REVIEW ARTICLE

Asbestos and Other Ferruginous Bodies

Their Formation and Clinical Significance

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Analyses of asbestos bodies from the general population have confirmed that these structures, like asbestos bodies from the lungs of asbestos workers, contain an asbestos core. In members of the general population this core is almost always an amphibole, whereas asbestos workers may have bodies formed on either amphibole or chrysotile. Most adults have a few bodies, and increasing numbers are seen in blue collar workers and others who handle small amounts of the fiber, with the highest levels being seen in asbestos workers. In men with minimal or extensive occupational exposure, asbestos bodies are formed on the commercial fibers, amosite and crocidolite, whereas women also form a significant number of bodies on the noncommercial fibers, anthophyllite and tremolite. These findings suggest that women may be exposed to specific asbestos-containing products, eg, cosmetic talc. The commercial fibers found in women and white collar men probably reflect atmospheric pollution with asbestos. At the highest levels of exposure, numbers of asbestos bodies correlate in a general way with the presence of asbestosis, although no precise value has been determined above which asbestosis is always found. In persons with much lower or environmental exposure, there does not appear to be any correlation between numbers of bodies and disease, in particular between numbers of bodies and carcinoma of the lung or gastrointestinal tract. The situation for mesothelioma is uncertain. (Am J Pathol 1981, 102:447–456)

EXPOSURE to large amounts of asbestos dust is known to cause asbestosis, malignancies of the lung and pleura, and carcinoma of the larynx and gastrointestinal tract.[1,2] For many years the asbestos body, a fiber of asbestos covered with an iron-protein coat, was thought to be a marker of asbestos exposure found only in primary asbestos handlers. The report by Thomson[3] that asbestos bodies could be found in the lungs of a substantial portion of urban dwellers raised the possibility that many persons who do not have obvious occupational exposure were inhaling asbestos. This notion has been strengthened by the finding of asbestos fibers in urban air and water supplies and as contaminants of many household products.[4-6]

The belief that asbestos bodies in the lungs of the general population represented a marker of asbestos exposure was challenged by Gross and his colleagues, who showed that morphologically identical structures (ferruginous bodies) could be produced in animals by inhalation of nonasbestos fibrous dusts.[7] They concluded that the bodies found in most persons probably were not the result of exposure to asbestos.[8]

Because of the carcinogenic effects of asbestos, even the low level of exposure encountered by city dwellers may be potentially dangerous; asbestos bodies, provided they contain asbestos, may provide one way to quantify such exposure. In this article we shall review the current concepts of the formation of asbestos and other ferruginous bodies, the nature of the cores of such bodies, particularly those found in the general population, and the clinical and epidemiologic significance of these structures.

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Nature of the Asbestos Minerals

Asbestos is a generic name for a variety of naturally occurring fibrous silicate minerals that have the common properties of excellent heat resistance, high tensile strength, and relatively good chemical resistance. Asbestos minerals may be separated into two broad classes: chrysotile, which comprises more than 90% of the asbestos used in this country, and the amphiboles. The amphiboles are further divided into the commercially used fibers amosite and crocidolite and a host of other forms that have little commercial importance but are widespread contaminants of other minerals. These forms of asbestos include the minerals anthophyllite, tremolite, and actinolite.[9]

History

The original reports of asbestos bodies have been summarized by Gaensler and Addington,[10] Suzuki and Churg,[11] and Davis.[12] The initial description of asbestos bodies was made by Marchand in 1906.[13] He called the structures "peculiar pigment crystals" and demonstrated that the pigment surrounding the central fiber was iron. Cooke labeled the bodies "curious bodies"[14]; neither Marchand nor Cooke associated the bodies with asbestos exposure. Stewart and Haddow were the first to realize that they were the result of asbestos inhalation and called them "asbestosis bodies."[15] It soon became apparent that asbestosis bodies occurred in any patient with high-level asbestos exposure and were only a marker of such exposure, rather than an indicator of disease. Hence the name was shortened to "asbestos body." By the early 1930s the concept that the asbestos body was composed of an asbestos fiber coated with iron and protein was firmly established[16]; further elucidation of the nature of the core and coat had to wait until the advent of electron optical methods of analysis (see below).

The term "pseudoasbestos body" has appeared sporadically through the literature without clearcut definition.[17] At least two different meanings have been used: 1) asbestos bodies of ordinary appearance found in the lungs of persons with no known asbestos exposure; 2) bodies with an iron-protein coat but a core with an unusual appearance. Based on his animal studies, Gross suggested that all bodies with an iron-protein coat be called "ferruginous bodies" unless the nature of the core was known.[7] Because we believe that in humans true asbestos bodies can be separated from other ferruginous bodies, we shall use the terms "asbestos body" to indicate bodies containing asbestos, and "ferruginous body" or "pseudoasbestos body" for all non-asbestos-containing structures.

Structure and Formation of Asbestos and Ferruginous Bodies

The asbestos body consists of a core of optically transparent asbestos surrounded by a golden yellow, iron-protein coat. The core (and body) is usually straight (Figure 1), but curved forms are sometimes seen.[18,19] The overall diameter of the body is usually from 2–5 μ and the length typically in the range of 20–50 μ. Whole bodies less than 10 μ in length are rare, although fragments may be shorter. Bodies up to 250 μ in length are sometimes observed. By electron microscopy the fiber cores usually vary from 0.1 to 1.5 μ in diameter, with a mean diameter (for bodies from the lungs of the general population) of about 0.4–0.5 μ.[20] The curved bodies are usually formed on the thinnest diameter amphibole fibers or on chrysotile.[19]

The coat may be variably segmented into spherical or rectangular units spaced along the fiber; the ends of the body are frequently knobbed. The fiber core may be seen between the blocks of coat material or protruding from the ends of the body. Sheathlike coats are also common. Gloyne originally illustrated a series of different coat structures that he believed formed a cycle of formation and dissolution of the asbestos body[21]; more recently Botham and Holt have confirmed this notion in an animal model.[22] They showed

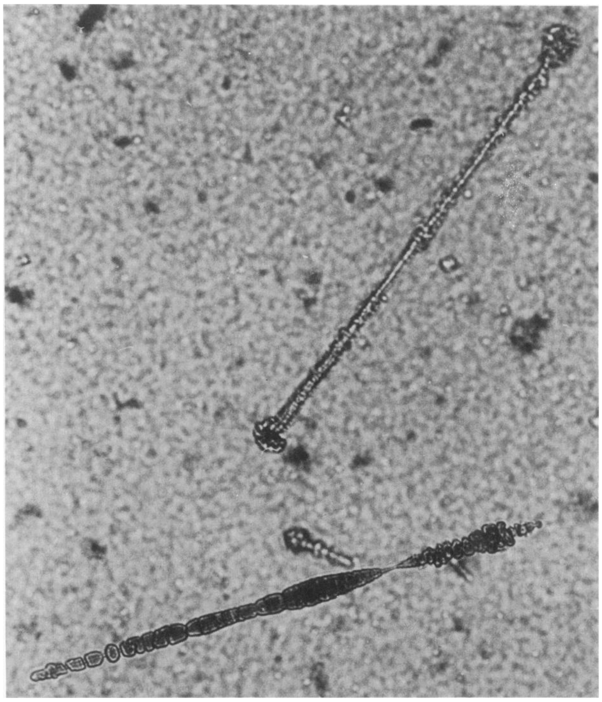

Figure 1—True asbestos bodies. Note the transparent colorless cores and the different patterns of deposition of coat material. (Millipore filter preparation, ×500) (with a photographic reduction of 10%)

that the earliest form of asbestos body has a sheathlike coat that with time becomes segmented. Eventually the body fragments. The entire cycle appears to require about 40 weeks in experimental animals.

Asbestos bodies may be branched at acute or right angles. Ultrastructural examination indicates that the acute angled forms develop on splayed fibers[19]; the nature of the forms with right-angled branches is unknown.

It is generally agreed that asbestos bodies are formed in macrophages; Suzuki and Churg have suggested that they are also formed in alveolar lining cells, which they demonstrated can phagocytize fibers, but this idea has not been further examined.[11] In all cases the initial event appears to be phagocytosis of the asbestos fiber by a macrophage or giant cell and incorporation into a phagosome. A mucopolysaccharide matrix is deposited on the fiber, and iron is added to this matrix.[12,23,24] Electron microscopy has shown that the coat material consists of dense granules about 60 Å in diameter, which represent either ferritin or hemosiderin.[11,24] It has been suggested that the source of iron is the hemorrhage that accompanies administration of asbestos to animals and presumably to humans,[11,22] but it is also likely that the iron is derived from circulating iron stores. Finally the cell dies, releasing the body into the pulmonary parenchyma.

In experimental systems as well as in humans, not all asbestos fibers acquire a coat. One of the major factors governing coat formation is length, as noted above. Most authors agree that fibers are rarely coated if they are less than 5–10 μ in length. Chrysotile fibers, in particular, have a tendency to fragment into very short, narrow fibers.[2] However, even with experimental or human inhalation of pure amphibole fibers, which do not tend to fragment as readily into very short segments, the number of uncoated fibers remains high many years after stopping exposure.[12,22,25]

Davis et al have examined the formation of ferruginous bodies with cores of fiberglass and synthetic aluminum silicate. At the light-microscopic and ultrastructural level the same sequence of events takes place with these fibers as with asbestos.[26]

Methods of Analysis of Cores of Asbestos Bodies

Because of their small size, positive identification of cores of ferruginous bodies requires an electron optical technique, which ideally should be a combination of morphologic examination, electron diffraction, and electron microprobe (X-ray energy spectroscopy) analysis to determine chemical composition. Under certain circumstances, identification can be performed without using all three techniques. Chrysotile, for example, has a tubular form and a diffraction pattern that are nearly unique; whereas its chemical composition cannot be relied upon to identify it, because magnesium is leached from fibers during residence in the body.[27] Identification of amphiboles is more difficult. In addition to a chemical analysis typical of one of the amphibole subtypes, one needs a diffraction pattern that is at least consistent with an amphibole. Preferably, such a pattern should be analyzed specifically for distances and angles between spots (indexed) for identification; Lee has recently pointed out that two indexed diffraction patterns are sufficient for a unique identification.[28] However, indexing of amphibole diffraction patterns is extremely time-consuming and may be difficult because of the presence of crystalline imperfections. In our experience, it is usually sufficient to base identification of amphibole fibers on a consistent but unindexed diffraction pattern and a microprobe analysis if these closely duplicate the results from analyses of standard samples.[29,30]

Ideally, identification of asbestos fibers should be attempted in a high-resolution (less than 200 Å probe spot size) scanning/transmission electron microscope (STEM). Systems with less (0.5 μ) resolution may be useful for pure samples, but mixed dust samples from the lung require high resolution for one to distinguish between particles. Furthermore, the higher the resolution, the more likely that analysis can be performed on a bare area between the blocks of iron coat of a body. The STEM system also allows for both diffraction and chemical analysis at the same time and permits the distinction of some minerals that have identical chemical compositions: eg, separation of anthophyllite and fibrous talc, which both have similar chemistries, can only be accomplished on the basis of distinctive electron diffraction patterns.

Asbestos Bodies in Asbestos Workers

Actual analyses of the cores of asbestos bodies, even in primary asbestos handlers, are surprisingly few, in part due to the technical difficulty of identifying a fiber that measures less than 1 μ in width and 10–100 μ in length. Sundius and Bygdén isolated asbestos bodies from asbestos workers' lungs by mechanical disruption of the tissues.[31] Chemical analysis showed that the cores were largely amphibole asbestos, despite the fact that the workers in question had been exposed primarily to chrysotile. This finding has been confirmed by modern methods using electron optical techniques. Pooley[18] examined bodies isolated from the lungs of persons exposed to known types of asbestos. He found that bodies were formed on all types of fiber examined, including chrysotile; however, the number of chrysotile bodies relative to fibers was much smaller than the number of amphibole bodies relative to fibers. Pooley ascribed part of the difference in frequency of body formation to the straight shape of amphibole fibers, compared with the tendency toward a curved shape in chrysotile fibers.[18]

Using an electron microprobe system, Langer et al examined bodies and uncoated fibers obtained from lungs of asbestos workers.[32,33] They found that amphibole fibers, amosite in particular, showed little chemical change from the original material despite years of residence in the lung, whereas chrysotile fibers showed a marked loss of magnesium.[33] Stumphius and Meyer examined eight bodies from lungs of shipyard workers and found an amphibole (amosite) core in all.[34]

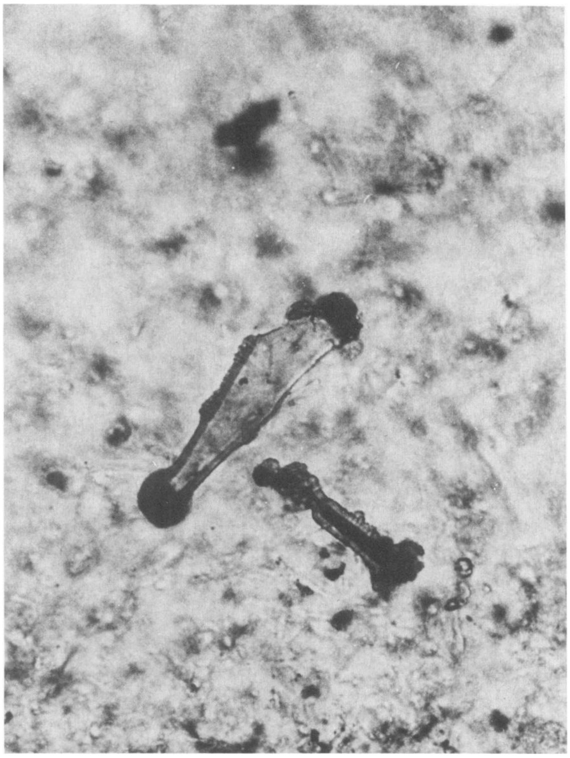

Figure 2—Ferruginous (pseudoasbestos) bodies. The smaller body has a black core composed of carbon, while the larger body has a broad yellow core of sheet silicate, in this instance, talc. (Millipore filter preparation of material from the lungs of a roofer exposed to talc, ×600)

Asbestos Bodies From the General Population

Analysis of the cores of asbestos bodies from the lungs of the general population presents considerably greater technical difficulties than are encountered with bodies from the lungs of asbestos workers. In large part this problem stems from the relatively small number of bodies such lungs contain: in a typical asbestos worker there are on the order of 10^5–10^7 bodies/gram of wet lung, whereas members of the general population more typically have 0–500 bodies/gram of lung, most persons having between 0 and 50. The technical methods required for individual particle analysis have only recently achieved a resolution sufficient to allow accurate definition of composition. As a result, studies in this area are few and contradictory. Gross et al isolated 28 bodies from the lungs of 28 persons in Pittsburgh and examined the cores by electron diffraction.[35] All 28 bodies contained crystalline cores. None of the diffraction patterns matched the pattern of chrysotile asbestos; hence they suggested that such data supported their notion that "asbestos" bodies in the general population are actually "ferruginous bodies" with nonasbestos cores. However, their published diffraction pattern is highly suggestive of amphibole asbestos.

Langer et al published two series of analyses of bodies from the general population. In one they examined 16 bodies from 7 patients, using a low-resolution electron microprobe.[36] They identified one core as amosite; 13 were possibly degraded chrysotile; 2 were possibly crocidolite. In a more extensive report they isolated 50 bodies from an unknown number of patients.[33] A small number of these bodies appeared to be amosite, but most were believed to be either degraded chrysotile or fibrous glass.

We have now examined close to 600 bodies from 82 patients who were not asbestos workers, using a high-resolution scanning transmission microscope.[19,20,29,30] Our overall results indicate that 98% of asbestos bodies from the lungs of this population have cores of amphibole fibers, and the remaining 2% have chrysotile fiber cores. This is true whether the patients are women and white-collar men, groups that in our hands tend to have fewer than 100 and usually fewer than 50 bodies/g of wet lung, or blue-collar men, a group which tends to have more than 100 bodies/g of lung. Combined diffraction/microprobe analysis has been carried out on 81 bodies from 42 patients. Of the 81 bodies, 59 were found to contain cores of the commercial fibers, amosite or crocidolite, while the remainder contained anthophyllite and tremolite.[29,30] The relation of these data to sex and occupation is discussed below. Correlation of morphologic studies with the chemical analysis of the cores of true and pseudoasbestos bodies convinces us that it is possible to distinguish the two with the light microscope and that

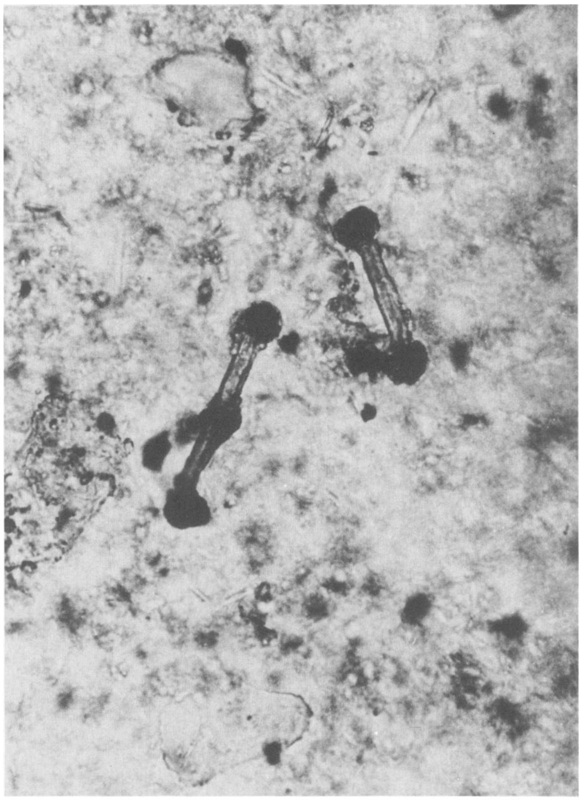

Figure 3—Ferruginous bodies mimicking true asbestos bodies. The bodies are from the same preparation as those in Figure 2. The cores of the bodies are actually bright yellow fibers of talc. Forms such as these may often be confused with true asbestos bodies. (Millipore filter preparation, ×600)

most of the bodies found during routine autopsies are indeed asbestos bodies.[19]

Pseudoasbestos (Ferruginous) Bodies

On the basis of the early reports of pseudoasbestos bodies it was appropriate for us to question the assumption that all of the bodies reported in routine autopsies did indeed have asbestos cores. The term "ferruginous body" was coined by Gross et al to indicate the nonspecificity of such coated, fibrous bodies.[7] They demonstrated that inhalation by animals of a variety of fibrous, nonasbestos dusts such as fibrous aluminum silicate, silicon carbide, and fiberglass resulted in structures identical (ie, containing transparent, colorless cores) to asbestos bodies in humans. The critical factor in the formation of these bodies was fiber size; in general, a fiber diameter from 0.1 to 3 μ and a minimum length of 5–10 μ were required for ferruginous body formation. These experiments were confirmed in part by Goldstein and Rendall.[37]

More recently Gross et al have described ferruginous bodies with black fibrous cores in human lungs.[38] They speculated that these cores were carbon, originating from inhaled smoke particles. In our own studies, 22 bodies with black cores were isolated from the lungs of the general population of Chicago, a city where coal burning was until recently quite prevalent[19] (Figure 2). Although many of the cores were fibrous, others consisted of large platelike sheets. All of the black cores were amorphous when examined by electron diffraction. Fiber cores examined with the microprobe contained no detectable elements (the lightest detectable element is sodium, atomic number 11).[19] It was concluded that these cores were indeed carbon. In several of the cases, bodies with black cores made up 75–90% of the total ferruginous bodies in the lung.

Another type of ferruginous body is that with a platy or fibrous yellow core (Figures 2 and 3). We have found a few cases in which they constitute up to 20% of the total ferruginous bodies, and many lungs from the general population contain small numbers.[19] These bodies appear to be formed on sheet silicates such as talc, mica, or kaolinite. The cores produce pseudohexagonal electron diffraction patterns, a feature typical of sheet silicates, and their chemical compositions as determined by microprobe analysis are consistent with such minerals. In some workers the source of exposure is apparent; for example, we have seen large numbers of such bodies in roofers and rubber factory workers, who are exposed to large amounts of talc on their jobs. The importance of recognizing these structures is that some (for example, Figure 3) may be mistaken for true asbestos bodies by light microscopy if the color and breadth of the core are not appreciated.

Other unusual types of ferruginous bodies in human lung have been shown to contain elastic fibers[39] and diatomaceous earth.[19] Although it is conceivable that structures identical to asbestos bodies might be found in someone with an unusual occupational exposure to a transparent fiber of the appropriate size, this phenomenon has not yet been demonstrated.

Extrapulmonary Asbestos Bodies

Asbestos bodies may also be found in extrapulmonary locations. Langer found occasional bodies and uncoated fibers in ashed thick sections of liver, pancreas, kidney, and spleen from 5 asbestos workers with very large numbers of bodies in the lung.[40]

Godwin and Jagatic examined 7 patients with pleural or peritoneal mesotheliomas and found asbestos bodies in 6 in regional lymph nodes.[41] In 2 cases asbestos bodies were found in tumor and intestinal wall in the abdomen. The lungs showed numerous asbestos bodies and reactive pulmonary fibrosis in all cases.

More recently, Auerbach et al counted asbestos bodies in many parenchymal organs, including abdominal viscera and brain.[42] They found that the numbers of bodies in extrapulmonary organs were proportional to the numbers in the lungs. The question of whether coated bodies migrate from the lung as such or are formed in the distant organ also remains to be determined. Kanazawa et al describe formation of asbestos bodies subcutaneously at the site of injection of asbestos in experimental animals,[43] and bodies are known to form when fibers are injected into the pleural space.[12]

Demographic Data

Knowledge about the methods of analysis for asbestos bodies is important for interpreting the reports from various laboratories. The frequency of bodies in smears, squeeze preparations, and thick paraffin sections is less than with digestion and filter-collection methods; hence many of the reports mentioned below are not strictly comparable. With the digestion technique, Smith and Naylor found bodies in lungs of 100% of urban adult patients.[44] Examination of the same lungs previously by the scrape and the tissue section methods had demonstrated bodies in only 4% and 18% of the lungs, respectively.[45] Digestion techniques have the advantage that bodies are freed from obscuring debris and concentrated. Membrane filters of pore size 0.45 μ or 5 μ have been shown to be equally effective for collection of asbestos bodies.

Ferruginous bodies have been related to age, sex, residence, occupation, and disease. Becklake has tabulated the results of many of the earlier studies and indicated the types of preparations examined.[1] Pooley et al, in a study of asbestos bodies in histologic sections of lung from persons in several European cities, conclude that differences reflect the general level of asbestos air pollution in these areas.[46] For example, asbestos bodies are more frequent in London than in Dublin or Galway, Ireland. Breedin and Buss, using lung digests, found that asbestos bodies could be found in the lungs of rural patients as frequently as in urban patients, although they tended to be more numerous in the urban persons.[47] Using basal smears and ashed tissue sections, Selikoff and Hammond demonstrated asbestos bodies in the general population of New York City in more men (51% of 1368) than women (39% of 607).[48]

Conflicting results have been obtained concerning whether bodies have increased in frequency over the past 30 years. Selikoff et al found that about 60% of routine autopsy patients over age 30 had asbestos bodies, both in 1934 and 1967.[48] Bhagavan and Koss, however, found a progressive increase in frequency of bodies and an increase in number of bodies with age over a similar 30-year period.[49] Um, using thick histologic sections, found that asbestos bodies increased in frequency from 1936 to 1966 from 0 to 20% of cases and increased slightly with age from 50 to 90 years.[50] In none of these studies is there matching for age, sex, or occupation. Since the frequency of positive cases is small, the results may reflect more a difference in occupation of the subjects in the 2 periods than a general increase in the use of asbestos.

Thomson, using basal smears, was the first to study systematically the differences in asbestos bodies within a population.[3,51] Differences in frequency of asbestos bodies among blacks, colored, and whites of Cape Town were interpreted as reflecting differences in occupation more than environment. In sections of over 10,000 lungs from miners, Goldstein and Rendall found that ferruginous bodies were most frequent in asbestos miners but also occurred in gold and coal miners.[37] Doniach et al, using thick histologic sections, found bodies more frequently in men in heavy manual labor and men in shipping, electrical engineering, and the transport industries than in others.[52] Classification of the men in New York City by occupation indicated that of those (51%) with asbestos bodies, 47% with white-collar jobs, but 50% with blue-collar jobs and 70% in construction or shipyard work had asbestos bodies in histologic sections.[48]

In a study of lungs from over 350 autopsied patients in the general population, we found that asbestos body counts varied with occupation and possibly with smoking.[53] Using the bleach digestion technique of Smith and Naylor,[44] we showed that only 7% of women and white-collar men, but 60% of construction workers, 41% of steel workers, and 25% of other manual laborers had more than 100 asbestos bodies/g wet lung. Bodies were found in 96% of all lungs, and smokers seemed to have more bodies than nonsmokers, but the number of nonsmokers was small.

When the cores of the bodies from these different occupational groups were analyzed, it was surprising to find that women differed from both white-collar men and manual laborers.[29,30] About half (12 of 21, or 57%) of the cores isolated from women with fewer than 100 asbestos bodies/g lung had anthophyllite or tremolite cores, whereas white-collar men and manual laborers had predominantly (48 of 57, or 84%) amosite or crocidolite cores in their bodies. The source is not clear. Urban air contains amphiboles, and anthophyllite and tremolite may contaminate some cosmetic talcs. The amosite and crocidolite in men with more than 100 asbestos bodies may be related to handling of specific asbestos-containing products.

Asbestos Bodies and Disease

Asbestosis

There are few reports of numbers of asbestos bodies in asbestosis. Ashcroft and Heppleston counted bodies by phase contrast microscopy in persons with mesothelioma and varying degrees of asbestosis.[25] Bodies increased from 1.26×10^6/g dried lung in patients with no fibrosis to 7.7×10^6 with mild fibrosis and to 71×10^6 with moderate fibrosis but did not increase further with progression to severe fibrosis. Sebastien et al studied 1 subject with moderate and 5 with heavy asbestos exposures and fibrosis varying from 1 to 4^+. Asbestos bodies varied from 1×10^3 to 1×10^6/ml wet lung.[54]

We analyzed lung digests from 6 asbestos workers and found a range of 8000 to 500,000 asbestos bodies/g wet lung (multiply by 10 to obtain bodies/g dry lung[53]), with numbers of asbestos bodies varying considerably from one region in the lung to another.[55] The extent of this variation in a particular lung and the degree of certainty about the actual count in a particular region in a lung with very high counts has not yet been studied.

Thomson originally made his smears for asbestos bodies from the lower lobes because early asbestosis begins in this region.[3] He believed that the fibrosis was related to the gravitational concentration of bodies in this region. Later, others were not able to find any difference in frequency of numbers of asbestos bodies in upper or lower lobes.[45,53,56] The pathogenesis of early asbestosis still remains to be explained.

Lung Cancer

It has been both affirmed and denied that asbestos bodies are related to lung cancer in persons without asbestosis.[37,47,52,56-58] Evidence that persons with lung cancer in the general population have a higher frequency of exposure to asbestos than normal controls depends heavily on the type of control population. If the control subjects are not matched for occupation, as well as age, sex, and smoking habits, there may be too many white-collar workers among control subjects and a spurious demonstration of a significant difference between patients with cancer and control subjects.[58,59] In a comparison of 100 cases of lung cancer in persons in the general population with control subjects matched for age, sex, smoking habits, and occupation, no differences in asbestos body counts were observed.[55]

Mesothelioma

Epidemiologic studies of patients with mesothelioma have indicated that a history of exposure to asbestos can be obtained in some, but not all.[60] Asbestos bodies have been found by various techniques in the uninvolved lung parenchyma in 10–100% of cases.[2] Because of the fact that some persons give histories of relatively minimal exposure to asbestos and have no evidence of asbestosis, it is hoped that quantification of asbestos bodies can help to define more precisely those patients in whom the asbestos is etiologically important. In a study of asbestos bodies with the electron microscope using ashed 6-μ sections from 120 cases of mesothelioma and 135 cases without mesothelioma, Pooley found asbestos bodies in lung parenchyma adjacent to tumor in only 18 of the cases with mesothelioma.[61] All of the asbestos bodies had amphibole cores. Asbestos fibers were also studied in the sections. Ninety-two percent of the mesothelioma cases had asbestos fibers, but less than 50% of the control group had fibers. Amphiboles predominated in the mesothelioma group, whereas chrysotile predominated in the control group.

Gastrointestinal Cancers

Asbestos bodies have also been looked for in the colon in relation to gastrointestinal cancer in persons in the general population. Rosen et al[62] were not able to find typical asbestos bodies in digests of colonic wall from 12 patients with cancer of the colon, although atypical ferruginous bodies, which appear to us to represent diatomaceous-earth-containing bodies, were found. However, none of the patients was an asbestos worker. We found no differences in the numbers of asbestos bodies in the lungs of 50 patients with gastrointestinal cancer and 50 controls matched for age, sex, and smoking habits.[55]

Pleural Plaques

Generally asbestos bodies have not been found in histologic sections of pleural plaques.[17] After bleach digestion, Rosen et al[63] were able to find a few typical asbestos bodies in 3 of 8 plaques, but Sebastien found that asbestos bodies ranged from 5 to 300/cu cm in 8 of 9 plaques examined.[54] By electron microscopy, chrysotile was found but not quantified.

Relationship of Coated to Uncoated Fibers

Several studies have attempted to relate numbers of asbestos bodies to total asbestos fibers in order to determine whether the ratio of the two is relatively constant. Comparison of results is difficult because of differences in technique. Gross et al, using light microscopy on material prepared by a concentration technique, found that uncoated fibers outnumbered bodies by a factor of 5 to 200 in material from the lungs of 6 random autopsy subjects.[64] However, Sebastien et al, in examining a similar group, found only asbestos bodies and no uncoated fibers by light microscopy.[54] Using phase contrast microscopy, Ashcroft and Heppleston[25] found that uncoated fibers ranged from 37 to 83% of the total in a series of heavily exposed persons with mild to severe asbestosis.

Electron-microscopic examination clearly indicates that any method of light-microscopic counting markedly underestimates the true number of fibers present in lung, although here again the ratio of bodies to total fibers is quite variable. In a study of 21 patients from the general population, we found that the average ratio of total fibers to bodies was approximately 10,000 to 1.[65] Sebastien et al determined that the ratio of total fibers to bodies was on the order of 20–100:1 in patients with both moderate and heavy exposure.[54] In a similar group of exposed patients, Ashcroft and Heppleston[25] concluded that fibers were 10–25 times the number of bodies. They also noted that the proportion of uncoated fibers remained constant regardless of the time between the last exposure and death, suggesting that progressive coating of uncoated fibers does not occur.

It appears likely that the ratio of bodies to total fibers is not very constant in those with low exposure, but bodies may be some indicator of total burden in those with very high exposure. However, even this conclusion must be tentative, since there does not appear to have been any study of persons with pure chrysotile exposure, a group in which fewer bodies would be expected (see above).

Conclusions

When present in large numbers, asbestos bodies may serve to confirm the etiology in a person with an asbestos-associated disease such as asbestosis or mesothelioma. The actual numbers that suffice for confirmation are yet to be defined. Because scarred lungs appears to have rather large variation in local fiber concentrations, examination should preferably be performed on autopsy lung for which several samples can be obtained. Provided one is careful to distinguish asbestos bodies from other forms of ferruginous body as described above, counting with a light microscope provides an inexpensive, rapid, quantitative method. Although histologic sections are occasionally useful in persons with very high exposure, concentration of bodies on a membrane filter as described here[44,53] should be used. This relatively simple technique using light microscopy provides an initial screening of a case, to be followed, if necessary, by electron optical examination.

In persons with little or no history of exposure, there does not appear to be any correlation between numbers of bodies and disease. Bodies are, however, only a partial indicator of lung asbestos burden; in particular, they appear to be an indicator of the numbers of long amphibole fibers. With low exposure, then, electron-microscopic enumeration and typing of fibers will be needed to establish a relation of asbestos to disease and to define the nature of the exposure. Our laboratory, as well as that of Sebastien et al,[54,64] has begun to enumerate the uncoated asbestos fibers that are present in every lung, and it appears that such uncoated fibers will always greatly outnumber asbestos bodies. Electron optical methods of counting and analyzing asbestos fibers are extremely time consuming and expensive, but such counts are especially important in establishing an etiologic role of asbestos in lung cancer or gastrointestinal cancer in persons without asbestosis. Establishment of a dose-response curve for fibers and disease, and more specifically for various subtypes and sizes of fibers and disease, awaits extensive documentation of the total fiber burden in lung.

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