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**Title:** On the effectiveness of steroids in acute lung injury: Experimental separation between inflammation and hypoxemia

Ms. Lucy Kathleen 87 Reiss kreiss@ukaachen.de<sup>1</sup> and Prof. Dr Stefan 1642 Uhlig suhlig@ukaachen.de<sup>1</sup>.  
Institute of Pharmacology and Toxicology, Medical Faculty of RWTH Aachen University, Aachen, Germany, 52074 .

**Body:** Acute lung injury (ALI) is defined by hypoxemia in the presence of excessive inflammation. Despite of a multitude of clinical trials the role of glucocorticoids in the treatment of ALI is under constant debate. The present study was designed to investigate the effectiveness of dexamethasone in dependence on the type and severity of lung injury and the fraction of inspired oxygen ( $FiO_2$ ). C57BL/6 mice were instilled intratracheally with 50  $\mu$ L HCl at pH 1.5 or 1.8 and were then ventilated with recruitment manoeuvres (RM) and  $FiO_2=0.3$  or 1.0. Another group was ventilated without acid instillation and without RM to induce atelectasis. Dexamethasone [1mg/kg] was injected intravenously at the beginning of ventilation. Lung mechanics were followed by the forced oscillation technique. Cardiovascular parameters, oxygen saturation and body temperature were monitored. Blood gases, cytokines, neutrophil recruitment, microvascular permeability and lung histology were examined. Dexamethasone attenuated inflammation (neutrophil recruitment, edema formation, cytokine liberation) in all models. Hypoxemia and lung mechanics were improved in the groups instilled with acid pH 1.8 (moderate injury), but not in the groups instilled with acid pH 1.5 (severe injury) or in those with atelectasis. A high  $FiO_2=1.0$  augmented acid-induced lung injury, but did not affect the effectiveness of dexamethasone. In the present study steroids were highly effective in preventing inflammation under all conditions, whereas they improved the clinical outcome in moderate, but not in severe lung injury or in cases of derecruitment, suggesting that steroids are effective only in a subclass of patients with ALI.