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Mammalian-Transmissible H5N1 Influenza: the Dilemma of Dual-Use Research

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ABSTRACT The National Science Advisory Board for Biosecurity (NSABB)’s recommendation to restrict publication of the details of the generation of mammalian-transmissible H5N1 influenza virus is unprecedented. Dual-use considerations indicated that the potential biosecurity risks of a transmissible H5N1 virus with a possible mortality of 50% in humans outweigh the substantial benefits of open and complete scientific exchange in this case, although the benefits include potential early detection strategies for H5N1 viruses with specific genetic markers and control strategies, including development of antivirals and vaccines. It is argued that both the funding agency (the National Institute of Allergy and Infectious Diseases) and the scientists were responding to societal needs and acted entirely responsibly. These studies usher in a new era for life sciences, compelling the research community to confront important decisions: under what conditions should such research be done? How can the principle of full release of information be balanced with the moral imperative to protect the public health?

The majority of biological scientists are surprisingly unaware of dual-use research and the role of the U.S. National Science Advisory Board for Biosecurity (NSABB), although influenza researchers did know that a review board had recommended publication of Jeffrey Taubenberger’s complete sequence of the 1918 Spanish influenza virus (1, 2), despite potential biosecurity risks. Consequently, authors and journals alike were surprised by the NSABB’s recommendation that the full details of the generation of mammalian-transmissible H5N1 influenza virus be withheld. Why the apparent reversal in policy? Why does the risk of publishing the details of H5N1 transmissibility in mammals outweigh the benefits of disseminating important new information of immense human and veterinary public health importance?

The reasons include the greater lethality of H5N1 influenza (>50%) than of Spanish influenza (2.5%) in humans, the availability of highly pathogenic H5N1 viruses in nature, and the nearly universal susceptibility of humans to H5N1 infection. This combination of factors creates an unacceptably high level of risk to humanity should mammalian-transmissible H5N1 virus be accidentally or intentionally released. To cope with this dilemma, the NSABB recommended publication of revised manuscripts that withheld some of the details. A full manuscript would be prepared for distribution to global health officials on a need-to-know basis after further consideration and planning.

Both the Fouchier and Kawaoka groups used the ferret model to demonstrate mammalian transmissibility of highly pathogenic H5N1 virus. While the ferret is considered the best available model of human influenza virus infection and transmission, we do not know whether the ferret fully recapitulates these events in humans. For one thing, H5N1 infection tends to be milder in ferrets than in humans; only a minority of H5N1 strains are lethal in ferrets, whereas lethality greater than 50% has been documented in humans. Thus, while we cannot confidently equate transmissibility and pathogenicity of influenza virus in ferrets and humans, can we afford to disregard data from the best available model?

Concern has been expressed that the agency funding the research (the National Institute of Allergy and Infectious Diseases [NIAID]) and the two groups of scientists conducting the research on H5N1 influenza transmissibility may have acted irresponsibly (3). However, after the 1997 emergence of H5N1 influenza in humans, with its greater than 50% lethality and its potential transmissibility from avians to humans, both the World Health Organization (WHO) (4) and a Blue Ribbon Panel of influenza research advisers to NIAID asserted that further H5N1 research was necessary (5). One of the research recommendations of the 2009 WHO Public Health Research Agenda for Influenza was to “Investigate virus-specific factors associated with zoonotic and pandemic potential (e.g., infectivity, transmissibility, and pathogenicity).” In 2006, the Blue Ribbon Panel on Influenza Research recommended to NIAID that “Learning more about how influenza viruses circulate between animal reservoirs and about the evolutionary pressures that lead to the emergence and spread of new viral subtypes—especially the factors that favor transmission from animals to humans—are urgent research priorities.” Unfortunately, neither the Blue Ribbon Panel nor WHO addressed the question of dual-use research. The focus was on the benefits of knowledge, including the development of better control strategies, such as novel antivirals and vaccines. Now that researchers have generated mammalian-transmissible H5N1 and the U.S. NSABB has raised the dual-use concern, there is a clear and acknowledged need for full discussion of the way forward. WHO has also raised considerable concern about the risk of developing mammalian-transmissible H5N1 viruses.

The two manuscripts formally demonstrating generation of mammalian-transmissible H5N1 influenza virus make major contributions to our knowledge and usher in a new era in the life sciences. The question before the scientific community is how to preserve scientific openness while minimizing risk to the public. Control strategies for influenza and other emerging diseases are not adequately developed; the Fineberg Report on the evaluation of WHO’s response to the 2009 H1N1 pandemic (6) emphasized...
that “the world is ill prepared to respond to a severe influenza pandemic or to any similarly global, sustained and threatening public health emergency.” The urgent need for general guidance in this matter is reminiscent of the dilemma addressed at the Asilomar conference on recombinant DNA molecules in 1975 (7). One possibility is to involve the national academies of science from all interested countries and WHO in considering the topic of dual-use research and an approach that both promotes research and maintains biosecurity. It has been argued that suppression of information serves no purpose, as the information will inevitably be “leaked.” Although this viewpoint is likely correct, I do not believe we should publish the detailed methods of preparing transmissible H5N1.

Further, we must consider and establish the biosecurity level needed for future work on transmissible H5N1. Because highly pathogenic H5N1 is enzootic in multiple regions of Eurasia, the use of biosecurity level 4 (BSL4) for all H5N1 research would markedly restrict advancement of knowledge needed for vaccine and antiviral research. Enhancing BSL3 biosecurity with electronic surveillance, advanced personal protective equipment (PPE), and dual-use assessment of proposed studies is a possibility for further consideration. It is noteworthy that in the United States there were 395 biosecurity breaches involving select agents and 7 laboratory-acquired infections during 2003 to 2009 (8). These incidents, which occurred in both BL3 and BL4 laboratories, highlight the potential risks and the need to fully consider improved biosecurity and the immunization of staff with regularly updated H5N1 vaccines.

The groundbreaking manuscripts by the Fouchier and Kawaoka groups will be of great interest to life scientists and will no doubt increase their familiarity with the concept of dual-use research. These two reports challenge us to take action to ensure that research and open dissemination of knowledge can be safeguarded without compromising biosecurity. Both causes are fundamentally important, but public safety must not be compromised. While bioterrorism is of real concern, nature has the potential to do much greater damage.

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