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A flu virus risk worth taking

By Anthony S. Fauci, Gary J. Nabel and Francis S. Collins, Published: December 30

A deadly influenza virus has circulated widely in birds in recent years, decimating flocks but rarely spreading to humans. Nonetheless, because of its persistence in bird flocks, this highly pathogenic avian influenza virus has loomed as a major public health threat. Seasonal influenza kills less than 1 percent of the people it infects. In contrast, human infections with H5N1, though exceedingly rare, are fatal in more than half of cases. Should this virus mutate in a way that allows it to be transmitted as efficiently among people as seasonal influenza viruses are, it could take an unprecedented toll on human life.

A number of important scientific and public health questions regarding this virus remain unanswered, including the likelihood of such mutations arising and the mechanisms by which they may occur. Two recent studies co-funded by the National Institutes of Health have shed light on how this potentially grave human health threat could become a reality. Working carefully with influenza viruses they have engineered in isolated biocontainment laboratories, scientists in Europe and the United States have identified several mechanisms by which the virus might evolve to transmit efficiently in the ferret, the best animal model for human influenza infection. This research has allowed identification of genetic pathways by which such a virus could better adapt to transmission among people. This laboratory virus does not exist in nature. There is, however, considerable concern that such a virus could evolve naturally. We cannot predict whether it or something similar will arise naturally, nor when or where it might appear.

Given these uncertainties, important information and insights can come from generating a potentially dangerous virus in the laboratory. While the World Health Organization and the Centers for Disease Control (CDC) and Prevention provide excellent public health surveillance for novel influenza strains, influenza outbreaks still occur suddenly and in unexpected places. The recent H1N1 pandemic exemplifies the problem: In 2009, a new influenza virus emerged. It was shown to have originated from an animal reservoir, and it spread so rapidly that it strained the pharmaceutical industry’s capacity to prepare vaccines fast enough to blunt its spread. We do not fully understand the underlying factors that allow influenza viruses to be transmitted efficiently in humans after they emerge from different species. The ferret transmission studies were intended in part to fill these important gaps in knowledge.

Understanding the biology of influenza virus transmission has implications for outbreak prediction, prevention and treatment. In defining the mutations required for mammalian transmission, public health officials are provided with genetic signatures that, like fingerprints, could help scientists more readily identify newly emergent, potentially harmful viruses, track their spread and detect threatening outbreaks. The ability to identify such viruses even a few months faster than by conventional surveillance provides critical time to slow or stop an outbreak. For example, the CDC implements public health protective measures and stockpiles antiviral drugs. Identifying threatening viruses can also facilitate the early stages of manufacturing vaccines that protect against such a virus in advance of an outbreak.

In addition, determining the molecular Achilles' heel of these viruses can allow scientists to identify novel antiviral drug targets that could be used to prevent infection in those at risk or to better treat those who become infected. Decades of experience tells us that disseminating information gained through biomedical research to legitimate scientists and health officials provides a critical foundation for generating appropriate countermeasures and, ultimately, protecting the public health.

The question is whether benefits of such research outweigh risks. The answer is not simple. A highly pathogenic bird flu virus transmissible in humans could arise in ways not predicted by laboratory studies. And it is not clear whether this laboratory virus would behave in humans as it does in ferrets. Nonetheless, new data provide valuable insights that can inform influenza preparedness and help delineate the principles of virus transmission between species.

Along with support for this research comes a responsibility to ensure that the information is used for good. Safeguarding against the potential accidental release or deliberate misuse of laboratory pathogens is imperative. The engineered viruses developed in the ferret experiments are maintained in high-security laboratories. The scientists, journal editors and funding agencies involved are working together to ensure that access to specific information that could be used to create dangerous pathogens is limited to those with an established and legitimate need to know.