Mechanisms and modification of chlorine-induced lung injury in animals.

Chlorine (Cl₂) is a reactive oxidant gas used extensively in industrial processes. Exposure of both humans and animals to high concentrations of Cl₂ results in acute lung injury, which may resolve spontaneously or progress to acute respiratory failure. Injury to airway and alveolar epithelium may result from chemical reactions of Cl₂, from HOCl (the hydrolysis product of Cl₂), and/or from the various reaction products, such as chloramines, that are formed from the reactions of these chlorinating species with biological molecules. Subsequent reactions may initiate self-propagating reactions and induce the production of inflammatory mediators compounding injury to pulmonary surfactant, ion channels, and components of lung epithelial and airway cells. Low-molecular-weight antioxidants, such as ascorbate, glutathione, and urate, present in the lung epithelial lining fluid and tissue, remove Cl₂ and HOCl and thus decrease injury to critical target biological targets. However, levels of lung antioxidants of animals exposed to Cl₂ in concentrations likely to be encountered in the vicinity of industrial accidents decrease rapidly and irreversibly. Our measurements show that prophylactic administration of a mixture containing ascorbate and desferal N-acetyl-cysteine, a precursor of reduced glutathione, prevents Cl₂-induced injury to the alveolar epithelium of rats exposed to Cl₂. The clinical challenge is to deliver sufficient quantities of antioxidants noninvasively, after Cl₂ exposure, to decrease morbidity and mortality.

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