

## Bird flu complacency

By James. A. Joyce  
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**“Society just can't accept the idea that 50 percent of the population could die, and I think we have to face that possibility.”**

-- Robert G. Webster, Bird flu expert

Earlier this year, the media deployed the best and brightest from the science world to discuss the imminent threat of bird flu mutating into a form that would allow for human-to-human infection. ABC News produced a special report on world-renowned researcher Robert G. Webster, who stated: “Society just can't accept the idea that 50 percent of the population could die, and I think we have to face that possibility.”

As time passed, however, the public became distracted by multiple wars in the Middle East, inflation, rising oil prices, tumbling financial markets, global warming and a host of other issues. Unfortunately, evolving evidence underscores the reality that bird flu, otherwise known as H5N1 Avian Influenza, is still a very real threat.

Influenza is already a big killer, as it is responsible for more than 35,000 deaths and over 200,000 hospitalizations in the United States each year. Avian flu occurs naturally in birds and has historically demonstrated the ability to infect humans. It already is unprecedented as an animal illness in its rapid expansion, and has cost 300 million farmers more than \$15 billion during its recent spread in poultry around the globe. World Health Organization officials claim the H5N1 strain of avian flu poses a greater challenge to the world than any other infectious disease, including AIDS. As of July 20, WHO officials confirm that of the 230 individuals known to have been infected, 132 died since the virus re-emerged in 2003.

Among humans, there is no natural immunity and no vaccine to treat the H5N1 strain of avian flu. WHO Assistant Director General Margaret Chan stated, “We have never seen such a high case-fatality rate where more than 50 percent of people affected by the infection die from the disease.” As a comparison, the fatality rate of the Spanish flu of 1918 (also a form of avian flu), which was only 2.5 percent, caused the deaths of over 40 million people during an 18-month period. To provide perspective, it has taken 25 years for AIDS-related deaths to reach such levels. Scientists, increasingly worried that the H5N1 strain of avian flu could mutate into a form that could be passed between humans, received bad news on June 23 when researchers documented that the virus had successfully mutated to be passed through human-to-

human transmission in a family in Indonesia. Fortunately, these same researchers reported that the virus did not pass beyond the infected family members, who all died from the infection.

In the face of such dire news, researchers are unraveling the mystery of why the H5N1 strain of the avian flu virus is so lethal. It appears H5N1 hyper-activates the immune response, a frightening trait also inherent in the Spanish flu. In the case of H5N1 infection, viral sepsis leading to major organ failure is often the cause of death. This is triggered when the immune system over-responds to infection by releasing a cascade of inflammatory cells and chemicals in what is known as a “cytokine storm.”

As a result, the likelihood of death in individuals with robust immune systems equals or exceeds the immune compromised who are normally most susceptible to regular seasonal flu strains. Unfortunately, antiviral drugs are unable to shut off a cytokine storm once it has been triggered. As a result, the antiviral drugs being stockpiled as part of a global strategy to treat avian flu have no therapeutic value once the cytokine storm has been triggered.

At present, only one antiviral, oseltamivir (Tamiflu), is known to offer some level of effectiveness against the H5N1 strain of avian flu. Tamiflu, however, is indicated only as a treatment for normal household varieties of influenza if administered within 48 hours of first symptoms. The treatment window for an ultra-virulent H5N1 strain is likely to narrow considerably. Reports indicate the potency of Tamiflu against the avian flu virus is reduced, even when taken within 24 hours of the first symptoms of the disease. In addition, the drug is directed toward symptoms and does not provide an anti-viral effect. Prolonged incubation combined with a short antiviral treatment window also concerns researchers. Dr. Tim Uyeki, a medical epidemiologist with the influenza branch of the Centers for Disease Control and Prevention, stated to The Wall Street Journal: “Patients aren't presenting (symptoms) early in the illness. If the cytokine storm has already been triggered, antiviral drugs aren't going to turn it off.” A successful global strategy against H5N1 will, at a minimum, have to rely on therapeutics that can modulate the overproduction of cytokines.

The March 2 issue of The Lancet reported that researchers at the well-regarded Karolinska Institute in Stockholm are proposing the use of chemotherapy to kill off excess immune cells as a means to curb the cytokine storm leading to viral sepsis in H5N1 patients. While the concept may seem radical, researchers are likely to agree that any treatment able to damp down the immune system might be helpful. Unfortunately, taming the immune system without destroying defenses against infection has yet to be demonstrated with drugs. Until effective therapeutics surface, we are all naked to the effects of H5N1 avian influenza. Let's hope the evolving evidence dissipates to justify bird flu complacency!

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***Joyce is chief executive officer of Aethlon Medical, a San Diego research laboratory that will file with the Food and Drug Administration for approval of its technology to treat avian flu.***