CHAPTER TWO

ASBESTOSIS

THE CHEMISTRY OF THE DUST AND OF THE PULMONARY PATHOLOGY

To THE MAN in the street asbestos is a material which does not burn and is therefore used to advantage in such products as the fireman's protective clothing and the stand for the housewife's iron. It is seldom recognised that asbestos has over the last 100 years played a considerable and increasing, though unobtrusive, part in the life of the community.

It is a mineral which has the unique property of occurring naturally as a fibre. Seams of asbestos are found in particular rock formations in many parts of the world; the main deposits which are commercially worked lie in Canada, South Africa, and the U.S.S.R., and to a lesser extent in Europe, particularly Italy. The structure of commercial asbestos is that of a closely compacted bunch of extremely fine crystalline filaments lying parallel to one another. The length of each filament may vary from a small fraction of a centimetre to several centimetres. The operations by which the mineral is extracted from the mother rock closely follow conventional mining practices, and both underground and opencast methods are used. The treatment at the mine includes cleaning and a pri-

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mary opening process, so that the bagged asbestos fibre despatched from the mines is ready for more refined processes at the manufacturing centres.

Asbestos appears in a variety of natural forms (all of them fibrous), and each has particular properties. Chrysotile or serpentine asbestos, a hydrated magnesium silicate containing small amounts of iron and aluminium, is commercially the most important variety of asbestos. It yields flexible filaments of up to 7.5 cm. in length, but more commonly of less than 3.75 cm. It varies in colour from white to greyish green and is used largely in the manufacture of asbestos textiles which give good heat resistance and resistance to attack by alkali chemicals. Most of this type of asbestos is associated with ultrabasic rock or igneous rock composed of ferro-magnesium silicates. It is found chiefly in the Thetford district of the Province of Quebec in Canada, the Bazhenov area of the Ural mountains in Russia, and in Southern Rhodesia. A less important magnesium containing asbestos which, like chrysotile, can be woven, is anthophyllite. It is found in Scandinavia, is used as a slag-producing coating for welding rods and is associated with pleural calcification in the human being.

Amosite, a form of amphibole asbestos, on the other hand, contains more silica, a much larger proportion of iron (mainly in the ferrous or less oxidised state), and much less magnesium. Its fibres are long, sometimes as much as twelve inches in length, but they are brittle and have a relatively low tensile strength. It is used mainly in thermal insulation materials. Another commercially important type of asbestos, crocidolite or "Blue," has the important property of superior resistance to acid attack which makes it extremely useful in certain industrial applications, such as acid resistant pipe packings in chemi-

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cal installations. Both these iron-containing forms of asbestos have associated with them traces of the carcinogenic polycyclic hydrocarbon 3:4 benzpyrene in the proportion of 3.0 μg/100 g. for crocidolite and 1.0 μg/100 g. for amosite. This may explain the association of blue crocidolite with pleural (and sometimes peritoneal) mesothelioma. Tremolite and actinolite are two less important types of asbestos which contain calcium and a trace of iron. They may also contain benzpyrene. Their industrial uses are not, however, important; tremolite is used in filters and actinolite to strengthen paper.

From the human point of view, chrysotile has been the most important of the several named forms of the mineral which is generally called "asbestos." In the gross it is in the form of long thin aggregated needles which have the important property of floating in the air like thistledown. The general chemical formula is $3\,Mg.2SiO_2.2H_2O$—an hydrated magnesium silicon dioxide in which there may sometimes be iron and aluminium contaminants. Outside the human respiratory tract these fibres may be up to 2 cm. long, but only a few microns in diameter. They are fragile, rigid, and snap cleanly across their transverse diameters. But the mineral also cleaves almost spontaneously in the plane of the long axis of its molecules. Hence the needle-like form of its particles. The molecules are formed of chains of silicon dioxide and magnesium which are coated with hydroxyl groups, and the spontaneous cleavage is along this coating.

The chrysotile molecule can be considered to be composed of a sheet of hydroxylated magnesium silicate formed into a helical tube. Moreover, the electron microscope reveals these tubes and it shows that they are mostly circular on cross section, although some appear polygonal. Each tube contains a rather thicker one inside, the outer

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tube averaging about 40Å thick and the inner 70Å. Each "tube in a tube" has relatively large areas of empty space both within it and between the inner and the outer one, and both tubes of the unit appear to be partially filled with chrystalline or formless material. Sometimes this takes on the appearance of radial lines which join the inner to the outer tube (Figure 5).

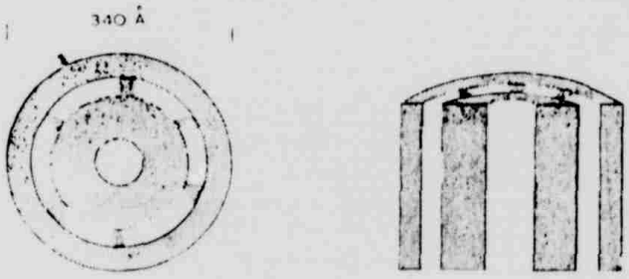


Figure 5. Simplified diagram of electron micrograph of a single asbestos fibre. It consists of one tube inside the other separated from it by amorphous material.

If an *asbestos needle* is snapped across, magnesium hydroxide is formed at the free end, and it gives an alkaline reaction when it is dipped in an indicator. Along the sides of the needle a series of chemical reactions, ill understood but unique in industrial pulmonary disease, take place to form the asbestos "body" in the lung. These bodies are about 3μ thick and 70μ long compared with the dimensions of the naked needles of asbestos lying free in the lung which average 30μ in length and 0.5μ in diameter. In shape they are usually described as "dumb bell" but often they look either like a chain of beads or *a match with heads at both ends*. These asbestos bodies are

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less fragile and less rigid than the naked needles which suggests that a physico-chemical change has occurred to the asbestos while it is in the lung. As it lies in the tissues the needle gradually becomes encapsulated with a clear substance which slowly becomes manifest after about two months in the lung (Figure 6).

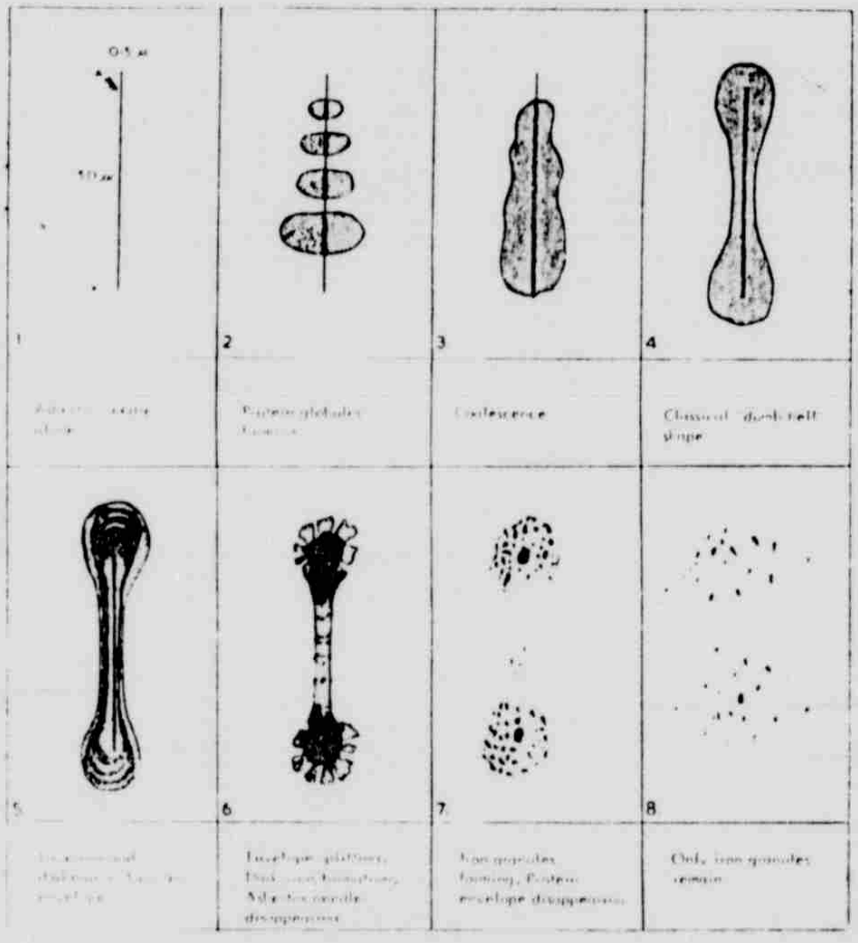


FIGURE 6. The chemical life history of the asbestos body.

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This coating first appears as globules along the centre of the needle which gives a chain-of-beads appearance. Then the ends become surrounded with a thicker curved covering which forms what the German workers picturesquely call a "hull." The material from which this "hull" is made is amphoteric, reacting with either acid or alkali; it gives a positive biuret reaction and it is dissolved by the proteolytic enzyme, trypsin. The evidence, therefore, strongly suggests that the substance which surrounds the asbestos needle to form the body is a protein. Indeed, a kind of asbestos body has, in fact, been synthesized by coating a needle with egg albumin. As the asbestos body becomes older, the needle in its centre becomes less noticeable, and finally disappears. No needles can be seen which are shorter than 10μ which suggests that they eventually go completely into solution. An asbestos needle count in the lung also suggests gradual solution, as the longer the patients survive after last inhaling asbestos, the smaller the intrapulmonary fibres appear to be (Figure 7). The whole asbestos body eventually becomes segmented and radial cracks appear in the bulbous rounded ends, and at last nothing is left but a string of dark granules which appear to be iron oxide which has gradually accumulated in the protein envelope as it has become older. What, therefore, started as a clear symmetrical asbestos needle ends as an opaque collection of amorphous iron granules. The source of this iron has yet to be traced. Has it been breathed in along with the asbestos? Is it a molecular contaminant, or has it come from the blood haemoglobin? Analysis of asbestos bodies which are beginning to develop dark granules shows that as much as 40 per cent is iron, 31 per cent organic, 6.9 per cent phosphorous pentoxide, and 1.6 per cent asbestos. The protein packaging of the asbestos needle may well minimise the

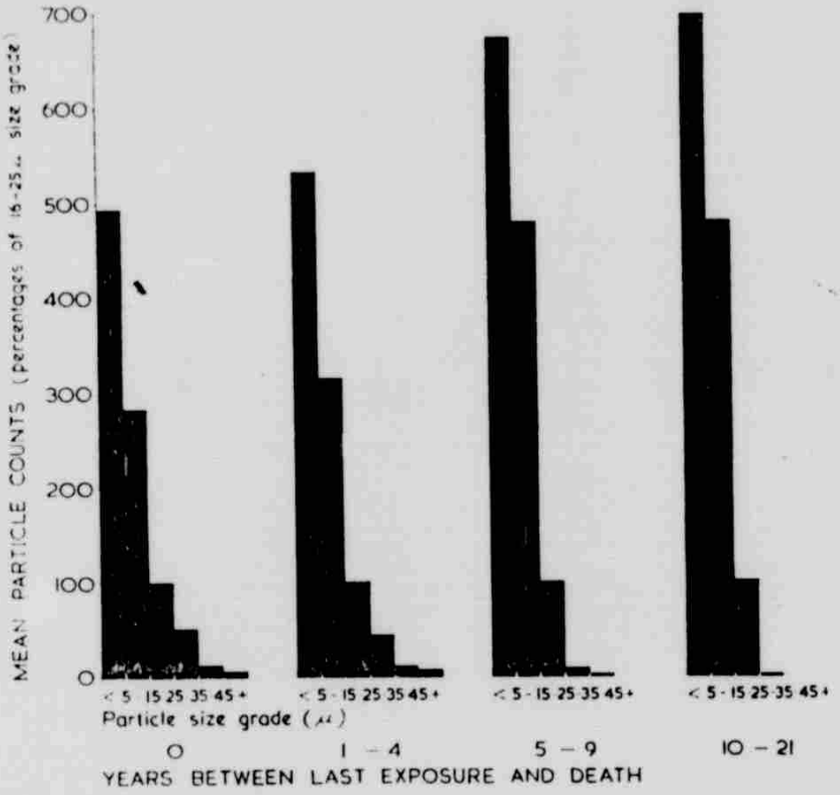


Figure 7. There are a smaller number of large particles and a greater number of small in the lungs the longer the patient survives.

biological harm which it does, as it has been shown that whereas inhaled asbestos needles produce a pulmonary reaction in guinea-pigs, asbestos bodies do not. But the human significance of the animal work is not very clear because of very different species' reactions. There may, however, be a physical as well as a chemical factor in the production of the disease, since it has been shown that it is more likely to be produced by long asbestos needles of between 20μ and 50μ than by those below 20μ.

Asbestos, or a material associated with it, appears to be carcinogenic, but the chemistry of this is by no means yet clear. More and more cases of mesothelioma of the pleura or peritoneum are being reported in cases of asbestosis. Similar tumours have been produced by the implantation of dusts in laboratory animals, and particularly the rat. But similar tumours were also produced by the injection of silica. The suggestion that asbestos is associated with an organic carcinogen of the 3:4 benzpyrene type has been made and, indeed, such a compound has been found in association with the crocidolite type of asbestos, but none with chrysotile or silica. This is a puzzling finding, because from a geological point of view the temperatures and pressures at which asbestos is formed make it most unlikely that an organic compound would survive.

THE CONSEQUENTIAL CHEMISTRY

The changes in the lung substance in asbestosis bring consequential changes in the chemistry of the pulmonary and blood gases. Because of the modification of the gross physical structure of the lung, there is a reduced maximum ventilation and vital capacity, and owing to the microscopic physico-chemical changes in the alveolar walls, the blood-gas barrier becomes less permeable and the passage of oxygen from alveolus to capillary is impeded. But on the other hand, the passage of CO_2 in the opposite direction is not obstructed because this gas is so very much more soluble than oxygen. The advanced case of asbestosis tends, therefore, to be anoxic, and increasingly so as exercise metabolises oxygen more quickly than it can be transported across the defective gas-blood barrier. Experimental work with carbon monoxide supports the idea that the transfer of oxygen from alveolus to blood is impeded.

But there is another factor quite as, if not more, important than the diffusion defect. There are relatively large unaerated parts of the lung in this disease through which blood flows without becoming oxygenated to mix with that which has, thus producing an oxygen saturation in the final mixture less than 100 per cent.

THERAPY

The fundamental therapeutic approach to asbestosis should be preventive, since it is a progressive disease for which there is no effective curative therapy. The three *important elements in prevention are:*

(1) Regular estimations of atmospheric asbestos at the working positions, together with fibre counts and length grading.
(2) Annual vital and diffusion capacity measurements.
(3) Annual large-size chest X-ray.

Congestive heart failure of the right-sided type is the commonest ultimate danger in this disease, and increasing breathlessness is the lot of its victims. A superadded acute winter chest infection is likely to push such a patient over the edge of his cardiac reserve, so that he becomes an overt case of heart failure. A higher than expected proportion of the cases also develops carcinoma or mesothelioma of the lung or pleura. Asbestosis is one of the pneumoconioses which carry an additional risk of this.

The therapeutic steps in the developed case should therefore be as follows: Men with X-ray evidence of the disease should be advised to take work which will not entail further exposure. Indeed, from a strictly pathological point of view, they will already be rather advanced cases. Consideration should be given to explaining to them that as they get older they will gradually become shorter in the wind, but probably less quickly than if they re-

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mained in their dusty job. The sinister fact is beginning to emerge that this disease becomes pathologically established before there are any warning signs or symptoms.

A large chest X-ray should be taken annually to detect a developing neoplasm. Superimposed acute chest infections should be treated either by half-a-million units of injected penicillin four times a day, or by one to three grammes of tetracycline three times a day. The treatment of the ultimate congestive cardiac failure has nothing about it which is specific to asbestosis.

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