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Supplementary appendix

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Public health concerns regarding avian influenza A(H7N9) virus

Virology and Pathogenesis

- *LPAI A(H7N9) viruses are circulating widely among poultry in China, with increased spread from eastern to central and western China, and potential for introduction into adjacent Southeast Asia countries
- *Recent evolution from LPAI to HPAI A(H7N9) viruses¹
- *Demonstrated binding to human upper and lower respiratory tract tissues (ability to infect the human upper respiratory tract is thought to be a pre-requisite for increased transmission among humans)
- *Has molecular markers conferring increased virulence, adaptation, transmissibility, and pulmonary replication in mammals
- *Infection triggers dysregulated cytokine response resulting in pulmonary inflammation
- *Resistant to the adamantane class of antiviral drugs
- *Evolution into multiple antigenic groups in poultry, no longer matched by currently stockpiled vaccines based on older virus strains

Epidemiology

- *Unique as a LPAI virus causing high number of human infections with high mortality
- *Annual fall-winter-spring epidemics of human infections since 2013
- *Human infections in current 5th epidemic exceed total infections in 3 prior epidemics
- *Highest number of human infections of all novel influenza A viruses
- *Human infections have occurred in many new areas in eastern, central, and western China in 2017
- *Human infections continue to be associated with exposures to poultry at live bird markets in urban, semi-urban and rural areas, and while raising backyard poultry
- *Limited human-to-human transmission between family relatives and between unrelated persons
- *Human infections have been exported in travelers from mainland China to Taiwan, Malaysia, and Canada
- *High severity with mortality of approximately 40% in hospitalized patients
- *Sero-surveys suggest very limited immunity among humans of all ages
- *Overall denominator of infected persons is unknown

Clinical

- *Wide clinical spectrum from asymptomatic infection, upper respiratory tract illness, to severe pneumonia, respiratory failure, ARDS, refractory hypoxemia, and multi-organ failure
- *High proportion of hospitalized patients have critical illness, requiring intensive care and advanced organ support
- *Resistance to neuraminidase inhibitor (NAI) antiviral drugs reported during treatment
- *No clinical trials of investigational therapies in A(H7N9) patients, including for treatment of NAI-resistant infections (limited treatment options)
- *Nosocomial transmission (patient-to-patient, and patient-to-health care worker) reported
- *Potential for even more severe disease and extrapulmonary dissemination with HPAI virus infection

¹LPAI = low pathogenicity avian influenza; HPAI = highly pathogenic avian influenza. Sources: Published case reports and case series, WHO Disease Outbreak News, WHO Monthly Risk Assessment Summaries

Public health preparedness needs for A(H7N9) and other novel influenza A viruses

- Enhanced surveillance for human illness (mild and severe) and timely reporting of infections
- Enhanced virologic surveillance of novel influenza A viruses in infected humans, with timely sharing of genetic sequence data and virus isolates for analyses, and for assessment of candidate vaccine virus development
- Detailed epidemiologic investigations (including joint public health-animal health investigations) of sporadic cases and clusters of human infection and monitoring of exposed close contacts to assess human-to-human transmission; for early isolation, testing, and treatment of symptomatic persons
- Expanded surveillance of influenza A viruses in animals (poultry, pigs) at the human-animal interface to inform pandemic risk assessment and preparedness
- New approaches for the timely development of high yielding candidate vaccine viruses
- Development of vaccination strategies that elicit more broadly protective and longer lasting immunity
- Development of new therapeutics against novel influenza A virus targets, with effectiveness against neuraminidase inhibitor-resistant viruses
- Increased animal health laboratory capacity worldwide for detection, isolation, and characterization of influenza A viruses circulating among wild birds and domesticated animals (poultry, pigs)
- Improved respiratory infection prevention and control measures in health care settings worldwide to reduce nosocomial influenza virus transmission
- Establishment of on-going prospective, multi-year, multi-site, and multi-country clinical trial networks and platforms for conducting randomized clinical trials of investigational therapies, including combination treatments, for treatment of severe influenza

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