Changing epidemiological patterns in human avian influenza virus infections

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Explosive geographical expansion of the avian influenza virus (AIV) continues to threaten human and animal health during and after the COVID-19 pandemic. Individuals from 17 countries across five continents have been infected by the five emerging (H5N8, H10N3, H3N8, H10N5, and H5N2) and four re-emerging (H5N1, H5N6, H7N9, and H9N2) subtypes of AIV since 2019 (appendix). H5N1 viruses, especially those of clade 2.3.4.4b, continue to diversify genetically, spread geographically, and infect humans, as illustrated by the first ever human infection in Victoria, Australia,[1] in May, 2024, and a presumed novel transmission from dairy cattle to a dairy worker from Texas, USA,[2] in April, 2024. Moreover, high viral concentrations have been detected in unpasteurised milk from infected dairy cattle. A comprehensive sequence-based analysis suggested that the viruses isolated from wild birds, cows, cats, and humans in Texas during March, 2024, share the same origin, ie, infected migratory wild birds.[3] The ever-growing list of potential sources, such as alpacas,[4] dairy cows, goats,[2] civets,[5] and minks,[6] raises immense concern regarding the consequences of exposure to AIV.

In humans with AIV infection, extra-pulmonary, beyond-influenza-like conditions and symptoms at the onset of the illness, including conjunctivitis (ocular), diarrhoea (gastrointestinal), and seizures (neurological), warrant special attention.[7] Reports of two fatal mixed infections in humans—one involving H10N5 and seasonal H3N2,[8] and the other involving H5N1 and influenza B/Victoria lineage viruses[9]—suggest that mixed infections not only increase mortality risk but also reassort with human influenza viruses and potentially adapt the viruses to humans with a risk of triggering a pandemic. Immunisation, particularly of those at high risk of exposure, is recommended to reduce the risk of coinfection of AIV and seasonal influenza viruses. In addition, educating physicians on the risk factors and natural history of human AIV infection can increase awareness and improve diagnostic ability.

Understanding the delay between illness onset and pathogen identification and hospital admission can help to tailor early risk assessment and mitigation strategies to improve prognosis and limit the spread of AIV. Compared to a 10·7-day delay during 2003–13,[10] the median time-delay from illness onset to laboratory confirmation in human H5N1 cases has been reduced to 8 days since 2019 (appendix). However, the viral identification of emerging AIVs took even longer, such as the first H10N5 human case (53 days)[8] and the first H5N2 human case (35 days),[11] despite the former case having a clear history of poultry exposure. The time from illness onset to admission varies among inpatients infected by H9N2, H5N1, and H5N6 viruses owing to the differences in the virus genotype, patterns in exposure, disease progression, and health-care services. These delays have contributed to fatal outcomes among inpatients, with half of the fatal cases characterised by a delay of more than 7 days. Collecting and reporting temporal data on pathogen identification and hospital admission in a standardised manner are recommended for better risk assessment. Addressing health inequities and unmet medical needs is also necessary.

Given the unpredictable risk posed by AIVs, the implementation of One Health-based prevention and control strategies is essential. The main challenges requiring attention are disease detection and diagnosis. Although the gold standard for the diagnosis of AIV is RT-PCR testing, current resource and capacity limitations in many countries, such as issues with storing and transporting samples, restrict the amount of testing. Thus, enhanced deployment of rapid influenza diagnostic tests in both humans and animals, including neglected mammals that come in close contact with humans, is imperative.

To characterise zoonotic AIVs, viral sequencing at different outbreak stages should be encouraged to identify genetic changes that could facilitate adaptation to mammals or humans. Understanding the mechanisms that determine the host range and virulence of AIVs is essential to ensure optimal preparedness. Stricter biosecurity measures are required in all commercial farms where farm workers might be in direct contact with animals. Furthermore, education, training, and support among farm workers might enable better self-protection and disease management. Vaccines for farmed mammals are urgently needed, particularly for species with high economic value, to reduce viral spread and economic losses and provide secondary protection to farm workers.

Moreover, given the multiple detections of AIVs in produce such as uncooked meats and milk from farms susceptible to the virus, food safety measures should be strengthened. Considerable collaboration is required to address socio-economic inequalities; overcome the limitations in access to diagnosis, treatments, and vaccines; and update strategies to combat AIVs.

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