

# Prolonged evolution of virus-specific memory T cell immunity after severe avian influenza A (H7N9) virus infection

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Since 2013, influenza A H7N9 virus has emerged as the most common avian influenza virus subtype causing human infection, and it is associated with a high fatality risk. However, the characteristics of immune memory in patients who have recovered from H7N9 infection are not well understood. We assembled a cohort of 45 H7N9 survivors followed for up to 15 months after infection. Humoral and cellular immune responses were analyzed in sequential samples obtained at 1.5 to 4 months, 6 to 8 months, and 12 to 15 months postinfection. H7N9-specific antibody concentrations declined over time, and protective antibodies persisted longer in severely ill patients admitted to the intensive care unit (ICU) and patients presenting with acute respiratory distress syndrome (ARDS) than in patients with mild disease. Frequencies of virus-specific gamma interferon (IFN- $\gamma$ )-secreting T cells were lower in critically ill patients requiring ventilation than in patients without ventilation within 4 months after infection. The percentages of H7N9-specific IFN- $\gamma$ -secreting T cells tended to increase over time in patients  $\geq 60$  years or in critically ill patients requiring ventilation. Elevated levels of antigen-specific CD8<sup>+</sup> T cells expressing the lung-homing marker CD49a were observed at 6 to 8 months after H7N9 infection compared to those in samples obtained at 1.5 to 4 months. Our findings indicate the prolonged reconstruction and evolution of virus-specific T cell immunity in older or critically ill patients and have implications for T cell-directed immunization strategies.