DEPARTMENT OF DEFENSE (AFHSB)
Avian Influenza A (H7N9) Surveillance Summary #78
21 JUN 2017 (next Summary 6 JUL 2017)

CASE REPORT: As of 21 JUN, according to WHO, FAO, China's National Health and Family Planning Commission (National HFPC) and provincial governments within China, the total influenza A (H7N9) human case count since the fifth seasonal epidemic of H7N9 began on 1 OCT 2016 is 906 (+17) cases with at least 269 (+30) deaths. The substantial increase in deaths reported since AFHSB's last summary is due to additional data included in the National HFPC monthly disease report for MAY. The number of new cases reported each week during the current seasonal epidemic has declined since the peak of activity in JAN 2017, with the Hong Kong Center for Health Protection (CHP) reporting 12 new cases for epidemiological week (EW) 23 (4 – 10 JUN) and just 5 new cases for EW 24 (11 – 17 JUN). The number of human cases identified this season accounts for approximately 51% of all human cases of H7N9 reported since 2013. The total case count since the disease was first identified in APR 2013 is 1,768 cases with at least 416 deaths (CDC reports at least 571 deaths as of 20 JUN) in China, Hong Kong, Macao, Taiwan, Malaysia, and Canada. All cases in Taiwan (6), Hong Kong (21), Macao (2), Malaysia (1), and Canada (2) are believed to have been imported from Mainland China. The overall case-fatality proportion among known cases is 33%; the average age of those affected is 55 years; and at least 455 (+3) (26%) of the cases reported have been female. The most recent known date of onset was 24 MAY. Since 2013, China has reported cases in 24 provinces and autonomous regions: Anhui, Fujian, Gansu, Guangdong, Guangxi, Guizhou, Hebei, Hubei, Henan, Hunan, Nei Mongol (Inner Mongolia), Jiangsu, Jiangxi, Jilin, Liaoning, Shaanxi, Shandong, Shaanxi, Shanxi, Sichuan, Tibet, Yunnan, Zhejiang, and Xinjiang; and four municipalities: Beijing, Chongqing, Shanghai, and Tianjin. During the fifth seasonal epidemic, cases have been reported from 23 different provinces and autonomous regions, and all four municipalities of China. Jiangsu Province has reported the most cases of any single province during this time period, 159 (18%) of 906 cases. On 19 JUN, FAO reported the first identification of H7N9 positive samples in poultry from a farm in Heilongjiang, which is China's northernmost province and borders Russia to the north and east. No human cases of H7N9 have been reported in Heilongjiang Province to date.

TRANSMISSION: In a CDC study published in APR 2015, H7N9 antibodies were found among 6.7% of case contacts identified between MAR 2013 and MAY 2014 in China, suggesting that human-to-human transmission does occur and could cause mild or asymptomatic infections. Since much of the reporting out of China occurs in monthly batches, with limited information on age, gender, and location, it is possible that only the most severe cases and fatalities are being reported by China. It is unknown how many mild or asymptomatic cases have occurred and how many cases have occurred without laboratory testing. This lack of information coupled with the infrequent reporting makes spatial and temporal cluster analysis difficult. CDC reports that at the conclusion of the fourth wave of H7N9, there had been 26 known disease clusters since the beginning of the outbreak in 2013, and that cluster-associated cases accounted for 7% of total reported cases. As of 21 JUN, AFHSB has identified 11 spatial clusters during this season of H7N9.

In a recent study in Nature Communications, researchers from Hong Kong University identified a mutation in the viral genome of H7N9—a unique nucleotide substitution (NS-G540A) acquired through prior reassortment with low pathogenic H9N2—which is responsible for its unique ability to circulate efficiently in avian hosts as well as replicate in mammalian cells. This particular mutation is also present in human infections with avian influenza subtypes H10N8 and H5N6. A recent Eurosurveillance study reported highly pathogenic H7N9 can mutate to include antiviral resistance during prophylaxis or treatment. In a 15 JUN PLOS Pathogens study, authors searched for mutations that might make H7N9 more transmissible among humans. They identified three mutations that could occur in the H7 hemagglutinin protein and would make the virus more likely to bind to human rather than avian airway receptors. The authors concluded that these findings could benefit risk assessment in the global surveillance of H7N9 in avian and human populations.

SURVEILLANCE: Reagents for surveillance testing purposes are available via the CDC website. NMRC has produced amplicon H7N9 positive testing control material using the published WHO primers/probes. Kits were sent to AFRIMS, NAMRU-3, NAMRU-6, NAMRU-2, Phnom Penh, NMRC-A, and NHRC for surveillance. Nineteen DoD laboratories were sent diagnostic kits, as have all 50 states, the District of Columbia, Puerto Rico, and more than 60 international labs.

INTERAGENCY/GLOBAL ACTIONS: On 26 JAN, the U.S. CDC announced a Level 1: Practice Usual Precautions travel advisory for China. U.S. CDC and WHO advise no special screenings at points of entry, and no trade or travel restrictions at this time.

(+xx) represents the change in number from the previous AFHSB Summary of 7 JUN 2017.
All information has been verified unless noted otherwise.
For questions or comments, please contact: dha.ncr.health-surv_list.afhs-jb-alert-response@mail.mil
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BACKGROUND: On 1 APR 2013, WHO reported three human cases of infection with a novel influenza A (H7N9) virus in China. This was the first time human infection with H7N9 had been detected. CDC believes the H7N9 virus is likely a reassortant of H7N3 viruses from domestic ducks and H9N2 viruses from other domestic poultry. Seasonality has been observed since the beginning of this outbreak with a consistent pattern of declining incidence through the summer months followed by a spike in cases in the winter months. Confirmed avian H7N9 has been rare and subclinical but has been previously identified. H7N9 is usually asymptomatic in birds and many bird owners are likely unaware of infections and the risk of transmission. Detection in birds requires routine active surveillance, which FAO reports has resulted in at least 4,242 virus-positive samples from the environment and chickens, pigeons, ducks, and wild birds since the beginning of the outbreak in 2013.

A recent CDC MMWR study reported that genetic sequences of 74 virus samples collected from infected persons or live bird markets during the fifth epidemic indicate H7N9 viruses have diverged into two distinct genetic lineages, the Pearl River Delta lineage and the Yangtze River Delta lineage; 69 of these samples were of the Yangtze River Delta lineage. CDC’s preliminary data suggests the Yangtze River Delta viruses are antigenically distinct from earlier H7N9 viruses and from existing candidate vaccine viruses (CVVs). On 2 MAR, experts from the WHO Global Influenza Surveillance and Response System recommended two new CVVs for development: 1) an A/Guangdong/17SF003/2016-like virus, which is a highly pathogenic virus from the Yangtze River Delta lineage; and 2) an A/Hunan/2650/2016-like virus, which is a low pathogenic virus also from the Yangtze River Delta lineage. On 23 MAY, CDC reported that development of the second of these two CVVs, which is matched to the H7N9 virus lineage that has predominated during the fifth seasonal epidemic, has been completed and is being shipped to various manufacturers in China. WHO posted information about the availability of this CVV on 18 MAY. On 12 JUN, China’s Ministry of Agriculture (MOA) announced it would initiate a H7 poultry vaccination program in Guangdong and Guaxi provinces in early JUL using a new recombinant, bivalent (H5 + H7), inactivated vaccine. Breeding farms in other provinces will also be able to carry out H7 vaccination following approval by their local veterinary authorities, and provincial veterinarians will be authorized to conduct emergency H7 vaccination to facilitate outbreak control.

RESEARCH & MEDICAL COUNTERMEASURES: On 27 FEB, WHO reported a change in the genetic sequence of isolates from two confirmed human H7N9 cases in Guangdong Province indicating the virus is evolving from a low pathogenic to a highly pathogenic avian influenza virus. Similar changes were also found in genetic sequence data from another recent case with travel history to Guangdong Province that was reported by Taiwan to WHO on 4 FEB. Following the identification of the first two human infections with highly pathogenic H7N9, provincial China CDC labs reportedly have been conducting genetic analyses of respiratory specimens from all confirmed human cases of H7N9 in the country. According to a CDC Emerging Infectious Diseases (EID) study on 1 JUN, there have been a total of eight human cases of infection with highly pathogenic H7N9 in three provinces (Guangdong, Guaxi, and Hunan) through MAR 2017.

China’s MOA notified OIE on 21 FEB that genetic sequences of virus samples from live poultry markets (LPMs) in Guangdong showed changes consistent with highly pathogenic avian influenza virus. As of 21 JUN, FAO and OIE have reported the highly pathogenic form of H7N9 in LPMs from Fujian, Guangdong, Guangxi, and Hunan provinces, and from farms and backyard flocks in Guaxi, Hebei, Henan, Hunan, Shaanxi, and Tianjin provinces. WHO has noted that there is no evidence this change from a low pathogenic to a highly pathogenic avian influenza virus has had any impact on the pathogenicity or transmissibility of H7N9 in humans. “Highly pathogenic” and “low pathogenic” refer only to the ability of influenza A viruses to cause disease in avian populations and do not describe disease severity, transmissibility, or pathogenicity of influenza A infections in human populations. However, the recent identification of a highly pathogenic form of H7N9 indicates yet another genetic change in the virus not observed in the previous four seasons and with unknown implications for human populations. A recent CDC EID study noted that highly pathogenic H7N9 viruses may pose a higher risk of zoonotic transmission as these viruses spread systematically within chicken[s] and are likely to be found at high titer in multiple organs while low pathogenic avian influenza viruses only infect the respiratory and intestinal tracts of birds.

A recent study from the Journal of Virological Methods describes a rRT-PCR assay developed to distinguish between highly pathogenic H7 virus and low pathogenic H7 virus. The study data showed that the new method is sensitive and gives specific results in detecting highly pathogenic H7 virus, and that it will play an important role in the rapid identification of highly pathogenic H7 virus.
Avian Influenza A (H7N9) Human Cases by Estimated Week of Onset
As of 21 JUN 2017 (N = 1,768)
*The above map does not include the recent identification of H7N9 on a farm in Heilongjiang Province. This map illustrates the geographic distribution of human H7N9 cases and H7N9-positive samples in birds or the environment in China since OCT 2015. Human cases are depicted in the geographic location where they were reported; for some cases, exposure may have occurred in a different geographic location. Precise location of 24 human cases in Anhui (2), Beijing (2), Guangdong (1), Guangxi (1), Hebei (3), Hunan (1), Hubei (2), Jiangsu (1), Jiangxi (6), Sichuan (2) and Zhejiang (3) provinces are currently not known; these cases are therefore not shown on the map.

Source: [FAO H7N9 Situation Update 14 JUN 2017](#)
Cumulative Human Cases of Avian Influenza A (H7N9)
1 APR 2013 - 21 JUN 2017

Cumulative Cases
(N = 1768*)
- No Reported Cases
- 1-15
- 16-25
- 26-115
- >115
- Imported Cases

*47 cases from China were reported without location information in 2015 – 2017

Season 1
APR 2013-SEP 2013
Season 2
OCT 2013-SEP 2014
Season 3
OCT 2014-SEP 2015
Season 4
OCT 2015-SEP 2016
Season 5
OCT 2016-JUN 2017

Since the beginning of the avian influenza A (H7N9) outbreak, spikes in cases have been associated with seasonality. These seasonal epidemics typically span 1 OCT to 30 SEP of the following year (see the above maps). These maps only illustrate autochthonous cases in China, not imported cases.