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Karolinska Institutet och Universitetssjukhuset

## ASPECTS OF INFLAMMATION IN COPD

A clinical study

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### AKADEMISK AVHANDLING

som för avläggande av medicine doktorexamen vid Karolinska Institutet,  
offentligen försvaras på engelska språket i Thoraxklinikernas föreläsningssal N2:U1  
Karolinska Universitetssjukhuset Solna  
Fredagen den 24 november 2006, kl. 10.00



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Institutet**

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**Stockholm 2006**

## ABSTRACT

Development of chronic obstructive pulmonary disease (COPD) involves an amplified inflammatory response to tobacco smoke that results in a limitation of airflow. At present, the mechanisms underlying these inflammatory processes are not fully understood and insight into these mechanisms could be obtained through comparison of the processes in patients with COPD and appropriate controls.

Here, in order to characterize inflammatory responses in different body compartments, bronchoscopy was employed to obtain bronchoalveolar lavage (BAL) fluid and mucosal biopsies and, in addition, blood samples were taken from patients with COPD (n=23), smokers without this disease (n=16) and non-smokers (n=15). In addition, all of the participants underwent dynamic spirometry, computerized tomography (CT), body plethysmography and determination of the diffusion capacity of their lungs (DLCO).

The volume of BAL fluid recovered from the patients was lower than from both groups of controls. From patients with an emphysema index of <1% (i.e., for whom less than 1% of the pixels in a CT scan using 10-mm slices demonstrated an attenuation of less than 950 Hounsfield units), a larger volume of BAL fluid was recovered than from those with a corresponding index of >1%. Thus, this recovery correlated negatively to the index of emphysema and positively to other, indirect measures of emphysema (i.e., the DLCO and the FEV1/VC ratio).

Examination by flow cytometry showed that in comparison to smokers without the disease, the alveolar macrophages in BAL fluid from patients with COPD exhibited an altered phenotype, i.e., attenuated expression of the co-stimulatory molecule CD86 and of CD11a, an adhesion protein. Other differences in the expression of surface molecules by alveolar macrophages from smokers and non-smokers suggest that cigarette smoke exerts direct effects on these cells.

Moreover, exploration of the infiltration of the bronchial epithelium by inflammatory cells revealed elevated numbers of lymphocytes in patients with COPD. The numbers of CD4+ cells in these patients was higher than in either control group, while their numbers of CD8+ cells were elevated only in comparison to non-smokers.

In addition, the oxidative burst produced by leukocytes in the peripheral blood of patients and smokers without disease was less pronounced than in non-smokers. Vascular alterations were also present in the patients with COPD, as reflected in an enhanced level of sICAM-1. At the same time, the ability to mobilize the adhesion molecule CD11b was reduced in those patients who had smoked during the 12-hour period immediately preceding bronchoscopy.

These findings emphasize the importance of characterizing patients with COPD in an appropriate manner. Furthermore, the alterations observed in the phenotypes of the inflammatory cells of patients with COPD indicate that the innate immune responses of these individuals may be impaired, e.g., their macrophages may be less capable of activating T-lymphocytes and their circulating phagocytes less responsive to stimulation. Moreover, the present investigation reveals that the amplification of inflammation associated with COPD also involves the airway epithelium, a region of the bronchial mucosa previously explored less extensively than the submucosa, and, finally, confirms that COPD influences not only the airways, but systemic inflammatory responses as well.

**Keywords:** Chronic obstructive pulmonary disease, bronchoscopy, bronchoalveolar lavage, inflammation, flow cytometry, bronchial biopsies

**ISBN:** 91-7140-990-4