Eur Respir J
1988, 1, 498–504

Antiproteases are increased in bronchoalveolar lavage in interstitial lung disease

Y. Sibille*†, J.B. Martinot*, P. Staquet*, L. Delaunois*, B. Chatelain**, D.L. Delacroix†

Antiproteases are increased in bronchoalveolar lavage in interstitial lung disease. Y. Sibille, J.B. Martinot, P. Staquet, L. Delaunois, B. Chatelain, D.L. Delacroix.

ABSTRACT: The present study evaluates different cellular and soluble components in the bronchoalveolar lavage (BAL) from patients with interstitial lung disease. We observed an increased T_4/T_8 lymphocyte ratio in BAL but not in blood from 24 patients with active pulmonary sarcoidosis compared to sixteen normal individuals and to eleven patients with inactive pulmonary sarcoidosis. Seven patients with hypersensitivity pneumonitis had a normal T_4/T_8 ratio. In the active sarcoidosis and hypersensitivity pneumonitis groups, α_1-Protease Inhibitor (α_1PI) in BAL is significantly higher than in the normal group and a significant correlation between the two antiproteases (α_2-macroglobulin and α_1PI) is observed. These data demonstrate that antiprotease levels (α_1PI and α_2M) are increased in the lower respiratory tract of patients with interstitial lung disease and that among cellular and soluble components of BAL, α_2M represents a sensitive marker of the alveolitis.

Eur Respir J. 1988, 1, 498–504.

* Pulmonary Section and
** Haematology Laboratory, University Hospital of Mont-Godinne, Belgium.
† Experimental Medicine Unit, Institute of Cellular and Molecular Pathology, Catholic University of Louvain, Belgium.

Correspondence: Y. Sibille, Cliniques UCL Mont-Godinne, B-5180 Yvoir, Belgium.

Keywords: Antiproteases; BAL; interstitial lung disease.

Received: July 15, 1987; accepted after revision August 8, 1987.

The interstitial lung diseases include disorders of unknown and known aetiology, and even distinguishing among the diseases of known cause is sometimes tedious. In addition to the problem of diagnosing specific causes of interstitial lung disease, the assessment of disease activity, especially in pulmonary sarcoidosis, remains an important issue. In recent years three techniques have been proposed to assess disease activity in sarcoidosis: ^{67}Gallium scan, Angiotensin Converting Enzyme (ACE) and Bronchoalveolar Lavage (BAL) [1–4]. In the past ten years BAL has been widely used and may be a useful technique in the management of interstitial lung diseases [5, 6]. The lymphocytosis of the BAL has been proposed as an index of disease activity in pulmonary sarcoidosis: a high percentage of lymphocytes in the BAL corresponding to a 'high intensity alveolitis' [7, 8]. Furthermore, the pre-treatment BAL lymphocytosis was recently reported to predict steroid responsiveness in sarcoidosis [9].

Other groups have, however, failed to demonstrate a correlation between BAL lymphocytosis and disease activity and consider an increased T helper/T suppressor ratio (T_4/T_8) in the BAL as a better index for active disease [10, 11]. This BAL T_4/T_8 has also been shown to drop to normal values with regression of the disease. In contrast with these cellular studies, the usefulness of soluble components in BAL has not yet been demonstrated [6].

We recently reported that BAL α_2-macroglobulin (α_2M) is increased in BAL from patients with active interstitial lung diseases [12]. These studies confirm and extend our previous observations and include data for α_1-protease inhibitor (α_1PI) which is the predominant antiprotease in the serum, whose fate in interstitial lung disease has not yet been explored. The purpose of this study is to evaluate in BAL different cellular parameters (including lymphocyte subpopulations) and soluble components (including the two major antiproteases α_1PI and α_2M) during the course of interstitial lung disease.

Material and methods

Study populations

1. *Single lavage group.* After agreement of the local Ethics Committee, the following non-smoking individuals were investigated: 16 normal volunteers (group I) and 35 consecutive patients with biopsy proven sarcoidosis (22 newly diagnosed and 13 with disease known for 1–5 years before referral to us) further subdivided into group II and group III. Group II consisted of 24 untreated patients defined as 'active' sarcoidosis based on BAL lymphocytosis $>15\%$. These included 10 patients with radiological stage I (hilar adenopathy), 7 with stage II (hilar adenopathy and lung infiltrates) and 7 with stage III (lung infiltrates alone). Group III included 11 patients with pulmonary sarcoidosis considered as 'inactive' based on BAL lymphocytosis $<15\%$ (3 stage I, 3 stage II, 5 stage III) including 3 patients treated with steroids. Group IV consisted of 7 untreated patients with typical hypersensitivity pneumonitis. Three patients were pigeon breeders, two fancy bird breeders and two had farmer's lung.

2. *Serial lavages group.* Twelve patients with

pulmonary sarcoidosis were sequentially lavaged (one, two or three times) after the initial BAL. This group included two patients under steroid treatment at the time they were referred to us.

Bronchoalveolar lavage

Bronchoalveolar lavage was performed as described [5, 12, 13] through the fibre-optic bronchoscope using 200 ml sterile 0.9% saline solution in 50 ml aliquots instilled and gently aspirated. The first aliquot (bronchial lavage) was discarded and the studies were performed on the three following aliquots. The recovered fluid was filtered through a single layer of gauze to remove gross mucus and an aliquot was saved for a total cell count, using a Coulter^R cell counter, and for cell differential. The lavage was then centrifuged and the cell pellet was used in lymphocyte subpopulation studies, while the supernatant was kept at $-20°C$ for protein analysis.

Cellular studies

Cell differentials were performed on cytospin preparations, using the same cytocentrifuge (Cytospin 1) at the same centrifuge speed to minimize artificial variations between the different samples [14]. Lymphocyte subpopulations in blood (obtained on the day of the lavage) and BAL were determined using the fluorescent monoclonal antibodies OKT_{11} (T lymphocytes), OKT_4 (helper) and OKT_8 (suppressor) according to REINHERZ *et al.* [15]. The cell bound fluorescence in the lymphocyte population was determined using an EPICS C Coulter^R flow cytometer. Data are expressed as percentage of positive (OKT_{11}, OKT_4, OKT_8) cells in the total lymphocyte population.

Proteins assays

Serum levels of albumin, IgG, IgM and α_1PI were determined by immunonephelometry [16]. The immunoradiometric assay (IRMA) was used for measurement of α_2M in the serum and for all proteins in BAL. This assay, previously described in detail [12, 17], does not require concentration of the BAL fluid. Results are expressed as previously in coefficient of excretion relative to albumin (RCE), to correct for both serum concentration of the different proteins and variable dilution of BAL [12].

$$RCE = \frac{\text{BAL protein}}{\text{serum protein}} \Big/ \frac{\text{BAL albumin}}{\text{serum albumin}}$$

Statistical analysis

Values in the different groups were tested for significance using an unpaired t-test and correlations between variables were evaluated by linear regression.

Results

Cell differentials and lymphocyte subpopulations

BAL volumes recovered, total cell counts and cell differentials in each group are given in table I. The lavage fluid from patients with active sarcoidosis and hypersensitivity pneumonitis contained more cells than the BAL from normal individuals and from patients with inactive sarcoidosis. Patients with active sarcoidosis also demonstrated a significantly higher percentage of lymphocytes than normals and patients with inactive sarcoidosis. Patients with hypersensitivity pneumonitis had higher percentages of both lymphocytes and polymorphonuclear neutrophils.

As illustrated in figure 1, the group of patients with active sarcoidosis had a significantly higher T_4/T_8 ratio in the BAL than the normal group or the groups of patients with inactive sarcoidosis or hypersensitivity pneumonitis. This increased T_4/T_8 ratio in the BAL from the active sarcoidosis group reflects a combined increase of BAL T_4 subpopulations and a decrease of BAL T_8 subpopulations. No significant difference was observed in the blood T_4/T_8 ratio between the different groups (data not shown).

Table 1. - Cellular components of BAL

	BAL recovery ml	Cell count x10^4/ml BAL	% macrophages	% lymphocytes	% PMN	%eosinophils
Normals n=16	160.9±19.1+	17.2±5.8	91.1± 8.4	8.2± 8.0	0.5±0.7	0.06±0.2
Sarcoidosis n=35	136.3±28.2	28.1±13.8*	76.4± 8.1*	22.6±12.8*	0.8±0.8	0.1 ±0.4
Active sarcoidosis n=24	133.6±30.7	30.9±12.9*	69.8±10.2*	29.3± 9.9*	0.6±0.8	0.2 ±0.4
Inactive sarcoidosis n=11	141.3±23.0	23.6±15.6	89.3± 3.8	9.7± 3.3	1.1±1.0	0
Hypersensitivity pneumonitis n=7	136.0±19.7	66.8±25.2*	38.7±20.7*	39.5±28.7*	6.5±5.6*	1.3 ±1.2*

+ Mean±SD. *p<0.05 when compared to normal group values. PMN: polymorphonuclear neutrophils

Table 2. - BAL immunoglobulins G and M (in RCE)

	Normals n=16	Active sarcoidosis n=24	Inactive sarcoidosis n=11	Hypersensitivity pneumonitis n=7
IgG	0.74±0.26⁺	1.90±0.90**	1.08±0.50*	2.28±1.02*
	(0.20–1.38)°	(0.64–3.62)	(0.60–1.80)	(1.42–4.00)
IgM	0.08±0.07	0.51±0.43**	0.28±0.20*	1.54±1.21**
	(0.01–0.16)	(0.08–1.65)	(0.12–0.49)	(0.40–4.75)

⁺mean±SD. ° range in brackets , *p<0.05, **p<0.01 when compared to normals, p<0.05 when compared to inactive sarcoidosis; RCE: relative coefficient of excretion.

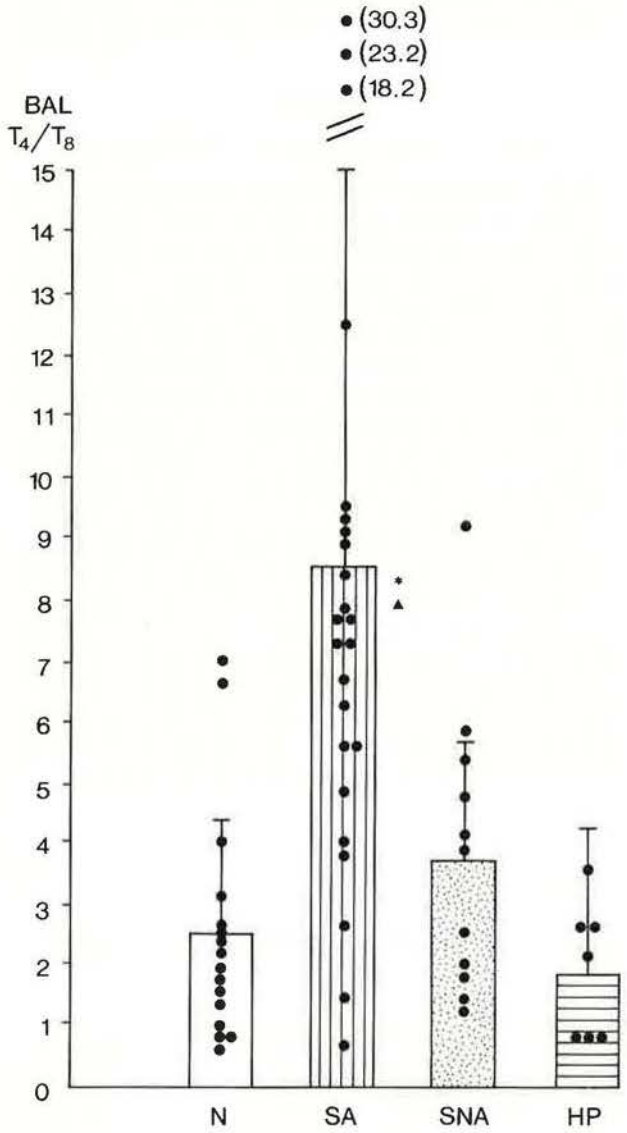

Fig. 1. The T_4/T_8 lymphocyte ratio in BAL from active sarcoidosis patients (SA) (n=24) is significantly increased when compared to normals (N) (n=16) and non-active sarcoidosis patients (SNA) (n=11). No significant difference was observed between hypersensitivity pneumonitis patients (HP) (n=7) and normals. Columns represent means and bars standard deviations. * $p<0.05$ when compared to normals. ▲ $p<0.05$ when compared to non-active sarcoidosis patients.

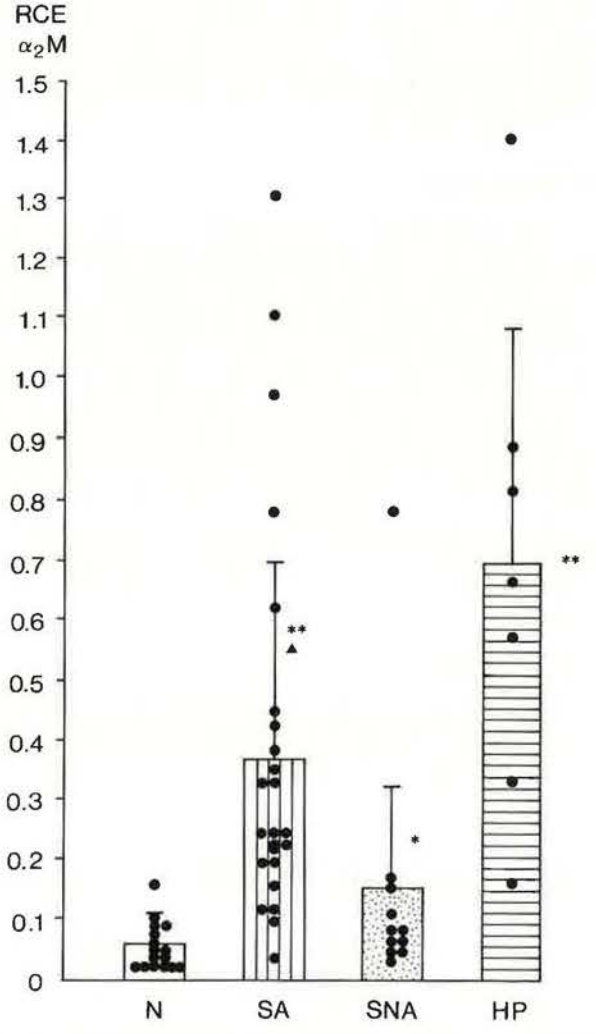

Fig. 2. α_2M RCE in BAL from (left to right) normals (□), active sarcoidosis patients (▥), inactive sarcoidosis patients (▤) and hypersensitivity pneumonitis patients (▤). Columns and bars represent respectively means and standard deviations. Significant differences are observed between SA and N, between SNA and N, between HP and N and between SA and SNA. Same symbols (*, ▲) as in figure 1, ** $p<0.01$ when compared to normals.

Immunoglobulins G and M and α_2-macroglobulin in BAL

A significant increase in RCE of α_2M (fig. 2) and IgG (table II) is observed in the active sarcoidosis

group (mean values respectively 0.39 and 1.90) compared to normals (respectively 0.05 and 0.74) ($p<0.01$). RCE of IgM for the active sarcoidosis patients (mean = 0.51) was also higher than that of the normals group (mean = 0.08) ($p>0.05$). Patients with hypersensitivity pneumonitis also demonstrated a significant increase in RCE of α_2M (0.69), IgG (2.28) as well as IgM (1.54) compared to the normal group (fig. 2, table II).

α_1-protease inhibitor levels in BAL

The RCE mean value of α_1PI in BAL from the normal group was 1.24, significantly lower than the corresponding RCE value in the active sarcoidosis group (2.04) ($p<0.01$) or the hypersensitivity pneumonitis group (1.83) ($p<0.05$). The mean RCE value in the non-active sarcoidosis group (1.08) was not significantly different from the normal value (fig. 3).

In the hypersensitivity pneumonitis group and in the inactive sarcoidosis groups, a significant correlation between α_1PI RCE and α_2M RCE is observed (respectively $r=0.86$ and $r=0.57$, $p<0.05$). In the active sarcoidosis group, there is no significant correlation between the two antiproteases RCE ($r=0.34$). However, in the group of 17 patients with radiographic stage I and II disease, a significant correlation is again demonstrated ($r=0.67$, $p<0.05$). In contrast, no correlation between α_1PI RCE and α_2M RCE is observed in the normal group. No other correlation between protein and cellular data of the BAL was significant in the patient groups.

Follow-up studies

In the group of 12 patients with sarcoidosis, who were lavaged at least twice, eight were considered initially as 'active' and remained untreated. These patients, except one, had initially high α_2M RCE and BAL T_4/T_8 ratios (table III). In subsequent lavages, both α_2M RCE values and BAL T_4/T_8 values remained above the mean range of the corresponding normal values except for one patient who initially suffered stage I disease with erythema nodosum and after eight months was considered free of disease.

Two other patients had initially 'active' disease and high α_2M RCE; their α_2M RCE dropped to the normal range under treatment (fig. 4).

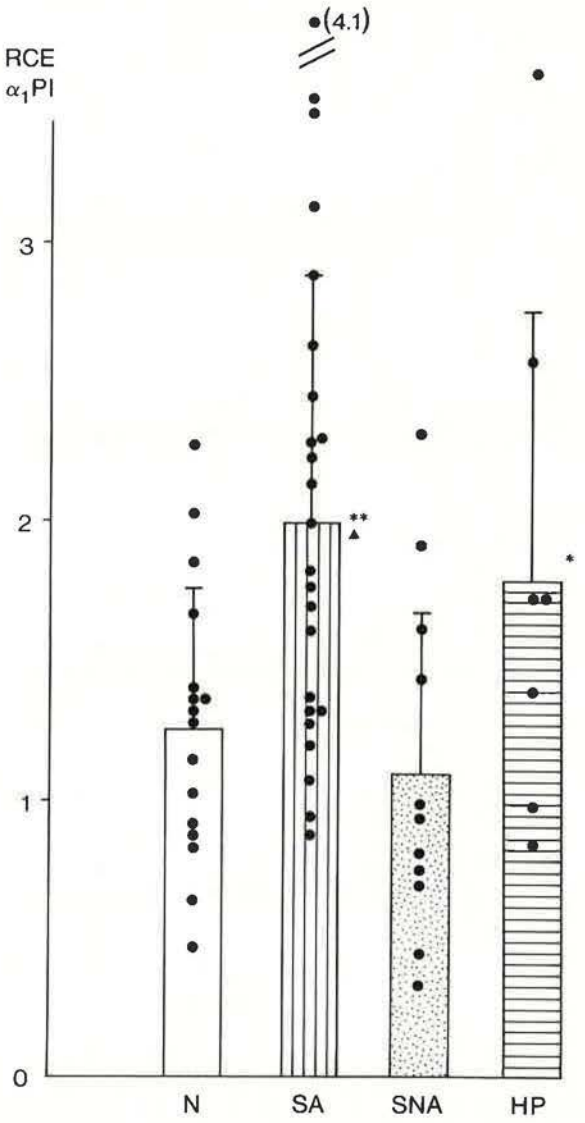

Fig. 3. RCE value of α_1PI in BAL from patients with active sarcoidosis (▥) or with hypersensitivity pneumonitis (▤) is increased when compared to normals (□) or to patients with inactive sarcoidosis (▨). Same symbols (* and ▲) as figure 1.

Finally, two patients were under steroid treatment before being referred to us. Parallel to the progressive withdrawal of the steroids, we observed a gradual

Table 3. - BAL data from sequential lavages in "active" untreated sarcoidosis patients

	Total cell count x10^6 cells/100 ml	Lymphocytes %	T_4/T_8	α_2M RCE
Initial BAL n=8	36.5+	27.4	9.7	0.37
Second BAL after 3-4 months n=8	32.4	28.2	13.8	0.45
Third BAL after 6-9 months n=4	26.3	14.7	10.6	0.32

+ mean values; RCE:relative coefficient of excretion.

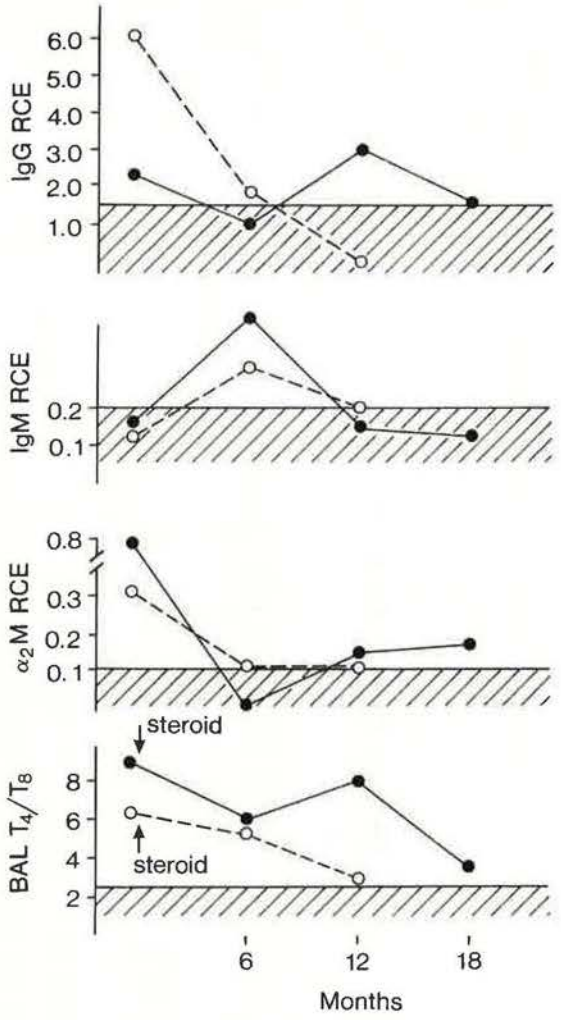

Fig. 4. Cellular (T_4/T_8 ratio) and protein (IgG, IgM and α_2M expressed in RCE) parameters in BAL from two patients with active sarcoidosis at the time of diagnosis (before steroid treatment) and 6, 12 and 18 months after the beginning of corticotherapy (32 mg Methylprednisolone daily). Dashed zones represent normal ranges (mean ± 1 standard deviation).

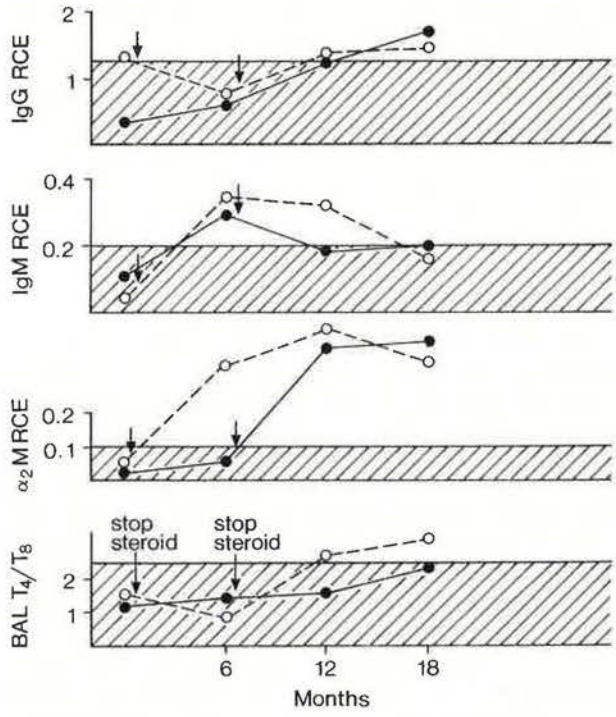

Fig. 5. Cellular (T_4/T_8 ratio) and protein (IgG, IgM and α_2M RCE) parameters in BAL from two patients treated with steroids at the time of diagnosis in which the corticotherapy was discontinued, immediately for (○——○) and 6 months later for (●——●) and these parameters were further followed 6, 12 and 18 months later.

increase of the α_2M RCE value prior to BAL T_4/T_8 changes (fig. 5).

Discussion

Much promise has been expected from the development of the BAL. For example, BAL lymphocytosis or BAL lymphocyte subpopulation studies were proposed as sensitive markers of sarcoidosis alveolitis [6, 8, 10]. Since previous reports suggested that a high lymphocytosis in the BAL reflects a 'high intensity alveolitis', we arbitrarily divided our patients with sarcoidosis into two groups ('active' and 'inactive') using 15% lymphocytes in the total BAL cell population as the discriminating criterion [7]. However, this criterion is not uniformly accepted and more sensitive criteria may be required [18, 19]. The study of lymphocyte subpopulations has been proposed by different groups to better assess the alveolitis in sarcoidosis [10, 20, 21]. As reported by others, we observed in the present study a significant increase of the BAL T_4/T_8 ratio in the active sarcoidosis group, without any significant change in the blood T lymphocyte subpopulations when compared to the normal and non-active sarcoidosis groups [10, 22]. No significant change is noticed in the blood or in the BAL lymphocyte subpopulations from patients with inactive sarcoidosis. Different groups reported an increased proportion of OKT_8 (suppressor) lymphocytes in BAL from hypersensitivity pneumonitis patients [23–25]. We observed that the mean value of the BAL T_4/T_8 in the hypersensitivity group was not significantly different from the normal group. This observation may be related to the delay between the last exposure to the allergen and the lavage procedure as previously reported [26], more than to methodological problems. Patients with active pulmonary sarcoidosis have a higher RCE for α_2M with little overlap with the normal group values. The group of patients with sarcoidosis considered as inactive (based on BAL lymphocytosis) expressed a significantly higher mean value of RCE for α_2M when compared to the normal group. However, ten out of the eleven patients in this group have a RCE for α_2M within the normal range and no symptoms; the α_2M RCE of 0.78 was observed in a patient with 7% lymphocytes in the BAL. However, the patient was symptomatic (fatigue and dyspnoea) and had a dramatic increase in BAL T_4/T_8 ratio of 9.3. This supports further the

concept that the BAL T_4/T_8 ratio provides a more sensitive cellular marker of the alveolitis than the BAL total lymphocytosis.

Although the follow-up studies concerned a limited number of patients over a limited period of time, we observed that patients with active disease kept α_2M RCE values above the normal range when untreated, while the values dropped to the normal range under steroid treatment. Patients with normal α_2M RCE under steroids demonstrated a rise of α_2M RCE back to abnormal values when steroid treatment was discontinued. Furthermore, in these patients, it appears that α_2M RCE changes occur prior to both the BAL lymphocytosis and T_4/T_8 ratio suggesting that α_2M better reflects early changes of the intensity of the alveolitis. As described for α_2M, the levels of the major antiprotease (α_1PI) were significantly increased in BAL from patients with active pulmonary sarcoidosis or hypersensitivity pneumonitis. Moreover, in the hypersensitivity pneumonitis and inactive sarcoidosis groups (but not in normal volunteers) we observed a linear correlation between the concentrations of these antiproteases after correction of the values for their serum concentration and dilution of the BAL. This occurred despite the large difference in their molecular weight (53.000 for α_1PI and 820.000 for α_2M). This correlation was also present in the 17 patients of the active sarcoidosis group with stage I and stage II disease. Whether the remaining 7 patients (stage III) with high α_2M RCE associated with relatively low α_1PI RCE represent a subgroup of patients, or have a different prognosis, remains unknown at this point.

Although our method of immunoassay does not allow us to distinguish between native and complexed antiproteases, or to estimate the antiprotease activity, it still demonstrates a local increase of the two major antiprotease levels in diseases where proteolytic activity is likely to be enhanced.

In conclusion, the measurement of soluble components in BAL in addition to cellular studies may help the clinician in the management of patients with interstitial lung disease. Moreover, three lines of evidence suggest that α_2M may be a better index of the alveolitis than the BAL lymphocytosis or T_4/T_8 ratio: a) the overlap of BAL T_4/T_8 ratios between normals and patients with active sarcoidosis is larger than the overlap of α_2M RCE values; b) in sarcoidosis, the changes of α_2M occur earlier than the changes of BAL T_4/T_8 ratios during the course of the disease; c) the RCE of α_2M is elevated in the acute phase of hypersensitivity pneumonitis while the T_4/T_8 ratios remain normal or decreased. Finally, the correlated increase of the two major antiproteases (α_1PI and α_2M) in BAL from patients with interstitial lung disease may be at least part of the defence mechanism against the potential proteolytic activity responsible for the fibrosis occurring in advanced sarcoidosis or hypersensitivity pneumonitis. However definitive analysis of these data awaits long term studies.

Acknowledgements: The authors wish to thank J.P. Dehennin and C. Desaeger for their excellent technical help, and Drs. Y. Coyette, J.L. Doyen, P. Minette, P. Lemaire and P. Scory who performed some of the bronchoalveolar lavages, Drs. M. Buysschaert, P. Dubois, W. Esselinckx, J. Prignot and J. Steyaert who referred their patients to the study and J.P. Delwiche for statistical help. They also acknowledge the excellent editorial help of M.P. Heylens and the graphical work of C. Deneffe.

References

1. Line BR, Hunninghake GW, Keogh BA, Jones AE, Johnston GS, Crystal RG. – Gallium-67 scanning to stage the alveolitis of sarcoidosis: correlation with clinical studies, pulmonary function studies, and bronchoalveolar lavage. *Am Rev Respir Dis*, 1981, 123, 440–446.
2. Lieberman J, Nosal A, Schlessner LA, Sastre-Foken A. – Serum angiotensin-converting enzyme for diagnosis and therapeutic evaluation of sarcoidosis. *Am Rev Respir Dis*, 1979, 120, 329–335.
3. Reynolds HY, Fulmer JD, Kazmierowski JA, Roberts WC, Frank MM, Crystal RG. – Analysis of cellular and protein content of broncho-alveolar lavage fluid from patients with idiopathic pulmonary fibrosis and chronic hypersensitivity pneumonitis. *J Clin Invest*, 1977, 59, 165–175.
4. Rossi GA, Hunninghake GW, Crystal RG. – Evaluation of inflammatory and immune processes in the interstitial disorders: use of BAL. *In*: Cellular biology of the lung, G. Cumming and G. Bonsignore eds. Plenum Press, New York, 1982, 107–139.
5. Reynolds HY, Newball HH. – Analysis of proteins and respiratory cells from human lungs by bronchial lavage. *J Lab Clin Med*, 1974, 84, 559–573.
6. Daniele RP, Elias JA, Epstein PE, Rossman MD. – Bronchoalveolar lavage: role in the pathogenesis, diagnosis, and management of interstitial lung disease. *Ann Intern Med*, 1985, 102, 93–108.
7. Crystal RG, Roberts WC, Hunninghake GW, Gadek JE, Fulmer JD, Line BR. – Pulmonary sarcoidosis: a disease characterized and perpetuated by activated lung T-lymphocytes. *Ann Intern Med*, 1981, 94, 73–94.
8. Keogh BA, Hunninghake GW, Line BR, Crystal RG. – The alveolitis of pulmonary sarcoidosis. Evaluation of natural history and alveolitis-dependent changes in lung function. *Am Rev Respir Dis*, 1983, 128, 256–265.
9. Hollinger WM, Staton GW, Fajman WA, Gilman MJ, Pine JR, Check IJ. – Prediction of therapeutic response in steroid-treated pulmonary sarcoidosis. Evaluation of clinical parameters, bronchoalveolar lavage, Gallium-67 lung scanning, and serum angiotensin-converting enzyme levels. *Am Rev Respir Dis*, 1985, 132, 65–69.
10. Ceuppens JL, Lacquet LM, Marien G, Demedts M, van den Eeckhout A, Stevens E. – Alveolar T-cell subsets in pulmonary sarcoidosis: correlation with disease activity and effect of steroid treatment. *Am Rev Respir Dis*, 1984, 129, 563–568.
11. Baughman RP, Fernandez M, Bosken CH, Mantil J, Hurtubise P. – Comparison of Gallium-67 scanning, bronchoalveolar lavage, and serum angiotensin-converting enzyme levels in pulmonary sarcoidosis. *Am Rev Respir Dis*, 1984, 129, 676–681.
12. Delacroix DL, Marchandise FX, Francis C, Sibille Y. – Alpha-2-macroglobulin, monomeric and polymeric immunoglobulin A, and immunoglobulin M in bronchoalveolar lavage. *Am Rev Respir Dis*, 1985, 132, 829–835.
13. Merrill WW, Reynolds HY. – Bronchial lavage in inflammatory lung disease. *Clin Chest Med*, 1983, 4, 71–84.
14. Saltini C, Hance AJ, Ferrans VJ, Basset F, Bitterman PB, Crystal RG. – Accurate quantification of cells recovered by bronchoalveolar lavage. *Am Rev Respir Dis*, 1984, 130, 650–658.
15. Reinherz EL, Nadler LM, Rosenthal DS, Moloney WC, Schlossman SF. – T-cell subset characterization of human T-cells. *Blood*, 1979, 53, 1066–1075.
16. Delacroix DL, Vaerman JP. – Influence of the molecular size

of IgA on its immunoassays by various techniques. III. Immunonephelometry. *J Immunol Methods*, 1982, 51, 49–55.
17. Delacroix DL, Hodgson HJF, McPherson A, Dive C, Vaerman JP. – Selective transport of polymeric Immunoglobulin A in bile: quantitative relationships of monomeric and polymeric Immunoglobulin A, Immunoglobulin M on other proteins in serum, bile and saliva. *J Clin Invest*, 1982, 70, 230–241.
18. Chretien J, Venet A, Danel C, Israel-Biet D, Sandron D, Arnoux A. – Bronchoalveolar lavage in sarcoidosis. *Respiration*, 1985, 48, 222–230.
19. Bauer W, Gorny MK, Baumann HR, Morell A. – T-lymphocyte subsets and immunoglobulin concentrations in bronchoalveolar lavage of patients with sarcoidosis and high and low intensity alveolitis. *Am Rev Respir Dis*, 1985, 132, 1060–1065.
20. Lin YH, Haslam PL, Turner-Warwick M. – Chronic pulmonary sarcoidosis: relationship between lung lavage cell counts, chest radiograph, and results of standard lung function tests. *Thorax*, 1985, 40, 501–507.
21. Ginns LC, Goldenheim PD, Burton RC *et al.* – T-lymphocyte subsets in peripheral blood and lung lavage in idiopathic pulmonary fibrosis and sarcoidosis: analysis by monoclonal antibodies and flow cytometry. *Clin Immunol Immunopathol*, 1982, 25, 11–20.
22. Hunninghake GW, Crystal RG. – Pulmonary sarcoidosis. A disorder mediated by excess helper T lymphocyte activity at sites of disease activity. *N Engl J Med*, 1981, 305, 429–434.
23. Leatherman JW, Michael AF, Schwartz BA, Hoidal JR. – Lung T-cells in hypersensitivity pneumonitis. *Ann Intern Med*, 1984, 100, 390–392.
24. Schuyler MR, Thigpen TP, Salvaggio JE. – Local pulmonary immunity in pigeon breeder's disease: a case study. *Ann Intern Med*, 1978, 88, 355–358.
25. Costabel U, Bross KJ, Ruhle KH, Lohr GW, Matthys H. – Ia-like antigens on T-cells and their subpopulations in pulmonary sarcoidosis and in hypersensitivity pneumonitis. Analysis of bronchoalveolar and blood lymphocytes. *Am Rev Respir Dis*, 1985, 131, 337–342.
26. Costabel U, Bross KJ, Marxen J, Matthys H. – T-lymphocytosis in bronchoalveolar lavage fluid of hypersensitivity pneumonitis: changes in profile of T-cell subsets during the course of disease. *Chest*, 1984, 85, 514–518.

RÉSUMÉ: Il s'agit d'une évaluation de différents composants cellulaires et solubles du lavage broncho-alvéolaire de patients atteints d'une maladie interstitielle pulmonaire. Nous observons une augmentation du rapport des lymphocytes T_4/T_8 dans le lavage broncho-alvéolaire, et non dans le sang, chez 24 patients atteints d'une sarcoïdose pulmonaire active, par comparaison avec 16 individus normaux, et avec 11 patients avec une sarcoïdose pulmonaire inactive. Sept patients atteints de pneumopathie d'hypersensibilité, ont un rapport T_4/T_8 normal. Dans la sarcoïdose active et dans le groupe de pneumopathie d'hypersensibilité, l'alpha 1 anti protéase (alpha 1 PI) du lavage broncho-alvéolaire est significativement plus marquée que dans le groupe normal, et l'on observe une corrélation significative entre les deux anti-protéases (alpha 2-macroglobuline et alpha 1 PI). Ces données démontrent que les niveaux d'anti-protéases (alpha 1 PI et alpha 2 M) sont augmentés dans le tractus respiratoire inférieur des patients avec maladie pulmonaire interstitielle et que, parmi les composants cellulaires et solubles du lavage broncho-alvéolaire, l'alpha 2-macroglobuline est un marqueur sensible de l'alvéolite.