

Opinion: H5N1 flu is just as dangerous as feared, now requires action

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The debate about the potential severity of an outbreak of airborne H5N1 influenza in humans needs to move on from speculation and focus instead on how we can safely continue H5N1 research and share the results among researchers, according to a commentary to be published in *mBio*, the online open-access journal of the American Society for Microbiology, on Friday, February 24.

H5N1 influenza has been at the center of heated discussions in science and policy circles since the U.S. National Science Advisory Board for Biosecurity (NSABB) asked the authors of two recent H5N1 investigations and the scientific journals that planned to publish the studies to withhold crucial details of the research in the interest of biosecurity.

In the mBio® commentary, Michael Osterholm* and Nicholas Kelley, of the Center for Infectious Disease Research and Policy at the University of Minnesota, present their case that H5N1 is a very dangerous virus, based on their analysis of published studies of the seroepidemiology of H5N1 in humans. H5N1 flu infections have exceedingly high mortality, they say, and current vaccines and antiviral drugs will not pull us out of a global H5N1 pandemic. "We believe that the assertion that the case-fatality rate of H5N1 influenza in humans may be overestimated is based on a flawed data analysis," Osterholm said.

Analysis of reports of H5N1 seroprevalence that include data from the 1997 Hong Kong outbreak as well as data from 2004 to date will give a

misleading impression because the 1997 outbreak was a very different “biologic event” that is recognized as such by the WHO, because the 1997 H5N1 virus has a significantly different genotype from that of later H5N1 viruses. This is why the WHO does not include the Hong Kong H5N1 virus data in any analysis of H5N1 transmission, and the 1997 Hong Kong virus is not recommended for inclusion in H5N1 vaccines, Osterholm explained.

Seroepidemiologic studies that have examined the exposure of various groups of people to H5N1 viruses only from 2004 onward indicate that only a small segment of the population has ever been exposed to H5N1, and that among those that have been exposed, many become seriously ill or die.

"The available seroepidemiologic data for human H5N1 infection support the current WHO reported case-fatality rates of 30% to 80%," Osterholm says. In the event of an H5N1 pandemic, they point out, if the virus is even one tenth or one twentieth as virulent as has been documented in these smaller outbreaks, the resulting fatality rate would be worse than in the 1918 pandemic, in which 2% of infected individuals died.

Vaccines will not head off an H5N1 pandemic either, the authors say, since the time required to develop and manufacture an influenza vaccine specific to new outbreak strain has resulted in “too little, too late” vaccine responses for the 1957, 1968, and 2009 influenza pandemics, and not much in the process has changed since 2009.

"The technology behind our current influenza vaccines is simply not sufficient to address the complex challenges associated with an influenza pandemic in the 21st century," Osterholm and Kelley say.

This is the heart of the matter, they say: there has been enough

discussion about how severe an H5N1 pandemic might be. Moving forward, the current controversy has provided a valuable opportunity for scientists and public policy experts to discuss influenza research and preparedness and create "a roadmap for the future." The discussion among scientists and policy makers needs to move on from whether H5N1 poses a serious international threat - as it clearly does - and begin discussing how we can prevent these viruses from escaping labs and how scientists can share their flu-related results with those who have a need to know.

There are critical questions that need to be answered, the authors say. For instance, how can scientists conduct virus-transmission studies in mammals safely and how can scientists share research methods and results with those who have a need to know? We also need to come to agreement on how to ensure that strains of H5N1 viruses created in the lab don't escape those controlled environments, the authors say. And new, more effective vaccine technologies are needed that can enable substantially faster production. Resolving these issues could allow H5N1 research and preparedness to serve as a springboard for solving similar problems with existing or emerging pathogens.

More information: *Michael Osterholm is a member of the National Science Advisory Board for Biosecurity.

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