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Emergence of a human co-infected with seasonal influenza A (H3N2) virus and avian influenza A (H10N5) virus, China, December 2023

KEYWORDS
Emergence;
H10N5;
Cross-species transmission;
Avian influenza virus

Dear Editor,

We read with interest a recent paper in Journal of Microbiology Immunology and Infection that reported Human infection caused by avian influenza A (H10N5) virus in China.[1] Although avian influenza viruses (AIVs) have a diverse range of hosts, human infections with avian influenza are typically associated with subtypes such as H5Nx, H7N9, and H9N2.[2,3] However, on January 27, 2024, the World Health Organization (WHO) reported the death of a 63-year-old woman in Anhui Province, China, due to co-infection with seasonal influenza A (H3N2) subtype virus and avian influenza A (H10N5) subtype virus.[4] Undoubtedly, this is the first time that human infection with H10N5 occurred.

On November 30, 2023, the patient chose to be hospitalized at a local hospital after experiencing symptoms of coughing, sore throat, and fever. Subsequently, on December 7, she was transferred to a neighboring medical institution in Zhejiang Province. Unfortunately, the patient passed away on December 16. Zhejiang Province health officials isolated seasonal influenza A (H3N2) subtype virus and avian influenza A (H10N5) virus from the patient's samples on January 22, 2024. Through investigation and detection, the patient had exposure to live poultry through the purchase of a duck on 26 November 2023. From the duck meat stored in the fridge, seven samples were found to be positive for H10N5 and two sample were positive for N5 (no result for haemagglutinin). It is understood that the patient had close contact with ducks before the onset of symptoms. As of now, no new suspected cases of human infection have been found.

Table 1 Homology analysis of 8 protein nucleotide sequences of ZJU01 strain (H10N5).

Segment	Strains	Accession	Similar (%)
PB2	A/*Anser albifrons*/South Korea/22JN-163-1/2022(H10N7)	OQ296821.1	98.73
PB1	A/Mallard (*Anas platyrhynchos*)/South Korea/KNU2021-17/2021(H3N8)	ON495686.1	98.04
PA	A/duck/Tottori/311215/2020(H5N2)	LC656332.1	98.39
HA	A/*Anser albifrons*/South Korea/22JN-163-1/2022(H10N7)	OQ296824.1	98.64
NP	A/duck/Vietnam/HN5076/2018(H5N3)	MW935999.1	97.57
NA	A/environment/Bangladesh/52110/2022(H10N5)	OP572292.1	98.34
M	A/Bean Goose (*Anser fabalis*)/Korea/KNU10/2022(H10N7)	OR674058.1	99.22
NS	A/Bean Goose (*Anser fabalis*)/Korea/KNU10/2022(H10N7)	OR674059.1	99.77

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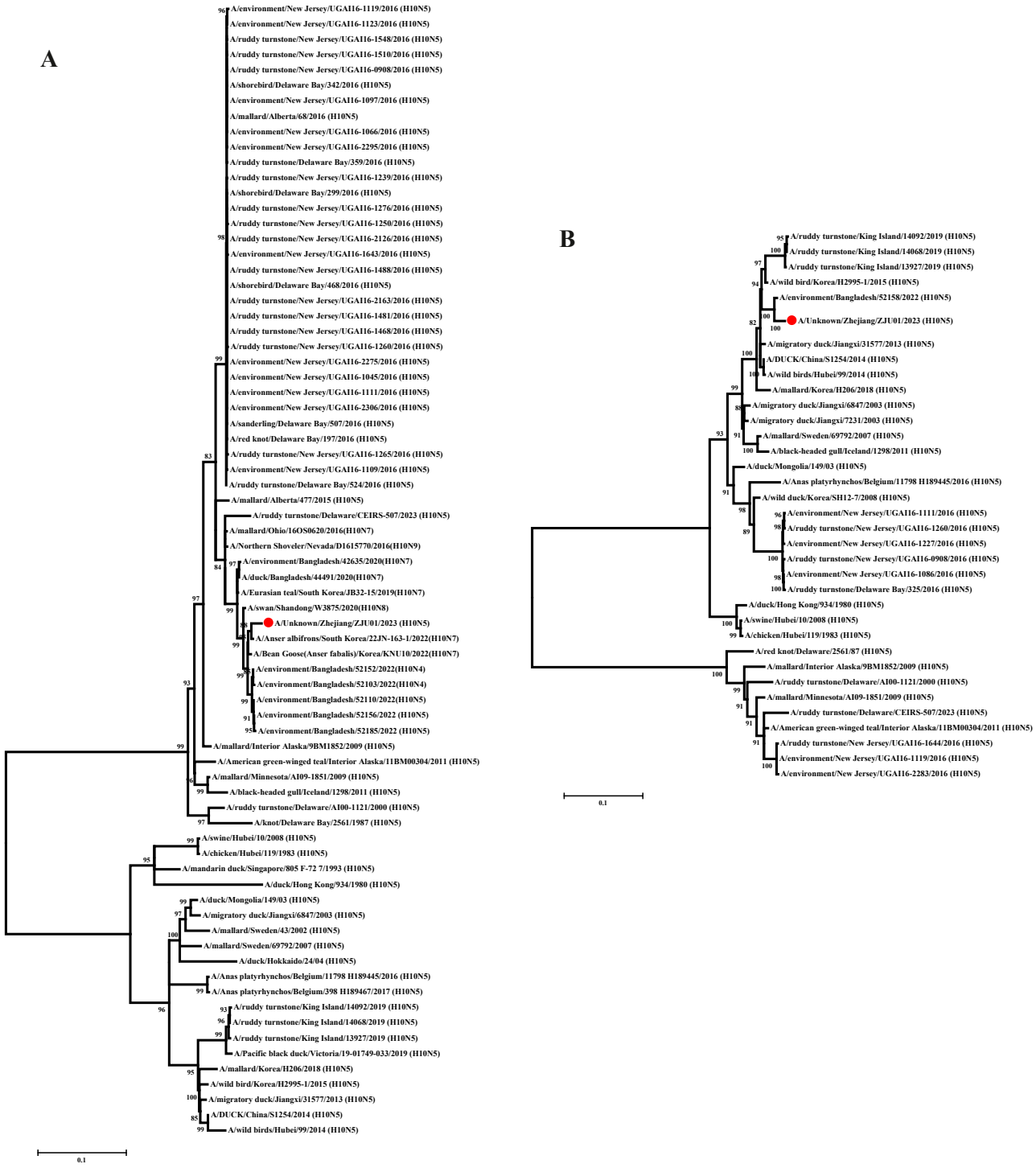

Figure 1. Phylogenetic analysis base on HA (A) and NA (B) gene of ZJU01/H10N5. The reference sequences were extracted from the GISAID and GenBank database. Phylogenetic trees were constructed using the maximum likelihood method with the best-fit model GTR + F + I in MEGA 7.0. Bootstrap majority consensus values based on 1,000 replicates are indicated at each branch point as a percentage.

BLAST searches in the GenBank database revealed that the ZJU01/H10N5 HA and NA segments in this case showed the highest nucleotide homology with A/*Anser albifrons*/South Korea/22JN-163-1/2022 (H10N7) and A/environment/Bangladesh/52110/2022 (H10N5), with identities of 98.64% and 98.34%, respectively (Table 1). Regarding the internal genes of ZJU01/H10N5, the PB2, PB1, M, and NS segment sequences exhibited high similarity

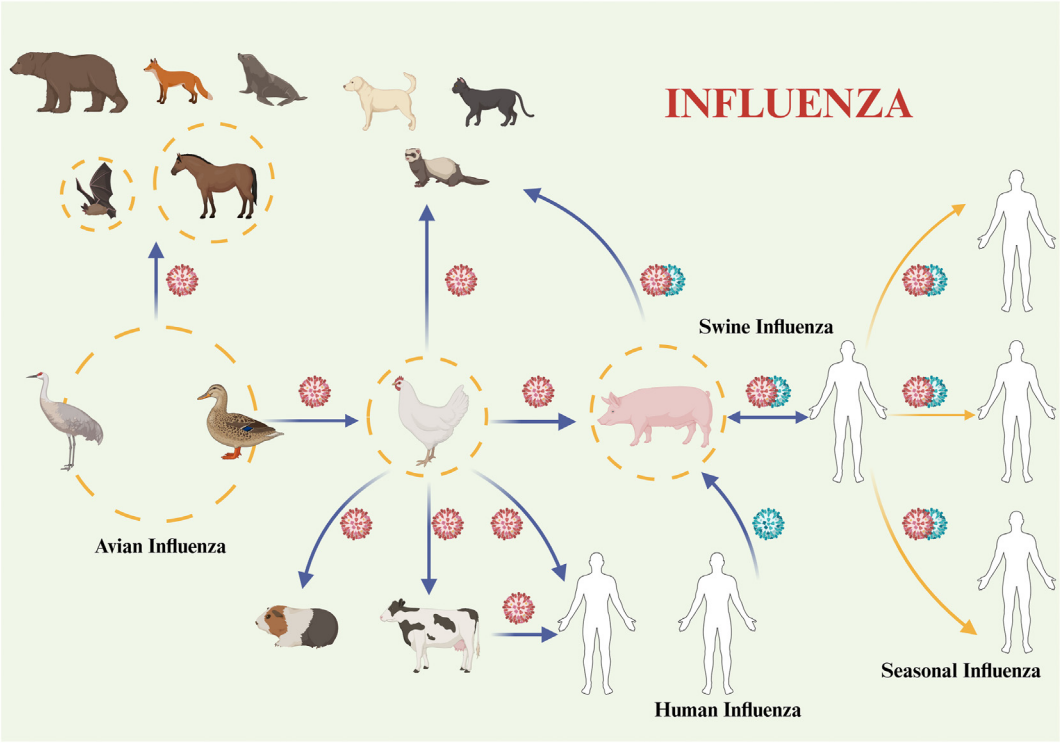

Figure 2. Diagram of Influenza Transmission Hosts. Certain subtypes of Influenza A virus (red virus) dominate and circulate within specific species (yellow dashed circles), achieving cross-species transmission through adaptive mutations (blue arrows). Pigs serve as mixing vessels, capable of being infected by both avian influenza viruses and human influenza viruses (green virus). In pigs, different influenza viruses may reassort, creating a new virus (red-green virus), which can then cross the species barrier and spread among humans.

to viruses identified in birds in South Korea, while the PA and NP segment sequences showed high similarity to those in Japan or Vietnam. The phylogenetic tree results indicated that the ZJU01/H10N5 HA and NA genes clustered within the avian-origin branches without forming new branch (Fig. 1).

In China, the seasonal influenza A (H3N2) subtype virus is one of the major strains transmitted during the flu season, and typically occurring in winter.[5] Infected individuals can spread the virus among the population through forms such as coughing, sneezing, or speaking. In contrast, the H10N5 originates from birds and usually does not have the ability to infect humans. Therefore, infections of H10N5 in human populations are rare. However, human infections can also occur when individuals have other complications that lead to a weakened immune system, or when a person's eyes, nose, or mouth are exposed a sufficient amount of virus.

The cross-species transmission of avian influenza is typically associated with HA receptor-binding characteristics. As we know, wild birds are the natural reservoirs for AIV, while pigs serve as mixing vessels (pig possess both α-2,3 sialic acid receptors and α-2,6 sialic acid receptors).[6] Different influenza strains may reassort within pigs, and acquire the ability for crossing the species barrier (Fig. 2). Briefly, the determinants for the transmission of influenza viruses across species barriers depend on the presence of corresponding sialic acid receptors on host cell membranes. The receptors recognized by seasonal influenza viruses are α-2,6 sialic acid receptors (on the human nasal cavity and upper respiratory tract), while those recognized by AIV are α-2,3 sialic acid receptors (on the intestines of birds and lower respiratory tract of humans).[7] Through multiple sequence alignment analysis, although we did not reveal previously reported key mutation sites, we identified three amino acid diversification sites in ZJU01/H10N5 HA: 145R, 246V, and 248K (Supplementary Table 1).[8] The functional implications of these mutation sites are currently unknown. Additionally, PB2 is a crucial protein for the pathogenicity of influenza viruses. However, we did not observe significant amino acid iterations in the key residues of H10N5 PB2 (Supplementary Fig. 1).

In conclusion, ZJU01/H10N5 likely does not possess the ability to transmit among humans based on the available epidemiologic information and genomic analysis.[2,9] Therefore, this outbreak is most likely an isolated case of interspecies transmission from birds to humans. It is worth noting that cross-border migration of infected wildlife may increase the likelihood of human co-infection, highlighting the importance of international information sharing in the face of influenza outbreaks. Importantly, we must not overlook the potential risks posed by co-infection of H3N2 and H10N5 to public health, as such combinations could potentially result in fatalities. Hence, it is recommended to strengthen research on influenza vaccines and develop targeted vaccines to prevent the risk of simultaneous infections by these viruses.

CRediT authorship contribution statement

Zimin Xie: Writing — original draft. **Fengxiang Xu:** Validation. **Rongmao Chen:** Software. **Ming Liao:** Writing — review & editing. **Manman Dai:** Writing — review & editing, Funding acquisition.

Declaration of competing interest

The authors declare no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jmii.2024.07.008.

References

1. Lai CC, Hsueh PR. Human infection caused by avian influenza A (H10N5) virus. *J Microbiol Immunol Infect* 2024;**57**(3):343—5.
2. CDC. *Influenza type A viruses*. 2024. Published, https://www.cdc.gov/flu/avianflu/influenza-a-virus-subtypes.htm. [Accessed 19 March 2024].
3. Philippon DAM, Wu P, Cowling BJ, Lau EHY. Avian influenza human infections at the human-animal interface. *J Infect Dis* 2020;**222**(4):528—37.
4. WHO. *Avian influenza A(H10N5) and influenza A(H3N2) coinfection - China. Published 2024*. https://www.who.int/emergencies/disease-outbreak-news/item/2024-DON504. [Accessed 19 March 2024].
5. Zhang B, Huang W, Pei S, Zeng J, Shen W, Wang D, et al. Mechanisms for the circulation of influenza A(H3N2) in China: a spatio-temporal modelling study. *PLoS Pathog* 2022;**18**(12):e1011046.
6. Ma W, Lager KM, Vincent AL, Janke BH, Gramer MR, Richt JA. The role of swine in the generation of novel influenza viruses. *Zoonoses Public Health* 2009;**56**(6—7):326—37.
7. Mair CM, Ludwig K, Herrmann A, Sieben C. Receptor binding and pH stability—how influenza A virus hemagglutinin affects host-specific virus infection. *Biochim Biophys Acta Biomembr* 2014;**1838**(4):1153—68.
8. Suttie A, Deng YM, Greenhill AR, Dussart P, Horwood PF, Karlsson EA. Inventory of molecular markers affecting biological characteristics of avian influenza A viruses. *Virus Gene* 2019;**55**(6):739—68.
9. L S. *Ducks identified as source of H10N5 avian flu in Chinese woman's coinfection*. 2024. Published, https://www.cidrap.umn.edu/avian-influenza-bird-flu/ducks-identified-source-h10n5-avian-flu-chinese-womans-coinfection. [Accessed 19 March 2024].

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