(so-called "pseudoasbestos" bodies). The asbestos body core color and shape are important: golden brown, beaded, dumb-bell shaped structure 20-50 p long and 2-5 p diameter with transparent core (Table 5).

Table 5. Color and shape of asbestos bodies.

Erionite	Transparent (identical to asbestos by light microscopy) electron microscopy and energy dispersive X-ray analysis useful. Geographic variation: Turkey, environmental exposure
Sheet silicates Talc Mica Kaolin	Blood yellow, platy, rectangular Occupation: miners, stone, steel, rubber, enamel glass, ceramics
Carbon	Black variable thin platy segmented/dittuse coat Perpendicular 90 0extensions Occupation: coal mining, foundry workers
Metals (Aluminium oxide) (Iron oxide)	Brown-black Occupation: arc welders, steel workers, metal polishers
Man-made mineral (Glass-fiber)	Ferruginous bodies rarely form but may be indistinguishable from asbestos cores

In individuals with a history of asbestos exposure, awareness that other conditions can, on occasion, mimic those changes usually associated with asbestos is important for medicolegal compensation purposes.

Electron microscopic mineral analysis is useful when asbestos-related disease is suspected and, i) light microscopy reveals advanced tibrosis and few asbestos bodies; ii) light microscopy reveals fibrosis and many ferruginous bodies (mixed asbestos and pseudoasbestos type); iii) malignant mesothelioma cases where no asbestos bodies are identified by light microscopy; and iv) lung cancer cases in which there is minimal fibrosis and sparse asbestos bodies.

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Pathology of nonasbestos pneumoconiosis (silicosis and mixed dust pneumoconiosis)

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Pneumoconiosis represents a variety of pathological reactions of lung tissue to permanent deposition of inhaled particulate or fibrous matter of occupational or environmental origin. The nomenclature or concept of pneumoconiosis is somewhat confusing because of overlap resulting from heterogeneous definition of the disease. There are quite a few pneumoconioses named after occupation. On the other hand, there are only limited numbers of patterns of reaction of lung tissue to inhaled dust. As a result, exposures to different dust may produce the same pathology. This is the very reason the author recommends concentrating on pathological patterns prior to taking occupational history or mineralogy into account.

Etiologically specific features can be distinguished from nonspecific patterns in the pathology of pneumoconiosis. There are the following specific lesions: macule, nodule (silicotic, mixed dust fibrotic), granuloma and massive fibrosis, which essentially are upper-lung diseases.

Macules

A macule appears macroscopically as a nonpalpable, pigmented spot in a centrilobular distribution throughout the lungs, and represents one of the initial changes of pneumoconiosis and may progress to nodular disease as described below. Histologically, macules consist of peribronchiolar or perivascular collections of dust-laden macrophages accompanied by a delicate meshwork of reticulin fibers. There is little collagenous fibrosis in the macules.

Nodules

A nodule is a palpable, firm lesion of up to 3 mm in size. Generally, two types of nodules are distinguished. Firstly the silicotic nodule is a well demarcated, extremely firm lesion with variable pigmentation, composed histologically of paucicellular, hyalinous collagen fibers in a whorled or concentric arrangement. Silicotic nodule develops primarily in the centrilobular and/or subpleural locations,

involving and destroying the blood vessels in the vicinity. It is considered a very specific lesion attributable to crystalline silica. Under polarized light, crystalline silica may appear as faintly birefringent fine particles. Strongly birefringent, platy or needle-shaped particles are not crystalline silica but mostly silicate minerals. Secondly, mixed dust fibrotic nodule (MDF) is an irregularly contoured (like Medusa head), fibrous lesion composed histologically of sparse, irregularly arranged collagen fibers accompanied by collections of dust-laden macrophages. MDF represents a wide spectrum of fibrous nodules ranging from macule-like "soft" lesions with minimal collagen to "hard" ones with abortive silicotic-type fibrosis developing in the center of the nodule. The histological transitions between the macule and silicotic nodule clearly corresponds to the crystalline silica content in the deposited dust: classic silicosis develops if the burden of crystalline silica in the lung exceeds 18% weight in the total deposited dust (1). Like macules, MDF extends into the surrounding lung tissue in a diffuse interstitial pattern.

Granuloma

Sarcoid-like granuloma is characteristic of beryllium disease. Ill-defined aggregates of foamy histiocytes indicate silicate pneumoconiosis (especially, talc pneumoconiosis or talcosis).

Massive fibrosis

Massive fibrosis is a fibrous mass lesion measuring greater than 2.0 cm (2) and composed essentially of either confluent nodules (silicotic nodule, MDF) or disorganized and/or degenerated collagen bundles alternating with massive deposits of dust. Massive fibrosis is associated with a number of heterogeneous lesion in or around massive fibrosis, which include collapsed and/or atelectatic lung tissue, alveolar proteinosis (3), tuberculosis and in some cases, nonspecific (nonpneumoconiotic) fibrosis. The nonspecific lesions include diffuse interstitial fibrosis, small airways disease, alveolar proteinosis and emphysema.

Diffuse interstitial fibrosis

Diffuse interstitial fibrosis (DIF) is a nonspecific dust-related lesion consisting of two pathologically distinct subtypes, as follows (4): i) upper-lung dominant, interstitial extension of macules and MDF with dust-laden macrophages and reticulin and/or faint collagen fibrosis; and ii) lower-lung dominant extensive deposition of collagen associated with parenchymal remodeling and honeycombing. The latter lesion is more important in that some cases closely resemble usual interstitial pneumonia (UIP) both clinically and pathologically (5). There are cases in which it is difficult or even impossible to draw the line between occupational and idiopathic cases. It is reasonable to assume any etiologic link between UIP (interstitial pulmonary fibrosis or cryptogenic fibrosing alveolitis) and pneumoconiosis-associated DIE.

The pathological diagnosis of asbestosis is entirely dependent on the detection of asbestos bodies in the lungs with DIE. To distinguish from nonasbestos ferruginous bodies, the following should be checked: i) translucent fibrous core; and ii) faint or absent birefringence of the fiber (6).

Small airway disease

Small airway disease is associated with fibrous or nonfibrous mineral dust particles (7).

Alveolar oroteinosis

Alveolar proteinosis is not a specific hallmark of acute silicosis (silicoproteinosis) but associated with diverse conditions including chronic pneumoconiosis with massive fibrosis (3) and exposures to different metals or organic dust (8).

Ernohvsema

Centrilobular emphysema may be associated with macules or MDF. If the patient is a smoker, it is difficult to decide its attributability (9). Paracicatricial, paraseptal or bullous emphysema may be seen in all kinds of pneumoconiosis. Pneumothorax is an important complication.

Other important complications of pneumoconiosis include tuberculosis, collagen disease, renal disease and malignancy.

Tuberculosis

Pathologically, two distinct types of tuberculosis are recognized (10). Combined-type (Kombinationstyp) disease represents a unique clinicopathological entity. The diagnostic hallmark is a tuberculo-silicotic nodule which consists of tuberculous coagulation necrosis surrounded by dense collagenous fibrosis of silicosis. These combined-type nodules lack typical granulomatous reaction and acid-fast bacilli are usually negative in Ziehl-Neelsen stain. The sole diagnostic clue is to demonstrate intact alveolar elastic (or reticulin) framework which is characteristic of tuberculous necrosis (11).

Collagen disease

A remarkably high association (ca. 10%) with collagen disease is reported in cases with accelerated silicosis (12). In chronic disease, however, its prevalence may be around 1% in autopsy series in Japan, in which rheumatoid arthritis is most common. Rheumatoid pneumoconiosis is characterized by necrobiotic nodules similar to those seen elsewhere in the body. Polymorphonuclear leukocytic infiltration in the nodule, destroyed alveolar elastic or reticulin framework, and intense plasmacytic infiltration serve to distinguish from tuberculosis. In contrast to classic co-worker pneumoconiosis-associated rheumatoid nodule described originally by Caplan (13) and Gough (14), silicosis-associated rheumatoid nodule consists of degenerated or necrotic silicotic nodule without dust ring and is much smaller than classic rheumatoid nodule.

In 1997, the International Agency for Research on Cancer evaluated crystalline silica as carcinogenic to humans (15) as asbestos fibers. Lung cancers do develop in ca. 20% of unselected autopsy cases with nonasbestos pneumoconiosis in Japan. However, there appears to be no dose-response relationship (16). Two-thirds of lung cancers in nonasbestos pneumoconiosis develop in peripheral lung tissue despite a high prevalence of smoking habit (>80%). Almost half are squamous cell carcinomas. Coal dust does not cause lung cancer (15, 17).

Options in pathological diagnosis

Macular oneumoconiosis

Macular pneumoconiosis exists if the lungs show only dust macules with no nodular lesions. Macules resulting from smoking usually contain a small number of birefringent particulate matter (silicates), and the diagnosis of macular pneumoconiosis should be made with caution, unless the deposited dust is convincingly distinguished from combustion products.

Silicosis vs. *mixed dust oneumoconiosis*

If the predominant lesion is silicotic nodule, the appropriate diagnosis is silicosis. Mixed dust pneumoconiosis may be defined as a pneu-

moconiosis consisting predominantly of MDF-type nodules with or without silicotic nodule or massive fibrosis. Classic silicosis is meant in cases where almost all lesions are silicotic nodule. Silicosis and mixed dust pneumoconiosis are distinct entities clinicopathologically (18). Massive fibrosis, active tuberculosis and alveolar proteinosis are more common in cases with silicosis. Mixed dust pneumoconiosis tends to be associated with DIE more frequently.

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Perspectives of cellular sociology in chronic interstitial lung diseases

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The development and outcome of chronic interstitial lung diseases is still subject of intensive scientific investigations. In particular, factors which are related to occurrence and prognosis are still missing. Similar to investigations in lung cancer, the analysis of basic structure elements in combination with the involved inflammatory cell types seems to be appropriate for the characterization of chronic interstitial lung diseases. Therefore, transbronchial lung biopsies taken from patients with chronic interstitial lung diseases were incubated with the following antibodies: CD3, CD2O, macrophage migration inhibitory factor (MIF), galectin-1, galectin-3, galectin-8, CD-34; and the biotinylated substances galectin-1, galectin-3, sarcolectin, and carrier-immobilized cortisone. Cases with various of the following rare interstitial lung diseases were analyzed in relation to the HR-CT findings: sarcoidosis, usual interstitial pneumonia, lymphoid interstitial pneumonia, pulmonary hemosiderosis, carbohydrate deficiency syndrome, systemic lupus erythematodes, pulmonary ossification, alveolar proteinosis, bronchiolitis obliterans, acute and chronic eosinophilic pneumonia, and inflammatory lung reaction due to various cytostatic drug regimes. The expression of binding capacities was measured by use of a semiautomated image analyzing system, and the spatial relation of the binding and nonbinding cells was calculated. The amount of fibrosis was measured by use of Sirius-red stain.

As a result, the expression of the analyzed determinants differs not only in the percentage of specific cells but also in the spatial arrangement. For example, the alveolar spaces of alveolar proteinosis are characterized by rare populations of B-cells and macrophages (and absence of macrophage migration inhibitory factor). Missing presence and binding capacities of MIF were, in addition, noted in sarcoidosis and cytostatic drug reactions. Vascularization was disturbed in cases with usual interstitial pneumonia (UIP) and lymphocytic interstitial pneumonia (LIP), whereas in cases with eosinophilic pneumonia the vascular arrangement was notably preserved. These investigations are derived from similar measurements of structure features and entropy of primary and metastatic lung tumors (1-3), and confirm the practical use of the analysis of tissue structures. In addition, the expression of binding capacities of immobilized sugar-binding substances (lectins) and their antibodies can be used to determine specific interactions of involved inflammatory cells in altered lung parenchyma due to various agents (4-6). Thus, modern image analyzing techniques in combination with immuno- and ligand histochemistry permit detailed insight into the arrangement of various cellular subpopulations and the underlying interstitial and vascular matrix. The response of the idiopathic lung diseases to corticosteroids is related to the amount of irreversible fibrosis (collagen IV) and the expression of binding capacities of cortisone. The spatial arrangement of the different cell types and cells with the different functional states seems to be of importance for the outcome of the various diseases.

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