two weeks and were then removed from the dusting tunnel. Animals were killed at intervals and changes in histological sections of the lungs were studied.

An animal was killed on the 7th day of exposure to crocidolite dust. A section of the lungs (Fig. 1) shows a terminal bronchiole plugged with cellular exudate which was pouring into the respiratory bronchiole. This exudate consisted mainly of macrophages, many of which were multinucleated and loaded to capacity with fine dust. An occasional dust-laden cell or short asbestos fibre occurred in the alveolar duct. The initial lesion then appears to be a bronchiolitis, with an extension along the respiratory bronchiole and alveolar duct.

Another guinea-pig was killed 190 days after the experiment started. Histological sections show severe damage to the terminal bronchiole and to the air spaces bordering the respiratory bronchioles. The alveolar ducts are still filled with cellular exudate which contains many macrophages loaded to capacity with fine dust. Asbestos bodies and asbestos fibres are numerous.

An animal killed 400 days after a similar exposure to chrysotile dust had extensive fibrosis around the terminal bronchioles. The fibrosis diminished progressively along the alveolar ducts into alveoli more remote from the bronchioles (Fig. 2).

Lung sections which had been treated with ferrocyanide showed asbestos bodies stained blue, indicating the presence of iron in the protein coating (Fig. 3). The very small dust particles which packed the macrophages also appeared blue at higher magnification.

Some of the fibres which penetrated into the lung were of considerable length. In one animal killed 195 days after exposure to crocidolite, an asbestos fibre traversed the whole of one alveolus, penetrating the wall and extending into an adjacent alveolar duct. This fibre was not uniformly coated. Silver impregnation showed one

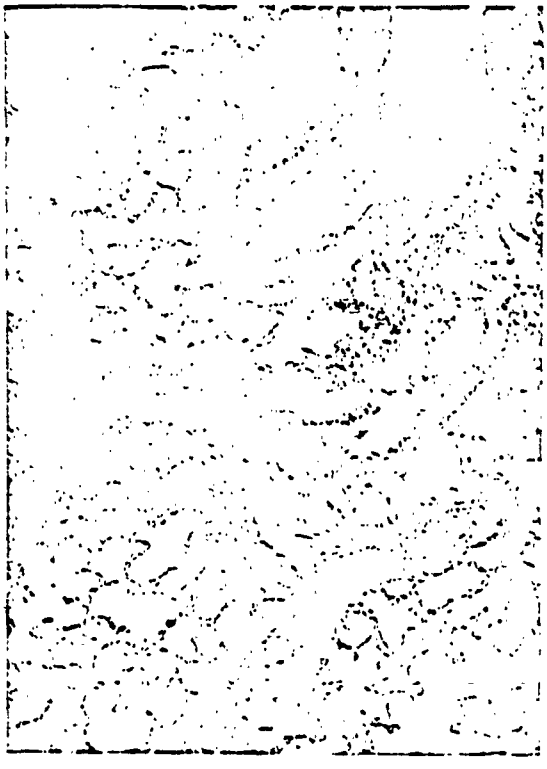

Fig. 1. Section of the lung of a guinea-pig killed after inhaling crocidolite asbestos dust for 50 hours during 7 days. A terminal bronchiole is plugged with cellular exudate which is pouring into the respiratory bronchiole. Macrophages filled with dust are in the exudate and occasionally in the wall of the duct. (X 175 Haematoxylin-eosin).

end to be heavily coated by some substance which greatly increased its thickness and which stains intensely. At the other end was a similar but lighter coating and in the middle, where the fibre penetrated the alveolar wall, there was scarcely any coating; the fibre was much thinner and yellow. This fibre also traverses a group of closely packed yellow granules which represent the load of dust carried by a macrophage, the cell itself remaining unstained by this technique.

Other fibres presented a beaded appearance and were stained heavily with silver. A short fibre nearby was unstained and appeared as a very fine uncoated filament. One fibre was unstained but appeared beaded and another had two black beads at one end, a thin, curved and unstained middle portion and a black bead at the other end.

These wide variations in the size, shape, thickness and staining properties of asbestos fibres, all of which had been in the lung for approximately the same time (between 195 and 181 days) were inexplicable. All the silver impregnated sections exhibited a diffuse reticulinosis of the alveolar walls.

The results of these experiments on guinea-pigs confirm the general findings resulting from the previous experiments on rats. The principal con-

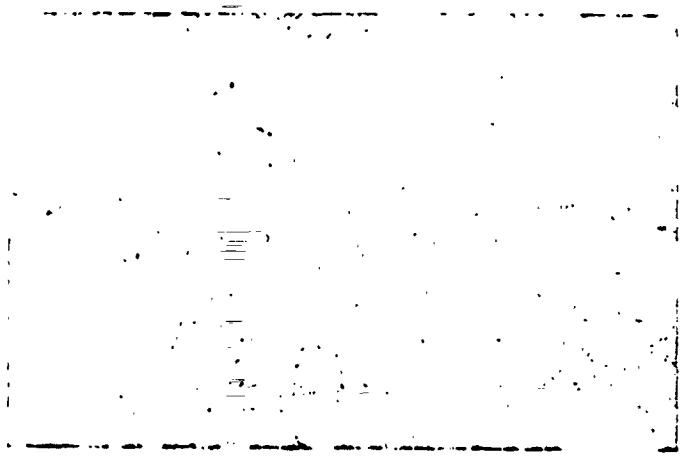

Fig. 2. Section of the lung of a guinea-pig killed 396 days after inhaling chrysotile asbestos for 14 days. A late stage of bronchiolitis with collagen infiltration in the surrounding alveoli. (X 40 Van Gieson).

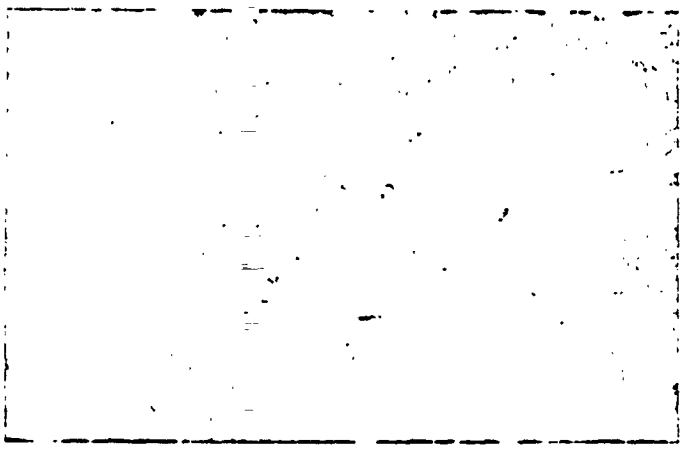

Fig. 3. Guinea-pig killed 181 days after inhalation period of 14 days. Crocidolite asbestos. Asbestos bodies stained deep blue indicate iron in the protein coating. Some fibres are not coated. Submicron asbestos particles in phagocytes stain blue. (X 200 Haematoxylin-eosin and Perl).

clusion resulting from our earlier work, that very fine particles of asbestos, even submicroscopic particles, can rapidly produce severe lesions in the lung, is reinforced. The difference between the lungs of the experimental rats and those of the guinea-pigs may be due to differences in the respiratory tract whereby the rat can efficiently remove from inhaled air particles down to a size of 1 μ or even less.

In some earlier publications emphasis has been laid on the importance of long asbestos fibres as the causative agent in asbestosis. Our results indicate that very small asbestos particles can certainly cause widespread damage in the lungs of small animals and this fraction of the dust cannot be ignored in the assessment of a hazard. The fact that the diameter of the ultimate fibres of the types of asbestos which are used in industry is smaller than the limit of resolution of the optical microscope indicates that electron as well as light microscopy should be used in the study of this hazard.

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