Cytology of Nonneoplastic Occupational and Environmental Diseases of the Lung and Pleura

Rodolfo Laucirica, MD; Mary L. Ostrowski, MD

**Context.**—Cytologic examination of the respiratory tract has been a useful diagnostic tool when evaluating neoplastic lesions of the respiratory tract. However, we have limited experience in the application of this technique in the management of nonneoplastic occupational and environmental diseases of the lung and pleura. This review focuses on the cytologic characteristics of a variety of occupational lung diseases, grouping them into 2 broad diagnostic categories: reactive cellular changes and noncellular elements. The former includes entities such as reactive mesothelial proliferation, goblet cell metaplasia, Creola bodies, and reserve cell hyperplasia, and the latter encompasses Curschmann spirals, Charcot-Leyden crystals, and asbestos bodies.

**Objective.**—To illustrate the cytologic features of several nonneoplastic occupational and environmental diseases and correlate the cytology with various etiologic agents.

**Data Sources.**—Case-derived material and literature review.

**Conclusions.**—The role of cytology in the diagnosis of nonneoplastic occupational and environmental lung diseases is limited. This may be because more than one agent can elicit a similar host reaction and/or the offending agent can be associated with more than one pathologic process. However, in the appropriate clinical and radiographic setting, the cytology can render valuable diagnostic information. Examples include pulmonary alveolar proteinosis in patients with acute silicoproteinosis and asbestos bodies in bronchoalveolar lavage samples of patients with asbestos exposure.

(ARCH PATHOL LAB MED. 2007;131:1700–1708)
Table 1. Mineral Dust Diseases

<table>
<thead>
<tr>
<th>Mineral Dust Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coal worker’s pneumoconiosis</td>
</tr>
<tr>
<td>Silicosis, silicatosis</td>
</tr>
<tr>
<td>Asbestosis</td>
</tr>
<tr>
<td>Berylliosis</td>
</tr>
<tr>
<td>Siderosis</td>
</tr>
<tr>
<td>Other metals (eg, mixture of tungsten or titanium carbide with cobalt or nickel)</td>
</tr>
</tbody>
</table>

Table 2. Pathologic Reaction to Lung Injury

<table>
<thead>
<tr>
<th>Pathologic Injury</th>
<th>Disease Process*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emphysema</td>
<td>CWP, smoking-related lung disease</td>
</tr>
<tr>
<td>Diffuse interstitial inflammation/fibrosis</td>
<td>Asbestosis, hard metal lung disease, hypersensitivity pneumonitis, chronic berylliosis, silicosis, complicated CWP</td>
</tr>
<tr>
<td>Granulomas</td>
<td>Chronic berylliosis, silicotuberculosis, hypersensitivity pneumonitis</td>
</tr>
<tr>
<td>Nodular/progressive massive fibrosis</td>
<td>Silicosis, complicated CWP</td>
</tr>
<tr>
<td>Dust macules</td>
<td>CWP, mixed dust pneumoconiosis</td>
</tr>
<tr>
<td>Pleuritis/pleural effusion, fibrosis, plaques, nodules</td>
<td>Asbestosis, silicosis</td>
</tr>
</tbody>
</table>

* CWP indicates coal worker’s pneumoconiosis.

Table 3. Reactive Epithelial and Inflammatory Changes

<table>
<thead>
<tr>
<th>Cytology</th>
<th>Disease Process</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesothelial hyperplasia</td>
<td>Asbestosis</td>
</tr>
<tr>
<td>Goblet cell metaplasia</td>
<td>Occupational/environmental asthma, environmental toxins</td>
</tr>
<tr>
<td>Creola bodies</td>
<td>Occupational/environmental asthma</td>
</tr>
<tr>
<td>Squamous metaplasia/reserve cell hyperplasia</td>
<td>Chronic berylliosis, hard metal lung disease</td>
</tr>
<tr>
<td>Multinucleated giant cells</td>
<td>Smoking-related lung disease, dust macules (coal worker’s pneumoconiosis, silicosis, siderosis)</td>
</tr>
<tr>
<td>Pigmented macrophages</td>
<td>Occupational/environmental asthma, parasitic/fungal infections, drug reactions</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>Farmer’s lung, maple bark stripper’s disease, hot tub lung, bagassosis, drug reactions</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Noncellular Elements

<table>
<thead>
<tr>
<th>Cytology</th>
<th>Disease Process</th>
</tr>
</thead>
<tbody>
<tr>
<td>Curschmann spirals</td>
<td>Occupational/environmental asthma</td>
</tr>
<tr>
<td>Charcot-Leyden crystals</td>
<td>Occupational/environmental asthma, parasitic/fungal infections, eosinophilic pneumonia</td>
</tr>
<tr>
<td>Asbestos bodies</td>
<td>Asbestosis*</td>
</tr>
<tr>
<td>Intra-alveolar granular material</td>
<td>Silica-related pulmonary alveolar proteinosis</td>
</tr>
</tbody>
</table>

* Asbestos bodies may also be seen in asbesostexposed individuals in the absence of asbestosis.

an overview of the various pathologic lesions associated with occupational lung diseases. Notice that the lung can react to the same agent in more than one way, depending on the type of dust particle and amount and duration of exposure. For example, individuals exposed to silica can display a variety of pathologic lesions including silicoproteinosis and nodular silicosis. With silicoproteinosis, the air spaces are filled with granular eosinophilic material, whereas nodular silicosis is characterized by a varied histologic pattern that includes collections of dust-filled macrophages and fibrotic nodules containing birefringent silica and silicate particles. This varied reaction pattern will therefore impact on one’s ability to obtain adequate material to render a cytologic diagnosis. The illustrations in this review are derived from pleural fluids, brushings, and BAL specimens. In patients with suspected pneumoconiosis, indications for performing BALs are as follows: (1) the exclusion of other causes of diffuse lung disease, such as sarcoidosis, tuberculosis, pulmonary hemorrhage syndromes, malignancies, and so forth in patients exposed to inorganic dust; (2) the documentation of mineral dust exposure in patients who may not be aware of being at increased risk of dust inhalation; and (3) the documentation of the local immune and inflammatory reaction (alveolitis).

Our discussion of the nonneoplastic cytologic manifestations of occupational and environmental lung diseases is divided into 2 broad diagnostic categories. The first encompasses reactive cellular changes associated with occupational and environmental lung diseases, and the second deals with noncellular elements. The former group includes reactive mesothelial proliferation, goblet cell metaplasia, Creola bodies, squamous metaplasia, reserve cell hyperplasia, and various inflammatory changes. Table 3 correlates these changes with various pathologic lesions related to the environment or the workplace. The group of noncellular elements includes Curschmann spirals, Charcot-Leyden crystals, asbestosis bodies (ABs), and intra-alveolar granular material in patients with pulmonary alveolar proteinosis (PAP) (Table 4).

**REACTIVE CELLULAR CHANGES**

**Mesothelial Hyperplasia**

Under normal conditions, only a small amount of fluid is present in the pleural space for lubrication purposes. Effusions arise when there is excess fluid, and based on their physical and biologic properties, they are divided...
Table 5. Cytologic Features of Reactive Mesothelial Cells

- Cells shed in 3-dimensional balls with scalloped periphery, sheets, and single cells
- Range in size and appearance of mesothelial cells
- Abundant cytoplasm that may be foamy, vacuolated, or dense (cyanophilic with Papanicolaou stain and basophilic with Diff-Quik stain)
- Peripheral “fuzzy” zone and empty intercellular space or “windows” between cells because of long microvillous processes
- Round to oval, central or eccentric nuclei with finely granular chromatin and 1–2 nucleoli

![Image](image_url)

Figure 1. Pleural fluid with a reactive mesothelial proliferation. Note the range in size and appearance of the reactive mesothelial cells (Papanicolaou, original magnification ×400).

into transudates and exudates. Effusions in occupational lung diseases are typically of the exudative type. When an effusion is present, cytologic examination of the fluid usually reveals variable numbers of reactive (hyperplastic) mesothelial cells. These reactive mesothelial cells represent a host response to various types of injury, including those that are occupational or environmental in origin, as a result of the inhaled particles or fibers associated with these diseases. Once inside the alveolar parenchyma, the mechanisms by which these inhaled inorganic particles or fibers reach the pleural surface are not well understood. Direct erosion from the underlying lung or spread via the lymphatic system are the 2 most favored hypothesized routes of spread. Only those particles whose mean diameter is less than 5 μm reach the alveolar spaces, whereas larger particles are trapped along the bronchial tree and cleared via the mucociliary system of the endobronchial cells. Fibers, particularly asbestos, behave quite differently. Deposition of these fibers in the alveoli appears to be more of a function of the diameter rather than fiber length. Thus, relatively long fibers with diameters less than 5 μm can be found in the alveoli. Among the different asbestos fiber types, amphiboles are considered more carcinogenic because of their biopersistence in pulmonary tissue.

The cytologic characteristics of reactive mesothelial cells in effusions are listed in Table 5 and illustrated in Figure 1. Given the range of atypia that reactive mesothelial cells can exhibit, it is important that one be familiar with potential pitfalls associated with reactive mesothelial proliferations. They include papillary fragments with or without collagenous cores (Figure 2, A), 3-dimensional cell balls (Figure 2, B), multinucleation (Figure 2, C), increased mitotic rate or nuclear-cytoplasmic ratios, and “signet ring–like” changes in the cytoplasm because of accumulation of fluid or lipid material (Figure 2, D). Figure 3 represents a histologic correlate of reactive mesothelial proliferation illustrating hyperplastic mesothelial cells and papillary fragments. Additional information regarding the cytologic features of asbestos-associated effusions is provided by Sporn et al.7

Pleural effusions represent one of the benign pleural disorders associated with asbestos exposure. The others include visceral pleural fibrosis, hyaline pleural plaques, and rounded atelectasis.8 Benign asbestos effusion is defined by 4 criteria: history of asbestos exposure, radiologic or thoracoscopic evidence of a pleural effusion, absence of another disease as the etiology for the effusion, and no history of malignancy for the past 3 years.2,8 Although the pathogenesis of benign asbestos effusion is unknown, experimental models suggest that mediators from asbestos-phagocytosing cells induce inflammation and mesothelial cell proliferation. The effusion usually precedes the development of pleural plaques and asbestosis, and the incidence is directly proportional to the dosage of asbestos exposure.10 About 50% of these asbestos effusions are hemorrhagic and 25% are eosinophilic.8 Asbestos fibers or bodies have not been reported in these effusions.

Goblet Cell Metaplasia

Goblet cells are normally interspersed between ciliated endobronchial cells along the mucosal surface. They usually proliferate in the presence of environmental toxins or chronic inflammation or irritation. Goblet cell metaplasia is present in large airways in asthma and chronic bronchitis, as is submucosal gland hypertrophy. Cytologic specimens, especially bronchial brushings, yield cohesive groups of cells with hypersecretory features. The goblet cells have single or multiple cytoplasmic vacuoles filled with mucin and peripheral nuclei (Figure 4, A). These cellular groups can be distinguished from mucinous adenocarcinoma by the lack of malignant features, such as single cells, nuclear enlargement, nuclear membrane irregularities, hyperchromasia, and chromatin clumping (Figure 4, B).

Creola Bodies

Creola bodies were described by Naylor11 as compact clusters of columnar epithelial cells exhibiting peripheral palisading that are seen almost exclusively in asthmatic patients. In his original paper, Naylor selected the term Creola body in honor of the patient in whose sputum specimen these cell groupings were first observed. In a follow-up article coauthored by Railey, the authors12 discussed the differential diagnostic points between Creola bodies and pulmonary adenocarcinomas in sputum specimens. The most useful features they found to help separate Creola bodies from pulmonary adenocarcinomas included the uniform size and shape of the nuclei, peripheral palisading of the papillary groups, and the presence of cilia. Several of these features are illustrated in Figure 5. Creola bodies have been reported in patients with occupational asthma–related lung disease.13
Figure 2. Examples of potential pitfalls in reactive mesothelial proliferations. A, Papillary fragment with community border and fibrous core (Papanicolaou, original magnification ×400). B. Three-dimensional cell ball of reactive mesothelial cells (Papanicolaou, original magnification ×400). C, Multinucleated giant cell (Papanicolaou, original magnification ×400). D, Mesothelial cell with “signet ring–like” change because of intracytoplasmic fluid accumulation (Papanicolaou, original magnification ×400).

Squamous Metaplasia and Reserve Cell Hyperplasia
Squamous metaplasia and reserve cell hyperplasia may be seen simultaneously in cytologic preparations. These changes typically result from chronic irritation and/or injury of mucosal surface of bronchi or bronchioles by an offending agent. Examples include the toxic effects associated with cigarette smoking or air pollution. Inflammatory processes or infections such as sarcoidosis, tuberculosis, chronic bronchitis, organizing pneumonia, or bronchiectasis may also result in squamous metaplasia and reserve cell hyperplasia. In brushings, metaplastic squamous cells exfoliate in sheetlike tissue fragments, whereas cell groups with more rounded contours are seen in liquid-based preparations. The individual cells have a dense cytoplasm and reactive nuclear changes (Figure 6). Reserve cell hyperplasia sheds as small tissue fragments with cells displaying regular periodicity. Reserve cell hyperplasia lacks the high nuclear-cytoplasmic ratio, extreme hyperchromasia, and nuclear molding seen in small cell carcinoma.

Multinucleated Giant Cells
Multinucleated giant cells (MGCs) are common in BAL fluids from patients with various interstitial lung diseases.
and even from healthy individuals, although the amount is limited, ranging from 0.25% to 2.5% of all alveolar macrophages.\textsuperscript{14} From an occupational standpoint, MGCs can be found in BAL specimens from a variety of diseases including chronic berylliosis, aluminosis, asbestosis, and hard metal (cobalt) disease.\textsuperscript{8,15} The chronic form of berylliosis represents a hypersensitivity reaction to beryllium, resulting in a noncaseating sarcoid-like granulomatous reaction (Figure 7). Patients with hard metal (cobalt) disease have a giant cell interstitial pneumonia pattern on histology characterized by syncytial giant cells lining alveoli and bizarre MGCs within alveolar spaces.\textsuperscript{8} Given their intra-alveolar location, these syncytial and MGCs may be seen in cytologic samples of patients with hard metal lung disease. The BAL specimen from these patients characteristically shows elevated MGC–alveolar macrophage ratios ranging from 4% to 11%.\textsuperscript{16,17} Cannibalism of inflammatory cells by these enlarged MGCs has also been described in the BAL fluid of hard metal workers.\textsuperscript{17}

**Pigmented Macrophages**

Several different types of pigmented macrophages can be seen in occupational lung disease, depending on the offending agent. Smoker's pigment has a finely granular, golden-brown appearance in BAL specimens (Figure 8, A). In contrast, hemosiderin pigment has a darker and coarser appearance (Figure 8, B). This difference is readily seen with Prussian blue iron stains that highlight the fine granules in smoker's pigment and the coarse dark blue granules present in hemosiderin. This pattern of reactivity is usually not seen with anthracotic pigment, given the large amount of carbon in anthracosis. The degree of cytoplasmic pigmentaion in smokers correlates with the number of pack-years smoked. Also, this pigment can persist in the lung for many years after cessation of smoking.\textsuperscript{18} Dust macules, which represent collections of pigmented macrophages associated with minimal fibrosis, may occasionally be seen in cytologic preparations.

**Eosinophils**

Normal BAL fluid contains less than 1% eosinophils.\textsuperscript{19} Their characteristic red granules are easily seen in Diff-Quik preparations (Figure 9, A). However, in ethanol-fixed Papanicolaou-stained preparations, these granules are not easily visualized. The only way to recognize these cells is by their bilobed nuclei (Figure 9, B). The most common causes of BAL-associated eosinophilia include interstitial lung diseases, acquired immunodeficiency syndrome-associated pneumonias, eosinophilic pneumonias, and drug-induced lung disease.\textsuperscript{20} Examples of potential occupational and environmental etiologic agents associated with increased numbers of eosinophils include wood dust exposure, di-isocyanates, anhydrides, plants, metals, chemicals, vegetable gums, insects, and so forth. Smoking and allergic bronchopulmonary aspergillosis may also result in BAL-associated eosinophilia.\textsuperscript{2}

**Lymphocytes**

In patients with BAL-associated lymphocytosis, there is a marked proliferation of mature-appearing small lymphocytes (comprise more than 50% of the cells in the BAL specimen). This reaction pattern is seen in patients with HP (extrinsic allergic alveolitis). This is a diffuse interstitial granulomatous disease that represents an immunologic reaction to inhaled organic antigens or simple chemicals. Examples include farmer's lung, bird fancier's lung, bagassosis, maple bark stripper's disease, and hot tub lung.\textsuperscript{21,22} The latter is thought to represent a hypersensitivity reaction to Mycobacterium avium present in water. Subtyping of BAL-derived lymphocytes is a useful ancillary test in the diagnosis of HP. Satake et al\textsuperscript{23} have shown that phenotypic characterization of BAL T lymphocytes may be useful in the differential diagnosis of several interstitial lung diseases including HP, pulmonary sarcoidosis, and bronchiolitis obliterans with organizing pneumonia (currently termed cryptogenic organizing pneumonia). They noted a significant increase in CD3 lymphocytes when compared with patients with sarcoidosis, cryptogenic organizing pneumonia, and healthy controls. Flow cytometric analysis of T-cell subsets revealed a relative increase in CD8 lymphocytes with decrease in CD4/CD8 ratio (usually less than 1.0).\textsuperscript{23} This is in contrast to BAL specimens from patients with sarcoidosis, in whom there is preferential expansion of CD4 T-helper cells.\textsuperscript{24} Other cell types seen in BAL fluids from patients with HP include mast cells. The finding of significant number of mast cells (more

---

**Figure 4.** Bronchial brush specimen of goblet cell metaplasia. A, This tissue fragment contains numerous goblet cells that have abundant intracytoplasmic mucin (Papanicolaou, original magnification ×200). B, The higher magnification illustrates basilar displacement of the nucleus by the intracytoplasmic mucin. The smooth nuclear contours and finely granular, evenly distributed, chromatin are benign features of this reactive process (Papanicolaou, original magnification ×400). Figure 4, B, reprinted with permission from Lippincott, Williams & Wilkins, from Laga et al.\textsuperscript{48}(p27)

---

**Figure 9.** A, Bronchial brush specimen of multinucleated giant cells. B, The higher magnification of the multinucleated giant cells shows multiple nuclei with different sizes. The nuclei are relatively large and arranged in a syncytial pattern (original magnification ×400).
than 1%), in combination with lymphocytosis, is specific for HP. Positive specific immune response to a given antigen by lymphocyte transformation testing may also aid in the diagnosis of HP. Although some may consider subtyping of BAL-derived lymphocytes and lymphocyte transformation testing ancillary studies in the evaluation of HP, these tests, in combination with the clinical history, radiologic studies, and pathology, form part of the criteria used in the diagnosis of HP. Lymphocyte transformation and proliferation assays have also been useful in the diagnosis of chronic berylliosis. In these patients, it is hypothesized that beryllium-specific T-cell clonal expansion and T-cell helper cytokine production may explain chronic beryllium disease and its development years after beryllium exposure has ceased.

NONCELLULAR ELEMENTS

Curschmann Spirals

The structures are named after the German physician, Dr. Heinrich Curschmann, who first reported these spirals in sputum samples from asthma patients. Curschmann spirals usually form as a result of excess mucus production and are associated with bronchial obstruction, often because of chronic bronchitis or asthma. Asthma-induced occupational and environmental lung disease may be associated with exposure to a variety of sensitizing agents including insects, plants, biologic enzymes, wood dust, diisocyanates, anhydrides, metals, and so forth. The Curschmann spirals represent inspissated mucus casts of bronchioles that typically arise from the deep lung tissue, possibly from seromucous bronchial glands. In cytologic samples, these structures have a densely staining core with a lighter staining periphery (Figure 10).

Charcot-Leyden Crystals

These are eosinophilic to orangeophilic structures that are typically rhomboidal or somewhat needle-shaped. They represent byproducts of eosinophil granules and, therefore, are seen in cases of hypereosinophilia. The latter include occupational and environmental asthma, fungal and parasitic infections, drug-induced lung disease, or eosinophilic pneumonia. Although frequently seen in BAL samples, these crystals have also been rarely reported in serous fluids from patients with eosinophilic pleural effusions. Allowing the fluid to stand at 4°C for at least 24 hours appears to enhance the formation of these crystals.

Asbestos Bodies

Asbestos bodies represent asbestos fibers that have been coated by an iron proteinaceous coat by alveolar macrophages. The presence of a thin transparent fibrous core helps to differentiate ABs from other ferruginous bodies such as those associated with mica, carbon particles, and inhalational talcosis. Other pseudoasbestos bodies that may be confused with ABs include erionite and refractory ceramic fiber bodies. These structures also have thin translucent cores that are indistinguishable from true ABs on routine phase-contrast light microscopy. In these cases, one may need to resort to x-ray spectrometry and chem-
ical analysis to separate pseudoasbestos fibers from true asbestos fibers. In cytologic preparations, ABs have a yellow-brown color and a characteristic beaded, dumbbell-shaped appearance (Figure 11). Asbestos body counting of digested lung tissue is routinely used to determine the extent of AB burden in the lung. Using this method, it appears that even individuals who have not been exposed to occupational asbestos may have ABs in the lung. Dodson et al and Roggli et al have determined that 0 to 20 ABs per gram of wet lung tissue (about 200 ABs per gram of dry lung tissue) represents the normal range of ABs in the general population. In contrast, patients with asbestosis have at least 2000 ABs per gram of wet lung tissue with a median concentration more than 100,000 ABs per gram. To provide a less invasive means to quantify ABs, attempts have been made to determine if BAL fluid samples can be used to document asbestos exposure. There appears to be a good correlation between AB concentration in BAL fluid samples and number of ABs per dry lung tissue. De Vuyst et al concluded that in patients with more than 1 AB per milliliter of BAL fluid, 85% had more than 1000 ABs per gram of lung tissue and 44% had more than 10,000 ABs per gram. This was also reported by Sebastien and colleagues who found that BAL concentrations of 1 AB per milliliter predicted parenchymal concentrations of ABs between 1050 and 3010 per gram of lung tissue. Roggli et al demonstrated that the presence of more than 1 AB per 10^6 cells or 1 AB per milliliter of BAL fluid correlated with asbestos exposure. They also noted a higher percentage of AB-positive BAL specimens in asbestos-exposed individuals compared with the non-asbestos-exposed population (75% vs 31%, respectively). In their study, patients were diagnosed with asbestosis when there was a history of occupational exposure and at least 2 of the following: increased interstitial markings on chest radiograph, inspiratory crackles, dyspnea on exertion.
tion, and restrictive changes on pulmonary function tests. Similar findings were also reported by Vathesatogkit et al., who found a higher prevalence of clinical and parenchymal abnormalities in AB-positive BAL samples. The parenchymal abnormalities they noted in the asbestos-exposed individuals included pleural plaques, diffuse pleural thickening, subpleural reticular changes, subpleural lines, fibrosis, and bronchiectasis.

**Pulmonary Alveolar Proteinosis**

Pulmonary alveolar proteinosis is a rare condition that is characterized by intra-alveolar accumulation of granular eosinophilic material that is periodic acid–Schiff positive and rich in lipids. It is thought to arise as a result of overproduction of surfactant by type 2 pneumocytes or impaired clearance by alveolar macrophages. This granular material can be seen in BAL specimens. In addition, the presence of globular material has also been described in BAL samples from patients with PAP.

These globules have a dense, green or orange appearance with sharp borders in Papanicolaou-stain smears (Figure 12). Quantification of these globules in BAL-derived samples has been used to differentiate PAP from other disease processes such as sarcoidosis, idiopathic pulmonary fibrosis, collagen vascular diseases, and immunodeficiency states. Chou et al. reported that when 18 or more globules are present in BAL specimens, this was a highly sensitive and specific marker for PAP. All 7 (100%) patients with PAP had 18 or more of these globules. In contrast, 6 (4.6%) of 128 patients with other pulmonary disorders displayed these globules in BAL fluids. In these patients, the number of globules was less than 18. No globules were seen in 11 healthy subjects. It is believed that these globules represent the multilamellated structures characteristic of PAP visible by electron microscopy. From an occupational standpoint, PAP has been linked to aluminum, titanium, and silica exposure. Pulmonary alveolar proteinosis represents one of the pathologic lesions associated with silica exposure (acute silicoproteinosis). This form of silicosis is seen in patients exposed to large quantities of finely granular silica (such as the sandblasting industry). Therefore, the cytologic presence of the granular material seen in PAP may be useful in the diagnosis of this disease, given the fact that there is light microscopic documentation that PAP occurs in silica-exposed individuals. Acute silicoproteinosis becomes apparent within 3 years of exposure and represents an aggressive, potentially lethal form of silica-related lung disease.

In conclusion, for most cases of occupational and environmental lung diseases discussed in this review, the cytologic findings are entirely nonspecific. This may be because more than one agent can initiate a similar host reaction and/or the offending agent can be associated with more than one pathologic process. However, there are few cases in which the cytology, in combination with the clinical and radiologic findings, can yield valuable diagnostic information. Examples of this include bizarre MGCs in...
workers with hard metal (cobalt) disease, PAP in patients with acute silicoproteinosis, and the presence of ABs in BAL specimens, which appears to correlate with asbestosis exposure.

References