



<http://www.onehealthinitiative.com/>

***“One Health is the collaborative efforts of multiple disciplines working locally, nationally, and globally to attain optimal health for people, animals, plants and our environment.”***

*“One Health implementation will help protect and/or save untold millions of lives in our generation and for those to come.”*

*“Between animal and human medicine there are no dividing lines--nor should there be.”*  
Rudolf Virchow, MD (the father of cellular pathology)

*Submitted to One Health Initiative website April 13, 2013 - Posted Wednesday, April 17, 2013*

## **The Novel H7N9 Influenza A Virus: Its Present Impact and Indeterminate Future**

**\*Robert E. Kahn, PhD and Juergen A. Richt, DVM, PhD**, Center of Excellence for Emerging and Zoonotic Animal Diseases (CEEZAD), Kansas State University, Manhattan, KS (USA)

Influenza A viruses are unpredictable in their emergence, ability to mutate or reassort, and especially their capacity to cross species. Each of these three aspects of unpredictability are evident in a puzzling new H7N9 influenza virus which began in China earlier this year and has become a significant public health hazard, but not (at least thus far) a harbinger of a pandemic. It appears that this virus is a newly emerging reassorted bird flu virus with the significant characteristic of travelling among numerous avian and maybe mammalian species as a low pathogenic avian influenza virus which surprisingly is a highly pathogenic virus for the human species. The good news is that there is no evidence of sustained human-to-human transmission, but the bad news is that this newly minted H7N9 avian virus can kill human beings who come in contact with birds or poultry that appear healthy but are in fact carrying a lethal zoonotic agent. As Timothy Uyeki and Nancy Cox have pointed out: “intensified surveillance for H7N9 in humans and animals is essential” (See “Global Concerns Regarding Novel Influenza A (H7N9) Virus Infections,” *The New England Journal of Medicine*, April 11, 2013 at: <http://www.nejm.org/?query=OF> ).

**The world is being given a crash course in the importance of “One Health”, because it is primarily through research at the human-animal-environmental interface that this virus can be better understood and hopefully controlled.** There are no existing vaccines for the H7N9 virus for any species, including humans. Already in Shanghai alone more than 110,000 birds have been culled (ProMed Digest 160 at: <http://www.promedmail.org/> 9 April: Avian Influenza, human [38] [5], China [SH, JS] H7N9 update).

Despite on-going laboratory investigations on the new viral pathogen in hundreds of laboratories, both in China and globally, the source and significance of H7N9 is not yet clear. The virus has been found in chickens, pigeons and ducks, but the prevalence of the virus in other species (especially wild and domestic birds, geese, pigs, quail and turkeys) remains unknown. Among 39 detected human infections as of April 12, 2013 in 11 cities in Eastern China (including the 23 million people in Shanghai) and one case already in the capital Beijing (with its 22 million people) – far away from the epicentre in Shanghai) -many (but not all) of the 10 people who have died and the 19 who are at present severely ill had extensive contact with poultry. Underlying health conditions may have been a significant contributory factor to their demise and severe illnesses, but the tracing of hundreds of human contacts has not found a single person who has definitely contracted H7N9 from those who have died or been sickened by the virus.

The current situation has been succinctly summarized by Moderator CP in ProMed Digest 164 of April 11, 2013: "Overall the pattern remains unchanged, the victims are mainly elderly males. Infection in children is rare and mild. Despite the speculation, there is no evidence so far of evolution of human-to-human transmissible virus. The case numbers are rising dramatically but this may in part be a consequence of greater availability of diagnostic agents" (at: <http://www.promedmail.org/> 11 April 2013: Avian Influenza, human [34] [6-Mod CP]). In public health parlance, the basic reproduction rate in humans is zero at this time. For an epidemic or a pandemic to take place, each person infected with the pathogen must pass it on to more than one other person. The question we could ask now is: What are we worried about?

We are worried about the ubiquity of cross-species transmission of avian influenza viruses. We are worried that **the astounding mixture of species in Chinese live bird markets has the potential for easy spread of the H7N9 from the unknown original host species to other hosts, just as happened with SARS (Severe Acute Respiratory Syndrome). In the U.S. and other Western countries, 'poultry' means basically chickens, ducks, and geese. "In China, besides those three species, practically every live market also includes pigeons, quail, pheasants, guinea fowl, and sometimes peafowl, and right next door you'll have open-air pet markets selling captive songbirds, many of them illegally caught from the wild," as well as pigs and maybe dogs. (See Merritt Clifton's comment in ProMed Digest Number 151 at: <http://www.promedmail.org/> 5 April 2013: Avian Influenza [28] [2] China (Shanghai) H7N9, OIE Update). In brief, the environment of a Southeast Asia wet market is an ideal breeding ground for influenza and other promiscuous viruses, both new and old, which is why the Chinese Government decided to close some of these markets in the epicenter of the H7N9 outbreak. While such closures are an important, sensible and necessary mitigation strategy, it is doubtful if this alone will be sufficient to stop the transmission and spread of this new virus entirely.**

Zeng Guang, Chief Epidemiologist at the Chinese Centre for Disease Control and Prevention, has recognized that "banning the [live poultry] trade and culling [i.e. killing] birds is only an expedient. Research into vaccines and effective medication are essential," he says (at: <http://www.promedmail.org/> 11 April 2013: Avian Influenza [34],[1]: China (ZH), LPAI H7N9 OIE Update). However, Helen Branswell of the Canadian Press, has set out significant problems in both the development and utilization of such a vaccine for human use: (See "Making vaccines for new flu H7N9 flu virus could be a challenge, experts say," 11 April 2013 at:

[http://www.huffingtonpost.ca/2013/04/11/making-vaccine-for-new-flu\\_n\\_3064478.html](http://www.huffingtonpost.ca/2013/04/11/making-vaccine-for-new-flu_n_3064478.html))). Furthermore, even if an H7N9 vaccine becomes available and is

shown to be safe and efficacious, it will be difficult, if not impossible, to convince poor farmers in Southeast Asia to vaccinate their flocks against a virus which does not cause any loss or obvious clinical disease (See ProMed Digest 166 at:

<http://www.promedmail.org/>, 12 April 2013: Avian Influenza [34] [3-Mod AS]).

Despite the significance of wet markets in the spread of H5N1 and SARS, H7N9 is a very different phenomenon than either H5N1 or SARS. The former virus emerged in Hong Kong in 1997 and re-emerged in Southeast Asia and Europe in 2003 killing more than 50% of infected humans; the latter virus emerged in China in 2002 and killed about 10 per cent of the 8,000 people it infected worldwide (See Karl Taro Greenfeld, *China Syndrome: The True Story of the 21<sup>st</sup> Century's First Great Epidemic*, Penguin Books, 2006). The fact that there appears to be no sustained transmission of H7N9 from humans to humans - similar to H5N1 - is reassuring, but not conclusive in assessing the significance of H7N9. As Anthony J. Michael has reminded us, we have to accept that "humans and microbes are not 'at war' (as much popular literature suggests). Rather, both parties are engaged in amoral, self-interested, co-evolutionary struggles " (See "Environmental and social influences on emerging infectious diseases: past, present and future" in A. R. McLean, R. M. May, J. Pattison and R. A. Weiss, *SARS: A Case Study in Emerging Infections*, Oxford University Press, 2005). As human beings we tend to search for culprits as to which species or place is responsible for the creation and spread of a dangerous pathogen. However, the reality is that both microbes and people are striving to live at the animal-human-environmental interface. **The precise identification of a new zoonotic pathogen requires animal, human and environmental scientists to carefully work together [i.e. One Health] in the field and laboratory to confirm (i) the identification of the original host species, (ii) its mode of transmission into intermediate host species including humans and (iii) its ecology and survival in the environment.**

Avian influenza viruses tend to bind to the *lower* parts of the human lung, which are not easily reached. Therefore, these influenza viruses are not easily transmissible between humans. However, mutations in the avian influenza genome can allow an avian influenza virus to bind to the human influenza receptor. Such mutations would then render these avian viruses transmissible between humans, as is feared could happen with the H5N1 avian flu virus. It must be emphasized that in the case of H7N9 this has already partially happened. The amoral reality is that influenza viruses are so unpredictable because they use sophisticated and efficient methods of molecular evolution, adaptation and cross-species transmission. One method is called "reassortment" or "genetic shift," which is the mixing of the gene segments from different influenza viruses. Another method is called "genetic drift," which is the constant introduction of mutations into the influenza genome with an unpredictable impact on the phenotype of the newly mutated influenza virus. In the case of H7N9, genetic shift has already occurred, as well as genetic drift with a partial adaptation to the human environment (See R. Gao et al, "Human Infection with a Novel Avian-Origin Influenza A(H7N9) Virus" *New England Journal of Medicine*, April 11, 2013 at: <http://www.nejm.org/?query=OF> ; and Y.-M. Wen & H.-D. Klenk, "H7N9 avian influenza virus – search and re-search, *Emerging Microbes & Infections*, April 10, 2013 at: <http://www.nature.com/emi/journal/v2/n4/full/emi201318a.html>). This is a very disturbing reality, as this new avian virus seeks not only to survive in avian species but is looking for new opportunities in mammalian and human populations. The outcome of this cross-species interaction with this new H7N9 virus is at present indeterminate. **What is determinate— what is conclusively settled—is that an increased commitment to the objectives and implementation of the "One Health" approach to medicine in general is now more urgent than ever.**

---

\***Dr. Robert E. Kahn**, Education Consultant, College of Veterinary Medicine, Kansas State University; and **Dr. Juergen A. Richt**, Regents Distinguished Professor, College of Veterinary Medicine, Kansas State University and Director, Center of Excellence for Emerging and Zoonotic Animal Diseases (CEEZAD); Please address correspondence to: [jricht@vet.k-state.edu](mailto:jricht@vet.k-state.edu)

**Note:** Drs. Kahn and Richt are recognized, prominent One Health supporter/advocates.