Title: Activation of the coagulation system following exposure of mice to chlorine

Body: Chlorine (Cl₂) is a highly irritant and reactive gas produced in large quantities throughout the world. The accidental release of large amounts of Cl₂ in 30 large cities world-wide, caused significant mortality and morbidity to humans and animals. Our previous findings show that exposure of rodent to Cl₂ causes both pulmonary and systemic injury (Zarogiannis et al. Am J Respir Cell Mol Biol. 2011;45(2):386-92; Honavar et al. Am J Respir Cell Mol Biol. 201145(2):419-25.) Herein we tested the hypothesis that exposure to Cl₂ activates intraalveolar and systemic coagulation cascades which in turn may contribute to the development of lung and other end-organ injury. Male C57Bl/6 mice (6-8 weeks) were exposed to either Cl₂ (600 ppm for 45 minutes in environmental chambers) or air (0 ppm). Mice were returned to room air and sacrificed immediately or at 1 h post-exposure and their lungs were lavaged. Mice exposed to Cl₂ had much higher levels of Thrombin/anti-Thrombin (TAT) complexes (measured by ELISA) as compared to those exposed to air both in the BAL (10 ± 2 ng/ml vs. 0.5 ± 0.1; mean + SE; n=6; p<0.01) and plasma (25±0.1 ng/ml vs. 0.1±0.05; mean + SE; n=6; p<0.01) at 1 h post exposure. In addition clotting time in the blood (measured by thromboelastometry) was significantly prolonged in Cl₂ exposed mice as compared with air controls (275 ± 25 sec. vs. 150 ±10; mean + SE; n=6; p<0.01). In contrast, there was no significant change in the clotting time blood taken from mice immediately after Cl₂. Taken together, these data demonstrates a strong activation of the coagulation within the airspaces as well as the development of a systemic disseminated intravascular coagulation after Cl₂ exposure in mice.