European Respiratory Society
Annual Congress 2012

Abstract Number: 1451

Publication Number: 4694

Abstract Group: 5.3. Allergy and Immunology

Keyword 1: Viruses **Keyword 2:** Asthma - mechanism **Keyword 3:** Inflammation

Title: Rhinovirus infection activates coagulation through eosinophilic airway inflammation

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Body: Introduction: Exacerbations in asthma are most commonly caused by rhinoviruses. Inflammatory conditions, like asthma, are known to activate hemostasis. Vice versa, a prothrombotic state in the lung can also induce or aggravate pulmonary inflammation. Hypothesis: Rhinovirus infection activates coagulation in patients with asthma, but not in normal control subjects. Methods: 14 patients with mild asthma and 14 healthy controls were nasally inoculated with rhinovirus type 16 (10 $TCID_{50}$) using a validated method. Bronchoalveolar lavage fluid (BALF) was retrieved by bronchoscopy at t=-1 and t=6 days. Microparticle-associated tissue factor(TF) activity in BALF was examined by a fibrin generation test (FGT). Thrombin-antithrombin complexes (TAT) and Eosinophil Cationic Protein (ECP) in BALF were measured by immunoassay. Eosinophils were counted on cytospin preparations. Results: On day 6 after rhinovirus infection, FGT in BALF became significantly shorter in asthma (t=-1: 672s vs. t=6: 516s (medians); p=0.013), whereas there was no change in healthy controls (t=-1: 695s vs. t=6: 707s (medians); p=0.75). At t=6 days, FGT correlated (Spearman) with TAT, eosinophils and ECP (r = -0.607, -0.583 and -0.682 resp., all $p<0.01$) and TAT with eosinophils and ECP (r = 0.482, 0.538, both $p<0.05$). Conclusion: Rhinovirus infection significantly shortens the clotting time (FGT) when induced by microparticles isolated from BALF of asthma patients, reflecting enhanced coagulant activity of TF-exposing microparticles. The strong correlations between FGT, TAT, eosinophils and ECP after rhinovirus infection in asthma suggest that eosinophils may play a critical role in the coagulation activation during viral airway infection.