CONCLUDING REMARKS

Clinical usefulness of bronchoalveolar lavage

P. Howard

Bronchoalveolar lavage (BAL) has been researched for about 15 yrs or more. This workshop has introduced new concepts which extend the usefulness of BAL. Standardization of procedures is welcome. Recommendations of a European Working Party will appear shortly in the European Respiratory Journal. The wedged bronchoscope method is simple but invasive. Analysis of specimens taken under strictly defined conditions requires identification. Transport of specimens at room temperature to regional laboratories was considered. In suitable media cells and constituents are preserved for up to 24 h, enabling overnight transport. Reservations were expressed as to whether cells, particularly neutrophils, will withstand such trauma. As clinical indications for BAL expand, availability of transport techniques raises questions as to which analyses may be conducted locally and which would be better transferred to regional laboratories.

BAL is most useful in detection of organisms by smear, culture or examination of macrophage inclusion characteristics in undiagnosed infection, human immunodeficiency virus (HIV), other immunocompromised pneumonias and atypical pneumonia in the normal host. *Pneumocystis carinii*, cytomegalovirus and other viral and fungal infections are readily recognized. Transbronchial biopsy and induced sputum techniques are competitive. Induced sputum is simple and should be tried first, followed by BAL. The complications of transbronchial biopsy, *e.g.* pneumothorax and haemorrhage, are reduced by applying this technique after induced sputum and BAL have failed.

The diagnostic value of BAL is limited in cryptogenic fibrosing alveolitis (CFA), hyper-sensitivity pneumonitis and occupational fibrosis, compared with transbronchial biopsy and clinical features. Work continues on the efficacy of sub-sets of lymphocyte populations. BAL is of diagnostic value for lipoid pneumonias, histiocytosis and berylliosis, which are all rare.

The use of BAL to guide corticosteroid and immunosuppressive drug therapy in CFA remains controversial. There are strong indications that steroids are beneficial when lymphocyte and neutrophil counts are high and cyclophosphamide when eosinophil counts are high but specificity is insufficient to alter the approach used by most clinicians *i.e.* prednisolone first and immunosuppressive drugs later. Response is generally poor.

University of Sheffield, Dept of Medicine, Royal Hallamshire Hospital, Glossop Road Sheffield, S10 2JF UK.

In patients of more than 65 yrs, particularly females, CFA can be remarkably benign. If BAL could be used to identify patients taking a more aggressive course it would be diagnostically valuable.

Occupational fibrosis seems to be caused by both inflammatory fibrosis and release of fibrogenic factors. BAL has provided evidence for both mechanisms but it is not known why so few heavily exposed individuals develop severe forms of the disease. Analysis of particles within alveolar macrophages reveals occupational exposure but does not indicate the likelihood of subsequent disease. This is hardly surprising given the time lag involved. BAL is so far of little use in occupational lung fibrosis except in berylliosis.

An account of the aetiology of sarcoid as an excessive but ordered T-lymphocyte proliferation demonstrated the research value of BAL. Unknown antigens on the surface of macrophages stimulate replication of T-lymphocytes largely through α/β surface receptors. Progression to lung fibrosis varies between countries. Sarcoid is relatively benign in the UK. More fibrosis occurs in the USA. Lymphocyte response is claimed to have diagnostic strength and therapeutic indication but total counts and sub-set analysis are probably not sufficiently specific for most clinicians to prefer BAL to other clinical indicators when determining corticosteroid treatment.

BAL performed at the same time as bronchoscopy is of value in the diagnosis of peripheral solitary lung lesions. A positive Papanicolau stain for malignant cells can save more invasive procedures. Research continues into biochemical markers of malignancy, macrophage and lymphocyte function and anti-tumour factors in BAL fluid.

Replacement of α_1-antitrypsin (using human or genetically engineered material) by injection or inhalation is now possible for patients with severe deficiency. Clinical usefulness cannot be determined for several years. Measurement of antiprotease activity in BAL fluid is used to determine the efficacy of the new preparations.

Potential use of α_1-antitrypsin for obstructive airways disease in the nondeficient patient is more complex. Many such patients have normal levels of antiprotease in BAL fluid but it seems functionally less active. Whether high dosing or combination with anti-inflammatory and anti-oxidant agents will be effective is unknown and difficult to prove. However, it is important that the potential of such therapy be explored as decline of airway function in bronchitis and emphysema has probably changed little in the past

decade despite increasing use of current anti-inflammatory agents and bronchodilator drugs.

Work continues on BAL in bronchial asthma. Solution of the major problems of sudden death and control of the relatively steroid resistant (10%) might be assisted by BAL but it is not yet used in routine clinical management of bronchial asthma.

Several new indications for the investigation of pulmonary toxic drugs were presented. Appearance of certain cells in BAL fluid is of diagnostic value for paraquat, bleomycin and amiodarone toxicity. They indicate contact with the agent but cannot so far be related to the intensity of disease. The agents probably act by a combination of oxidant injury and hypersensitivity inflammation. In the future, BAL may be used to detect toxic lung changes producing hypersensitivity reactions by sub-typing lymphocytes.

The major complications of lung transplantation are infection, bronchiolitis obliterans, graft *versus* host disease, toxicity of drugs used for immunosuppression and a number of sequelae to surgery. In the detection of infection, immunological reactions and drug toxicity, BAL and transbronchial biopsy are necessary monitoring procedures. Whether one or both should be routinely used is being studied. It is hoped that BAL will replace at least some need for more invasive transbronchial biopsy. In transplantation infection, effective recognition of *P. carinii*, viruses, fungi and standard organsims is claimed. Legionella has not been fully evaluated. Detection of *Aspergillus* spp. seems less good.

Conclusion

Clinical uses for BAL increase but diagnosis of infection in immunocompromised and atypical pneumonia remains the major indication. Diagnosis of a number of rare conditions is helpful and value in malignancy clear. Guide to therapy is controversial. New indications include monitoring transplantation problems and detection of pulmonary drug toxicity. The technique remains of great scientific interest and further developments of clinical value can be expected.