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Editorial

Two linked clinical cases of avian influenza in Cambodia: what threat to public health in southeast Asia does this pose?

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Highly pathogenic avian influenza A (HPAI H5N1), more commonly known as bird flu – is, as the name suggests – primarily a disease that affects birds, yet it can also infect mammals, including humans. Since emerging in southern China in 1996, with the first human case a year later, outbreaks have occurred with great regularity across the world. The most incidence is in southeast Asia, although less frequent over the last decade [1]. Indeed, in Vietnam, the first new case in eight years was reported in October 2022, that of a 5-year old

girl who became seriously ill in the northern province of Phu Tho, close to the capital city of Hanoi [2]. According to the Vietnam Ministry of Health this brought the number of confirmed cases of A/H5N1 since the first report in 2003 to 128. This has resulted in 64 deaths, a mortality rate of precisely 50%. It is in this context that the recent confirmed human cases of A/H5N1 in one Cambodian family, with the death of an 11-year-old girl, in the border Prey Veng province [3], has caused appreciable concern in densely populated southern Vietnam [4,5].

Human transmission risk

The majority of human cases of bird flu recorded to date have occurred through direct contact with infected birds or via their contaminated products or environments. There is an occupational risk for poultry farmers or stallholders in live-bird markets that are common in southeast Asia [6]. However, there have been instances of human-to-human transmission of bird flu, particularly in situations where there is extended close contact with an infected person, such as within families or healthcare settings [7]. Transmission of A/H5N1, a respiratory virus, is primarily by inhaling aerosols from an infected individual nearby. This concept is

familiar to us from the related A/H1N1, A/H3N2 and B subtypes that seasonally infect humans, against which an annual trivalent vaccine is made, as well as airborne viruses with a similar transmission route – for example, those that cause the common cold or COVID-19 [8].

Heightened surveillance

Battery farming practices, in which chicken and ducks are kept in enclosed, cramped conditions, provide ideal conditions for bird-to-bird transmission. The typical ‘quick fix’ response from all nations to a widespread outbreak is the questionably effective practice of culling. This has a devastating financial impact on the poultry industry [9], as does the knock-on effect of a loss of public trust in chicken and duck meat and eggs [10]. In the current scenario, at the time of writing the proportionate response of the Vietnam Ministry of Agriculture and Rural Development to the outbreak in its neighboring country is to enforce monitoring of poultry and poultry product imports from Cambodia [5]. Inspection and control measures are being strengthened at land border crossings, air and sea ports to apply strict sanctions on illegal trading. Any confiscated items will be tested, then destroyed. Moreover, the Pasteur Institute in Ho Chi Minh City, a World Health Organization (WHO) National Influenza Center, has alerted hospitals and clinics in southern provinces of both Cambodia and Vietnam to ramp up surveillance of viral pneumonia among residents [3,4].

Outbreak source

A rapidly assembled taskforce of experts from the WHO is now working with Cambodia’s public health authorities to seek to determine how the family members were exposed to the virus [3]. Most likely this was through close contact with domestic birds or aquatic wild birds, or possibly even one of a number of mammal species – intermediate hosts in a zoonotic transmission cycle [11]. However, for the girl’s father, a smallhold livestock farmer who became ill an unspecified time later, did he catch the virus from his daughter? If not, one might predict there to be only occasional cases of viral pneumonia contracted by people who come into regular close contact with infected poultry, such as through occupational exposure – for example, battery farm and abattoir workers. On the other hand, if the answer is yes, so the source was propagated and not arising from a single point, infection could potentially spread within local

communities. The usually very measured WHO acknowledges that this latter scenario raises the concerning possibility of human-to-human transmission [3]. The medical condition of relatives and other close contacts of the father and daughter is being monitored.

Virus mutation

For a respiratory virus of animal origin to cross host species boundaries to infect humans requires a sudden and significant change to the composition of its surface proteins via the process of genetic reassortment. For HPAIs, this enables better adaptation of the receptor-binding protein hemagglutinin and the receptor-cleaving enzyme neuraminidase to facilitate entry into host epithelial cells of a less frequent host species [12]. When such an antigenic shift event happens, most people have negligible protective immunity to the new virus subtype. There have been four influenza A pandemics since the start of the twentieth century: Spanish (A/H1N1, 1918–19); Asian (A/H2N2, 1957–58); Hong Kong (A/H3N2, 1968–69); and swine (A/H1N1, 2009–10). Three ‘pseudopandemics’ of A/H1N1 (USA, 1947 and 1976; Russia, 1977) have also contributed to the evolution of this pathogen [13]. Hence, recent history foretells that it is only a matter of time and misfortune, through the random event of genetic mutation, before a novel avian influenza strain of high virulence emerges [14]. If and when this happens, the blueprint for preparing the seasonal flu vaccine would be readily adapted so that a modified preparation could target the potentially pandemic pathogenic avian strain [15].

Conclusion

Highly pathogenic avian influenza is a persistent public health threat as a leading cause of severe respiratory disease. While the source of infection of the A/H5N1 isolate that caused the death of a child in Cambodia may never be determined unequivocally, this emergency event should sound a warning of what may be to come. With the virtue of hindsight, in all but a handful of countries the real time surveillance and early detection system in place at the start of the COVID-19 pandemic for control of community transmission was grossly inadequate and need of major overhaul [16]. Striking a positive note, those hard-learned lessons are now helping to ensure better outbreak preparedness and threat mitigation for a virulent strain of bird flu should it spread to, and between, humans.

Authors' contributions

Article conception, both authors; literature search and data collection, N.K.Q.; interpretation of information, both authors; writing — original draft preparation, N.K.Q.; writing — editing critically for important intellectual content, A.W.T-R. Both authors approved the final version submitted.

Conflicts of interest

Both authors have no conflicts of interest to declare

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