13 Chan YH, Wong KM, Lee KC, *et al.* Pneumonia and mesenteric lymphadenopathy caused by disseminated *Penicillium marneffei* infection in a cadaveric renal transplant recipient. *Transpl Infect Dis* 2004; 6: 28–32.
14 Wu TC, Chan JW, Ng CK, *et al.* Clinical presentations and outcomes of *Penicillium marneffei* infections: a series from 1994 to 2004. *Hong Kong Med J* 2008; 14: 103–109.
15 Sripa C, Mitchai J, Thongsri W, *et al.* Diagnostic cytology and morphometry of *Penicillium marneffei* in the sputum of a hypogammaglobulinemia with hyper-IgM patient. *J Med Assoc Thai* 2010; 93: Suppl. 3, S69–S72.
16 Lin JN, Lin HH, Lai CH, *et al.* Renal transplant recipient infected with *Penicillium marneffei*. *Lancet Infect Dis* 2010; 10: 138.
17 Luo DQ, Chen MC, Liu JH, *et al.* Disseminated *Penicillium marneffei* infection in an SLE patient: a case report and literature review. *Mycopathologia* 2011; 171: 191–196.

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Surfactant protein A in chronic extrinsic allergic alveolitis

To the Editors:

The chronic form of extrinsic allergic alveolitis (EAA) may have some common features with idiopathic pulmonary fibrosis (IPF). The clinical, radiological and histopathological presentation of both diseases may be similar. Surfactant protein (SP)-A can be detected in serum of patients with IPF and concentrations of SP-A were found to be elevated in these patients [1]. The aim of the present study was to compare serum SP-A concentrations in IPF and chronic EAA patients and detect possible relationships between SP-A levels, bronchoalveolar lavage (BAL) fluid differential cell counts, high-resolution computed tomography (HRCT) patterns and pulmonary function tests in both diseases.

13 patients with chronic EAA and seven patients with IPF were enrolled in the retrospective study after informed consent was obtained. The mean$\pm$SD age of IPF patients was 63.7$\pm$12.4 yrs and the mean$\pm$SD age of the EAA group 60.3$\pm$11.3 yrs. Only one IPF patient was a smoker, all others were nonsmokers.

All of the enrolled subjects underwent a diagnostic programme including history assessment, physical examination, pulmonary function tests, blood tests including evaluation of SP-A serum concentrations, HRCT of the chest, bronchoscopy with BAL and transbronchial biopsy. HRCT alveolar and interstitial scores were assessed according to the criteria of GAY *et al*. [2] by a pneumologist experienced in radiology.

Patients with IPF who fulfilled diagnostic criteria presented in the official American Thoracic Society/European Respiratory Society/Japanese Respiratory Society/Latin American Thoracic Association statement were included [3]. There are no widely accepted diagnostic criteria for chronic EAA, so data obtained by aforementioned procedures have to be evaluated with care.

Serum samples were collected in the same month as pulmonary function tests and HRCT of the chest were performed. Serum SP-A concentrations were measured according to manufacturer's instructions (Human Surfactant Protein A ELISA; BioVendor, Brno, Czech Republic).

Results are expressed as mean$\pm$SD. Differences between two variables were assessed with the Mann–Whitney U-test. p-values <0.05 were regarded as significant. Spearman's correlation was used to analyse correlations between pulmonary functions, HRCT scores and SP-A serum concentrations.

Pulmonary function tests, HRCT scores, BAL fluid samples and SP-A serum concentrations are summarised in table 1.

We found negative correlation between forced vital capacity (FVC) and SP-A serum concentrations in IPF patients ($p<0.01$). The chronic EAA group exhibited negative correlation between FVC ($p<0.05$), diffusing capacity of the lung for carbon monoxide ($D_{L,CO}$) ($p<0.01$) and BAL fluid eosinophils, and positive correlation between HRCT interstitial score and BAL fluid eosinophils ($p<0.01$).

While the radiological pattern of IPF should not contain extensive areas of ground-glass opacities, these might be present in chronic EAA patients and usually represent potentially reversible alveolitis indicating continuous exposure to inhalation antigen. TILLIE-LEBLOND *et al*. [4] presented, in their recent study, patients with chronic progressive EAA presenting with ground-glass opacities on HRCT scans. In accordance with IPF radiological definition, we found significantly lower HRCT alveolar score in the IPF group than in chronic EAA patients ($p<0.01$). Interstitial score did not differ between both groups, giving evidence for similar extent of fibrotic changes.

Despite the fact that chronic EAA patients showed more advanced deterioration on HRCT, they had significantly higher $D_{L,CO}$ than IPF patients ($p<0.01$). $D_{L,CO}$ is also influenced by alveolar volume, which is known to be reduced in IPF patients. We found no difference in $D_{L,CO}$ when adjusted for alveolar volume between both groups.

In EAA histology specimens, staining for SP-A was positive in the cytoplasm of all regenerating alveolar epithelial cells, in Clara cells and in elastic fibres in vascular walls. Areas of impaired pulmonary structure showed SP-A positivity in

TABLE 1 Pulmonary function tests, high-resolution computed tomography (HRCT) scores, bronchoalveolar lavage results and surfactant protein (SP)-A concentrations in patients with idiopathic pulmonary fibrosis (IPF) and extrinsic allergic alveolitis (EAA)

	IPF	EAA	p-value
FVC % pred	66.5±14.1	69.3±15.8	0.75
FEV_1 % pred	72.0±18.4	74.1±14.6	0.62
TLC % pred	59.8±5.2	68.1±20.0	0.69
$D_{L,CO}$ % pred	29.7±9.0	43.5±18.3	0.02*
K_{CO} % pred	60.6±19.1	70.9±18.5	0.19
HRCT alveolar score	0.6±0.7	2.1±1.0	0.003**
HRCT interstitial score	2.8±0.5	2.4±1.1	0.5
Alveolar macrophages %	68.9±13.0	67.7±24.1	0.6
Polymorphonuclear cells %	16.6±12.3	8.8±4.7	0.2
Lymphocytes %	3.4±1.2	16.5±17.8	0.4
Eosinophils %	11.1±3.7	5.8±7.2	0.1
SP-A ng·mL^{-1}	9.3±2.4	8.3±3.0	0.3

Data are presented as mean±SD, unless otherwise stated. FVC: forced vital capacity; % pred: % predicted; FEV_1: forced expiratory volume in 1 s; TLC: total lung capacity; $D_{L,CO}$: diffusing capacity of the lung for carbon monoxide; K_{CO}: $D_{L,CO}$ adjusted for alveolar volume. *: $p<0.05$; **: $p<0.01$.

endothelial cells of lymph vessels as well as their contents [5]. We detected no significant difference between serum SP-A levels in chronic EAA and IPF patients which, together with similar HRCT interstitial involvement, may suggest similar alveolar epithelial cell behaviour in both diseases. It is possible that, in chronic EAA, derivation of SP-A from hyperplastic alveolar epithelial cells into the serum by lymphatic vessels may contribute to serum SP-A presence. MAZUR *et al*. [6] recently found that plasma SP-A levels are associated with age and smoking history. SP-A is expressed mostly in alveolar epithelium in nonsmokers, while in smokers the locations differ and SP-A is expressed in bronchial epithelium as well. As both the IPF and EAA groups did not significantly differ in age and only one enrolled patient was a current smoker, these factors do not interfere with the present study.

No correlations among serum SP-A concentrations, pulmonary function tests and HRCT patterns were found. It could be simply explained by the fact that fibrosis and inflammation do not reflect only the activation status of alveolar epithelial cells. Moreover, immunohistochemical studies found that the number of alveolar epithelial cells expressing SP-A varies, ranging from cases in which almost all cells expressed SP-A to cases in which expression was scarce. Because SP-A serum levels and either pulmonary function tests or degree of HRCT score reflect distinct aspects of the fibroproliferative process, the observed values should not inevitably show a correlation.

ISRAËL-ASSAYAG and CORMIER [7] demonstrated that SP-A in EAA may have a direct impact on BAL fluid lymphocytosis. At first they suggested alterations of surfactant immunosuppressive activity at alveolar macrophages, which may lead to lymphocytic alveolitis. Nevertheless, further studies pointed out that EAA patients have impaired lymphosuppressive function of regulatory T-cells, which contributes to lymphocyte accumulation in the lung and maintenance of inflammation [8]. We indeed observed higher lymphocyte BAL fluid percentage in EAA patients with higher SP-A levels, even though it did not reach statistical significance.

Our study shows that SP-A serum concentrations do not differ between chronic EAA and IPF patients and thus should not be used as a biomarker for IPF detection. Prognostic value of serum SP-A concentrations in chronic EAA patients should be the aim of further studies.

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REFERENCES

1 Goldmann T, Kähler D, Schultz H, *et al.* On the significance of surfactant protein-A within the human lungs. *Diagn Pathol* 2009; 4: 8.
2 Gay SE, Kazerooni EA, Toews GB, *et al.* Idiopathic pulmonary fibrosis: predicting response to therapy and survival. *Am J Respir Crit Care Med* 1998; 157: 1063–1072.
3 Raghu G, Collard HR, Egan JJ, *et al.* An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir Crit Care Med* 2011; 183: 788–824.
4 Tillie-Leblond I, Grenouillet F, Reboux G, *et al.* Hypersensitivity pneumonitis and metalworking fluids contaminated by mycobacteria. *Eur Respir J* 2011; 37: 640–647.
5 Ohtsuki Y, Nakanishi N, Fujita J, *et al.* Immunohistochemical distribution of SP-D, compared with that of SP-A and KL-6, in interstitial pneumonias. *Med Mol Morphol* 2007; 40: 163–167.
6 Mazur W, Toljamo T, Ohlmeier S, *et al.* Elevation of surfactant protein A in plasma and sputum in cigarette smokers. *Eur Respir J* 2011; 38: 277–284.
7 Israël-Assayag E, Cormier Y. Surfactant modifies the lymphoproliferative activity of macrophages in hypersensitivity pneumonitis. *Am J Physiol* 1997; 273: L1258–L1264.
8 Girard M, Israël-Assayag E, Cormier Y. Impaired function of regulatory T-cells in hypersensitivity pneumonitis. *Eur Respir J* 2011; 37: 632–639.

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