Clearance of asbestos bodies from the lung: a personal view

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ABSTRACT  In histological sections asbestos bodies in human lungs may be either transparent, yellow, strongly Perls-positive structures as described in published reports, or opaque, black structures, the ferroprotein coating having been converted into haemosiderin. The transparent asbestos bodies fragment into segments; the black asbestos bodies disintegrate into a mass of haemosiderin granules that accumulate as dense deposits, particularly near to blood vessels. The presence of haemosiderin granules indicates that asbestos bodies have broken down. When a patient has died with a mesothelioma there is little evidence of phagocytic activity in many areas of the lung. When exposure to asbestos ceased many years before a mesothelioma developed there may be few recognisable asbestos bodies remaining in the lung.

The relation between mesothelioma and asbestos is now well established, but there are often few asbestos bodies in the lungs of patients who have died with mesotheliomas even when the patients were known to have been exposed to asbestos. Asbestos bodies were found in only 12 of one group of 45 patients1 and only 18 of another group of 45 patients2 who died with mesotheliomas. None was found in the lungs of a welder and an asbestos gasket worker, known to have been exposed to asbestos, who died with mesotheliomas.3

The lungs may still retain many uncoated asbestos fibres; among 88 cases of mesothelioma with a history of asbestos exposure only one had fewer than 20000 asbestos fibres per g dried lung tissue,4 and a patient who died 60 years after less than one year’s exposure retained >500000 fibres per g dried lung tissue.

The breakdown of asbestos bodies in the lung was first suggested by Beger,5 who made an early and extensive study of the effects of asbestos, and more recently by Hourihane.6 The breakdown of asbestos bodies in the lung of experimental animals was observed by Botham and Holt.7 Both Beger and Hourihane observed dark brown or black granules of iron oxide or haemosiderin resulting from the decomposition of the asbestos bodies.

A study of histological sections from the lungs of three patients who died with mesotheliomas and who had inhaled asbestos in contrasting circumstances has been used to throw light on the removal of asbestos bodies from the lung.

Histological material and observations

Lungs from three patients who died with mesotheliomas were studied. One patient probably had a heavy exposure to asbestos over a period of 20 years, and a second had a light exposure, probably for 50 years. A third patient after exposure for two years had no known exposure until she died many years later.

CASE 1

A man worked for 20 years with an asbestos firm. He was employed in a chemical factory and later became an agricultural worker. He died aged 46, that is 27 years after his first known exposure to asbestos. Many asbestos bodies were visible, all of which were transparent, golden yellow structures (fig 1). There were areas in which asbestos bodies had broken down leaving many transparent yellow fragments that were all extracellular. Heavy deposits of black or dark brown granules (haemosiderin), some in the shape of asbestos bodies, were scattered throughout the tissue and were concentrated at the periphery of blood vessels (figs 1 and 2). In some areas the granules were intracellular. A few uncoated fibres

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were observed. In one section macrophages were attached to both ends of an asbestos body, one macrophage having granules in the cytoplasm.

CASE 2
A man who died at the age of 70 had worked for about 50 years as a plumber, mainly lagging pipes with asbestos. A post-mortem examination showed a mesothelioma of the pleura that had grossly thickened the chest wall and affected the diaphragm, pericardium, and mediastinum.

A few uncoated asbestos fibres were seen. There were scanty asbestos bodies, some of which were transparent and golden yellow (fig 3) but others were black (fig 4). Some of the asbestos bodies had fragmented, one or more beads having separated (figs 3 and 4). Black or brown granules were scattered extensively throughout the tissue with dense deposits near blood vessels (fig 5). Some of these granules were still in the form of asbestos bodies (figs 6 and 7). There were numerous macrophages that contained haemosiderin granules (for instance, fig 7). Most of

Fig 1  Mesothelioma. Lung 1. Transparent yellow asbestos bodies and black haemosiderin granules in human lung. (Haematoxylin and eosin × 1000.)

Fig 2  Mesothelioma. Lung 1. Note position of haemosiderin granules, some of which (arrows) still retain shape of asbestos bodies, relative to a blood vessel. (H and E × 470.)

Fig 3  Mesothelioma. Lung 2. Transparent yellow asbestos bodies showing disintegration (arrows) at one end. (H and E × 1000.)

Fig 4  Mesothelioma. Lung 2. Black asbestos body. End segment has separated as structure disintegrates. There are many brown and black granules derived from other fragmented asbestos bodies. (Eosin only × 1000.)
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the tissue was devoid of Perls-positive material, but a few areas disclosed rounded, Perls-positive macrophages that contained haemosiderin, many of which were vacuolated.

CASE 3

As a child a woman inhaled asbestos dust when she lived near to an asbestos factory between the ages of 5 and 7 years. During the subsequent 37 years she had no known exposure to asbestos. She died with a malignant mesothelioma that almost completely replaced the right lung and infiltrated the right side of the pericardium. There were extensive metastases.

Few asbestos bodies were seen but several were very long. None was transparent, all were black and opaque. Deposits of black granules were visible, especially near to blood vessels. There were a few randomly scattered granules; they were almost all extracellular and deposits were less dense than in lung 2. Sections treated with Perls' reagent were almost devoid of Perls-positive material. An

Figs 6 and 7  Mesothelioma. Lung 2. Haemosiderin granules as remnants of asbestos bodies. Many scattered extracellular granules indicate that other asbestos bodies have disintegrated. Some granules appear in macrophages in fig 7. (Eosin only × 1000.)

Fig 8  Mesothelioma. Lung 3. X-ray analysis of a silicate mineral particle several μm across (A) and of granules (haemosiderin) <0-5 μm across (B) in residue after digesting lung in hypochlorite.
occasional rounded structure that stained weakly blue may have been a modified macrophage, but it showed no nucleus. Asbestos bodies seen in sections from these subjects were found only in lung tissue; there were no asbestos bodies in the tumours. Hourihane reported that asbestos bodies are rarely seen within tumour tissue.

**Composition of the Granules**

Sections from lung 3 were scanned in a Jeol 100S electron microscope with a link system and energy dispersive microanalysis attachment. Since, except near to blood vessels, the granules were widely dispersed, it was not possible to locate them. A piece of the tissue was digested with sodium hypochlorite, and the residual matter was separated centrifugally. A part of the residue was transferred to a stub and coated with gold. Particles were seen under the electron microscope that were larger than one micron but there were many smaller particles less than 0.5 μm. X-ray analysis showed that the former particles were silicates (fig 8a), but the latter gave a single peak at about 6.2 keV, showing that iron was the only metal present (fig 8b) and confirming that the particles were haemosiderin.

**Discussion**

When asbestos dust is inhaled some of the fibres become coated with a ferroprotein, forming asbestos bodies. These structures were observed by the earliest investigators, and a detailed description appeared in the remarkable paper of Beger, who studied the lungs of a dead asbestos worker. Beger described asbestos bodies as transparent, golden-yellow structures, many having the form of a dumb-bell or a string of beads, with a central asbestos fibre and a ferroprotein coating that was much thicker than the fibre. He showed the presence of ferric iron in the coating by a positive Perls reaction. Later studies on the mechanism by which asbestos bodies are formed have been published, for example by Das et al.

Beger described the manner in which asbestos bodies eventually break down by fragmentation, a process that can readily be shown in the lungs of guinea pigs that have inhaled asbestos. Asbestos bodies begin to form in the guinea pig lung about four weeks after the dust is inhaled, and fragmentation is first seen about 22 weeks later. They may form in the human lung within 20 days of the dust being inhaled.

Although in the human lung asbestos bodies are usually transparent and golden yellow, as described in published reports, they are sometimes opaque, black structures. In the present series of mesothelioma cases three lungs are described: the first showed only golden-yellow asbestos bodies, the third only opaque, black asbestos bodies, and the second both types. Fragmentation of some transparent asbestos bodies was observed, single beads having separated from beaded structures (fig 3) as has previously been described. The black asbestos bodies sometimes fragmented in a similar manner (fig 4), but other structures appeared to break up into a large number of small opaque particles that were identified by x-ray diffraction as haemosiderin. Stages in the fragmentation of these asbestos bodies are seen in figs 6 and 7. Although these fragments were seen in histological sections as granules sometimes several μm in size, electron microscopy showed that the granules were in fact agglomerates of particles less than 0.5 μm in diameter. They were easily differentiated from a few larger particles that were identified as mineral silicates by x-ray diffraction (fig 8).

Haemosiderin particles were sometimes found in macrophages (fig 7), but there were few macrophages in most sections. No macrophages were identified with certainty in lung 3; there were a few rounded, non-nucleated, Perls-positive structures in lung 2 that contained granules and may have been the remnants of macrophages. Lack of macrophage activity may be due to poor oxygenation; Green has shown that phagocytic activity is seriously impaired if the partial pressure of oxygen is decreased. Since the formation of an asbestos body implies the intervention of a macrophage lack of macrophage activity would explain why there are few asbestos bodies but many uncoated asbestos fibres in the lungs of some mesothelioma patients. Since asbestos bodies eventually fragment, it is not surprising that no relation has been found between the number of asbestos bodies and fibres in the lungs of mesothelioma patients.

Apparently there are two routes by which asbestos bodies may be removed from the lung. Transparent structures may break up to give small fragments that are phagocytised and dissolved by macrophages. Alternatively, ferroprotein may be converted into haemosiderin, the structure then fragmenting into granules that are smaller than 0.5 μm. Initially the haemosiderin may be phagocytised and heavy deposits are found near to some blood vessels (fig 5), but later phagocytosis is less important because there are few macrophages.

Beger and Hourihane recognised that the granules represent residual debris of disintegrated asbestos bodies, but their presence is often ignored when the histological appearance of lung sections is considered in relation to possible asbestos exposure. Milne, who made a retrospective survey of 32 cases of mesothelioma with regard to asbestos exposure, stated that, in assessing the number of asbestos bodies...
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“granules were disregarded and unless an unmistakable beaded body was seen it was not considered a positive finding.” The presence of haemosiderin cannot be ignored; the granules may indicate that asbestos bodies originally present have broken down.

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