

Studies of neutrophilic inflammation in tobacco smokers

AKADEMISK AVHANDLING

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av

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Avhandlingen baseras på följande delarbeten:

- I. Andelid K, Bake B, Rak S, Lindén A, Rosengren A och Ekberg-Jansson A. **Myeloperoxidase as a marker of increasing systemic inflammation in smokers without severe airway symptoms.** Respiratory Medicine 2007; 101(5): 888-95.
- II. Glader P, Eldh B, Bozinovski S, Andelid K, Sjöstrand M, Malmhäll C, Anderson GP, Riise GC, Qvarfordt I och Lindén A. **Impact of acute exposure to tobacco smoke on gelatinases in the bronchoalveolar space.** European Respiratory Journal 2008; 32(3): 644-50.
- III. Andelid K, Tengvall S, Andersson A, Levänen B, Christiansson K, Jirholt P, Åhrén C, Qvarfordt I, Ekberg-Jansson A och Lindén A. **Systemic cytokine signaling via IL-17 in Smokers with Obstructive Pulmonary Disease. A Link to Bacterial Colonization?** Submitted manuscript.
- IV. Andelid K, Glader P, Yoshihara S, Åhrén C, Jirholt P, Gjertsson I, Ekberg-Jansson A och Lindén A. **Systemic Signs of Neutrophil Mobilization during Stable Clinical Conditions and Exacerbations in Smokers with Obstructive Pulmonary Disease: A Link to Hypoxia?** Submitted manuscript.



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ABSTRACT

The general aim of this thesis was to characterise markers of neutrophilic inflammation in smokers with and without obstructive pulmonary disease with chronic bronchitis (OPD-CB) in a clinically stable state and during exacerbations compared to healthy controls. *Methodology:* I) Blood samples were obtained from male smokers without airway symptoms and never-smokers at year 0 and 6. II) Non-atopic and atopic, occasional-smokers plus never-smokers underwent two bronchoscopies, including bronchoalveolar lavage (BAL). III & IV) Smokers with OPD-CB (n=60,) and control groups (n=10 each), underwent blood and sputum sampling every 15: th week and during exacerbations for 15 months. *Results:* I) Blood MPO was higher in smokers than in never- smokers at year 6. MPO was negatively correlated with time after cessation of smoking. II) Gelatinases in BAL fluid were unchanged after acute exposure to tobacco smoke. III) The concentrations of IL-17A and GRO- α protein were lower in blood from smokers with severe OPD-CB and in smokers with OPD-CB colonised with opportunistic pathogens. IV) In smokers with OPD-CB, blood MPO and NE proteins were increased during exacerbations; the corresponding mRNA was undetectable. *Conclusions:* Acute exposure to tobacco smoke does not exert a pronounced, lasting impact on gelatinases in the airways of occasional-smokers. During stable clinical conditions, neutrophil and MPO concentrations are increased in smokers without OPD-CB and even more so during exacerbations in smokers with OPD-CB. In smokers with severe OPD-CB, and in those colonised with opportunistic pathogens, specific neutrophil-associated cytokine signaling is down-regulated at the systemic level. The lack of detectable mRNA for MPO and NE in the blood of smokers with OPD-CB makes the location of production uncertain for these markers of neutrophil activity.

Keywords: smoking, neutrophils, inflammation

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