The Locus of Pathogenicity of Asbestos Dust

A Theory

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Documented experimental evidence, as well as the results of preliminary experiments, are presented which indicate a reduction in pathogenicity as the polyfilamentous arrangement of asbestos dust particles is replaced by a monofilamentous structure. On the basis of this evidence, it is proposed that the locus of pathogenicity of asbestos dust particles resides in their polyfilamentous structure.

Asbestos minerals are silicates, but the pathogenicity of their dusts is unmatched by that of any other silicate, and the fibrogenicity is equalled only by that of crystalline silica. There has been much speculation regarding the reason for this high degree of pathogenicity of the dust of the asbestos minerals, but today no satisfactory hypothesis remains.

Similar to the theories proposed for the pathogenic potential of silica dust, the first theory was a mechanical one based on the notion that inhaled asbestos particles tend to produce microtraumata by piercing and impaling delicate lung cells. This concept proved untenable when the dust of fibrous glass[1] and ceramic aluminum silicate fibers[2] were shown to be nonfibrogenic in the lungs.

A theory based on chemical structure became unsatisfactory when synthetic chrysotile, which has the same chemical composition as the natural product, produced no fibrogenic response in the lungs.[1] This nonfibrogenic response in the lungs of rats to synthetic chrysotile also destroyed the validity of the theory that the crystalline character of the asbestos fibers determined their pathogenicity. It is to be noted that synthetic chrysotile has the same crystalline structure as the natural product since it yields the same roentgenographic and electron diffraction pattern; and, like natural chrysotile, it also exhibits a tubular crystalline structure under the electron microscope.[1]

The presence of trace metals on the asbestos particles has also been considered a possible cause for their pathogenicity.[4] However, in a recent investigation, when neither the removal nor the addition of trace metals altered the pathogenicity of asbestos dust, this theory had to be abandoned (P. Gross, MD and R.A. Harley, Jr., MD, unpublished data).

The discovery that, when asbestos is ground to a fiber size less than 5μ long its fibrogenicity for the lungs disappears,[5] astounded the scientific community. This finding, subsequently confirmed,[6,7] proved to be an enigma that ultimately resulted in a new concept of the locus of pathogenicity of asbestos dust.

Although the new concept rests

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pational physicians and industrial hygienists in plants with relatively few employees. In any well-operated industry, there is a limit of overhead expenditure, but the necessary services of occupational physicians and hygienists can be obtained within reasonable limits, approximately proportional, within industries of comparable types, to the size of the population to be served. Medical-hygienic organizations in the community can be designed to serve all of its industries. In the past, their greatest obstacle has been their failure to supply the needed services.

The physician practicing occupational medicine alone, simply as a physician, is not capable of providing more than general advice and incomplete help in matters of environmental appraisal and control, yet these are absolutely essential for the safety of the employees engaged in certain types of industrial activity. Such a physician should be linked in his occupational practice with a qualified industrial hygienist, who must have a good laboratory at his disposal, just as the physician requires access to a trustworthy and well-equipped clinical diagnostic laboratory.

The owner or manager of a small industry is loath to employ a private medical-hygienic organization which is (or may be) also employed by his competitor. (Here, again, the physician engaged in the field of occupational medicine is not trusted to act as a physician should act. The physician in industry is often believed to differ from the one who serves the individual or family, who may be trusted with the most intimate information. If he is not a hireling, he will have to prove that he is not.)

Another factor which has hindered the organization of such private medical-hygienic units as are suggested above, is that they would have to be initiated, under present conditions, by physicians whose careers in occupational medicine have yet to be established, and who must make considerable capital expenditures without any assurance of the success of their professional efforts. (I know, personally, of several instances of this type in which the economic risk was too great to be assumed.) It seems likely, however, that the stern necessity of meeting certain governmental requirements on the part of small industries will alter this situation. A factor in this professional dilemma has been that in most states there has been no necessity for industry, either large or small, to meet standards of quality in matters of the health of its employees, and there has been almost no public demand for these standards which, in line with general experience and custom, were believed to be unattainable. This situation may, hopefully, be altered in the near future and create such a demand for medical services, in coordination with those of industrial hygiene, as to be irresistible. It would seem that some such demand must be made emphatically and effectively, if any reasonable sort of success is to be achieved in combatting the hazards of American industrial production.

No attempt has been made in this article to provide details of the organization of the industrial medical department, or of such a medical and hygienic facility as that envisaged for the small plant. Nor has any reference been made to the role occupied by the industrial nurse in either of these situations. These aspects of industrial health units within industry, or in the private practice of occupational medicine, are not considered to be of minor concern. Rather, they are recognized as essential features of the organization which must be dealt with by the individually responsible physician to suit the attendant circumstances. The position and functions of the nurse in industry, for example, while variable, are as well established as are those of the nurse in the doctor's office. They need not be discussed here. On the other hand, the relationship of the physician in industry to the industrial hygienist is a matter which requires repetitious statement. The complementary relationship between the physician in industrial practice, and the technologist in industrial hygiene, is an expression of the fact that neither individual in the combination can accomplish his task without the help of the other. It is hardly to be supposed that one man can achieve competence as a physician, and at the same time, possess the corresponding knowledge and skill to handle the technological problems concerning control of materials and types of energy. To protect the health of the people who work in certain industries, the utmost of competence is required of both the physician, and the industrial hygiene technologist. The requirements of the physician's practice, as well as the industrial hygienist's, may not be, or may not seem to be, as exacting in some industries as in others. It is nonetheless true that the professional man in occupational medicine or in industrial hygiene will have little difficulty finding problems of human health, on the one hand, and problems of environmental hazard, on the other, worthy of his greatest competence.

upon an embarrassingly obvious structural characteristic of asbestos. It is supported by uncontested documented experimental findings as well as by data from some promising preliminary experiments. The latter, however, require confirmation.

Theory and Supportive Data

The new theory is simply this: the locus of pathogenicity of asbestos dust resides in the polyfilamentous structure of its fibrous particles. Various data support this theory.

Man-made mineral fibers, in contrast to polyfilamentous asbestos fibers, are monofilamentous. The dust of those monofilamentous fibers (fibrous glass,[1] ceramic aluminum silicate,[2] and silicon carbide whiskers[4]) that have been studied have proved to be nonfibrogenic when inhaled or injected intratracheally.

Synthetic chrysotile is nonfibrogenic when it is injected intratracheally. It is monofilamentous. It differs from natural chrysotile in that its tubular crystals are discrete and not in close parallel apposition to each other, as is the case with the natural product.

When a grinding force is applied to asbestos fibers, they tend to split longitudinally rather than to fracture transversely. Consequently, asbestos that has been ground to a fiber length of less than 5μ will consist largely of fibers that are monofilamentous. Those bundles of fibers still remaining will be greatly reduced in thickness and will approach the monofilamentous state. It is the fact that most of the fibers in such finely ground asbestos are either monofilamentous or nearly so, that offers a logical explanation of its nonfibrogenicity.

When asbestos is heated to 1,000 C, its pathogenicity is either lost or severely reduced (P. Gross, MD and R.A. Harley, Jr., MD, unpublished data). At this temperature, the fibrils composing the bundles tend to become fused into unitary structures, ie, the fibers tend to become monofilamentous (Fig 1). Although chemical changes do occur as a result of the heat, such changes have no bearing on the resulting loss of pathogenicity since it has been shown (with synthetic chrysotile) that the chemical composition of asbestos is not responsible for its pathogenicity.

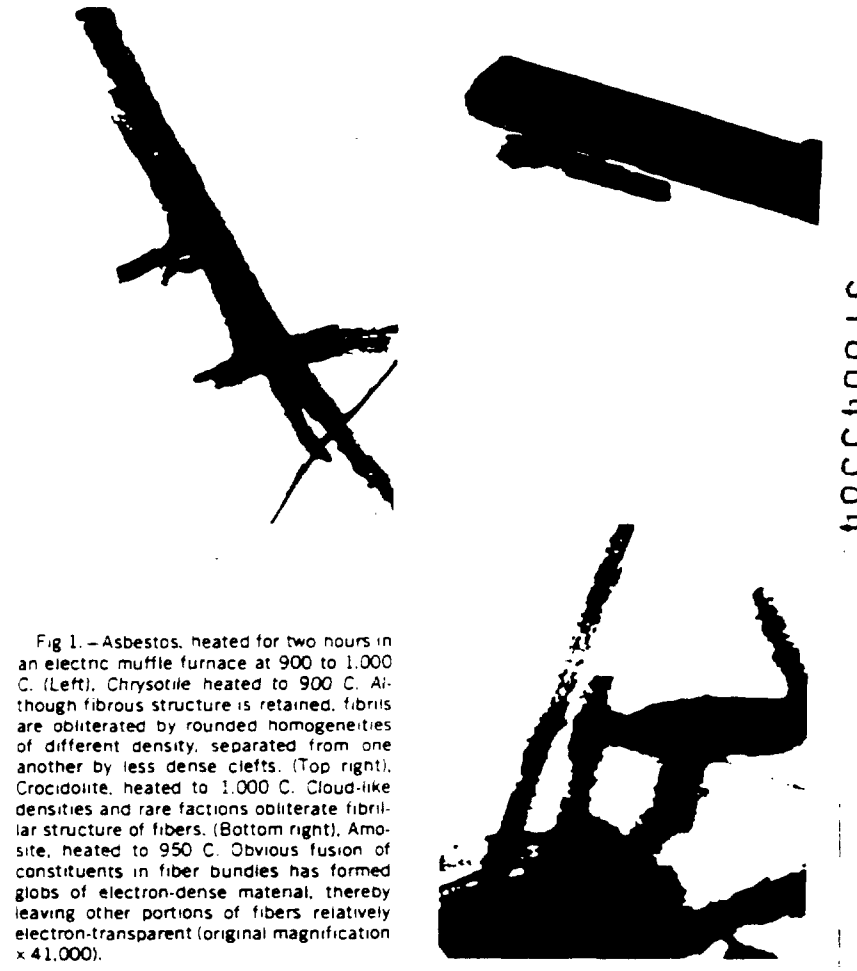

Fig 1.—Asbestos, heated for two hours in an electric muffle furnace at 900 to 1,000 C. (Left). Chrysotile heated to 900 C. Although fibrous structure is retained, fibrils are obliterated by rounded homogeneities of different density, separated from one another by less dense clefts. (Top right). Crocidolite, heated to 1,000 C. Cloud-like densities and rare factions obliterate fibrillar structure of fibers. (Bottom right). Amosite, heated to 950 C. Obvious fusion of constituents in fiber bundles has formed globs of electron-dense material, thereby leaving other portions of fibers relatively electron-transparent (original magnification x 41,000).

By cementing the fibrils of asbestos fiber bundles together chemically, it is possible to convert the polyfilamentous structures into monofilamentous ones. This has been successfully accomplished with various silicates such as those of lead, iron, and magnesium. The use of other water-insoluble cementing substances, such as those of magnesium and calcium pyrophosphate, calcium hypophosphate, and calcium metaphosphate, is contemplated.

The method has been to suspend finely ground asbestos in a dilute solution (1% to 5%) of an appropriate soluble metal salt (lead nitrate, iron chloride or magnesium chloride). After washing the asbestos free of all excess salt, it is suspended in a 1% solution of sodium silicate. The latter

Fig 2.—Chrysotile fibers cemented with lead silicate. Presence of lead silicate indicated by electron-dense stippling within lumen of the fibrils and elsewhere (original magnification x 143,000).

Fig 3.—Rat injected intratracheally with 10 mg iron silicate-cemented chrysotile, found dead six months later. Highly cellular inflammatory focus surrounds terminal bronchiole. An occasional giant cell is present, although in adjoining region many giant cells were observed. There is early fibrosis (hematoxylin-eosin, original magnification × 500).

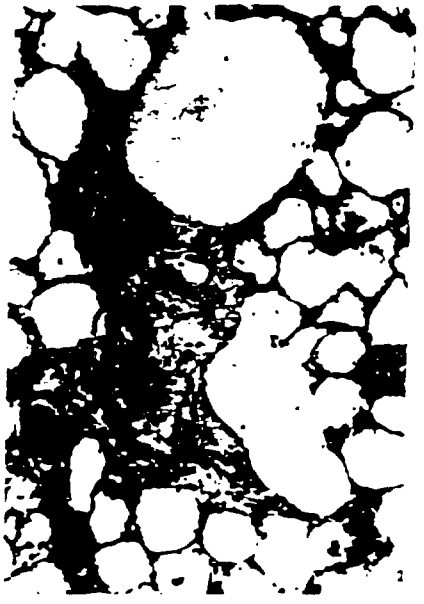

Fig 4.—Rat died 6¾ months after having been injected intratracheally with 7 mg unaltered chrysotile. Area of collagenous fibrosis is adjacent to respiratory bronchiole also involved in fibrosis. This fibrosis differs from that in Fig 3 as it is more collagenous and less cellular, ie, much more advanced. Granular material in collagen is brown pigment (hematoxylin-eosin, original magnification × 260).

reacts with the adsorbed metal salt to precipitate the insoluble silicate. From electron photomicrographs (Fig 2), it appears that solutes are capable of penetrating not only between the fibrils but also within the tubular lumen of chrysotile crystals.

In a preliminary study, the lead silicate- and ferric silicate-cemented asbestos were injected intratracheally into a few rats. Their lungs were examined three months after the intratracheal injection. The predominant pulmonary lesion produced by the lead-cemented asbestos was minimal in character, consisting of prominent giant cells, few histiocytes, little reticulin, and no collagen fibers (Fig 3). In contrast, the lesions of the same age produced by the unaltered asbestos consisted of collagen as well as reticulin fibers and histiocytes. Foci consisting of the minimal reaction, as were noted secondary to the "cemented" asbestos, were not found in lungs injected with the unaltered asbestos (Fig 4).

In an in vitro study it was found that lead silicate-cemented crocidolite caused only 30% hemolysis of human red blood cells whereas, under identical conditions, the unaltered crocidolite caused 100% hemolysis.

Iron silicate was less effective in reducing the pathogenic potential of chrysotile than was lead silicate. The reason for this was a gradual disappearance of the iron from the asbestos stored in the lungs. However, as observed in a tall glass cylinder, the iron silicate-cemented chrysotile stains a deep blue color with acidic potassium ferricyanide and retains this blue color. It settles rapidly, leaving a colorless supernatant which remains colorless over many months.

Because of obvious inadequacies in these experiments with cemented asbestos, the results can be termed only suggestive. But in conjunction with the other findings, they tend to support the thesis that when polyfilamentous asbestos dust particles are converted toward a monofilamentous state, a reduction in their pathogenicity takes place.

An extensive inhalation study with cemented and unchanged asbestos will soon be initiated, as well as an investigation of the comparative fibrogenic and cancerogenic potential of the polyfilamentous, versus the cemented asbestos dust injected intrapleurally.

Thus, the documented evidence points to a sharp difference in pathogenicity between polyfilamentous dusts on the one hand and monofilamentous dusts on the other, and to a significant reduction in the pathogenicity of asbestos dust when its particles are rendered monofilamentous either by grinding or by thermal fusion of fibrils. Preliminary unconfirmed experiments suggest that a similar reduction in the pathogenicity of asbestos dust may be accomplished by chemical fusion of fibrils, ie, the deposition of insoluble cementing materials between the fibrils of the fiber bundles.

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