## THE BIRD FLU THREAT - WHY AREN'T WE WORRYING?

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The World Health Organization (WHO) and influenza experts worldwide are concerned that the recent appearance and widespread distribution of an avian influenza virus, influenza A/H5N1, has the potential to ignite the next influenza pandemic. It is estimated that even in the best-case scenarios, the pandemic will cause 2 to 7 million human death and tens of millions would require medical attention. If the pandemic virus is a very virulent strain, deaths could be dramatically higher.

The global spread of influenza pandemic cannot be stopped but preparedness will reduce its impact. Given the current threat, WHO has urged all countries to develop or update their influenza pandemic preparedness plans for responding to the widespread socioeconomic disruptions that would result from having large numbers of people, including health care workers, unwell or dying. Some of the countries have already developed structures and processes to counter this threat but some plans are far from complete and many countries have yet to begin. While it is impossible to accurately forecast the magnitude of the pandemic, it is a fact that much of the world is unprepared for a pandemic of any size. Why is there such complacency in the face of a very urgent and serious threat?

Influenza, to most people, is "just the flu" - an annoying, but tolerable upper respiratory tract infection. Thus, to generate widespread concern about its power as a global threat was as hard as creating interest in the power of asthma, another hidden killer. Why worry about an influenza virus while there are so many more exotic viruses, like Ebola, to fret about? Even the virus that caused the SARS outbreak in 2003 got more front-page coverage than the current outbreaks of bird flu, caused by yet another respiratory virus.

For all its familiarity and apparent

harmlessness, complications of influenza had killed 10,000 to 20,000 people in the United States yearly. In the most devastating influenza pandemic that occurred in the winter of 1918-1919 (dubbed the "Spanish flu"), 196,000 Americans died in the month of October 1918 alone. Before the dreadful winter was over, 2 billion people around the world had come down with influenza with worldwide death estimated at 20 to 40 million. The "Spanish flu" had caused more deaths and socioeconomic disruptions in one six-month period then any other comparable period - more than the Black Death of the 14th century, more than the smallpox of the  $16^{\text{th}}$  century and even more than AIDS has killed so far. The rapid onset and dissemination of influenza relates to its short incubation period (which averages 2 days) and the high concentrations of the virus in aerosolized respiratory secretions (caused by coughing, sneezing, or speaking).

Modern medicine has given us an influenza vaccine, efficacious anti-influenza drugs and plenty of antibiotics (to treat secondary bacterial infections). All these led many to believe that whatever was killing people so ruthlessly in 1918 must certainly be something we can now treat, if history repeats itself. But during the 1918 debacle, many victims fell ill without prodrome and death occurred within hours of disease onset, making treatment a mockery. Once pandemic caused by a new influenza virus had started, prevention and control by vaccination would not be worthwhile as by the time the vaccine is ready for use (at least six months are needed for a vaccine to be concocted) the pandemic had already peaked and near ending. The current influenza vaccine offers no protection at all against bird flu, because no one can see it coming. Thus a global surveillance system for influenza is a necessity for detection of novel viruses before pandemics begin, as it would dramatically

increased the time to organize a response, including production and distribution of vaccines.

H5N1 is now widely entrenched in Asia and this signals that the world has moved closer to the next pandemic. Poultry husbandry in much of East Asia generally pays scant regard to hygiene practices and the movement of infected poultry, either by design or accident, is thought to have played a part in spreading the disease. Domestic and international trade in wild birds for both food and caged pets, involves millions of individuals annually and the frequent occurrence of mixed markets could allow viruses to pass between species and cross borders. The hiding of fighting cocks to avoid slaughter in Thailand may also have contributed to the spread, or at least hampered eradication. The role of migratory birds in the movement of H5N1 could not be discounted but it is noteworthy that surveillance of wild birds has resulted in very few isolations of H5N1 during either the current or previous Asian outbreaks.

Prior to 1997, avian influenza was confined to animals with no direct spread to humans. However in 1997, 18 human cases of avian influenza with 6 deaths were reported in Hong Kong. Coinciding with outbreaks of highly pathogenic H5N1 in poultry. In 2003, two other avian influenza viruses, A/H7N7 and A/H9N2, had also caused human illnesses in the Netherlands and Hong Kong respectively.

Since time immemorial, influenza A virus had been evolving with the production of totally different subtypes every 10 to 15 years. The evolution is largely due to its unique segmented genome that allows for easy recombination of its genetic materials when two different strains of influenza viruses infect a cell. Environmental factors provide selective pressure in producing mutant viruses and it was postulated that the current A/H5N1 virus could have resulted following widespread vaccination of poultry with H5 vaccine in mainland China, as a preventive response to the 1997 Hong Kong's avian influenza outbreak. The role of influenza vaccine in the prevention of avian influenza in poultry is controversial, at best. Despite vaccination, sub clinical infections could still be occurring and these would not be detected if post-vaccination surveillance were not put in place. The scenario allows the virus to circulate longer than usual in the avian host population with the risk of viral mutations highly likely to occur. Animals are almost always involved in production of new influenza viruses and in each of the three pandemics – the 1918 "Spanish flu", the "Asian flu" of 1957, and the "Hong Kong flu" of 1968 – the viruses originated in Asia, most likely somewhere in China.

Since January 2004, the outbreaks of H5N1 avian influenza in Asia had caused 50 deaths in 80 confirmed human cases, with cases reported only from Vietnam, Thailand and Cambodia. Why make a fuss when the mortality is small? This is precisely the right time to make a fuss. The last global influenza pandemic, in 1968, spread around the world killing 45,000 people within five months following detection of a single case. The H5N1 virus had already caused limited human-to-human transmission and it is only a matter of time before the virus adapt more efficient human transmission method. The advent of air travel adds more concern about the magnitude of a future pandemic as the spread of the new epidemic strain may be hastened.

As the scientific community continues to be on alert to the inevitable and possibly imminent massive influenza pandemic, the general public is only now gradually, grudgingly, learning that all our medical sophistication is still relatively helpless in the face of the elusive tactics of our tiniest enemy.

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