Avian influenza A H10N8--a virus on the verge?

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Avian influenza A H10N8—a virus on the verge?

Avian influenza A viruses of different subtypes sporadically infect people and cause a wide range of clinical outcomes, from asymptomatic infections to fatal pneumonia. Most infections result in no person-to-person pathogen transmission, but in some rare cases close contacts (eg, relatives or carers) can be infected. Of all the possible influenza A viruses with various combinations of haemagglutinin (H) and neuraminidase (N) genotypes circulating in wild birds, only a handful have been documented to have successfully crossed the bird–human species barrier, all of which had a domestic poultry intermediate. H6N1, H7N2, H7N3, H7N7, H9N2, and H10N7 viruses have caused conjunctivitis or mild respiratory symptoms, or both, in people, although some severe cases have been reported. Human infections with avian influenza A H5N1 and H7N9 viruses are more commonly detected and can result in fatal pneumonia. Live poultry markets seem to increase transmission of these viruses in birds and increase the number of human infections.

In December, 2013, Chinese health officials confirmed the first human case of avian influenza A H10N8 virus infection. In The Lancet, HaiYing Chen and colleagues report the clinical data for this case, which coincided with a second wave of avian influenza A H7N9 virus infections in eastern China. A woman aged 73 years was admitted to hospital and shown to have avian influenza A H10N8 virus infection, having become ill 4 days after visiting a live poultry market in Jiangxi province, China. The virus—designated as A/Jiangxi-Donghu/346/2013(H10N8), henceforth JX346—was identified by sequencing of tracheal aspirate samples obtained 1 week after illness onset. Preliminary phylogenetic analysis of the retrieved sequences suggests that JX346 originated through reassortment of H9N2 strains circulating in poultry and recorded in environmental samples from Jiangxi, with one or two viruses contributing haemagglutinin and neuraminidase genes. The data suggest that JX346 arose by reassortment events in domestic birds. JX346 has avian-like receptor specificity, which might contribute to the fatal outcome of infection. It was previously postulated that infection of lower lung sections expressing avian-like sialic acid receptors with avian influenza A H5N1 virus infection might determine the severity of infection outcomes.

So far, only two H10N8 viruses have been reported in China: one environmental isolate from a water sample in Hunan province, China, in 2007, and one from a live poultry market in southern China in 2012. However, phylogenetic analysis shows that JX346 is different from these previously identified viruses. Increased sampling efforts might identify the ancestors of JX346. Sequence analysis of the JX346 haemagglutinin gene shows no indications for a multibasic cleavage site, suggesting low pathogenicity in poultry. As for the newly emerged avian influenza A H7N9 virus, this low pathogenicity will make surveillance efforts substantially more difficult.

JX346 is the third virus strain generated by reassortment in avian species that are transmitted to people, and all internal gene segments (PB2, PB1, PA, NP, M, and NS) are derived from H9N2 viruses. This gene cassette might thus be a genetic platform for new strains with zoonotic potential.

As reported by Chen and colleagues, the woman infected with avian influenza A H10N8 virus had several underlying medical conditions (hypertension, coronary heart disease, and myasthenia gravis) and had undergone a thymectomy in December, 2012, which together probably resulted in substantial immune deficiency. So far, only one additional human case of avian influenza A H10N8 virus infection has been reported: on Jan 26, 2014, health authorities announced infection in a 55-year-old woman in Nanchang, Jiangxi province. This patient developed flu-like symptoms after visiting an agricultural market, and was admitted to hospital 1 week after onset of illness. More surveillance will be needed to establish the origin of H10N8 and monitor potential future transmission events.

Does H10N8 pose a pandemic threat? The introduction of a new influenza A subtype into people is always a public health concern. However, pandemic viruses are characterised by high transmission. Sustained person-to-person transmission has not been reported with influenza A virus subtypes other than H1, H2, and H3 viruses, and so far H10 viruses are no exception. JX346 did not successfully spread to close
contacts,1 and mild cases of H10N8 virus infection in Australia and Egypt did not transfer to exposed relatives.1 Experiments done to improve understanding of what is necessary for sustained transmission of avian H5N1 influenza A viruses in ferrets in laboratory settings10,11 showed several mutations throughout the viral genome (mainly in haemagglutinin and the polymerase complex) that are needed for this adaptation. Of those, JX346 shows PB1 polymorphisms at positions 99 and 368, which are associated with enhanced replication and transmissibility in ferrets, and the well characterised mammalian adaptation PB2 627KLYs. However, despite more than 15 years of H5N1 transmission events from birds to people, none of these mutations resulted in a strain that could be transmitted between people.13

How virulent is the H10N8 virus? Although H10N8 is predicted to have low pathogenicity in poultry and other avian species, it is too early to say anything conclusive about its virulence in people because of the small number of cases. Even for avian influenza A H5N1 and H7N9 viruses, the real frequency of mild and asymptomatic infections is unknown, despite the many deaths associated with human infections, because diagnosis and detection is generally done only when patients are admitted to hospital, and therefore is biased towards severe cases.

While increased surveillance might also be responsible for the increase in number of human infections with avian viruses, most human infections are associated with avian viruses containing the H9N2 internal gene cassette, on the basis of available sequences.13,14 Studies are needed to understand how this internal cassette helps avian influenza viruses seemingly well adapted to poultry to also jump more frequently into people and cause disease. More human cases of avian influenza A H7N9 virus infection have been reported in China in the past year than with H5N1 viruses since their emergence in 1997.10,11 Both reopening of live poultry markets and seasonality might have contributed to an apparent re-emergence of H7N9 human infections in the past month. Whether cases of avian influenza A H10N8 virus infection are going to increase is unknown, because how widely these viruses are circulating in poultry is unknown. More surveillance will be needed to establish the origin of H10N8 and to monitor potential future transmission events. Additionally, other new avian influenza virus subtypes, reassorting with H9N2 viruses, might emerge in the near future and cause human infections.

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AG-S has received remuneration for participation in scientific advisory boards for Vivaldi Biosciences, a privately held company that he cofounded, and Medivector; has consulted for Avirem; and holds patents related to vaccine development licensed to Vivaldi, Medimmune, and Avirem. MS declares that he has no conflicts of interest.

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