



# Global changes in the epidemiology of Highly Pathogenic Avian Influenza Viruses



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The recent worldwide distribution of (HPAIV) seriously impacts animal and public health, wildlife conservation, biodiversity, and agricultural productivity, especially poultry meat production and milk production in the near future. HPAIVs have been transmitted to poultry in many countries, causing high mortality and economic losses due to the mortality and mass culling of birds. In addition, recent reports of sporadic human infection with HPAIVs in association with close contact with infected poultry indicate the intrinsic potential of these viruses to cause a human pandemic in the future.

Since 2020, a dramatic change in ecology, epidemiology, and pathogenesis of HPAIV H5 subtype (clade 2.3.4.4b) viruses caused a worldwide expansion of these viruses, and

continuous mutations and adaptations finally caused the emergence of the clade 2.3.4.4b Eurasian lineage of H5N1 HPAIVs which were able to expand their geographic areas in Asia, Europe, and Africa, and eventually extending into North America (2021-2024), Central and South America (2022-2024), and the Antarctic (in February 2024), along with high mortality in a broad range of wild birds and different wild mammalian species, such as sea mammals, raccoons and foxes (1, 2). The recent transmission of these viruses to unusual hosts such as goats and dairy cows and the shedding of the virus via milk were significant milestones in the ecology and epidemiology of HPAIVs (3).

The segmented RNA genome of influenza A viruses allows them to have a high mutation rate and adaptability. A combination of 19 different hemagglutinin and 11

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neuraminidase proteins on the surface of influenza A viruses and eight genes encoding these and other proteins of these viruses brings an advantage of exchange rate among different strains (4, 5). This may facilitate expanding the host range of the new influenza viruses together with various levels of pathogenicity for previously resistant species.

Clade 2.3.4.4b of H5N1 HPAIVs already generated many different genotypes and new subtypes via reassortment with other LP or HPAIVs. Descending subtypes such as H5N6 and H5N8 viruses have shown an additional potential to infect different species, including humans. These viruses have been responsible for several epidemic waves of HPAI in different continents and caused high mortality and culling of tens of millions of poultry. The new waves of epidemics will continue to happen (6).

Infection of dairy cattle by clade 2.3.4.4b of H5N1 HPAIVs has caused clinical signs in affected cows and a decrease in milk production, and cattle-to-cattle transmission of the virus and high shedding of the virus in milk may facilitate the further transmission of the virus to humans and increase the concern regarding the generation of a pandemic HPAIV (3).

We need to revise national and international influenza outbreaks contingency planning documents, emergency management and risk assessment, HPAI prevention and control processes, monitoring and surveillance systems, including accurate and updated diagnostic tests, outbreak investigation, and compensation policies to mitigate long-term and sustainable health of humans, animals, and environment. Mammalian hosts play a significant role in the potential zoonotic adaptation of influenza A viruses, which may facilitate a human pandemic; therefore, we need to continue monitoring studies of avian and mammalian species, especially live birds, wild animals, dairy cattle farms, and animal markets. Developing countries with more vulnerable poultry production systems and lower capacity for rapid identification and eradication of HPAIV outbreaks should improve their surveillance, disease prevention, and sanitary systems, including even milking hygiene protocols.

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