

Highly pathogenic avian influenza A(H5N1) virus: How far are we from another pandemic?

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Abstract

The present Editorial deals with the pandemic risk brought about by the highly pathogenic avian influenza A(H5N1) virus. Such pandemic alarm is justified, among others, by the progressively and rapidly expanding range of virus-susceptible hosts, including humans alongside a huge number of domestic and wild avian and mammalian species, several of which distantly related to each other. Despite its documented zoonotic potential, no clear-cut evidence of viral interhuman transmission has been thus far reported. Should this happen sooner or later, it could pave the way for a new pandemic.

Keywords: highly pathogenic avian influenza.

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Editorial

While the COVID-19 pandemic cannot be considered yet behind our shoulders, due to the repeated appearance of new SARS-CoV-2 variants and subvariants able to bypass the population's immunity conferred by infection and/or vaccination, the highly pathogenic avian influenza (HPAI) A(H5N1) virus is increasingly perceived as a global threat.

Since its first description in 1959 in Scottish poultry farms [1], the A(H5N1) virus was subsequently identified in 1996 in intensively reared ducks and chickens from China [2], with the first human infection case having been additionally reported in 1997.

Nowadays, approximately 1,000 disease episodes caused by HPAI A(H5N1) virus (mostly characterized by severe pneumonia and, occasionally, by encephalitis) have been ascertained in people on a global scale, with a 50% case-fatality rate and with 23 different Countries being also affected [3].

Within this framework, the recent migratory bird-driven spread of A(H5N1) virus clade 2.3.4.4b to a huge and progressively growing number of domestic and wild avian and mammalian host species from Eurasia, North and South America, up to the Arctic and Antarctica regions - including South American sea lions (*Otaria flavescens*) and elephant seals (*Mirunga leonina*) as well as a polar bear (*Ursus maritimus*) in Alaska [4-6] -, is of concern, according to the Scientific Community, the World Health Organization, the World Organization for Animal Health and the public health Authorities from many European and extra-European Countries. More in detail, the consistent viral neurotropism and neuropathogenicity [6,7], coupled with a high infection's lethality rate and the well-established propensity of influenza viruses to undergo mutations [8] - especially at the level of haemagglutinin and polymerase genes -, are of crucial relevance, given the already threatened health and conservation status of several A(H5N1) virus-susceptible wildlife species.

Indeed, the aforementioned mutations have allowed, and continue still to allow, a successful pathogen's adaptation to a consistent and progressively growing number of avian and mammalian hosts, including species that are phylogenetically distant from each other. The last one in

chronological order is represented by the ovine species, with a case of A(H5N1) viral infection having been recently reported in a sheep from Yorkshire [9].

Within such context, cattle are of significant concern, given their well-known susceptibility to HPAI A(H5N1) viral clade 2.3.4.4b. As a matter of fact, since the bovine mammary gland may be targeted by both avian and human origin viruses - with viral infectivity having been clearly shown in unpasteurized milk -, this could "accreditate" cattle as a further "mixing vessel" allowing the genetic reassortment and recombination between avian and human viruses, similarly to swine.

Cases of severe respiratory and neurological A(H5N1) viral disease have been also described in cats following the consumption of raw milk from infected cattle [10] as well as in farm workers from Texas, Michigan and other USA regions, in whom a bilateral conjunctivitis is commonly observed, sometimes accompanied by a febrile syndrome with mild respiratory signs [11].

Despite the hitherto available "absence of evidence" towards HPAI A(H5N1) virus interhuman transmission, the recently demonstrated susceptibility of mice and ferrets to a viral strain recovered from the conjunctiva of a patient in Texas should be viewed as another serious concern issue. Such experimentally challenged animals developed, in fact, a lethal systemic infection characterized by severe bilateral pneumonia and encephalitis [12].

Finally, since we are dealing with a zoonotic infection, in a similar manner to what happens with "emerging infectious diseases", whose proven or suspect origin lies for two thirds of them in one or more animal reservoirs, the main take-home messages for efficiently tackling and counteracting HPAI A(H5N1) virus spread among birds and mammals as well as from birds and mammals to humans, with special emphasis on interhuman transmission, may be summarized by the following key words:

Multidisciplinarity, intersectorial cooperation, predictive epidemiology, tracking of viral genetic mutations, open data sharing and, last but not least, One Health.

Declarations

Conflict of Interest

The Author declares that there is no conflict of interest.

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