390. Diffuse parenchymal lung disease IV

**P3670**

Coagulation factor IX deficiency does not afford protection from pulmonary fibrosis in the experimental murine bleomycin model

Karen Bloomstrand1, Lin Cong1, Bruno Crestani1, Olivier Christophe2, Arnold Spek1 1INSERM U790, Faculté de Médecine Xavier Bichat, Paris, France; 2Center for Experimental and Molecular Medicine, Academic Medical Center, Amsterdam, Netherlands; 3Pulmonaryology, Hospital Bichat, Paris, France; 4INSERM U797, Hôpital le Kremlin Bicêtre, Le Kremlin-Bicêtre, France

**Introduction:** Animal and human studies strongly suggest the importance of the coagulation cascade in acute and chronic lung injury. Indeed, beyond their role in hemostasis, coagulation factors can signal via their cellular receptors, the protease-activated receptors. We hypothesized that the absence of coagulation FactorFIX, which is essential for the activation of the coagulation cascade would reduce fibrosis development and progression.

**Methods:** We used the murine model of bleomycin-induced pulmonary fibrosis in wild-type (WT; n=14) and FIX deficient mice (n=13). After 14 days, we assessed markers of tissue fibrosis, inflammatory cell influx in the bronchoalveolar lavage fluid (BALF), and cytokines levels in the BALF, blood and homogenate of the animals.

**Results:** Mortality during the experiment was higher in the FIX deficient mice compared to wildtypes (23% versus 7%). The remaining FIX deficient mice (n=10) developed pulmonary fibrosis to a degree similar to WT (n=13). There was no significant difference in the Ashcroft score between WT and FIX deficient mice (4.01±0.4 versus 4.2±0.4), in the alpha-actin score (0.94±0.09 versus 0.70±0.07) and in the inflammatory cell number. In contrast, we observed in the plasma of the FIX deficient mice significant elevations in levels of cytokines IL-12, TNFs, IFNγ, MCP-1 and IL-6.

**Conclusion:** Mice with a congenital deficiency of FIX are not protected against bleomycin-induced pulmonary fibrosis. These data strongly argue against an important role of the blood coagulation cascade in the progression of pulmonary fibrosis, and raise important concerns about the use of anticoagulant therapy in patients.

**P3671**

Aggravation of bleomycin-induced pulmonary fibrosis in senescence-accelerated mouse

Baibei Lou, Qian Ye, Huaping Dai, Kewu Huang, Chen Wang. Department of Respiratory Medicine, Beijing Chao-Yang Hospital, Beijing Institute of Respiratory Medicine, Beijing, China

**Objective:** Idiopathic pulmonary fibrosis (IPF) is predominantly a lung fibrotic disease of older adults, and the process underlying aging might significantly influence the development of pulmonary fibrosis. Bleomycin-induced lung injury was investigated in murine models of accelerated senescence (SAMPS) and of normal aging (SAMR1). The levels of Thi1/Th2 related cytokines were also measured.

**Methods:** Bleomycin or PBS was injected into the tracheal lumen of 12-month-old SAMR1. The levels of Th1/Th2 related cytokine were also investigated in murine models of accelerated senescence (SAMP8) and of normal aging (SAMR1). The levels of Th1/Th2 related cytokines were also measured.

**Results:** The aggravated bleomycin induced lung injury was observed in 12-month-old SAMPS comparing with 4 and 12-month-old SAMR1 mice. Seven, 14 and 28 days after the injection, the mice were killed and the lungs were harvested for pathological examination, hydroxyproline assay and protein detect. Lung TGF-β1 expression was determined by western blot, and the levels of IL-4 and IFN-γ were detected by ELISA.

**Conclusion:** The aggravated bleomycin induced lung injury was observed in 12-month-old SAMPS comparing with 4 and 12-month-old SAMR1 mice. Twenty eight days after injection of bleomycin, Aschoft score was significant higher in 12-month-old SAMPS than in 4 and 12-month-old SAMR1 (P<0.05, respectively). Seven days, 14 days and 28 days after bleomycin injection, lung TGF-β1 expression was increased in 12-month-old SAMPS and SAMR1 compared with 4-month-old SAMR1. Similarly, the level of IL-4 and the IL-4/IFN-γ ratio of the lungs tended to be higher in 12-month-old SAMPS and SAMR1 than in 4-month-old SAMR1, but the differences were not statistically significant.

**Conclusion:** Bleomycin-induced pulmonary fibrosis in SAM was aggravated by aging. The old SAM with bleomycin-induced pulmonary fibrosis might be inclined to Th2-biased immune responses.

(This work was funded by National Natural Science Foundation of China Grants 81070046).

**P3672**

Lung function progression in Langerhans cell histiocytosis

Sophie Kryvinska1, Philip Indy1, Anthony Chu2 1Respiratory Medicine, Imperial College Healthcare Trust, Hammersmith Hospital, London, United Kingdom; 2Dermatology, Imperial College Healthcare Trust, Hammersmith Hospital, London, United Kingdom

**LCH is a rare, multisystem dendritic cell disorder commonly involving the lungs. The natural history is variable with little lung function outcome data. In our database of 92 patients referred to AC for treatment, 51 patients were male, mean age at diagnosis was 31 (range 1-77) years (y). 1702 patients, 10 male, mean age 31 y, had primary lung disease (PLLCH). 1475 had systemic LCH with lung involvement (SLLCH). All PLLCH had smoked with mean 13 pack-y; 9/17 continued smoking after diagnosis. Initial lung function (n=18) showed mean %predicted FEV1 76 (34-113)%; VC 81 (53-114)%; TLCO 67 (19-108)% 2 patients had obstructive, 3 restrictive, and 3 mixed lung disease. 9/14 SLLCH patients were male, mean age 25y, 10 had smoked; mean 12 pack-y, 7 continued smoking after diagnosis. Initial lung function (n=90) showed mean %predicted FEV1 83 (72-105)%; VC 89 (72-104%); TLCO 67 (49-106)%

**Conclusion:** At diagnosis, 8 of 14 smokers continued smoking. Initial %predicted FEV1 was 70.1 (30-103)%; predicted VC was 84 (51-109%); TLCO was 63 (17-105)% . Mean change in FEV1 was -7.39 to +12% in VC was (+1.9 to +14%); in TLCO was -10 to -49 to +29% 11/17 patients received treatment. To date 3 have died, 10 are in remission and 4 have active disease.

In SLLCH (n=60) at mean follow up of 6 (2-22) y mean FEV1 was 83 (66-101)%; predicted VC was 92 (79-103%); TLCO was 93 (82-94%). Mean change in FEV1, was -3 to +9 to +5% in VC was -1 to +12% and in TLCO was 14 (2 to +45%); 12/14 patients received treatment. To date 1 has died, 8 are in remission and 5 have active disease.

**Conclusion:** LCH is rare but in this relatively small, selected series lung function is worse and declines more in patients who present with primary lung involvement than those with lung involvement in systemic LCH.
P3675 Electrocardiographic characteristics in patients with sarcoidosis
Elias Gialafos1, 2, Vasiliki Kourouna1, 2, Alfonso Jurado Roman3, Maria Gallego4, Juan Jiménez5, Anastasios Kallianos6, Ormania Anagnostopoulou7, John Aragis7, Aggeliki Rapti4, George Tzelepis1. 1 11st Cardiology Unit, University of Athens, Athens, Greece; 2 5th Pulmonary Clinic, General Hospital of Chest Diseases “Sotiria”; Athens, Greece; 3 Cardiology Clinic, Heart Hospital UCL, London, United Kingdom; 4 2nd Pulmonary Clinic, General Hospital of Chest Diseases “Sotiria”, Athens, Greece; 5 Department of Therapeutics, University of Athens, Greece

Background: Several studies have emphasized on the importance of early identification of cardiac sarcoidosis. Aim of our study is the evaluation of electrocardiographic (ECG) characteristics in a cohort of sarcoidosis patients indicating myocardial involvement.

Methods: Consecutive patients with biopsy-proven sarcoidosis (n=315) were ex- amined from October 2002 through October 2011. Exclusion criteria were presence of pacemaker and/or implantable cardioverter defibrillator. Heart rate (HR), PQ, QT and QT corrected intervals, PQRS and T wave axis were collected. Also, complete and incomplete right (RBBB) and left (LBBB) bundle branch block, right (RVH) and left (LVH) ventricular hypertrophy, repolarization and intraventricular abnormalities were noted.

Results: Only 59 out of 315 patients had a normal ECG. Mean HR was 75±13.5 beats/min, QT=390±33 ms, QTC=417.58±21.2 ms while axis of P, QRS and T wave was: 42.6±19.8°, 20.79±34.0° and 34.5±25.9° respectively. Six patients were found at atrial fibrillation while the rest were at sinus rhythm. PQ interval was 156.89±24.91 ms and the QRS interval was 97±17.56 ms. RBBB was detected in 55 (11 complete and 44 incomplete) and LBBB in 9 patients (8 complete and 1 incomplete). Sixty patients were found with ventricular hypertrophy (56 LVH/4 RVH). At least at one lead repolarisation abnormality was found in 177 patients including inferior lead abnormalities at 28, anterior leads abnormalities at 23 and lateral leads abnormalities at 23 patients.

Conclusion: Although ECG is a widely available tool used in the diagnosis of cardiac sarcoidosis various abnormalities were described implying necessity of extensive investigation in order to detect cardiac involvement.

P3676 Survival predictors in a cohort of patients with idiopathic pulmonary fibrosis biopsy-proven
Mauricio Salinas1, 2, Matias Florenzano3, Gabriel Cavada1, Álvaro Underaga4.
1Medicina, Instituto Nacional del Torax, Santiago, Region Metropolitana, Chile; 2 Facultad de Medicina, Universidad de Chile, Santiago, Region Metropolitana, Chile

Idiopathic Pulmonary Fibrosis (IPF) is a bad prognosis disease with heterogeneous progression. Only few studies, including relative small sample size, have searched for bad prognosis factors. The aim of this study was to analyze survival predictors in a retrospective cohort.

The study was conducted at the National Thorax Institute in Santiago, Chile. Registres of patients in the period between 1991 and 2008 with clinical, radiological and surgical biopsy concordant with IPF were analyzed. We performed survival analysis with mixed models and proportional Weibull hazard models. A total of 142 patients were analyzed. The average age was 58 years and 41.5% were males.

The mean survival was 80 months. In univariate analysis we predictors of mortality: diffusing capacity of the lung for carbon monoxide (DLCO) less of forty percent and desaturation during six minute walk test (6MWT) at baseline. The rate of decline of forced vital capacity (FVC) was mortality predictor. The rate of decline of FVC is a strong mortality predictor in this study and allows distinguishing bad prognosis groups.

P3677 Pathological findings in histiocytosis X with pulmonary hypertension
Javier Villuela1, Jose Cifrian2, Beatriz Abascal1, Alejandro Daly1, Carlos Amado1, Sonia Fernandez-Rozas1, David Irube1, Felipe Zuriano1, Roberto Moms1, Javier Gomez-Román1, 2 Pneumology, Hospital Marques Valdecilla, Santander, Spain; 3Pathology Department, Hospital Marques Valdecilla, Santander, Spain; 4Thoracic Surgery, Hospital Marques Valdecilla, Santander, Spain.

Objective: To evaluate the hemodynamic characteristics, pulmonary function and pathological findings in patients with Langerhans cell histiocytosis (LCH) and Pulmonary Hypertension (PH) not explained otherwise.

Methods: A retrospective study was conducted in patients with Langerhans cell histiocytosis. Echocardiogram, lung biopsies, lung function tests and hemodynamic registries were reviewed.

Results: Twenty patients were studied, with a mean age of 41±10 years. 8 patients (40%) had severe PH. The median delay between the diagnosis of LCH and PH was 2±1.1 years. Six minute walk distance was 49±101m. Systolic PAP: 62±16 mmHg. FVC was 62±15% of predicted, FEV1 59±21% and DLco 41±13. All patients were on long-term oxygen therapy. After a median follow-up of 9.1 years, 1 patient is clinically stable, 1 patient had died of cardiac arrest while waiting for lung transplant, and 6 patients had undergone lung transplantation with 83% survival at 1 and 3 years. Histopathological lesions studied in explanted lungs suggested a veno-occlusive origin for this kind of complication, with capillary and venular obliteration, and granulomatosis-like changes and fibrosis of septa, something that has rarely been described in LCH.

Otherwise, it is interesting to remark the presence of three cases of malignant neoplasias in the global series. This association has been described as isolated cases in literature review. Two patients suffered from malignant lymphoma and one female patient had an uterine cervix carcinoma.

Conclusions: Pulmonary Hypertension could have a veno-occlusive origin in LCH. A relationship between malignant neoplasias and LCH may be possible.

P3678 A combinational approach to optimize biomarkers efficacy in identifying patients with sarcoidosis and monitoring respiratory functional worsening
Giussepino Paone1, 2, Gian Luca Di Tanna2, Sandro Batzella3, Francesco Belli4, Salvatore D’Antonio1, 5, Mario Giuseppe Alma1, Giovanni Schmid4, Giovanni Pugliis1, Anna Maria Vestri2, Department of Cardiovascular, Respiratory, Nephrologic and Geriatric Sciences, University “La Sapienza”, Rome, Italy; 3 Department of Public Health and Infectious Diseases, University “La Sapienza”, Rome, Italy; 4 Department of Respiratory Diseases, S. Camillo-Forlanini Hospital, Rome, Italy; 5 S. Maria della Pace, IRCCS Don Gnocchi Foundation, Rome, Italy

Background: Sarcoidosis is a multisystemic granulomatous disease of unknown aetiology which affects lungs and lymphatic system. Its diagnosis is established by histologic evidence of non-caseating granuloma and the clinical course is unpredictable.

Aims: We aimed to investigate whether a panel of biomarkers combined together may help identify sarcoidosis and predict its functional worsening.

Methods: We analyzed 30 subjects with sarcoidosis and 34 with IPF. Participants underwent PFTs, radiologic investigations, and fiberoptic bronchoscopy. We examined BALF cellular profiles and BALF and serum concentrations of ECP, MPO, tryptase, procollagenIII, sIL-2R, IL-6, and TNFα.

Results: The linear predictor score based on the combination of BALF lymphocytes, CD4, CD8, and ECP, correctly allocated 29 patients with sarcoidosis (97% of correct classification; 95% CI, 84.4%-99.8%) and 28 with IPF (82% correct classification; 95% CI, 68.8%-92.2%). The AUC was 0.93.

We analyzed PFTs of participants with sarcoidosis during a 2-years follow-up period. At revaluation 76% of participants had stable disease, and 24% experienced a worsening of the respiratory function. The combination of BALF neutrophil percentage, ECP, and tryptase, yielded a 100% correct classification of patients (95% CI, 90.6%-100%); the AUC was 1. None of the markers analyzed as a single variable reached a similar allocation rate and a dissatisfying discrimination was obtained using markers from peripheral blood.

Conclusion: This combinational method could be a valuable approach to optimize biomarkers performance in the effort to identify sarcoidosis and to predict its clinical course.

Table 1. Results of pulmonary function tests at baseline

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forced vital capacity (mL)</td>
<td>4800 (770)</td>
</tr>
<tr>
<td>Forced vital capacity (%)</td>
<td>73 (20)</td>
</tr>
<tr>
<td>DLCO (mL/mmHg)</td>
<td>14 (4.8)</td>
</tr>
<tr>
<td>DLCO (%)</td>
<td>57.8 (16.3)</td>
</tr>
<tr>
<td>DLCO (mL/min/mmHg)</td>
<td>14.0 (4.8)</td>
</tr>
<tr>
<td>6MWT (m)</td>
<td>477 (83)</td>
</tr>
<tr>
<td>6MWT (%)</td>
<td>95.3 (15.4)</td>
</tr>
</tbody>
</table>

SD: Standard deviation; DLCO: diffusing capacity of the lungs for carbon monoxide; 6MWT: Six minute walk test.
Thematic Poster Session

P3679

Characteristics of gender distribution in sarcoidosis

Aglaia Vlassopoulou-Ioannou 1, Violeta Vuckovic 1, Snezana Filipovic 1, Vladimir Zgaga 1, Jelena Stojic 2, 1Pulmonology, Clinic for Lung Diseases and Tuberculosis, Belgrade, Yugoslavia; 2Pathology, Institute for Pathology, Belgrade, Yugoslavia

Introduction: Sarcoidosis is granulomatous disorder of unknown etiology, predominantly manifesting in female patients. It is the same or similar to mentioned in patients from the Clinic for lung diseases and tuberculosis CC Serba in Belgrade.

Method: Retrospective analysis were obtained on 857 patients incoming to the Clinic (F 587:68.5% - 44.7; M 270:31.5% - 47.8) years with previously obtained diagnosis of sarcoidosis.

Results: Acute onset of sarcoidosis is predominantly in younger (less than 35 years) with similar gender distribution, 153 F/132 M. The onset of sarcoidosis in older patients (over 35 years) was less acute notify in more male patients, 381, than 191 female accompanying with prolonged duration of sarcoidosis (5.3/3.1 yrs M/F) and frequently more than one organ involved with sarcoidosis. Lung involvement were the only symptom in patients with sarcoidosis. Only nonpulmonary involvement is in less numbered – 117 pts (eyes - 35, skin - 37, cerebri - 7, spleen – 5, bones – 3, liver – 9, per isl.-57; 47FB; gl.parotis – 11, heart – 7) with male predominated: 51 pts/36pts. F: Lung and nonpulmonary sarcoidosis were notified in 134 Female and/22 Male patients.

Conclusion: Due to analysis, the numbered patients with obtained diagnosis of acute onset of sarcoidosis are female. Male patients with nonpulmonary sarcoidosis predominated over the female. Duration of sarcoidosis course is much longer in male patients.

P3680

Prevalence of pulmonary involvement in rheumatoid arthritis patients in Indian population

Krishana J. Kanitkar, Diksha Tyagi, Harpreet Singh, Sarita Magu. Respiratory Medicine, Pt. B.D. Sharma Post Graduate Institute of Health Sciences, Rohtak, Haryana, India; Respiratory Medicine, Pt. B.D. Sharma Post Graduate Institute of Health Sciences, Rohtak, Haryana, India Radiology, Pt. B.D. Sharma Post Graduate Institute of Health Sciences, Rohtak, Haryana, India

Rheumatoid arthritis (RA) is the most common chronic connective tissue disorder that significantly affects the lungs. The aim was to evaluate the pulmonary involvement in RA patients and its correlation with RA.

A total of 100 diagnosed cases of RA, divided into two groups of 50 patients each on the basis of duration of RA i.e. <5 years and >5 years were evaluated. All the patients were assessed for clinical characteristics, high resolution computed tomography (HRCT) thorax and Spirometry findings. Disease severity was assessed by DAS28 score. Respiratory symptoms were present in 41% patients. Pulmonary involvement (either abnormal HRCT thorax/Spirometry or both) was found in 67% patients with abnormal Spirometry in 51% and abnormal HRCT in 59.30% patients. Chest radiographs were abnormal in 22% patients. Most common radiological finding on chest radiography was interstitial lung disease suggestive findings (31%) and bronchectasis (29.41%). On Spirometry, restrictive defect was found in 33% obstructive defects in 12% and mixed defect in 6%. FEF25-75% was abnormal in 18% patients. Risk factors for the presence of pulmonary involvement were increasing age and presence of rheumatoid factor. No association was found with gender, duration of disease, severity of disease.

A high prevalence of pulmonary involvement was found in RA independent of duration of illness. HRCT appeared to be more sensitive tool.

P3681

Is T-SPOT.TB performance in bronchoalveolar lavage usful in differential diagnosis between sarcoidosis and tuberculosis? - Pilot study

Anna Kemény 1, Piotr Radwan-Rohrenschel 1, Dagmara Borkowska 2, Ewa Augustynowicz-Kopeć 3, Jan Kus 4, 1Department of Lung Diseases, National Tuberculosis and Lung Diseases Research Institute, Warsaw, Poland; 2Department of Microbiology, National Tuberculosis and Lung Diseases Research Institute, Warsaw, Poland

Introduction: Both sarcoidosis and tuberculosis are similar in their radiological and histological pictures. Sometimes it is difficult to distinguish between these two diseases. The only reliable diagnostic tool for M. tuberculosis (MTB) is cultures. Unfortunately we have to wait for several weeks for culture results to make final diagnosis.

Object and rationale: IGRAs as peripheral blood detect MTB infection but do not discriminate latent from active TB. The aim of this study was to evaluate utility of T-SPOT.TB test in BAL and its advantages over T-SPOT.TB test in peripheral blood in differential diagnosis between sarcoidosis and tuberculosis.

Material and method: 11 subjects (4 female, 7 male; mean aged 45.8±12) suspected for sarcoidosis were included in this study. 1 was withdrew because of bronchial obstruction which made the BAL impossible. T-SPOT.TB tests in peripheral blood and in BAL were performed in 10 subjects.

Results: All 10 patients were AFB and MTB DNA negative in BAL. T-SPOT TB test was positive in peripheral blood in 2/10 and in BAL in 1/10. The culture of BAL was positive for MTB only in the case who had positive T-SPOT TB test both in BAL and in peripheral blood.

Conclusion: Positive T-SPOT TB performed in BAL could be helpful in differential diagnosis between sarcoidosis and tuberculosis. Further studies are needed.

P3683

Sarcoidosis in Sao Paulo, Brazil: Clinical, tomographic and lung functions data from 72 patients

Agostinho Hermes Medeiros-Neto, Fabiola Gomes Rodrigues, Carlos Roberto Ribeiro Carvalho, Ronaldo Adib Kafiulla. Pulmonary Division, Heart Institute (InCor), University of Sao Paulo Medical School, Sao Paulo, SP, Brazil

As part of major study on prevalence of pulmonary hypertension in outpatients with sarcoidosis, a sample of patients underwent prospective clinical, tomographic and lung function evaluation.

Objective: To describe clinical, imaging and lung function data of 72 consecutive patients with sarcoidosis.

Methods: Between September 2008 and September 2010, 72 consecutive patients underwent evaluation in a prospective fashion. All patients underwent clinical interview, chest radiography, high resolution computed tomography and lung function tests (spirometry, lung volumes by pletysmography and carbon monoxide diffusion DLCO).

Results: Clinical characterization: 69.4% female, age 54.9±12.6. Smoking status: 63.9% non-smokers. Disease duration at diagnosis was the most prevalent (91.7%), followed by lymph nodes and cutaneous involvement. Number of extra pulmonary organ involvement was 1±1.1 organ per patient. Near 62% of patients had interrupted working activity during an AE and showed a significant increase in CCL18 (p=0.04). Of note, 5 patients underwent bronchoscopy before and after an AE and showed a significant increase in CCL18 (p=0.04).

P3684

Coeistence of idiopathic pulmonary hemosiderosis and celiac disease: Complete remission with gluten free diet

Mehmet Avdologan 1, Alper Gundogan 2, Ergun Ucar 1, Cemal Tasci 3, Seyitettin Gunus 2, Zulfikar Polat 4, Omer Demir 2, Erzun Tozkoparan 2, Metin Oztkan 1, Hayati Bilgic 1, 1Pulmonary Medicine, Galipha Military Medical Academy, Ankara, Turkey; 2Gastroenterology, Galipha Military Medical Academy, Ankara, Turkey

Idiopathic pulmonary hemosiderosis is a rare disease of unknown etiology usually characterized by recurrent episodes of alveolar hemorrhage, hemosiderosis and iron deficiency anemia. It occurs most frequently in children but rarely in adults. The combination of idiopathic pulmonary hemosiderosis and celiac disease is extremely rare. A 24-year-old man with history of recurrent hemoptysis and anemia was diagnosed with the combination of idiopathic pulmonary hemosiderosis and celiac disease. The patient was started on a gluten-free diet and has had no recurrence of hemoptysis over 2 months’ follow-up. Hemoglobin at 2 months’ follow up was normal and grand glass opasites in HRCT scan completely disappeared.

P3685

M2 chemokines during acute exacerbations of IPF

Jano Schupf, Corna Kollert, Benedict Jager, Joachim Muller-Quernheim, Antje Prasse. Department of Pneumology, University Medical Center, Freiburg, Germany

Background: Alternative activation of macrophages is a well-recognized phenomenon in patients with IPF and is associated with poor prognosis. The most common cause of death in IPF is Acute Exacerbations (AEs).

Objectives: Evaluation of the alternative activation state of macrophages during acute exacerbations in patients with IPF.

Methods: 61 patients with IPF and 14 healthy volunteers underwent bronchoscopy with bronchoalveolar lavage, one million BAL cells were cultured for 24 hours without further stimulation and the conditioned medium was harvested. Spontaneous M2 chemokine production (CCL2, CCL17, CCL18, CCL22 and IL-1Ra) was measured by ELISA. AEs were defined according to the criteria of Collard et al. (Collard, HD et al. AJRCCM 2007; 176:636-643).

Results: BAL cells of patients with IPF produced significantly more CCL2, CCL17, CCL18, CCL22 and IL-1Ra compared to cells of healthy volunteers. Seventeen patients suffered from an AE at the time point of bronchoscopy. The spontaneous production of CCL2, CCL18, CCL22 and IL-1Ra were significantly increased of BAL cells from patients with AE in comparison to patients without AE (all p<0.05). Furthermore, 5 patients underwent bronchoscopy before and during an AE and showed a significant increase in CCL18 (p<0.04). Of note,
M2 chemokine production was elevated despite a decrease in the percentage of alveolar macrophages during AE.

Conclusion: We could show a further increase of M2 chemokines during AEs in patients with IPF. High state of alternative activation of macrophages is associated with an increased risk for AEs and might therefore be a therapeutic target for AE prophylaxis.

P3686
Effects of aerobic and strength training on symptoms and exercise capacity of IPF patients
Robert Jackson1, Carol Ramos1, Diana Cardenas1,2, Constanza Sol3, Meryl Cohen3, Ignacio Guzman1, Nicole Eustis1, Orlando Gomez-Marin1,4.
1Research Service, Miami VAHS, Miami, FL, United States; 2Department of Rehabilitation Medicine, University of Miami, FL, United States; 3Department of Physical Therapy, University of Miami, FL, United States; 4Epidemiology and Public Health, University of Miami, FL, United States

Patients with idiopathic pulmonary fibrosis (IPF) have limited exercise capacity due to dyspnea, abnormal lung mechanics, pulmonary hypertension and other mechanisms. We tested the hypothesis that 24 sessions of exercise in the form of a rehabilitation program would improve six-minute walk test (6-MWT) distance, peak exercise oxygen uptake (VO2 peak) and dyspnea (Borg dyspnea index) after exertion in patients with typical IPF. We investigated possible underlying mechanisms including hypoxemia, oxidant stress and pulmonary hypertension. Subjects with IPF defined by clinical criteria were randomly assigned to a 3-month pulmonary rehabilitation program or to a control group that did not participate in rehabilitation. Before and after the 3-month rehabilitation or observation, subjects underwent 6-MWT and exercise gas exchange studies (cycle ergometry). Blood samples were obtained for 15-F2t-isoprostanes, lactate and NT-proBNP measurements immediately before and after cycle ergometry. Rehabilitation did not cause a significant increase in 6-MWT distance or a decrease in dyspnea. Subjects who completed pulmonary rehabilitation maintained VO2 peak at baseline over three months. The control group had a significant decrease in VO2 peak over the same 3 months. Plasma lactate increased significantly after ~50-watt cycle ergometry exercise testing at 0- and 3-month evaluations in both groups; this was associated with significant decreases in arterial oxygen saturation. Pulmonary rehabilitation maintained peak oxygen uptake, but did not improve exercise capacity of patients with moderately severe IPF. Low-level exercise was associated with significant hypoxemia and systemic oxidant stress.