

Bronchoalveolar lavage phospholipid abnormalities in HIV-infected patients

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Bronchoalveolar lavage phospholipid abnormalities in HIV-infected patients. R. Escamilla, M-C. Prevost, C. Cariven, C. Hermant, M. Krempf, H. Chap. ©ERS Journals Ltd 1993.

ABSTRACT: Our aim was to evaluate the quality of pulmonary surfactant, a non-specific defence system, during the course of human immunodeficiency virus infection.

Protein and phospholipid composition were determined in 127 bronchoalveolar lavage (BAL) fluids from 89 HIV seropositive patients (54 acquired immune deficiency syndrome (AIDS), 35 non-AIDS) and 11 healthy controls.

In all of the HIV BAL samples, biochemical abnormalities were found. In subjects with pulmonary infection or Kaposi's sarcoma, the phospholipid/protein ratio was decreased, mainly because of elevated protein levels (15.8 and 20, respectively, vs 7.2 mg-100 ml⁻¹ for controls, $p < 0.05$). In subjects without obvious pulmonary involvement, phospholipid was decreased (1.3 ± 0.2 vs 2.9 ± 0.3 mg-100 ml⁻¹ for controls, $p < 0.001$), whereas the protein was not altered. Phospholipid composition was also altered: the phosphatidylcholine percentage was decreased, whilst the other main phospholipids were increased.

We conclude that the alveolar lining is altered, whatever the stage of HIV disease. In most patients, it results from an increase of vascular permeability, with an influx of serum proteins. However, changes in phospholipid composition suggest that, in some cases, surfactant is also altered.

Eur Respir J., 1993, 6, 1301-1307.

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Keywords: Bronchoalveolar lavage
human immunodeficiency virus
phospholipids
proteins

Received: November 10 1992
Accepted after revision May 5 1993

This work is supported, in part, by a grant No.90 MR11 from the Comité National contre les Maladies Respiratoires et la Tuberculose.

Bronchopulmonary involvement occurs frequently during the course of human immunodeficiency virus (HIV) infection [1, 2]: opportunistic infections, malignancies and lymphocytic alveolitis are usually described. If immunosuppression represents the main mechanism leading to pulmonary involvement, other possible factors, such as changes in alveolar environment and, in particular, in pulmonary surfactant may be implicated. Pulmonary surfactant, a phospholipid and protein complex, has been shown to have a non-specific anti-bacterial effect [3], and an immunosuppressive effect on T-lymphocytes [4]. Therefore, alveolar lining changes could predispose to pulmonary infection, and to a partial lack of the regulation of mitogenic lymphocyte response to nonspecific stimuli. In HIV seropositive patients, common pathogen infections and T-lymphocytic alveolitis are frequently observed before profound immunodepression, thus, it was of interest to determine the surfactant quality. Recently, PHELPS and ROSE [5] demonstrated an increase of a specific surfactant protein, SP-A, in acquired immunodeficiency syndrome (AIDS)-related pneumonia, but surfactant phospholipid composition was not studied.

Consequently, we analysed protein and phospholipid content of bronchoalveolar lavage (BAL) fluids in HIV-infected patients, with or without obvious infection or

tumoral pulmonary involvement, and compared the results with those obtained in healthy controls.

Methods

Subjects

Eighty nine HIV-1 seropositive patients, 69 men and 20 women (63 smokers and 36 nonsmokers), were evaluated. Among these, 55 were intravenous drug abusers (IVDA), 26 were homosexual men, 5 were transfusion recipients, and 3 were partners of known HIV-infected subjects. According to the Center for Disease Control Classification [6], 54 were AIDS (CD4 cells: $0.109 \pm 0.0165 \times 10^9 \cdot l^{-1}$) and 35 non-AIDS (CD4 cells: $0.492 \pm 0.064 \times 10^9 \cdot l^{-1}$). At the time of the study, 31 were being treated with zidovudine, and 26 were receiving prophylactic treatment for *Pneumocystis carinii* pneumonia (PCP) by aerosolized pentamidine. Sixty three subjects underwent one BAL, and iterative BALs were performed on 26 patients (2 BAL for 16, 3 BAL for 8, and 4 BAL for 2).

The control group consisted of 11 medical students (5 smokers and 6 nonsmokers), with no respiratory disease and with normal chest X-ray and pulmonary function tests.

Characteristics of patients and controls are reported in table 1.

Table 1. — Clinical details of HIV-infected patients and control subjects

	HIV-infected patients				
	Controls n=11	IVDA n=55	Homosexuals n=26	Heterosexuals n=3	Transfusion recipients n=5
Age yrs	24±0.8	30±0.7	37±1.7	46±8	49±7.7
Sex ratio F/M	4/7	18/37	0/26	1/2	1/4
Smokers	5	51	10	1	1
Packs-yr ⁻¹	1.4±0.14	19.4±1.7	8±2.8	5	5
AIDS		26	23	1	4
Non-AIDS		29	3	2	1
Zidovudine		21	9		1
Pentamidine		16	9		1
Methylprednisone		1	1		3
Bleomycin		1	4		

IVDA: intravenous drugs abusers; HIV: human immunodeficiency virus; AIDS: acquired immune deficiency syndrome.

Table 2. — Clinical diagnosis and BAL findings in 127 BAL from 89 HIV-infected patients

Diagnosis	BAL n
Non infection or tumour	36
Pulmonary infection	84
Opportunistic	56
<i>Pneumocystis carinii</i>	42
Cytomegalovirus	7
<i>Cryptococcus neoformans</i>	5
<i>Candida albicans</i>	1
<i>Aspergillus fumigatus</i>	1
Bacterial*	13
<i>Streptococcus pneumoniae</i>	7
<i>Staphylococcus aureus</i>	1
Gram-negative bacilli	5
Mycobacteria	15
Tuberculosis	10
Atypical	5
Kaposi's sarcoma	7
With pulmonary involvement	5
Without pulmonary involvement	2

*: bacterial infection was assessed for 10³ cfu·ml⁻¹ on brush. BAL: bronchoalveolar lavage; HIV: human immunodeficiency virus.

BAL specimen study group

From January 1988 to September 1990, 127 BAL samples were analysed: and divided into three groups, according to diagnosis at the time of lavage (table 2).

BAL samples from patients without obvious pulmonary infection or tumour (n=36). BAL was performed to discard an opportunistic infection either because of persistent cough and/or minor radiological abnormalities.

BAL samples from patients with progressive bronchopulmonary infection (n=84). All patients had fever, respiratory symptoms and/or abnormal chest X-rays. An opportunistic infection was found in 56 patients. Among these, 35 presented diffuse interstitial pneumonitis with hypoxaemia (arterial oxygen tension (Pao₂) 59.5±13 mmHg (7.9±1.7 kPa)). Thirteen subjects presented a bronchial and/or segmental or lobar pulmonary infection due to common pathogens, and in 15 cases, *Mycobacterium tuberculosis* or atypical *Mycobacteria* were the source of infection.

BAL samples from patients with Kaposi's sarcoma (KS) (n=7). All patients presented a cutaneous KS previously treated with bleomycin in four cases. Parenchymal opacities were present in all patients, and trancheobronchial involvement was revealed by means of bronchoscopy in five.

Clinical status assessment among patients with iterative BAL

Among the 26 patients who underwent iterative BAL, we compared the clinical status course at the time of each BAL. When pulmonary infection was present on the first BAL, improvement or recovery was considered on the following criteria: temperature resolution, respiratory symptom relief, chest roentgenogram resolution, negative result for both systemic and pulmonary microbiological investigations. Biochemical analyses were used to investigate the permeability of the alveolar-capillary barrier by protein level and the phospholipid/protein ratio. At the time of initial BAL, 20 subjects had pulmonary infection; and at the time of last BAL, an improvement was observed in 13 cases. In seven cases, including five pneumocystosis and two tuberculosis, infection was still present; secondary improvement was obtained in all cases after continuation, or adequate change, of initial therapy. Six subjects showed no obvious pulmonary involvement on the first BAL; a pulmonary infection was found in the second BAL in two of these cases.

Bronchoalveolar lavage

An informed oral consent for lavage procedure was obtained from all patients. The bronchoalveolar lavage was performed as described previously [7]. One hundred and fifty to 250 ml of 0.9 % saline solution was instilled in 50 ml aliquots. Total number of cells was determined by haemocytometer. Differential cell counts were performed on Giemsa's stained cytocentrifuged preparation and results were expressed as the percentage of total cells. We routinely performed the same microbiological studies on all patients, including direct examination of touch imprints (Giemsa, Gram-Weigert, Ziehl-Nielsen and modified Grocott stains), culture for bacteria, mycobacteria, fungi and viruses,

immunofluorescence assays for virus (cytomegalovirus, herpes viruses, adenovirus) and *Pneumocystis carinii*. For *Legionella* and *Cryptococcus neoformans* antibody estimation was performed. Bacterial infection was assessed for 10^3 cfu·ml⁻¹ on brush.

Biochemical studies

After cytological studies, the supernatant was submitted to a second centrifugation ($1,000 \times g$ for 10 min) in order to eliminate all cells and cell fragments; this supernatant was then stored at -20°C until it could be studied. Total proteins were quantified by the sodium dodecyl sulphate (SDS) method of LOWRY *et al.* [8], and expressed in mg·100 ml⁻¹ of BAL fluid. Total phospholipids were extracted according to the method of BLIGH and DYER [9], and quantified by the method of BÖTTCHER *et al.* [10], after mineralization with 0.3 ml of perchloric acid at 200°C , and expressed as mg of phospholipids·100 ml⁻¹ of BAL fluid. Total phospholipids were separated with bidimensional thin layer chromatography (TLC) on high performance TLC (HPTLC) Merk's plates ($0.2 \times 10 \times 10$ cm). In the first dimension, the solvent system was $\text{CHCl}_3/\text{CH}_3\text{OH}/\text{CH}_3\text{COOH}$ (65/25/10, v/v/v); and in the second dimension, the solvent system was $\text{CHCl}_3/\text{CH}_3\text{OH}/\text{HCOOH}$ (65/25/10, v/v/v). This allowed us to separate the main phospholipids which were identified by co-migration with commercial standards. All the spots on the plate were visualized in iodine vapour and through the use of Zinzadze reagent [11], which is specific for phosphate. The spots were scraped off and measured for phosphorus by the method of BÖTTCHER *et al.* [10]. Results were expressed either in $\mu\text{g}\cdot 10\text{ ml}^{-1}$ of BAL fluid, or as percentage of total phospholipids. Phospholipid composition could only be studied in 55 HIV+ subjects, because of too little phospholipid for quantification by our technique, or because of a non-workable migration.

Pulmonary function studies

In order to determine the relationship between biochemical abnormalities and pulmonary functions, 19 patients without obvious pulmonary involvement were submitted to pulmonary function tests including spirometric study, flow volume curves, and steady-state carbon monoxide diffusing capacity (DLCO). Results were expressed as percentage of normal values [12].

Statistical analysis

The data are reported as mean value \pm SEM. Differences between groups were tested by using the non-parametric Kruskal-Wallis one-way analysis of variance (ANOVA). When significant, this global test was followed by a non-parametric Mann-Whitney U-test to compare couples of groups. The Wilcoxon matched-pair test was used to compare results in subjects with iterative BAL. For correlation study, protein and phospholipid levels and leucocyte counts were logarithmically transformed, because of their skewed distributions. The relationship between biochemical parameters and other variables were then evaluated by linear regression analysis, except that involving DLCO, in which

Spearman rank correlations were used [13]. A p value <0.05 was considered significant. All statistical tests and parameter estimates were computed using the statistical package StatView II (Abacus Concepts).

Results

Lavage fluid recovered was significantly lower in all HIV+ patient groups (table 3).

Cellular characteristics of BAL

Compared to controls, BAL fluids in patients without obvious pulmonary involvement were similar, except for a small but significant neutrophil increase. In 12 cases, a lymphocytic alveolitis was present (mean lymphocyte % $31.5 \pm 3.5\%$). Patients with pulmonary infection or Kaposi's sarcoma presented an increase of total cell number, with enhanced lymphocyte and neutrophil percentage. As expected, neutrophil percentage was significantly higher when a bacterial infection was present (mean neutrophil % $29.8 \pm 8.3\%$; $p < 0.005$ vs controls).

Biochemical characteristics of BAL

As shown in table 3, HIV+ subjects exhibited a significant decrease of phospholipid/protein ratio. This ratio, independent of BAL dilution, allows the evaluation of both inflammation and permeability of alveolar-capillary barrier by protein increase, and alteration of surfactant by phospholipid decrease.

In patients without obvious tumour or infection, phospholipids decreased without any protein modification. No difference was observed when lymphocytic alveolitis was present, except for a nonsignificant increase of protein levels (11.8 ± 2.6 vs 7.2 ± 1.1 mg·100 ml⁻¹ in patients without lymphocytic alveolitis). Moreover, we did not observe significant differences between smokers and nonsmokers (fig. 1).

In patients with infection or tumoral involvement, elevated protein levels represented the main factor in phospholipid/protein ratio decrease. Phospholipids were also diminished except in the group with Kaposi's sarcoma. When an infectious process was present, we did not find particular biochemical abnormalities related to the various agents involved (data not shown). Compared to controls, HIV+ subjects showed a different BAL phospholipid composition. When expressed as total mg recovered from 10 ml of BAL (table 3), the amounts of phosphatidylcholine (PC) were significantly decreased in all groups, with a drop of the phosphatidylcholine/sphingomyelin ratio to 8.1 ± 0.7 vs 37.1 ± 3.8 for controls ($p < 0.001$); lysophosphatidylcholine and sphingomyelin were increased in BAL samples with bacterial infection (12.6 ± 1.9 mg·10 ml⁻¹, $p < 0.01$ vs controls) and in KS patients. Phosphatidylethanolamine and phosphatidylglycerol amounts were decreased.

The emergence of less polar compounds, the characterization of which is still in progress, was one of the main factors contributing to the change of phospholipid composition. Such

Table 3. - Cellular, protein and phospholipid content of BAL in HIV+ patients according to the diagnosis at the time of BAL

	Controls	HIV+ without pulmonary involvement	HIV+ with pulmonary infection	HIV+ with Kaposi's sarcoma
BAL n	11	36	84	7
Recovery ml	115±7	100±6*	84.5±3.8*	85.3±13.5*
Recovery %	75±2.2	55±2*	53±1.3*	56±3.8
Leucocytes 10 ³ .ml ⁻¹	182±54	444±95	615±86	494±74
Macrophages %	89±2.1	80±2.3*	69±2.3*	60±9.9*
Lymphocytes %	10±2	16±2.2	19±1.9	28±10*
Neutrophils %	1.4±0.2	3.2±0.4*	11±1.9	9.8±3.1
PR mg·100 ml ⁻¹	7.2±0.7	9±1.2	15.8±1.3*†	20±5.2*†
PL mg·100 ml ⁻¹	2.9±0.3	1.3±0.2*	1.3±0.1*	2.7±0.6†
PL/PR ratio	0.44±0.06	0.22±0.03*	0.11±0.01*†	0.17±0.05*
PL µg·10 ml ⁻¹	n=11	n=21	n=31	n=3
Lyso PC	4.5±0.5	6.6±0.8	8.4±1.1	17.3±9.3*†
Sph	5.2±0.5	7.1±1	9.3±1.2	11±7
PC	192.2±23.7	56.4±8.2*	66.3±11.8*	77.3±54*
PI+PS	21±4.8	13.8±2.4	17.6±2.1	16±3.2
PE+PG	37.8±4.9	19.1±2*	22.4±3.4*	27.3±17
PA+CL	4.1±2.2	4.9±0.8	5.4±0.8	6.7±3.4
lpPL	6.7±1.5	17.9±3.6*	19.2±1.8*	18±4.5

Data are shown as mean±SEM. Differences between groups were evaluated by using Mann Whitney U-test. (*: p<0.05 compared to the control group; †: p<0.05 compared to the HIV+ without pulmonary involvement group; ‡: p<0.05 compared to the HIV+ with pulmonary infection group. PR: proteins; PL: phospholipids; Lyso PC: lysophosphatidylcholine; Sph: sphingomyelin; PC: phosphatidylcholine; PI: phosphatidylinositol; PS: phosphatidylserine; PE: phosphatidylethanolamine; PG: phosphatidylglycerol; PA: phosphatidic acid; CL: cardiolipids; lpPL: less polar phospholipids. For further abbreviations see legend to table 2.

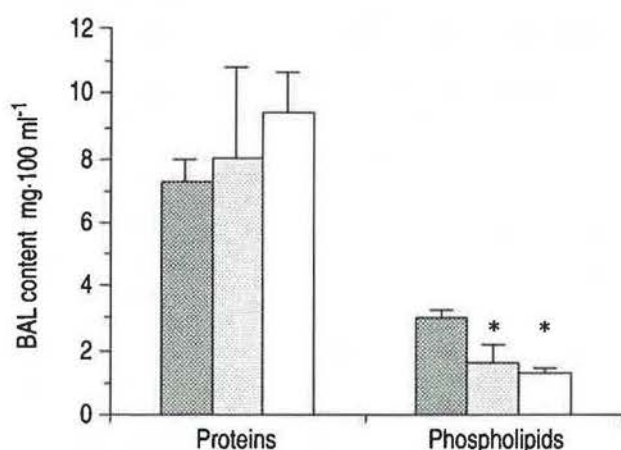


Fig. 1. - BAL protein and phospholipid contents in HIV+ patients, without obvious infectious or tumoral involvement, with regard to tobacco smoking. Phospholipids are significantly decreased in HIV+ patients vs controls. No difference was found between smokers (S HIV+; n=26 BAL samples) and nonsmokers (NS HIV+; n=10 BAL samples). *: p<0.05 vs controls (Mann Whitney U-test). ▨: controls; ▩: NS HIV+; □: S HIV+. BAL: bronchoalveolar lavage; HIV: human immunodeficiency virus.

compounds represented less than 3% of the total phospholipids in controls, but in HIV+ patients they reached more than 20%. If these compounds are not considered, phospholipid composition, expressed as percentage of total main phospholipids, remained strongly altered (table 4). All HIV+ BAL specimens showed a significantly lower percentage of phosphatidylcholine than the control group, and consequently, a relative increase of the other main phospholipids was observed.

Relationship between biochemical and cytological composition of BAL

Alveolar protein levels correlated with the number of leucocytes in BAL (fig. 2). This might simply reflect the increase of vascular permeability with serum protein influx into alveoli during infectious or lymphocytic alveolitis.

Relationship between BAL biochemical composition, clinical findings and the outcome of patients

We were unable to find a correlation between biochemical abnormalities of BAL fluids and tobacco smoking, or

Table 4. - Percentage distribution of phospholipids in BAL from HIV-infected patients and control subject

Phospholipids	Controls	HIV+ without infection or tumour	HIV+ with infection	Kaposi's sarcoma
%	n=11	n=21	n=31	n=3
LypsoPC	1.8±0.2	6.7±0.5*	7.5±0.7*	12.5±1.5*†
Sph	2±0.2	6.8±0.5*	8±0.8*	6.8±1.8
PC	73.3±1	50.3±2.3*	47.6±1.8*	42.3±7.8*
PI+PS	7.33±0.9	12.7±1.1	14.6±1.1*	17.2±7.2
PE+PG	14.3±5.4	18.3±0.9	17.2±1.1	16.7±2.6
PA+CL	1.2±0.6	5.2±0.8	5.2±0.7	4.4±0.2

Data are shown as mean±SEM. Percentages are calculated, excluding lpPL, and expressed as mass of each PL × 100/total PL. Differences between groups were evaluated by using Mann Whitney U-test. *: p<0.05 compared to control group; †: p<0.05 compared to others HIV+ groups. For definition of abbreviations see legends to tables 2 and 3.

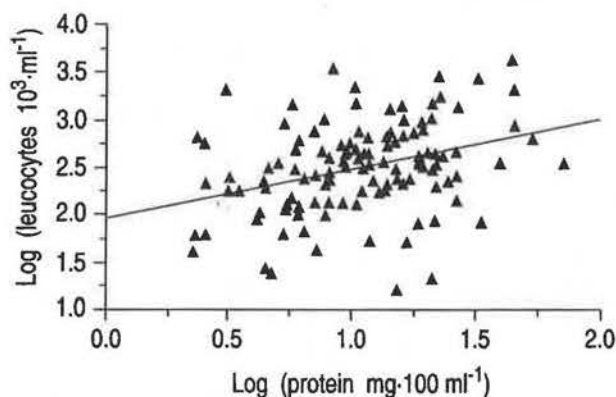


Fig. 2. - Relationship between alveolar protein amount and leucocyte number in BAL. Because of non-normal distribution, proteins and leucocytes were logarithmically transformed and expressed as log (protein mg·100 ml⁻¹) and log (leucocytes 10³·ml⁻¹). BAL protein content correlation significantly with leucocyte number (linear regression r=0.36; p<0.001). BAL: bronchoalveolar lavage.

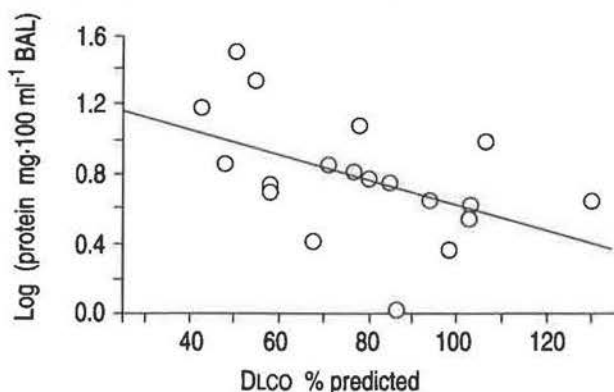


Fig. 3. - Relationship between BAL protein content and DLCO among 19 HIV-infected patients, without obvious infectious or tumoral pulmonary involvement. Protein levels were logarithmically transformed and expressed as log (proteins mg·100 ml⁻¹ of BAL); DLCO is expressed in percentage of normal predicted values. A significant inverse correlation was found between BAL protein content and DLCO. (Spearman r=-0.569; p=0.028).

belonging to a specific risk group, or with the clinical and microbiological findings. Similarly, we did not observe any distinct biochemical characteristics in patients previously treated with prophylactic aerosolized pentamidine, or with bleomycin. In subjects without infectious or tumoral involvement submitted to pulmonary function tests (data not shown), an inverse correlation was demonstrated between alveolar protein level and DLCO (fig. 3). Among patients with pulmonary infection, although biochemical abnormalities, by themselves, did not have a predictive prognostic significance, iterative BAL showed that the phospholipid/protein ratio and the clinical status had a similar course: so a significant correlation was found between phospholipid/protein increase and the recovery of pulmonary involvement. When infection was present, the phospholipid/protein value was 0.07±0.005 and it increased to 0.14±0.02 with recovery (p=0.007). Compared to non-infected patients, the phospholipid/protein ratio remained lower even with recovery, but phospholipid composition was not different.

Discussion

The aim of this report was to evaluate the quality of pulmonary surfactant during HIV infection, by analysis of phospholipid composition of BAL fluids. We hypothesized that, in addition to the immunodeficiency, nonimmunological factors, such as alveolar lining changes, could take part in the various pathological processes occurring in HIV+ patients. We found quantitative and qualitative changes in phospholipid contents of BAL from patients with infection or KS, but the major finding was that these abnormalities were also observed in patients without obvious pulmonary involvement. In BAL fluids from patients with pulmonary infection or KS, phospholipid amounts were low but the main finding was an elevated protein content, which correlated with the number of leucocytes. Elevated protein content in BAL fluid from patients with pneumonia and other respiratory problems is widely thought

to result from serum protein influx, due to an increase in vascular permeability [14]. We supposed, that such a mechanism could be involved in the alveolar lining changes that we found. The transudation of serum proteins may lead to a possible disruption of normal surfactant function, as suggested previously [15]. Thus, in infectious processes, including acute bacterial pneumoniae and respiratory distress syndrome, surfactant alteration has been reported [16]. The causative mechanism could require alveolar macrophages and polymorphonuclear neutrophils (PMN) that may release mediators with bactericidal activity, such as free radicals, some of which have been claimed to be responsible for alveolar barrier alteration [17]. In PCP, alteration to the pulmonary epithelium has been demonstrated experimentally in rats [18], and has more recently in HIV+ subjects by increased 99m-Tc diethylenetriamine penta acetate (DTPA) clearance [19]. In a previous work, we have shown that such surfactant abnormalities could play a role in the saprophyte-pathogen transformation of *Pneumocystis carinii* [20]. Among patients with KS, pulmonary epithelial damage may also be relevant to a specific toxicity of cytostatic drugs [21], such as bleomycin, usually prescribed in this infection, but we were unable to evaluate this parameter because of the small size of the group studied.

In patients without pulmonary infection or tumours, an immunological disorder with lymphocytic alveolitis is commonly observed [22]. In this instance, pulmonary epithelial alteration has also been reported. A study using labelled DTPA clearance showed that pulmonary epithelial permeability was enhanced in patients with only T8 cytotoxic lymphocytic alveolitis [23]. More recently, it was demonstrated that alveolar macrophages could constitutively synthesize and release tumour necrosis factor- α (TNF- α) which increases pulmonary vascular permeability [24]. In our report, two additional factors, *i.e.* tobacco smoking and drug addiction, must be considered. Tobacco smoking may itself lead to a reversible alteration of pulmonary epithelial permeability [25]. Moreover, pulmonary oedema, by means of a specific effect of cocaine and/or opiates, is commonly reported among drug addicts [26, 27], but chronic adverse effects of drugs on the alveolar-capillary barrier remain to be evaluated.

As a whole, the alveolar lining changes encountered during either current pulmonary infection or immunological disorder could be explained by enhanced vascular permeability. However, in HIV+ patients without tumoral or infectious involvement, we observed a fall of phospholipid amounts, whilst protein level remained unchanged. This decrease of phospholipids recovered by BAL could be explained by a lower recovery of instilled fluid into the alveoli [16]. Nevertheless, some factors allowed us to suppose that the surfactant itself was altered. Firstly, phospholipid composition was markedly modified: we observed phosphatidylcholine decrease with increased lysophosphatidylcholine as described in several pulmonary pathological processes with surfactant involvement [16, 28]. Elevated lysophosphatidylcholine amounts might be also relevant to change of phospholipase A2 activity, previously reported in experimental *Pneumocystis carinii* pneumonia [29], or due to bacterial infections. We could not exclude the possibility that some of our patients had subclinical infection. On

the other hand, we were surprised by the presence of less polar compounds representing about 20% out of total BAL phospholipids. The precise nature of these compounds remains unknown; investigations are still in progress, but preliminary results (data not shown) lead us to presume that they are hydrophobic proteins, which may bind to phospholipids [30]. The source of these proteins may be either plasmatic or cell membrane contamination, or abnormal surfactant metabolism. PHELPS and ROSE [5] recently demonstrated an increase of SP-A, a specific surfactant protein, in AIDS-related pneumonia, but surfactant hydrophobic proteins were not studied. Thus, the correlation between phospholipid abnormalities and abnormal surfactant metabolism remains hypothetical.

During HIV infection the quality of pulmonary surfactant seems to be altered, whatever the stage of the disease and the clinical status of the patients. This change of the alveolar lining might, in part explain some of the events observed in the course of HIV infection. Firstly, whilst surfactant enhances alveolar macrophage phagocytosis of common pathogens, such as *Staphylococcus aureus* [3], its alteration might favour bacterial bronchopulmonary infections, which are frequently encountered among HIV+ patients, even before a severe immunodeficiency state [31]. Second, the DLCO decrease often observed in seropositive subjects without overt pneumonitis [32] may be related to alveolar-capillary barrier damage, with the presence of an elevated protein level in the alveoli. In our patients with pulmonary infection, the phospholipid/protein ratio had a similar course to pulmonary improvement, and might be considered as an additional recovery index, although the intensity of initial biochemical alterations did not have a predictive significance.

We conclude that surfactant quality is altered early in HIV+ patients with or without obvious pulmonary involvement. This change of the alveolar lining is mainly due to an increase of vascular permeability during immunological or infectious processes. However, this abnormality is not constantly found, and the precise pathophysiological mechanisms of surfactant alteration remain to be determined. From a clinical point of view, the consequences of the alveolar lining changes are still hypothetical, but the alteration of the surfactant quality may lead to macrophage dysfunction, and favour the occurrence of bacterial infections.

Acknowledgements: The authors wish to thank J.P. Charlet and J.B. Ruidavets for their expert statistical assistance.

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