## Protective effect of low-concentration chlorine dioxide gas against influenza A virus infection

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低濃度二酸化塩素ガスによるインフルエンザ A ウイルスに対する予防効果

## [Abstract]

Influenza virus infection is one of the major causes of human morbidity and mortality. Between humans, this virus spreads mostly via aerosols excreted from the respiratory system. Current means of prevention of influenza virus infection are not entirely satisfactory because of their limited efficacy. Safe and effective preventive measures against pandemic influenza are greatly needed. We demonstrate that infection of mice induced by aerosols of influenza A virus was prevented by chlorine dioxide (ClO<sub>2</sub>) gas at an extremely low concentration (below the long-term permissible exposure level to humans, namely 0.1 p.p.m.). Mice in semi-closed cages were exposed to aerosols of influenza A virus (1 LD50) and ClO<sub>2</sub> gas (0.03 p.p.m.) simultaneously for 15 min. Three days after exposure, pulmonary virus titre (TCID<sub>50</sub>) was 10<sup>2.6±1.5</sup> in five mice treated with ClO<sub>2</sub>, whilst it was  $10^{6.7\pm0.2}$  in five mice that had not been treated (P=0.003). Cumulative mortality after 16 days was 0/10 mice treated with ClO<sub>2</sub> and 7/10 mice that had not been treated (P=0.002). In in vitro experiments, ClO<sub>2</sub> denatured viral envelope proteins (haemagglutinin and neuraminidase) that are indispensable for infectivity of the virus, and abolished infectivity. Taken together, we conclude that ClO<sub>2</sub> gas is effective at preventing aerosol-induced influenza virus infection in mice by denaturing viral envelope proteins at a concentration well below the permissible exposure level to humans. ClO2 gas could therefore be useful as a preventive means against influenza in places of human activity without necessitating evacuation.

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