Bronchoalveolar lavage

Bronchoalveolar lavage is generally performed through the flexible fiberoptic bronchoscope. Use of the flexible bronchoscope became routine after 1973 and since that time has virtually revolutionized the practice of pulmonary medicine because it provides easy and safe access to the tracheobronchial tree. In 1974, the use of the fiberoptic bronchoscope was extended to the performance of bronchoalveolar lavage in normal volunteers. This was followed by a number of studies wherein cells and proteins were analyzed in lung washings from normals.[1,2] Most of the recent information dealing with the immunology of the human lung has been obtained from the analysis of bronchoalveolar lavage specimens and of corresponding peripheral blood samples.[3]

Details about performing bronchoalveolar lavage have been well established and an extensive list of related publications is developing. The lavage is a safe procedure in both normal, healthy volunteers and in patients with interstitial lung disease.[4] Only minor complications are encountered and consist of transient fever, bleeding, and bronchospasm in less than 5% of procedures. The fiberoptic bronchoscope is securely wedged into a small bronchus of the lingula or middle lobe. Sterile saline (0.9%) is instilled in 50-mL aliquots and suctioned back after each instillation. Between 150 and 300 mL are instilled with about 50% to 60% of fluid being retrieved, which is then processed to obtain the cellular pellet and cell-free supernatant. The cells recovered by bronchoalveolar lavage in a normal, non-smoking patient number $5–10 \times 10^6$, of which $93\% \pm 3\%$ are alveolar macrophages, $7\% \pm 1\%$ are lymphocytes, and less than 1% are polymorphonuclear leukocytes. The cell-free fluid obtained from the lavage contains a variable amount of lipids, proteins, immunoglobulins, and proteases.

The use of bronchoalveolar lavage-cell analysis to quantify and characterize the alveolitis of the interstitial diseases is dependent on the assumption that lavage cells accurately reflect the population of inflammatory and immune cells in the lung parenchyma. Initial data suggested that the neutrophil was the major inflammatory cell present in the lavage fluid of patients with idiopathic pulmonary fibrosis.[5] An increased neutrophil count seemed to be associated with active disease and an increased likelihood of response to corticosteroids. Inherent in these data is the implication that patients with idiopathic pulmonary fibrosis who have a normal lavage cell analysis are in a quiescent stage of the disease. Similar data also exist for sarcoidosis, except that the major lavage effector cell appears to be the T lymphocyte, and those patients with greater than 28% T lymphocytes on lavage analysis would progress if untreated.[6] The lavage-cell analysis in pulmonary sarcoidosis remains unchallenged, but there have been controversies dealing with the interpretation of bronchoalveolar cellular analysis in patients with idiopathic pulmonary fibrosis. Even though earlier studies indicated that lavage cellular analysis does accurately sample parenchymal cells, some recent studies, including a prospective analysis of the value of bronchoalveolar lavage differential counts in patients with idiopathic pulmonary fibrosis, have shown that increased lymphocyte percentages were found to be associated with responsiveness to therapy.[7] The major problem in the comparison of bronchoalveolar lavage data is the variation from one laboratory method to another. Part of the variability may be related to the absence of specific markers for lavage cells. It can be difficult to distinguish large lymphocytes from small macrophages. The exact procedures used by different investigators is also not standard, with the lavage volume ranging from 100 mL to more than 500

Table. Bronchoalveolar lavage (BAL) findings in diffuse lung disease

Disease	BAL fluid and cells
Idiopathic pulmonary fibrosis	—Alveolitis (usually polymorphonuclear cells, but lymphocytes may be increased) —IgG elevated —Immune complexes, collagenase, and fibronectin present
Sarcoidosis	—Lymphocytes increased (T cell with T-helper cells high in active phase) —Activated lymphocytes —Spontaneous secretion of lymphokines —Angiotensin-converting enzyme and fibronectin present
Hypersensitivity pneumonitis	—Lung cell recovery increased with a high percentage of lymphocytes (T lymphocytes predominant, suppressor cells can be increased) —Abnormal surfactant
Chronic eosinophilic pneumonia	—Markedly elevated level of eosinophils (42 ± 22%). Lymphocytes may be increased —Reduction in eosinophils during steroid therapy
Pulmonary histiocytosis X	—Increased cellularity —Increase in percentage of neutrophils or eosinophils —OKT6 reactive cells —*Langerhans cells* —Histiocytosis X cells on electron microscopy

mL in some cases. Also, even within a single study, the volume of lavage fluid infused may vary from 1 patient to another.

In the diagnosis of chest diseases, bronchoalveolar lavage has limited value (*Table*). It can be useful for diagnosing some infectious diseases, intra-alveolar hemorrhage, alveolar proteinosis, chronic eosinophilic pneumonia, and histiocytosis X.[8–11] The interstitial lung diseases have been extensively studied by bronchoalveolar lavage. However, only one interstitial disease, histiocytosis X, can be diagnosed with reasonable accuracy by ultrastructural study of the cell pellet.

Bronchoalveolar lavage fluid analysis has been the favorite way to characterize the peripheral air spaces for the past decade. It has led to better concepts of immunopathology of many diseases and provided new ways to monitor the evolution of the diffuse interstitial lung disorders. It is also possible that through further study and correlation of distinctive lavage findings with other parameters that similar information may be obtained by less invasive procedures. For example, in a recent study of patients with idiopathic pulmonary fibrosis, Edmur et al[12] have shown a significant positive correlation between the degree of neutrophilic alveolitis and the expression of excessive helper function by peripheral blood T cells. The cause-and-effect relationship between these observations remains speculative, yet the possibility exists that a peripheral blood test may accurately reflect the inflammatory status of the lung. Limitations to lavage fluid analysis are many, and one must be cautious not to overinterpret results. However, there are studies where correlation between cells in the bronchoalveolar lavage fluid and those extracted from lung biopsy is surprisingly good,[13,14] but more studies of this relationship are needed. The clinical interpretation of lavage fluid analysis is not as yet well validated and must still be considered in an experimental stage. Application of these results re-

quires more research, standardization, and the use of prospective patient protocols.

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