yrs in the former [58], but only 3 mths [65, 66] and 6 mths [65] in the latter. Thus, it is still premature to draw conclusions on the clinical value of lavage cell counts in monitoring the progress of IPF patients.

Serial lavage studies have also recently shown that proportions of phosphatidylglycerol, which are reduced in the BAL fluids of many untreated IPF patients [67, 68], return to normal in patients responding to prednisolone but not in non-responders [67]. It has been suggested that such changes may reflect the extent of damage to the alveolar epithelium in IPF.

In conclusion, preliminary reports indicate that BAL may be of clinical value to monitor changes in the lungs associated with therapeutic response in IPF, but further information is required. In particular, independent prospective studies are needed where patients are evaluated over comparable long-term periods, and details are required of survival as well as radiological and functional response to therapy.

Conclusions

Current published evidence suggests that lavage is of value to aid the diagnosis and management of patients with IPF. BAL cell counts are only a guide to the differential diagnosis of IPF because of the variability within and overlap between diseases. Nevertheless, BAL is of particular value to identify and exclude some of the rarer lung diseases which must be considered in the provisional diagnosis. BAL can provide some useful prognostic indicators in IPF which may aid therapeutic decisions, and serial BAL measurements may have a place in assessing suppression of inflammation in patients responding to therapy. However, at this stage in our knowledge caution should be given to the interpretation of BAL findings, and they are most useful when considered and interpreted in the context of the overall clinical and other investigatory techniques used in the diagnosis and management of patients with this serious lung disease.

Collagen-vascular diseases

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Inflammatory processes that develop in the lung in many of the collagen vascular diseases (CVD) usually result in a diffuse interstitial lung disease (ILD) similar to idiopathic pulmonary fibrosis. Chronic alveolitis, as assessed by bronchoalveolar lavage, revealed the same characteristic pattern of alveolar inflammation associated with idiopathic pulmonary fibrosis; which is evidence of neutrophil accumulation and macrophage activation [38, 45, 50, 69–85]. However, there is a considerable overlap for each disease and type of alveolitis. In addition, inflammatory alveolitis may also be present in a high proportion of patients with CVD and without clinical or radiological evidence of pulmonary involvement, suggesting the presence of an ongoing subclinical alveolitis.

Cellular characteristics of alveolitis

Total number of recovered cells is increased in patients with overt ILD but not in patients without ILD. In addition, total number of cells is progressively reduced in advanced progressive systemic sclerosis [77]. The distribution of BAL cell type according to the disease and to the presence of an associated ILD is summarized in table 1. In addition, alveolar macrophages are "spontaneously" activated and release various bioactive mediators that could be relevant to the pathogenesis of ILD: superoxide anion (various CVD), neutrophil chemotactic factors (various CVD), fibronectin (various CVD), alveolar macrophage derived growth factor for fibrosis (AMDGF) (progressive systemic sclerosis) and tumour necrosis factor (TNF) (rheumatoid arthritis).

It appears that symptomless patients with CVD can have a similar pattern of alveolar inflammation including accumulation of neutrophils and/or lymphocytes and activated alveolar macrophages [86–91].

On the other hand, some cell activities may be defective: since decreased antibacterial activity of alveolar macrophages has been reported in systemic lupus erythematosus but not in other CVD [92, 93].

Biochemical characteristics of alveolitis

The biochemical analysis of BAL fluid shows an increased transudation of serum factors and/or an increased secretion of mediators: albumin, immunoglobulin G (IgG), IgM, alpha-2 macroglobulin, plasminogen activator, procollagen peptide (progressive systemic sclerosis), collagenase, elastase [73, 76, 83, 84, 94, 95]. So far, the value of biochemical analysis of BAL fluid in diagnosis and management of ILD CVD remains to be established.

Clinical significance of alveolitis in CVD

Since alveolar inflammation is a characteristic feature of CVD patients with or without associated ILD, the BAL cytology is by no means a reliable argument for the diagnosis of ILD in this context. However, BAL may be useful for the diagnosis of an associated

Table 1. – BAL cytology in collagen vascular diseases

Disease	With ILD	Without ILD	Ref.
Progressive systemic sclerosis	neutrophils eosinophils	neutrophils eosinophils	[38, 70–72, 74, 75, 86]
Rheumatoid arthritis	neutrophils lymphocytes	lymphocytes (CD4+, T5/9)	[76, 79, 83, 85, 86, 90] [78]
Primary Sjögren syndrome	neutrophils, lymphocytes (CD8+)	lymphocytes (CD4+)	[86–88, 100]
Systemic lupus erythematosus	neutrophils, lymphocytes	lymphocytes	[92]
Dermatopolymyositis	neutrophils	neutrophils	[86, 99]
Mixed connective tissue disease	neutrophils	neutrophils	[86]
Secondary Sjögren syndrome	neutrophils, lymphocytes (CD8+)	neutrophils, lymphocytes (CD8+)	[86, 88]

Presence of ILD is judged by clinical and radiological findings.

lung disease (infection, pulmonary haemorrhage, alveolar proteinosis *etc.*) or of drug-induced lung disorder [96–98]. BAL may also be useful to assess the activity of acute or chronic ILD in patients with scleroderma or with dermatopolymyositis [72, 82, 99]. In general, when increased numbers of lymphocytes are present in BAL fluid, lung disease is associated with a relatively good prognosis, whereas the presence of a predominantly neutrophilic or eosinophilic alveolitis is associated with a higher risk of functional and radiographic deterioration.

The role of BAL in therapeutic decision in symptomless patients with CVD is unclear since its prognostic value is still controversial. Preliminary data suggest that: 1) lymphocyte alveolitis is of good prognosis; 2) neutrophil alveolitis is associated with progressive deterioration of pulmonary function test (PFT) over a 1 yr follow-up in untreated patients. However, corticosteroid treated patients can improve their PFT while the alveolar neutrophilia persists.

In summary:

1) BAL may be useful for the diagnosis of lung complications in CVD; there is as yet no convincing evidence that BAL provides any help in the diagnosis and the management of chronic ILD-CVD.

2) BAL may be useful in the clinical management of acute ILD-CVD .

The value of bronchoalveolar lavage in the diagnosis and prognosis of sarcoidosis

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There is a consensus that BAL changes in sarcoidosis reflect the pathological process [101–110]. Furthermore by analysis of CD4/CD8 lymphocytes BAL can be of benefit in distinguishing sarcoidosis from other granulomatous diseases, such as hypersensitivity pneumonitis [111, 112]. Whether BAL can be used diagnostically and/or prognostically depends, however, on two factors. Firstly, for lavage analysis to be diagnostic, features have to be recorded that together with clinical investigation represent a unique picture of this disease and discriminate it from other interstitial lung diseases. Secondly, there has to be a clear clinical understanding of the level of disease "activity" for the features identified in lavage to be measured against. This second condition is somewhat difficult to satisfy as there appears to be no easy clinical measure of activity. It is only when patients have advanced to fibrotic forms of disease that clear clinical reflections of disease outcome are observed. The values of BAL to diagnosis and prognosis are commented on in tables 1 and 2. Emphasis on the prognostic value of a mere increase of the BAL lymphocyte count, interpreted as high intensity alveolitis [109] weakened as it was made obvious that even advanced cases may show a normal BAL lymphocyte count [113, 114]. BAL lymphocyte counts appear too unreliable as a single investigative tool to be of help regarding therapeutic decisions in patients receiving corticosteroid treatment [115].

A characteristic pattern of BAL macrophage phenotypes identified by monoclonal antibodies