

# MAMMALIAN SPREAD OF H5N1 AND ITS PANDEMIC POTENTIAL

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Avian influenza, or bird flu, is a highly contagious viral infection that primarily affects birds. Infrequently, the virus can infect mammals from birds, a phenomenon called spillover, and rarely can spread between mammals. There are several different subtypes of avian influenza viruses, ranging from low pathogenic to highly pathogenic types that can cause severe illness and death in birds. H5N1 is a highly pathogenic subtype of avian influenza that causes severe disease and death in birds. This subtype has caused a number of human infections through close contact with infected birds, or contaminated environments and is often fatal. Recent reports of H5N1 transmission between mammals therefore raise concerns about its potential to cause a human pandemic.

The H5N1 subtype has the potential to spill over to other mammals such as minks, ferrets, seals and domestic cats when the animals come in contact with infected birds or their feces or consume carcasses of infected birds and further serve as reservoirs. It is also possible that over time, the virus could evolve through mutations or recombinations with other influenza viruses to adapt to new hosts, leading to further outbreaks.

Recently, scientists have been investigating a potential mammalian spillover event after a mass mortality event which killed over 700 seals along Russia's Caspian Sea coast where a H5N1 variant was detected in wild birds a few months ago. More recently in February 2023, Peru reported cases of H5N1 avian influenza in sea lions and a dolphin, and a lion dying from H5N1 in a zoo. The U.K. has also reported deaths of otters and foxes due to infection by H5N1 subtype. In the past, seals and other mammals, such as foxes, minks, ferrets and domestic cats, have been reported to be infected by H5N1 through contact with birds. Wildlife, including foxes, coyotes and raccoons, often scavenge on infected birds or consume infected bird carcasses. However, the only recorded incidents of intra-mammal transmission of the virus have been among mink bred in close quarters in captivity at a farm in Spain, which were reported recently in 2022.

If the H5N1 variant of avian flu has evolved to be transmitted between mammals, there is a rare possibility of another evolutionary jump resulting in human transmission and outbreaks. The recent findings of transmission of H5N1 between mammals thus raise concerns on the potential for H5N1 to cause a pandemic in humans if it were to spill over and become transmissible among humans.

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The H5N1 avian influenza virus was first detected in 1996 on a goose farm in China. Subsequently, a major outbreak was reported in 1997 among poultry in Hong Kong, also leading to human infections of H5N1, which left 6 people dead and 18 infected. In 2004, H5N1 was reported in several countries in Asia, and further a global outbreak which continues to date. In 2013 and 2014, many countries in Europe and Asia reported H5N1 in poultry. Over the years the virus has caused outbreaks across the world, predominantly spread by migratory birds. Till date, over 800 cases of human H5N1 infections have also been reported, with a high fatality of 53%.

A new strain of H5N1, named 2.3.4.4b, emerged in 2020 and rapidly spread across Asia, Africa and Europe and subsequently to North and South America by 2021 and 2022, respectively. Many mammals were also infected in these outbreaks, including human infections. H5N1 sequenced from the mink farm in Spain also show several mutations, including (T271A) that enhances viral replication in mammalian tissues. The impact of this mutation in helping the virus spread to and among humans, therefore, remains unknown. Influenza H5N1 can rarely infect humans through direct contact with animals, but often causes severe disease and death. In addition, the widespread H5N1 outbreaks have substantial economic impact, resulting from significant losses to the poultry industry and threatening food and vaccine security (due to the use of eggs for vaccine production), apart from raising animal welfare and environmental concerns.

Preventing H5N1 spillovers and outbreaks requires a combination of measures including vaccination of poultry, safe disposal of dead birds, quarantine and culling of affected animals, wearing personal protective equipment when handling birds, and improved surveillance and monitoring of H5N1 in birds and other animals.

Human vaccines against H5N1 avian influenza have been designed to protect against the most severe forms of the disease. However, the highly mutable nature of the H5N1 virus could potentially decrease vaccine efficacy over time. Therefore, molecular surveillance of avian influenza and its subtypes is essential in understanding and responding to outbreaks. Genome sequencing can be employed to monitor mutations in the virus, the emergence of new subtypes, and keep a close watch on mutations and virulence factors that may increase the ability to infect humans. This can inform public health decisions and guide the deployment of more effective control measures.

In summary, although the risk of H5N1 to infect and spread among humans has been evaluated as low, disease and genomic surveillance as an integrated approach to controlling avian influenza are needed to keep a close watch on the outbreak. As we learned from the COVID-19 outbreak, monitoring the evolution of the shapeshifting virus can add to the preparedness against another potential pandemic.

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