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First confirmed human case of H5N2 virus infection in Mexico: an emerging zoonotic concern

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Dear Editor,
H5N2, a subtype of the avian influenza A virus, primarily infects birds (chickens, ducks, turkeys, ostrich, falcons, wild birds). Its impact varies based on whether it is a highly pathogenic (HPAI) or low pathogenic (LPAI) strain [1, 2]. HPAI-H5N2 can cause severe disease and high mortality rates in birds, often requiring the culling of thousands of birds in poultry farms. LPAI-H5N2 results in milder symptoms, and infected birds often do not appear ill. H5N2 spreads through direct contact with infected birds or contaminated environments, similar to other avian influenza viruses [3]. In 2004, LPAI-H5N2 [4] was detected in ducks on a farm in South Korea. The following year, it affected 40 chicken farms in Japan, culling >5.7 million birds. In 2006, an outbreak on a farm in South Africa destroyed 60 ostriches. In 2007, 25,000 turkeys were culled in the USA, and 15 roosters and two hens were killed in the Dominican Republic despite showing no symptoms. Haiti experienced three outbreaks in 2008 involving chickens, turkeys, and fighting cocks in different locations. A 2009 outbreak in Canada led to the culling of 60,000 turkeys to prevent further virus spread, and a similar outbreak in Sri Lanka in 2012 destroyed 6,000 chickens. Another outbreak involving ducks was reported in Canada in 2016 [5-7].
The HPAI-H5N2 outbreaks have been significant [4]. In 1983, chickens and turkeys in the USA were affected. Mexico had poultry outbreaks in 1994 and 1995, which were controlled following vaccination. Another outbreak was reported in March 2024, followed by Italy in 1997 [7, 8]. Taiwan and South Africa reported outbreaks in 2012, resulting in the culling of 41,000 ostriches. In 2015, the USA faced further outbreaks in chicken and turkey farms, leading to the mass culling of >50.5 million birds to contain the virus. That same year, the largest US egg producer saw 30 million chickens killed, causing severe economic losses and a surge in egg prices. In 2017, H5N2 was detected in a duck in the USA

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and first reported in Russia, leading to the culling of over 660,000 birds.

Another subtype of influenza A virus is HPAI-H5N1 [9]; ten human infections were reported in 2024. Notably, three of these were due to cow-to-human-transmission, marking the first documented instances in dairy cattle [10]. Since 2003, H5N1 has resulted in 892 cases and 463 deaths across 24 countries, reflecting a very high CFR of 52%. Initially circulating primarily in birds, the virus has spread to mammals, including mink, goats, bears, foxes, sea lions, farmed goats, mountain lions, dolphins, seals, coyotes, otters, skunks, squirrels, cats, and dogs [11]. In contrast, H5N2 is less commonly reported in mammals and primarily infects birds. Although zoonotic transmission of H5N2 to humans is rare, a possible first human transmission was reported in Japan in 2005 following a chicken outbreak. Seropositive antibodies were detected in 257 workers at 35 chicken farms, none of whom reported any symptoms [12]. Another report from Nigeria documented clinical features of conjunctivitis in seropositive humans [13]. These instances suggested the possible zoonotic transmission of H5N2, though it remains uncommon. This distinguishes H5N2 from other avian influenza subtypes like H5N1, which have a higher zoonotic potential and have caused significant human illness. The geographical spread of H5N2 is more limited and less virulent than H5N1, posing minimal risk to humans. Both subtypes have led to significant economic losses in the poultry industry due to the need for culling, with more drastic measures for H5N1 due to its severe impact on human health.

On May 23, 2024, LPAI-H5N2 was confirmed in a 59-year-old in Mexico with multiple underlying conditions, who had been hospitalised on April 17, with symptoms including shortness of breath, nausea, diarrhoea, and fever, and subsequently died on April 24 (Figure 1) [14]. The death was not associated with the infection. The patient had no history of exposure to poultry or other animals, and it is unclear if there is a connection to the ongoing outbreaks of poultry within the state. However, after sequencing analysis of the respiratory sample, the H5N2 virus found in the infected individual exhibited a 99% genetic match to the LPAI-H5N2 strain previously identified in birds in the nearby state of Texococo. This is the first confirmed human case of H5N2 virus infection globally and the first instance of avian H5 virus infection in Mexico. Although the current risk to the general population from this initial H5N2 human case is low, the infection highlights a potential new zoonotic threat. H5 viruses do not currently spread between humans, but this could change. Other outbreaks in the last 5 years have included SARS-CoV-2 [15], MERS [16], Ross River virus [17-19], Oropouche virus [20], Japanese encephalitis [21], Murray Valley encephalitis [22], tomato flu, hand-foot-mouth disease [23] and monkeypox virus [24, 25]. In order to prevent human infections of H5N2 and other H5 influenza viruses such as H5N6 [26], it is relevant to develop vaccines. Also, therapeutic drugs are needed

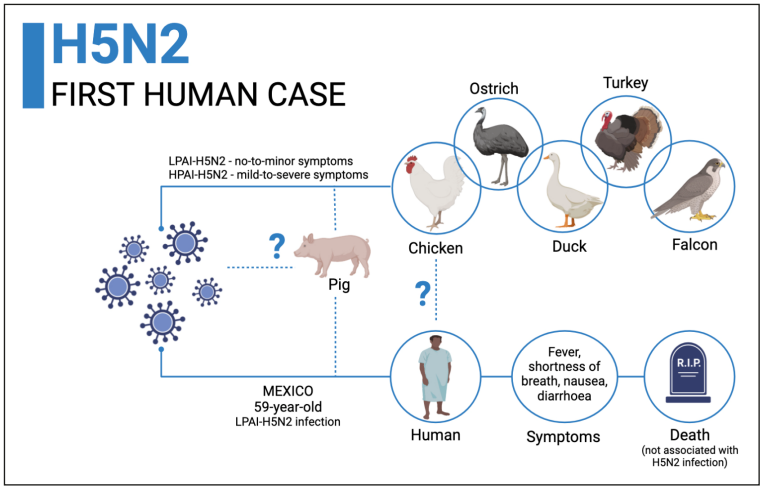

Figure 1
The first recorded H5 virus was in Mexico, and the first globally recorded human H5N2 infection was on May 23, 2024. In Mexico, a 59-year-old who presented with shortness of breath, fever, and diarrhoea was admitted to the hospital on April 24, 2024, and died the same day; an LPAI-H5N2 virus infection was confirmed but not associated with the death. This infection highlights a potential new zoonotic threat to humans. Figure made using biorender.com.

Abbreviations: HPAI-H5N2, highly pathogenic avian influenza virus subtype H5N2; LPAI-H5N2, low pathogenic avian influenza virus subtype H5N2.

[27-31]. Additionally, improving diagnostic methods for its detection is essential to prompt treatment initiation. In the event of a confirmed or suspected human infection with the LPAI-H5N2 virus, which has pandemic potential, a comprehensive epidemiologic study should be conducted, even while awaiting lab confirmation of a suspected case. This should include contact tracing as well as a thorough history of animal exposure and travel. Identifying any unusual events that might indicate person-to-person transmission of LPAI-H5N2 is important. Clinical samples from suspected cases should be collected, tested, and forwarded for further characterisation

Conflict of interest
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Author contributions
All authors contributed to this letter. Vasso Apostolopoulos and Ranjit Sah, contributed equally and may be considered both first author.

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