

A(H5N1) Avian Influenza Virus: A New Pandemic Threat on the Horizon?

Giovanni Di Guardo^(a)

^(a) Retired Professor of General Pathology and Veterinary Pathophysiology at the Veterinary Medical Faculty of the University of Teramo, Localita' Piano d'Accio, 64100 Teramo, Italy.

Correspondence to: gdiuardo@unite.it

Published: 2 Jun 2024

Keywords: A(H5N1) avian influenza virus; viral neurotropism; viral neuropathogenicity; zoonoses; zoonotic pathogens; interhuman transmission; pandemic potential; One Health.

Abstract

The present Editorial deals with the highly pathogenic avian influenza (HPAI) virus A(H5N1), whose clade 2.3.4.4b has been identified in several domestic and wild bird and mammalian species, both terrestrial and aquatic, with mass mortality outbreaks also affecting South American sea lions.

Within this fast evolving scenario, the progressively and consistently expanding range of virus-susceptible host species alongside the prominent viral neurotropism and neuropathogenicity are a matter of concern, with A(H5N1) virus having additionally spread among USA cattle, which may also shed it through their milk.

© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License (<https://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, sharing, adaptation, distribution and reproduction in any medium or format, for any purpose, even commercially, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

Although it is not happening at the moment, the possibility A(H5N1) virus may sooner or later become easily transmissible between people appears to be largely plausible.

A collaborative, intersectorial and multidisciplinary approach, based upon the "One Health" concept/principle is strongly needed in order to properly counteract the global menace brought about by the HPAI A(H5N1) virus, thereby taking inspiration from the lessons learned during the COVID-19 pandemic.

Editorial

The remarkable neurotropism and neuropathogenicity exhibited by the highly pathogenic avian influenza (HPAI) virus A(H5N1) in several bird and mammalian hosts - with special reference to the 2.3.4.4b viral clade - are a matter of concern, together with the largely and rapidly expanding number of virus-susceptible animals, including several species phylogenetically distant from each other (1-6). Additional worrisome issues are represented by the transmission of A(H5N1) virus from wild birds to cattle, with cows from 9 States in USA having tested positive to laboratory investigations (7). Noteworthy, while most infected bovines tend to develop mild clinical signs - with the subsequent risk of getting A(H5N1) avian influenza virus frequently undetected in cattle - consistent amounts of viral infectivity may be also found in raw, unpasteurized cow milk (8). In this respect, a surprisingly high expression of both the avian - sialic acid (SA) α -2-3-galactose (gal) - and the human - SA- α -2-6-gal - influenza virus receptors has been recently reported within the mammary gland tissue (but not in the upper airways and in the brain) from cattle (9), thus "candidating" the bovine species as a new "mixing vessel" potentially allowing the genetic reassortment/recombination between influenza viruses originating from different animal sources, as it "historically" happens in pigs with avian and human viruses (9). Although there is a paucity of studies aimed at defining how A(H5N1) avian influenza moves between cattle and people, one dairy worker in Texas - where the first case of this viral infection in cows was ascertained in March 2024 - developed a bilateral, virus-induced conjunctivitis (10), followed by a similar ocular disease case ascertained thereafter in another farm worker from Michigan (<https://www.nytimes.com/2024/05/22/health/h5n1-bird-flu-dairy.html>).

Noteworthy, despite the almost 900 human cases of A(H5N1) viral disease which have been reported from 2003 until now by the World Health Organization (WHO) - 52% of which being characterized by a lethal outcome - an efficient and sustained interhuman infection transmission's chain of such viral pathogen has never been documented, thus far. Nevertheless, based upon the high propensity of influenza viruses to undergo mutations in their genomic make-up through the well-known mechanisms of genetic reassortment/recombination, coupled with the rapidly and consistently expanding viral host range, the possibility the A(H5N1) virus will become easily transmissible between people, thereby acquiring a "pandemic behaviour", appears to be more than plausible (1).

Consequently, an "ad hoc" robust and multidisciplinary "preparedness and readiness effort", strongly relying on the lessons learned from the COVID-19 pandemic and accompanied by a close intersectorial collaboration between human and veterinary medicine, is urgently needed in order to properly counteract this alarming scenario, within a sound One Health perspective's framework.

Declarations

Conflict of Interest

The Author declares that there is no conflict of interest.

References

1. Di Guardo, G., Roperto S. (2024). AH5N1 avian influenza, a new pandemic behind the corner? (Rapid Response). BMJ <https://www.bmj.com/content/380/bmj.p510/rr>.
2. Ariyama, N., et al. (2023). Highly Pathogenic Avian Influenza A(H5N1) Clade 2.3.4.4b Virus in Wild Birds, Chile. *Emerg. Infect. Dis.* 29:1842-1845. doi: 10.3201/eid2909.230067.
3. Puryear, W., et al. (2023). Highly Pathogenic Avian Influenza A(H5N1) Virus Outbreak in New England Seals, United States. *Emerg. Infect. Dis.* 29:786-791. doi: 10.3201/eid2904.221538.
4. Gamarra-Toledo, V., et al. (2023). Mass Mortality of Sea Lions Caused by Highly Pathogenic Avian Influenza A(H5N1) Virus. *Emerg. Infect. Dis.* 29:2553-2556. doi: 10.3201/eid2912.230192.

5. Thorsson, E., et al. (2023). Highly Pathogenic Avian Influenza A(H5N1) Virus in a Harbor Porpoise, Sweden. *Emerg. Infect. Dis.* 29:852-855. doi: 10.3201/eid2904.221426.
6. Murawski, A., et al. (2024). Highly pathogenic avian influenza A(H5N1) virus in a common bottlenose dolphin (*Tursiops truncatus*) in Florida. *Commun. Biol.* 7:476. doi: 10.1038/s42003-024-06.
7. Reardon, S. (2024). Bird flu in US cows: Where will it end? *Nature* <https://www.nature.com/articles/d41586-024-01333-9>.
8. Gerhard, D. (2024). Deciphering the unusual pattern of bird flu symptoms in cows. *The Scientist Magazine*. <https://www.the-scientist.com/deciphering-the-unusual-pattern-of-bird-fl....>
9. Kristensen, C., et al. (2024). The avian and human influenza A virus receptors sialic acid (SA)- α 2,3 and SA- α 2,6 are widely expressed in the bovine mammary gland. *bioRxiv* 2024. 05.03.592326.
10. Uyeki, T.M., et al. (2024). Highly pathogenic avian influenza A(H5N1) virus infection in a dairy farm worker. *N. Engl. J. Med.* doi: 10.1056/NEJMc2405371.