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ASBESTOS AND FERRUGINOUS BODIES

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Are we adding fibers of many kinds to our environment, giving a confusing picture in our human samplers?

W. C. Cooper, 1967. (1)

Asbestos body-like structures (»ferruginous bodies«) found in some of the smears prepared from lungs of 450 consecutive necropsies in Zagreb were studied with particular reference to the morphological features of the iron-staining reaction of ferruginous coating. From this study it appears that there are no differences in iron staining properties of the coating which would serve to distinguish between ferruginous bodies of asbestotic and those of nonasbestotic origin. The colour pictures of the unstained (native) and the corresponding stained ferruginous bodies are presented.

The unexpectedly high incidence of asbestos bodies reported all over the world (2–9) in sections of lung from routine necropsies of people without disctinct asbestos exposure, indicates either a seriously widespread air pollution with asbestos, or a hitherto unappreciated possibility of pseudo-asbestos bodies being formed. In the majority of these reports the bodies have been defined morphologically and described as »asbestos bodies« because the only asbestos fibers were considered to be responsible for their formation and to be at their core. However, there is abundant evidence in the literature that the bodies can be formed in workers exposed to fibers other than asbestos. Thus *Gloyne, Marshall* and *Hoyle* (10) as early as 1949 reported on bodies similar to asbestos bodies in the lung of workers exposed to graphite. *Meurman* (11) 1966 described

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bodies with complete resemblance to asbestos bodies but having at their core elongated or fibrous material from a variety of other minerals instead of asbestos (including biotite-fusain, hornblende-rutile, diatomaceous earth, graphite and carborundum). Moreover, *Gross, de Treville, Cralley and Davis* (12) showed that the bodies morphologically indistinguishable from the asbestos bodies could be experimentally produced in hamsters by different man-made non-asbestos fibrous materials. After all, *Cralley* et al. (13) have shown that respirable fibrous dust particles, both natural and synthetic are ubiquitous in the modern urban environment and it is quite possible that at least some of them could form the core of »asbestos« bodies or better to say of pseudoasbestos bodies.

It has been well established that all the bodies regardless of the nature and origin of the central core contain iron and it seems that so far the only undisputable common characteristic of these bodies is their iron-containing coating. For this reason *Gross* et al. (12, 14–18) adopted and recommended for them the general term »ferruginous bodies« which most adequately encompasses all such bodies »unless and until the central fiber has been positively identified as asbestos«.

Although many authors have emphasized the fact that both asbestos bodies and pseudoasbestos bodies when sequestered in the lung develop an iron-protein complex coating demonstrable by Prussian blue reaction, there are few if any reports in the literature dealing with details of this colour reaction as seen with a light microscope.

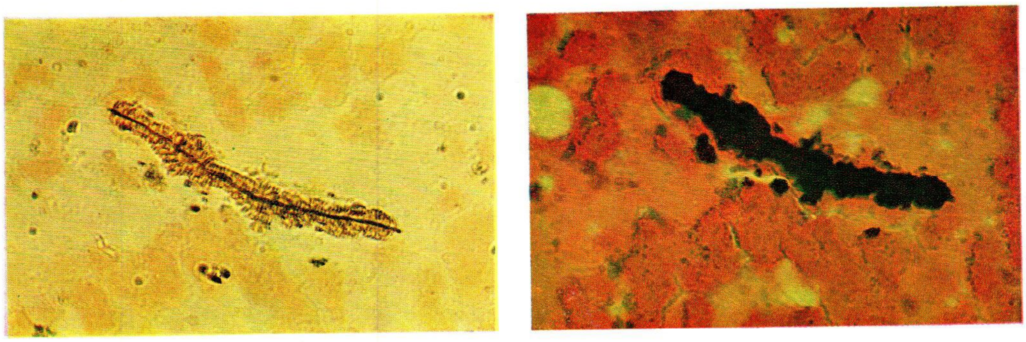
The purpose of this work was 1) to study the morphologic features of the iron staining reaction of ferruginous coating; 2) to find out whether any colour differences might serve to distinguish between ferruginous bodies of asbestotic origin and those of nonasbestotic origin, and 3) to present the colour pictures of the unstained (native) and the corresponding stained equivalents of ferruginous bodies in humans.

MATERIALS AND METHODS

Smears were prepared from the lungs of a series of 450 patients coming to consecutive necropsies in the Department of Pathology, University of Zagreb. After an incision was made in the base of either lung the cut surfaces were scraped with a knife and the exuding fluid was smeared on a standard microscope slide.

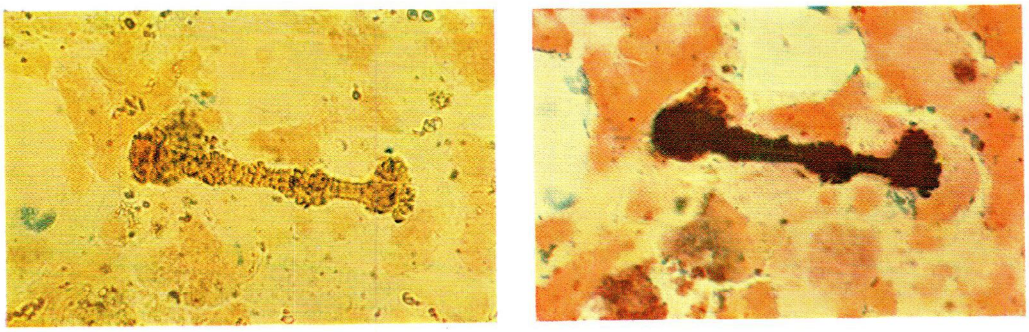
To analyze the staining properties of individual bodies they were in many smears photographed both before any staining and after being submitted to the Prussian blue reaction and the subsequent counterstaining. The Prussian blue method stains the iron-containing coating material of the ferruginous bodies a dense blue, making them easily visible against the background of a red (safranin) counterstain.

Ferruginous bodies a) *in the unstained smear,* b) *in the smear stained for iron*



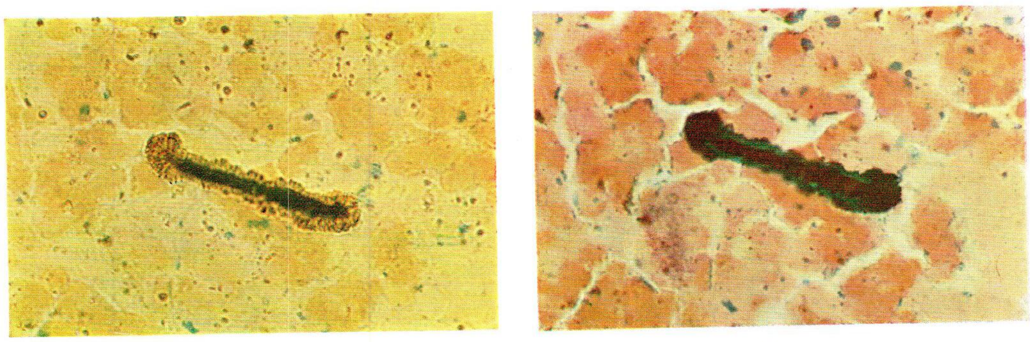
a) b)

Fig. 1. *Ferruginous body, corrugated but not clubbed with a clearly visible black core (probably »pseudoasbestos body«)*



a) b)

Fig. 2. *Ferruginous body with invisible, translucent core and clubbed ends (probably a true asbestos body)*



a) b)

Fig. 3. *Ferruginous body, corrugated and partly clubbed with a thick black, opaque core (probably »pseudoasbestos body«)*

RESULTS

The bodies were found in 18% of smears from 450 necropsies. Whenever stained by the Prussian blue method they gave a positive reaction. Nonstained and respective stained identical morphological examples are shown in each figure of the colour photomicrograms (figs. 1–3). In the nonstained smears the bodies are seen as golden-yellow corrugated and incompletely beaded rods with more or less clubbed ends. The shaft is usually straight, sometimes curvilinear, in rare instances also circular. The core may be visible or invisible. When visible it is usually black, surrounded by a variable amount of yellow coating. When stained for iron the dense blue stain of the Prussian blue reaction may cover the structure, completely masking the core from direct view (fig. 1) or the black central fiber may remain well visible (fig. 3). However, there were no differences in the iron-staining properties of the coating in relation to the visibility or non-visibility of the central core. In other words, the nature and origin of the central fiber – as far as can be judged by the staining characteristics of these bodies – do not seem to have any influence on the iron-staining property of the coating.

DISCUSSION

Since the time these bodies were described for the first time, they have several times changed their name in accordance to the corresponding level of the knowledge of their nature or significance at the time of the respective description. In 1906 *Marchand* (19) was the first to note »peculiar pigment crystals« in the lungs. Within the alveoli he found masses of light yellow to reddish-brown rod-shaped structures with clubbed ends. Because they turned black near the areas of putrefaction, *Marchand* suspected that the yellow pigment contained iron; this he confirmed by intense blue coloring with potassium ferrocyanide. At first the bodies were thought to be pathognomic of asbestosis: *Stewart* and *Haddlow* (20) described them as an integral part of asbestosis and coined the term »asbestosis bodies« but as soon as it was understood that they were not directly related to fibrotic disease but solely to asbestos exposure the term was changed to »asbestos body«. It is under this name that the bodies are still most often called although recently in many of them the asbestos nature of the core has been questioned. It has repeatedly been shown that the bodies may be formed from a number of different mineral fibers and that their fine structure is identical with that of genuine asbestos bodies. For this reason *Gough* (21) prefers to call them »mineral-fibre-bodies«. When it was established that all the bodies that develop in response to the presence of filamentous dust in the lung have a coating of iron-containing protein as a common feature, *Gross* and his coworkers (16) proposed, as already mentioned, the term »ferruginous bodies«, pointing out that »this generic term encompasses both asbestos and pseudoasbestos bodies as previously employed«.

Contrary to the prevailing opinion, the differentiation between asbestos and nonasbestos ferruginous bodies is pretty difficult. *Ashcroft* (8) adopted the following criteria for the acceptance of asbestos bodies: refractility, a pale central fiber, smooth or segmented yellowish encrustation and clubbed or rounded ends. *Roberts* (6) defines a pseudoasbestos body simply as »having a black carbonaceous centre«. *Thomson* (3) has particularly stressed the difference on the basis of the transparency or opacity of the central fiber. *Gross* et al. decline this proposal as inappropriate, inasmuch as they have demonstrated that a number of transparent fibers of respirable size other than asbestos are capable of producing ferruginous bodies that are indistinguishable from those produced by asbestos. On the other hand, *Stumphius* and *Meyer* (22) gave evidence that the existence of pseudo-asbestos bodies must be considered extremely doubtful: in all the cases investigated by electron diffraction and by X-ray microanalyzer, the core of the supposed pseudoasbestos bodies proved to consist of asbestos.

If we adopt the »classical« criteria for asbestos bodies and pseudoasbestos bodies then the structures at the top and bottom of our color photomicrographs are probably pseudoasbestos bodies while the one in the middle fulfils the criteria for a genuine or true asbestos body. As was also pointed out by *Gross* et al. (12), when stained for iron the outlines and the finer structure of these bodies are indistinct due to the diffusion of the pigment. However, comparing the iron content of the bodies one might conclude that neither the intensity of iron staining nor any morphological feature of the ferruginous coating could serve for distinguishing between ferruginous bodies of true asbestos and those of nonasbestos origin. In this connection it should be noted that *Stumphius* and *Meyer* (22) have found that the iron concentration decreases with the decreasing thickness of the coating due to the fact that the iron content of the protein coat is higher than the iron content of the asbestos.

The origin of iron in the ferruginous body has not been definitely established though it has many interesting aspects. *Davis* (23–27) has demonstrated with the electron microscope that ferruginous bodies are formed within macrophages by granules of ferritin or a ferritin-like protein that are precipitated upon and around some foreign materials. The deposition of iron-protein starts at both ends and later on the shaft. According to *Botham* and *Holt* (28, 29), the Prussian blue positive material is »apparently derived from red cells« which is deposited on them. *Davis* (25, 26) reported, however, that these structures were always formed intracellularly within macrophages or giant cells.

Of special interest is the relationship between iron and asbestos bodies with regard to the kind of the asbestos inhaled. The most commonly used commercial form of asbestos is chrysotile, a hydrate magnesium silicate which does not contain iron at all while amphibole asbestos (crocidolite and amosite) is composed of silica and iron. Thus it would logically be expected that some if not most of the cores of asbestos bodies are composed of chrysotile. Yet, in a study of the central fiber of human pulmonary ferrugionous bodies, *Gross, deTreville* and *Haller* (17) were able to exclude chrysotile as a constituent of all 28 ferruginous bodies that had been investigated from as many Pittsburgh city dwellers, in spite of the fact that more than 90% of the asbestos used in USA were chrysotile. Similar observations were made by *Stumphius* and *Meyer* (22): out of 27 uncoated asbestos fibres investigated by electron diffraction, 17 appeared to belong to chrysotile and 15 to amphibole but all the cores of asbestos bodies collected from the same sample consisted only of the amphibole.

Regarding the role of iron in the asbestos body formation, it might be worth while to quote another interesting finding of *Stumphius* and *Meyer* (22). These authors have noted objects similar to asbestos bodies in the lungs of shipyard-workers in whom typical asbestos-initiated tumours – pleural and peritoneal mesothelioma – were found at an unusually high frequency, though only slight asbestos exposure had taken place. The affected workers, however, had been exposed to high concentrations of iron oxide (flame cutters and welders). Originally the authors thought that the bodies were pseudoasbestos bodies containing an iron oxide core, and it was suspected that pseudo-asbestos bodies might play a part in the genesis of the tumours. Investigations carried out with the aid of electron diffraction and electron microscopy have shown, however, that the core of the bodies contained asbestos of the amphibole type and that, therefore, they were not pseudo but »normal« asbestos bodies. *Stumphius* and *Meyer* concluded that the simultaneous exposure to low concentration of asbestos and high concentrations of iron oxide might be an important cofactor in the genesis of mesothelioma found in ship-yard-workers.

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Sažetak

AZBESTNA I FERUGINOZNA TJELEŠCA

Tvorbe nalik na azbestna tjelešca (»feruginozna tjelešca«) nađene u stanovitom broju razmaza priređenih iz rezova pluća kod 450 redom izvršenih obdukcija u Zagrebu, proučavali su autori s naročitim obzirom na morfološke karakteristike pozitivnih reakcija na željezo što ih daju feruginozne ovojnice. Prema tim proučavanjima čini se da nema razlika u reakcijama na željezo koje bi mogle poslužiti za diferenciranje feruginoznih tjelešaca azbestnog i feruginoznih tjelešaca ne-azbestnog porijekla. Prikazane su i mikrofotografije u boji i to neobojenih (nativnih) i odgovarajućih obojenih feruginoznih tjelešaca.

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