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P1-105

Inactivation of the novel avian influenza virus A (H7N9) under physical conditions or chemical agents treatment

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Background: During the spring of 2013, the emergence and spread of a novel avian-origin influenza A (H7N9) virus in humans in eastern China has raised concerns that a new influenza pandemic could occur. The potential effect of chemical agents and physical conditions on inactivation of the novel H7N9 virus has not been assessed. Materials and Methods: To determine the survival of the H7N9 isolates under various physical and chemical treatments, two H7N9 isolates, A/Anhui/1/2013 and A/Shanghai/1/2013, were treated by varied temperatures, ultraviolet light, varied pHs and disinfectants. The viruses with a concentration of $10^{7.7}$ EID50 were exposed to physical (temperature, ultraviolet light and pH) and commercial chemical (chlorine, Virkon S, and ethanol) agents. Harvested allantoic fluid from embryonated SPF chicken eggs inoculated with H7N9 treated virus was subjected to haemagglutination assay. Results: Both the tested viruses can tolerate 15-min exposure to 56°C but lost their infectivity totally when exposed to the temperature of 56°C for 30 min, and also readily inactivated by 65°C for at least 10 min, 70°C for 5 min or 100°C for 1 min. It was also observed the H7N9 viruses lost their viability after they were exposed to ultraviolet light radiation for 30 minutes or longer. Additionally, acidic pH 1-3 was virucidal after 0.5 h (pH1-2) or overnight (pH3) contact time. But, the virus retained infectivity after contacting pH 4-12 for 24 h. In addition, the virus would lose infectivity when exposed to chlorine, Virkon S and ethanol at recommended concentrations after only 5-10 min. Conclusions: The novel virus can be inactivated by general physical or chemical treatments, but presents a high tolerance on acidic or alkali conditions. The results provide support for public awareness of protection against the novel virus or the decontamination method of the novel virus at laboratory and field conditions.

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Pathogenesis of the novel avian-origin influenza A (H7N9) virus in human lower respiratory tract

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Background: As of May 2013, 131 laboratory-confirmed human infections with a novel influenza H7N9 virus had been reported from China. The source of human infection appears to be poultry. There is so far no evidence of sustained human-to-human transmission. Genetic analysis revealed that all eight gene segments of H7N9 were of avian origin; six internal gene segments from avian influenza H7N9 viruses, while hemagglutinin and neuraminidase genes were derived from influenza viruses circulating in ducks and wild ducks, respectively. The emergence of the H7N9 influenza virus catches global attention about whether the new virus could spark another pandemic. The majority of the infected patients were hospitalized and suffered from ARDS, with a fatality rate of about 37%. Our study aimed to determine the mechanism contributing to the pathogenesis of the H7N9 virus. A panel of proinflammatory cytokines and chemokines will be examined upon influenza H7N9 virus infection in alveolar epithelial cells in order to examine if these mediators were induced differentially when compared with the highly pathogenic avian influenza (HPAI) H5N1 and the 2009 pandemic H1N1 virus. Moreover, because cleaved caspase 3 is commonly employed as a marker for the indication of apoptosis, we further examined the extensiveness of cleaved caspase 3 in influenza virus infection in

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human lung ex vivo cultures. Materials and Methods: Fresh biopsies of human lung tissue were obtained from patients undergoing surgical resection of lung tissues. Lung tissue fragments were cultured with F12K medium incubated at 37°C. For viral infection experiments, influenza viruses A/Shanghai/1/2013 (SH1, H7N9), A/Shanghai/2/2013 (SH2, H7N9), A/Hong Kong/483/97 (H5N1), and A/California/07 (Ca07, H1N1pdm) at a viral titer of 10^6 $TCID_{50}$/mL were used for ex vivo lung culture infection. Infected lung tissues were collected in 10% formalin at 24, 48, and 72 hpi for immunohistochemical staining. Costaining of cleaved caspase 3 and influenza virus nucleoprotein was carried out for the detection of apoptosis. Furthermore, primary culture of human alveolar epithelial cells was isolated from human lungs by mincing the lung, followed by filtration and centrifugation. Human alveolar epithelial cells were infected with the novel influenza H7N9, the HPAI H5N1, and the pandemic H1N1 virus. Virus replication was monitored by measuring infectious viral particles using $TCID_{50}$. mRNA and protein expression of proinflammatory cytokines and chemokines were quantified by real time qPCR and ELISA. Results: We found extensive apoptosis in influenza H7N9 (both SH1 and SH2) and H5N1, but not H1N1pdm infected ex vivo lung tissues, suggesting that both avian influenza viruses can induce apoptosis and cause severe cell death in human lung tissue. Furthermore, unlike HPAI H5N1 which induces dysregulated proinflammatory cytokine responses, the novel influenza H7N9 virus elicited poor proinflammatory cytokine responses, inducing type I and III interferon in ex vivo human lung explant cultures. The novel influenza H7N9 virus is an intrinsically more potent inducer of proinflammatory cytokine than the H1N1pdm virus but less than the H5N1 virus. Conclusions: The proinflammatory cytokine and chemokine responses may contribute modestly to the severity of human H7N9 disease, but it is likely that direct viral cytopathology is probably playing a more important role in pathogenesis of human H7N9 diseases. The recognition of the role of cleaved caspase 3 in severe human infection of avian influenza virus can provide insights on the development of novel therapeutic approaches for the preparedness of the future outbreak of pandemics.

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Antigenic and genetic evolution of low pathogenic avian influenza viruses (H7N3) following heterologous vaccination

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Background: Italy experienced H7N3 low pathogenic avian influenza (LPAI) outbreaks between 2002 and 2004 in a densely populated poultry area in the northeast. The H7N3 virus was first detected in October 2002 in poultry. This virus continued to circulate and the infection was controlled by August 2003 by stamping out, control of movements, improved bio-security, and heterologous vaccination. A vaccination program was designed based on a “DIVA” strategy and was carried out using an AI inactivated heterologous H7N1 vaccine and implemented from December 2002 to August 2003. In 2003, the virus circulated in unvaccinated and vaccinated poultry farms. In September 2004, approximately 1 year after the depopulation of the last LPAI affected flock, the AI virus of the H7N3 subtype re-emerged. This occurrence required the application of strict control measures in association with the rapid implementation of a booster immunization of the susceptible population. During the 2002-2004 Italian LPAI H7N3 epidemic, a longitudinal collection of H7N3 viruses was obtained and archived. To shed light on the occurrence, temporal pattern and genetic basis of antigenic drift for avian influenza (AI) viruses in absence and presence of heterologous vaccination, these viruses were subjected to genetic and antigenic characterization. Materials and Methods: H7N3 AI isolates were selected in this study according to the following criteria: 1) year of isolation; 2) vaccination status of the flock from which they were isolated. A total of 37 H7N3 isolates were selected. In particular, 16 H7N3 isolates were isolated during the 2002 epidemic (no vaccination campaign in place); 11 isolates collected in 2003 from unvaccinated (4 viruses) and vaccinated flocks (7 viruses); and 10 H7N3 isolates sampled from vaccinated farms during the 2004 epidemic were analysed, the latter were all available viruses isolated in 2004. Turkey sera were generated against representative H7N3 isolated

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