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Hot News

The risk for pandemic avian influenza

The first fatal case of H5N1 avian influenza in humans was reported on January 6 in the United States (*CDC, 2025*). He has been called the "*Louisiana patient*." He was a 65-year-old man with several chronic diseases that was infected with the flu virus after being exposed to the poultry and wild birds he raised. He developed pneumonia and respiratory failure, which required admission to an intensive care unit, where he died a few weeks later.

The influenza virus is an RNA virus, such as SARS-CoV-2 (COVID-19), HIV (AIDS), Ebola, or hepatitis C. Uniquely, the flu virus has its genome divided into 8 fragments, which increases its capacity for mutation by genetic recombination.

Avian influenza is an infectious respiratory disease that usually affects birds. The D1 variant was first identified in Southeast Asia in 1996. Since then, it has been responsible for the most serious avian influenza epidemic in history. It has decimated the bird population in some regions of the planet.

Severe forms of avian influenza belong to the H5 and H7 variants. Since 1955, most outbreaks in birds have been caused by 3 lineages. In infected poultry, *subtype 2.3.4.4b* emerged and has spread throughout the world and has also infected a variety of mammals. The first outbreak in humans was described in 1997, with 18 sick and 6 deaths. All had been exposed to infected birds.

During recent decades, a growing number of cases have been described in mammals, such as foxes that fed on dead and infected birds. In South America, outbreaks of H5N1 infection in sea lions have devastated their populations in some regions. In Spain, in 2022, there was an outbreak of avian flu in Galicia on a fur farm where 50,000 minks were raised, which were slaughtered.

So far, the circulating variant of avian influenza H5N1 only jumps from animals and infects humans in cases of very close and prolonged exposure. That is why they are sporadic and almost all in personnel with occupational exposure to birds or other animals (farmers, veterinarians, etc.).

The most unexpected and concerning change in H5N1 occurred in 2024 in Texas, when the virus became isolated in dairy cattle. Since then, more than 700 farms in the U.S. have reported cattle cases of H5N1. The new variant of the virus replicates in the mammary glands of infected cows, making unpasteurized milk a dangerous source of contagion.

During the year 2024, 66 human cases of H5N1 avian influenza were identified in the USA, almost all in patients with mild clinical manifestations (*Garg et al. N Engl J Med 2024*). All were zoonoses, that is, infections after exposure to infected animals. They harbored the D1.1 genotype from birds or the B3.13 genotype from cows. No cases of human-to-human transmission have been reported so far.

Genome studies in wastewater are an effective tool for monitoring the circulation of viruses in distinct communities. These analyses have become very relevant for epidemiological surveillance and epidemic prevention by public health agencies. In the United States, recent studies have alerted to the growing and widespread circulation of H5N1 in multiple regions (*Tisza et al. N Engl J Med 2024*).

The possibility of mutating H5N1 into forms with easy human-to-human transmission would be the prerequisite for an epidemic outbreak and an eventual pandemic (*Lin et al. Science 2024*). On the other hand, it remains to be seen how pathogenic a pandemic variant of H5N1 could be. In contrast to the high mortality of avian influenza in humans described in Southeast Asia and Egypt, the severity has been low in the human cases reported so far in North America (*Ison & Marrazzo. N Engl J Med 2024*).

Unlike COVID-19, there are already vaccines and antivirals to confront H5N1. The biggest challenge would be in its rapid and wide accessibility. Regarding vaccines, seasonal flu vaccines may produce some cross-protection and could be useful before specific vaccines are available. The CDC has recently reviewed the use of antiviral treatment in influenza to reduce the risk of developing resistance to oseltamivir and baloxavir. To this end, it recommends considering prolonging treatment beyond 5 days, doubling the dose and using combinations of antivirals.

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