Reprinted from the A. M. A. Archives of Industrial Health
September 1955, Vol. 12, pp. 280-287

The Biological Action of Glass Wool

Studies on Experimental Pulmonary Histopathology

G. W. H. SCHEPERS, M.D., D.Sc., Saranac Lake, N.Y.

Glass wool is fabricated by ejecting molten glass by means of supercharged steam into a chamber where fragments varying from 25 to 30 cm. in length fall.[1] During the process of manipulating this product in the manufacturing of textiles, fragments are released into the air and have been known to act as skin irritants,[2] but they have not been incriminated as a cause of pulmonary fibrosis,[3] though occasional cases have been cited in connection with which the inhalation of glass-wool dust has been implicated as a contributing cause of pulmonary disease of variable severity.[4] At the most, these reactions have been attributed to mechanical irritation, as glass does not contain any free silica. Powdered glass has been shown to be inert for subcutaneous or ocular tissues.

The increasing exploitation of glass wool and of glass fibers in industry and the similarity between glass spicules and asbestos fibers necessitate constant vigilance concerning the properties of these glass fibers. The description of the pulmonary lesions resulting from the introduction of glass wool into guinea pig lungs will serve to show that, though the silicon element in the glass is present as a silicate and thus does not provoke the characteristic nodular disease associated with quartz inhalation, glass fibers of the caliber and length used in this study, when effectively lodged within the lung tissue, are nevertheless capable of producing quite remarkable lesions.

Recorded for publication July 11, 1955.
Director, The Saranac Laboratory.

The observations flowing, respectively, from the intratracheal and the inhalation experiments described by Schepers and Delahant [5] will be presented separately.

INTRATRACHEAL STUDY: 20μ-50μ GLASS WOOL

One month after the intratracheal introduction of glass-wool fibers, areas of lung tissue are demonstrable in which the alveoli contain numerous multinucleated giant cells in which glass fibers may be found. Some alveoli may contain several such giant cells, and in others the giant cells are so large as to fill the greater part of the alveoli. The smaller the fibers introduced, the larger are the associated giant cells. No free-lying glass fibers could be observed. The alveolar walls are infiltrated by macrophage cells and occasional polymorphonuclear leucocytes at numerous points. There is, however, no appreciable hyperemia, and only isolated glass fibers have penetrated into the alveolar walls, either separately or in a phagocytosed state. Many of the longer fibers appear also to have either extremity embedded in an adjacent alveolar wall (Fig. 1*A*).

At several sites these islands of phagocytic reaction involve the lung lymph nodes, which are considerably hypertrophied, with lymphocytes overflowing into proximal alveolar walls (Fig. 1*B*). Glass fibers are not, however, found in the parenchymal lymph nodes. The hilar lymph nodes show some endothelioid cell hyperplasia and prominent lymph follicles in which macrophages, with minute glass spicules, may be found.

The lung fields intervening between these affected areas appear relatively normal, except for a measure of incipient atrophic emphysema.

Around some of the smaller bronchioles the cellular infiltration may be quite abundant.

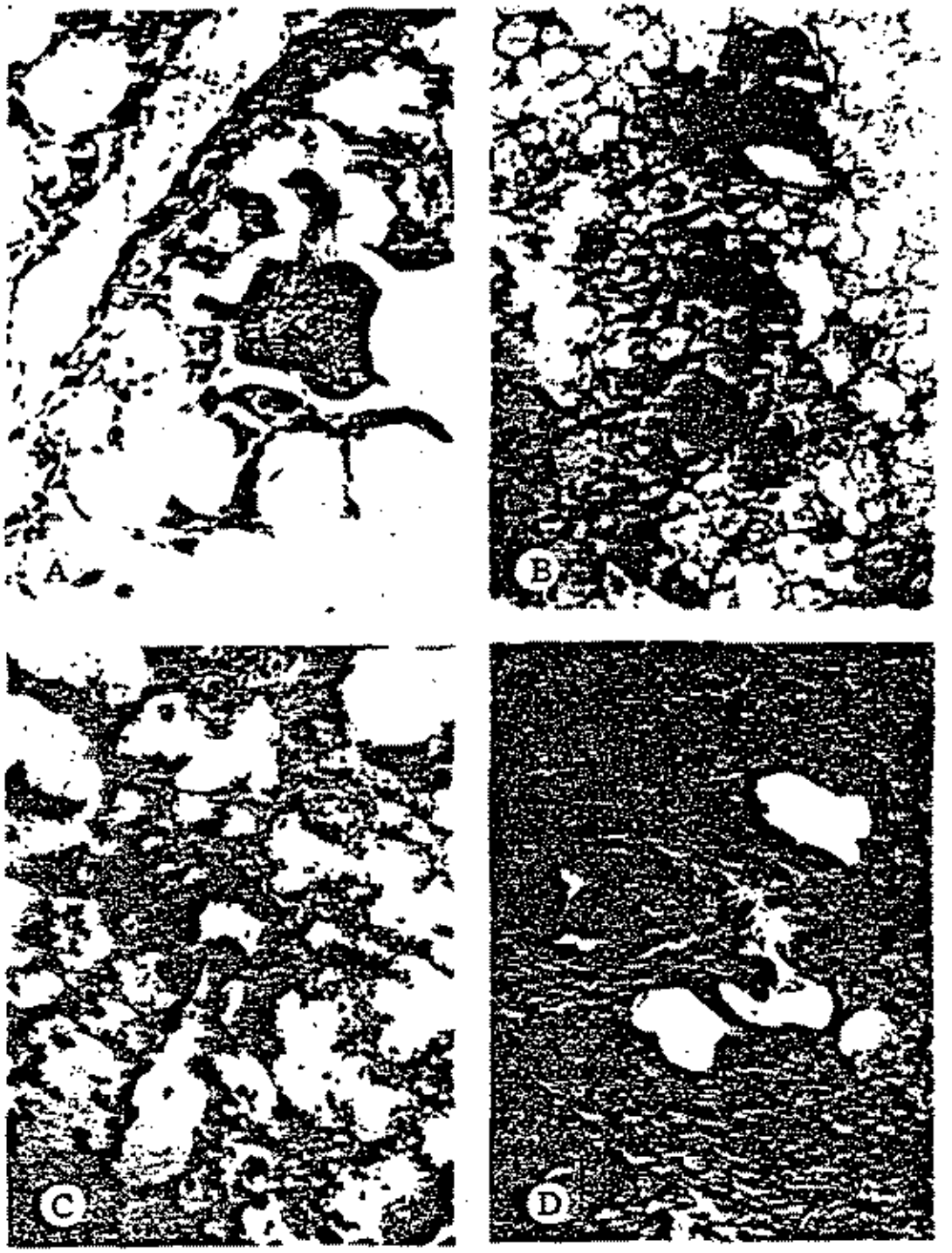

Fig. 1.—Acute pulmonary tissue reaction to long-fiber glass wool—guinea pigs; intratracheal injection of 20μ–30μ fibers; result after one month. *A*, giant macrophage filled with glass spicules, some of which are seen to penetrate the alveolar walls and blood vessel walls. *B*, proliferation of lymph nodes and extension of the cellular reaction into adjacent alveolar walls. *C*, peribronchiolar cellular inflammatory reaction, with epithelialization of adjacent alveoli. *D*, wide zone of cellular infiltration around a bronchiole, which is distorted and linked to atrophic alveolar ducts; degenerative changes in adjacent vascular bundle.

and the lining epithelium shows considerable hyperplasia, with some superficial desquamation. Very occasionally, glass fibers may be seen adhering to the surfaces of the bronchial epithelium, but there is no mucosal reaction to their presence. These affected bronchi and bronchioles occur in proximity to the islands of parenchymal reaction (Fig. 1*C*).

At isolated sites there is a broad reactive cellular zone around the smaller bronchi, which completely obscures the pulmonary histioarchitectonics. The trapped bronchus may be distorted and distended (Fig. 1*D*).

The tracheal epithelium tends to be somewhat hyperplastic and is covered by a thin layer of exudate which contains polymorphonuclear leucocytes.

Two months after the introduction of the glass-wool dust, much of the reaction seen within the first month has receded. There now are fewer parenchymal islets in which glass-filled macrophages occur within the alveoli. More frequently, these macrophages are to be seen diffusely scattered throughout the lung tissue. Isolated foci of intense, and even confluent, interstitial cellular infiltration also occur.

A new feature is the abundant presence of eosinophile cells within the alveolar walls, the peribronchial or perivascular tissues, and also sometimes within alveoli or bronchiolar lumina. The bronchi and trachea show no material pathological deviations at this stage.

The lymphatic reaction has become modified, and the lymphocytes now occupy perivascular and pericapillary positions mainly. This change is fairly diffusely disseminated. The hilar lymph nodes show no further reaction.

At the end of 12 months, a considerable amount of glass still persists within the lung tissue, and there are isolated islets of confluent cellular pneumonitis. More of these fibers are now to be found within the interstitial pulmonary tissue in areas where such proliferation persists and such fibers tend to be relatively long. Generally the short fibers are within macrophages with relatively atrophic alveoli, and the larger fibers are to be found in the alveolar walls. The bronchioles show some superficial epithelial desquamation (Fig. 2*A*).

Occasional bronchioles may be trapped within hyperplastic areas and appear stenosed. These areas differ from those demonstrated after the first month in that there are many more fibrocytes than inflammatory cells and the tissue has a poorer blood supply (Fig. 2*B*).

In the lymph nodes, the glass is now condensed into formless focal deposits, with no evidence of macrophages but with some cellular condensation around them (Fig. 2*C*). The lymph nodes of the lung parenchyma are normal once more.

At the end of 18 months, the interstitial parenchymal reaction may yet persist but is now minimal in degree. Glass fibers are now but scantily represented and occur mostly in the alveolar macrophages. Some glass rods may, however, be displayed within the interstitial tissues, and some are still seen to transfix alveolar walls. The main abnormality now concerns the bronchi and bronchioles which tend to be regionally distended and display many crypts and papillae covered by a thin lining of cuboidal or squamous cells. This bronchiectasia and bronchiolectasia had already commenced at 12 months, but the crypt and papillary formations are later trends. The condition is more marked with exposure to the shorter, narrower fibers (Fig. 2*D*).

INHALATION EXPERIMENT: 6μ AND LESS FIBERS

The essential difference between the result of the introduction of glass wool by means of a single intratracheal injection and the slower inhalation of the fibrous particles under experimental conditions is quite striking.

There is no acute response of the bronchial mucosa to the inhaled glass-wool spicules which impinge upon its surface (Fig. 3*A*). Very little reaction occurs before the fourth month, whereas in the intratracheal experiment the maximal effect is achieved within the first month. By the fourth month there are many macrophages in the alveoli.

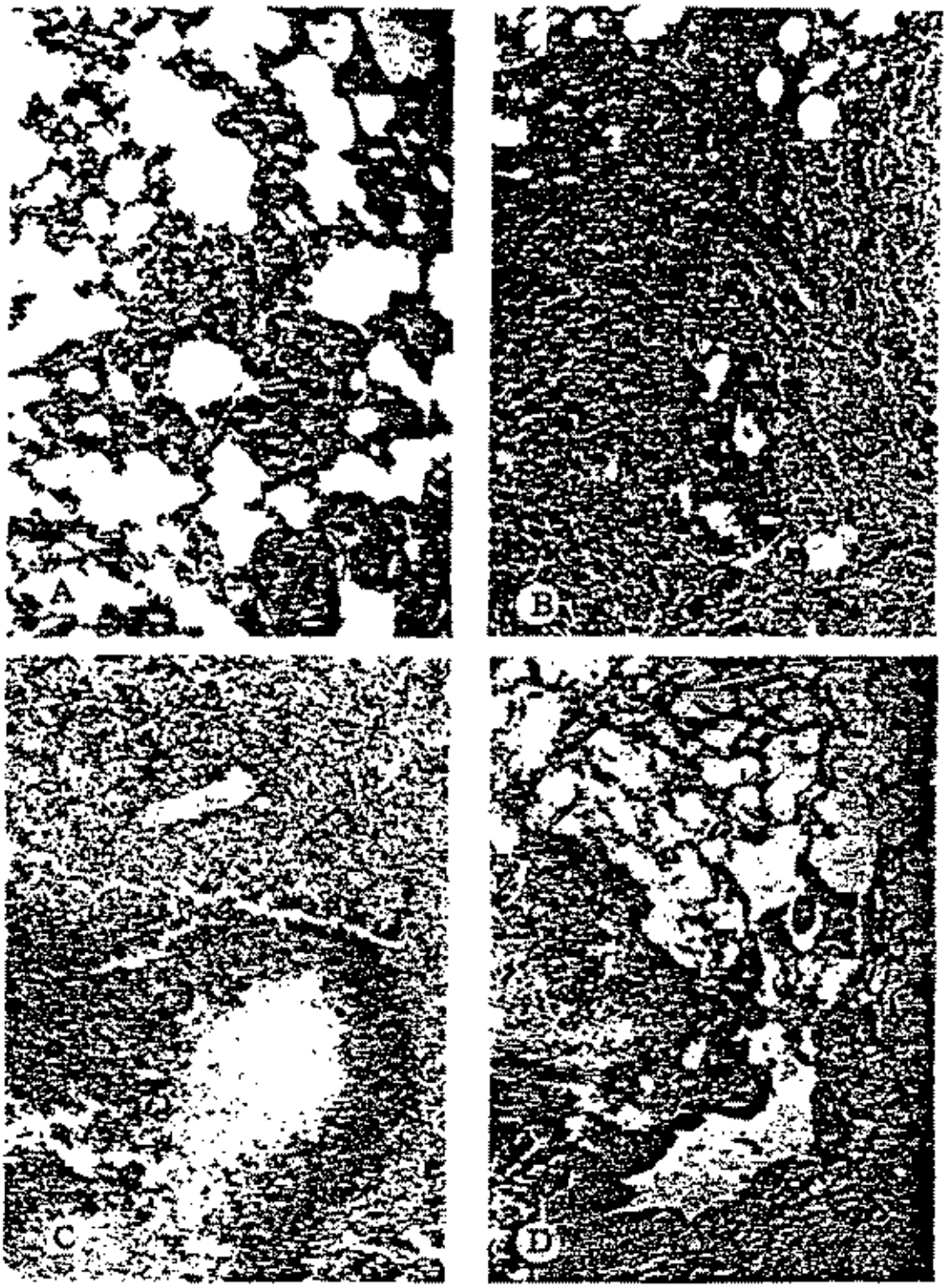

Fig. 2.—Chronic pulmonary reaction to long-fiber glass wool—guinea pigs: intratracheal injection of 20μ–30μ fibers; result at 12 months. *A*, persistent dominantly cellular reaction around a distorted bronchiole; numerous glass fibers discernible. *B*, diffuse peribronchial cellular reaction now largely fibrocytic in character. *C*, amorphous accumulation within a lymph node, with a reactive surrounding zone. *D*, distortion and incipient crypt formation in a bronchiole which is surrounded by a fibrotic process.

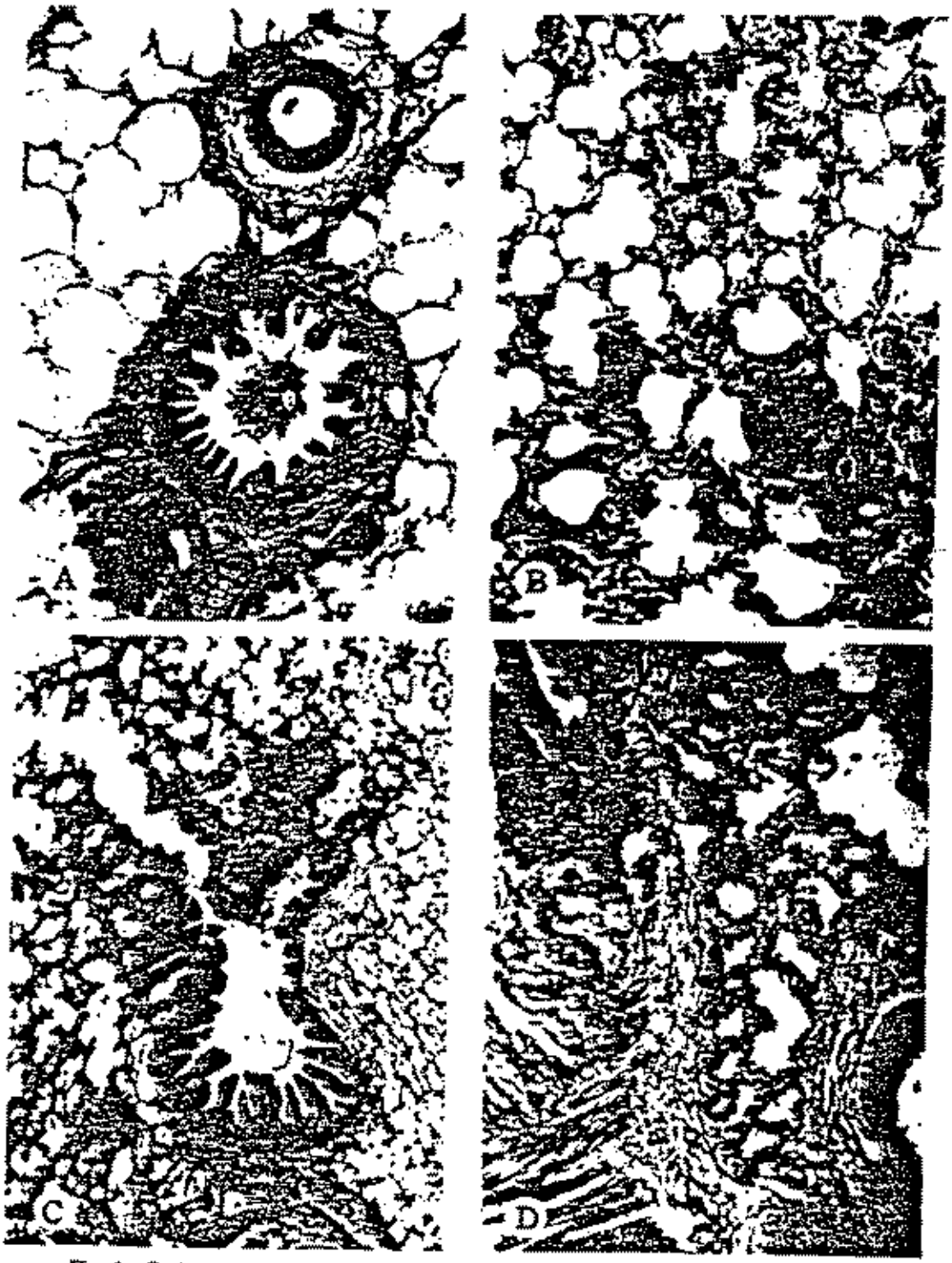

Fig. 3.—Early response to inhaled short-fiber glass wool—guinea pigs: inhalation study of less than 6μ fibers. *A*, presence of glass-wool dust within a bronchus on the 18th day, showing absence of immediate reaction. *B*, cellular infiltration of alveolar walls, with hyperplasia of parenchymal pulmonary lymph nodes (reaction at four months). *C*, epithelial hyperplasia and peribronchiolar fibrocellular reaction, bringing about progressive narrowing of the lumen (reaction at four months). *D*, epithelialization of the alveoli adjacent to a bronchus (reaction after a year).

These are separate cells, and there is very little of a tendency to giant-cell formation. Eosinophiles are fairly numerous now, whereas they appeared later only in the intratracheal experiment. Glass fibers, on the contrary, are very scarce, and because the inhaled substance contains fibers less than 6μ only, they are limited to short spicules, all of which are intracellular.

In the lung parenchyma, there are patches of almost solid cellular reaction around the lymph nodes whose proliferating cells overflow into adjacent alveolar walls, while the presence of large numbers of macrophages within such alveoli contribute to the impression of a diffuse pneumonitis (Fig. 3*B*). There is no hyperemia. The hilar lymph nodes show no particular reaction.

In the bronchi, there is considerable epithelial hyperplasia and cellular desquamation, and a tendency to papilloma formation is present in the smaller bronchioles, with mucosal hypertrophy in the larger air passages. There tends to be marked peribronchial cellular infiltration at this stage, with the evolution of multiple bronchial glandular cysts and mucosal papillae. A tendency toward bronchiectasia and bronchiolectasia has commenced (Fig. 3*C*).

By the end of nine months, glass fibers commence to make their appearance in clusters within alveoli as well as in the koniophores. The bronchiolar crypts are more prevalent, and there is fairly considerable peribronchial and perivascular cellular infiltration, with some collagen deposition.

A year after the commencement of the glass-wool inhalation experiment, the guinea pig lungs show a bronchitis and bronchiectasia, with marked focal cellular pneumonitis.

The bronchial (bronchiolar) disease consists of epithelial proliferation and distention of the lumina, with extension of the bronchiolar epithelium over the walls of the proximal alveoli. This produces a very characteristic lesion, comprising a dilated bronchiole surrounded by a zone of epithelialized alveoli (Fig. 3*D*). A fibrocellular reaction about these bronchi may enclose such epithelialized alveoli, creating a spurious adenomatous effect (Fig. 4*A*). A considerable degree of bronchial epithelial hyperplasia has supervened, and the lining shows marked rugosity and incipient metaplasia. There is no ulceration or submucosal infiltration (Fig. 4*B*).

The parenchymal islets of reaction are composed of thickened alveolar walls, with multinucleated giant cells and macrophages occupying the majority of such alveoli and containing many glass fibers. Occasional eosinophile cells are to be seen, but there is no hyperemia or collagenosis (Fig. 4*C*).

In the vicinity of lymph nodes, there is considerable dissemination of lymphocytes into adjacent alveolar walls. Many blood vessels also are ensheathed in fairly thick collections of lymphocytes. Some such arteries show medial myohypertrophy. The hilar lymph nodes are enlarged, owing mostly to medullary endothelial hyperplasia and infiltration by means of macrophages, many of which contain glass fibers.

By the 18th month of glass-wool dusting, the pulmonary tissue pathology ceases to reveal any significantly new features.

There still is intense alveolar wall thickening due to macrophage and plasma cell invasion, and there is also almost universal minor capillary hyperemia, with conspicuous perivascular macrophage infiltration. In numerous areas there is merely abundant intra-alveolar macrophage formation and no alveolar wall reaction of any consequence (Fig. 4*D*).

The parenchymal lymphatic tissue still escapes, even when lymph nodes may be almost completely surrounded by an extensive accumulation of macrophages. The bronchitis persists and comprises mainly epithelial hyperplasia, with increased goblet-cell activity and cellular catarrh, and there is also considerable peribronchial cellular infiltration.

Glass fibers are present everywhere. In stained sections they may be difficult to see, but scattered giant cells are to be found within alveoli. Dark-field examination of unstained sections shows up the universal distribution of the glass to good advantage.

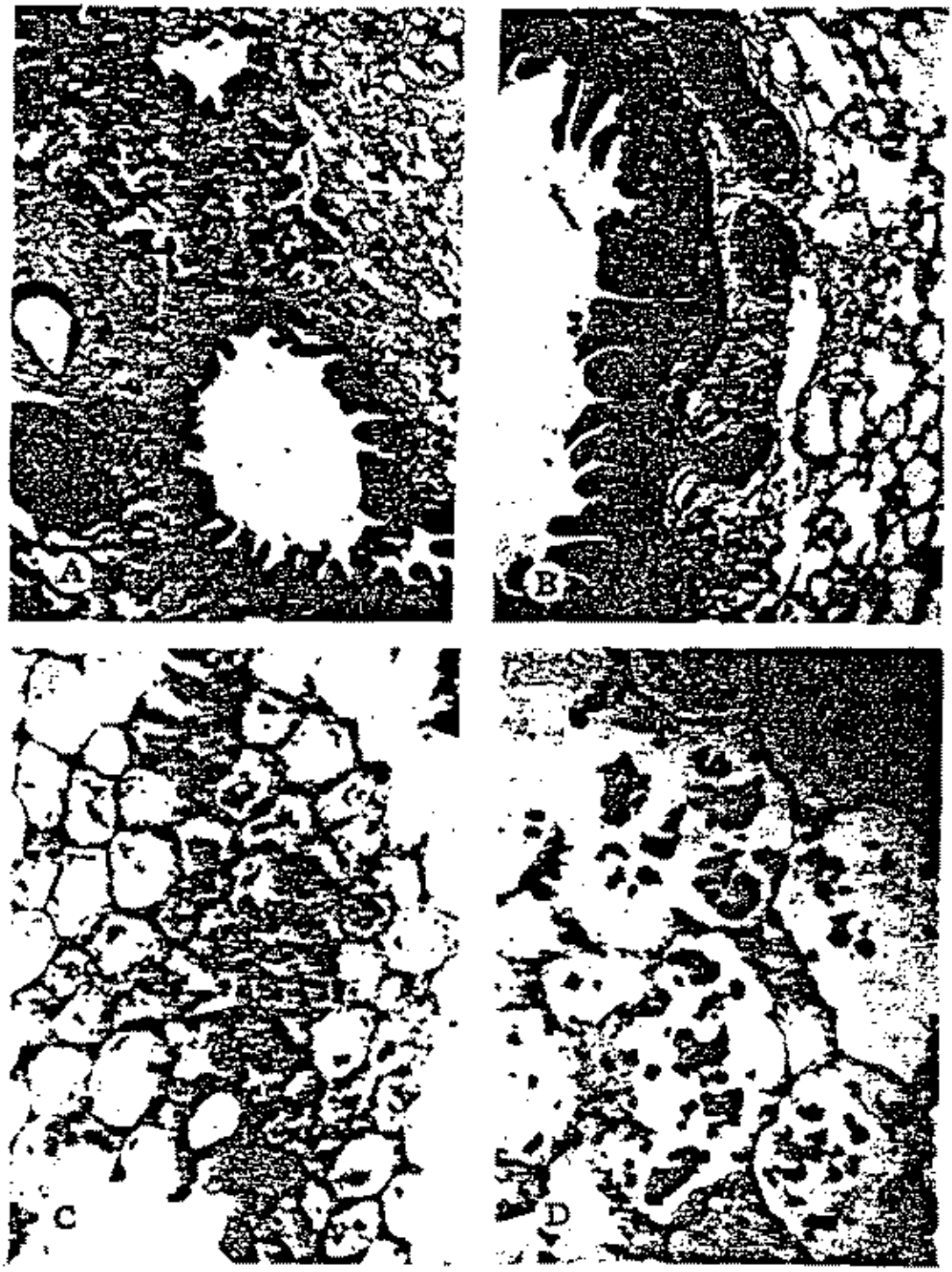

Fig. 4.—Chronic reaction to inhaled short-fiber glass wool—guinea pigs: inhalation study of less than 6μ fibers. *A*, peribronchial fibrocellular reaction which has surrounded epithelialized alveoli, thus producing a spurious adenomatous appearance (reaction at one year). *B*, hyperplasia of bronchial epithelium without inflammatory reaction in the mucosa (one-year result). *C*, focal parenchymal cellular reaction, with alveolar wall reaction and macrophage catarrh (one-year result). *D*, glass-fiber-filled macrophages, occupying alveoli whose walls show no significant reaction (result at 18 months).

COMMENT

These intratracheal and inhalation studies with glass wool have confirmed fairly conclusively that glass is not fibrogenic when retained in the lung tissue. At the same time the gravity of the type of bronchial lesion provoked necessitates caution in dismissing glass wool as innocuous. Indeed, it should be regarded as a potentially harmful substance in circumstances leading to the inhalation of large quantities of the type of product studied in these experiments. Other modern types of glass wool or fiber glass may not have any comparable effects.

In several respects, the pulmonary reaction to glass wool is similar to that produced by asbestos fibers, which the glass spicules resemble. However, despite the prominence of glass spicules in the lung tissue, no "glass-wool bodies" were observed which could be compared to "asbestos bodies." It is therefore not the shape alone of the asbestos fiber which leads to the formation of asbestos bodies.

It is to be noted also that asbestos fibers are intensely fibrogenic, whereas the lung tissue reacts to the glass fibers by means of a cellular response chiefly. This contrast again emphasizes the fact that the physical resemblances between glass wool fibers and asbestos do not determine their respective pathogenic propensities.

Obliterative damage to the bronchioles and the proliferative reaction of the bronchiolar and bronchial epithelium are obviously the more important lesions caused by the glass wool. There is but a limited range of substances which can provoke epithelial hyperplasia in experimental animals,[6] and the specific effect of glass wool thus extends the list. The significance of this observation in relation to oncogenesis needs further clarification.

SUMMARY AND CONCLUSIONS

When introduced intratracheally, long-fiber, medium-caliber glass-wool dust provokes early marked bronchiolar damage, which persists for more than a year without leading to well-defined fibrosis.

Some of the glass wool is transferred to the hilar lymph nodes where it accumulates without inducing local fibrosis.

Inhalation of short-fiber, medium-caliber glass wool produces a retarded pulmonary reaction, comprising partly an interstitial pneumonitis but dominantly an endobronchiolar and peribronchiolar lesion.

A tendency toward bronchial epithelial hyperplasia arises under the influence of prolonged short-fiber, medium-caliber glass-wool inhalation.

REFERENCES

1. Dhers, V.: L'industrie de la fibre de verre, Arch. mal. profess. 7:19-23, 1946.

2. Pellerat, J., and Coudert, J.: La dermatose de la laine de verre, Arch. mal. profess. 7:23-27, 1946.

3. Roche, L.: Le danger pulmonaire dans l'industrie des fibres de verre, Arch. mal. profess. 7:27-28, 1946.

4. Kahlau, G.: Tödliche Pneumonie nach Glasstaub inhalation durch Verarbeitung eines Kunststoffes aus Glaswolle, Frankfurt. Ztschr. 59:143-150, 1947.

5. Schepers, G. W. H., and Delahant, A. B.: An Experimental Study of the Effects of Glass Wool on Animal Lungs, A. M. A. Arch. Indust. Health 12:276-279, 1955.

6. Schepers, G. W. H.: The Biological Action of Tungsten Carbide and Cobalt: Studies on Experimental Pulmonary Histopathology, A. M. A. Arch. Indust. Health 12:140-146, 1955.

Printed and Published in the United States of America