

Cl ketoixmes. Notably, some newly synthesized Cl-Ketoximes demonstrated enhanced in vitro reactivation kinetics of sarin- and/or VX-inhibited AChE compared to 2-PAM and TMB-4.

WG 1 (Chemical, Biological, Radiological and Nuclear materials)

## Whole-Body Exposure of Rats to High Concentration Chlorine Gas: Clinical and Histological Evaluation

**Adi Neufeld-Cohen, Hila Gutman, Shlomit Dachir, Mordi Hotoveli, Shlomy Maimon, Maayan Cohen, Tamar Kadar, Tamar Klapholtz, Eldar Peretz, Inbal Egoz, Rellie Gez, Eyal Dor, Ariel Gore, Vered Horwitz.**

Israel Institute for Biological Research, Department of Pharmacology.

Chlorine is a corrosive irritant widely used in the chemical industry. Since it was first used as a chemical warfare agent in World War I in the battle of Ypres, Belgium, hundreds of attacks were reported, many of which in the last two decades in Syria. Acute exposure to chlorine gas due to industrial accidents or military activity may cause severe airway irritation and inflammation, respiratory distress and pulmonary edema injury, and in severe cases respiratory failure and death. Survivors of acute chlorine exposure present long-term effects such as bronchitis, emphysema, airway obstruction, encephalopathy and cardiac pathology. Currently, the treatments of acute inhalation of chlorine gas are supportive and symptom oriented.

Our work aims to characterize a rat model of acute and chronic injuries following a whole-body exposure to high concentrations of chlorine gas, which can serve for evaluations of emerging treatments.

Groups of awake adult Sprague-Dawley rats were exposed to 500ppm or 600ppm chlorine gas for 20-30 minutes in 70% humidified whole-body exposure system. Clinical evaluations including body weight, clinical severity score, respiratory functions, circadian activity and changes in blood count were performed for a period of 16 days after the exposure. Following euthanasia, lung and trachea tissues were processed for histological evaluation.

Exposed rats developed chlorine acute intoxication symptoms including skin injuries, changes in white blood cells counts, breathing difficulties, impaired circadian activity and weight loss. Death rates after 24 hours were 11% and 25% for 600ppm for 20 min and 500ppm for 30 min, respectively. Although gradual healing process was seen clinically, respiratory measurements using plethysmography presented ongoing dysfunction during the 16 days of monitoring. In addition, skin injuries around the eyes, nose and tail, did not heal during the follow-up period. Histological analysis revealed inflammatory cell infiltration and airways obstruction in the lungs, tracheal obstruction and severe damage to tracheal cilia and epithelium.

This study presents a model of an acute injury following a whole-body exposure of rats to a high concentration of chlorine, as expected in a real scenario. A comprehensive characterization of various clinical and histological parameters of acute chlorine induced injury was performed. This model will serve as a tool for emerging treatment evaluation.