Avian H5N1 influenza
In or out flew-enza?

John G. Morgan
Department of Microbiology; University College Cork; Cork, Ireland

The recent controversy about the potential dangers of publishing scientific methodologies on the generation of variants of avian H5N1 influenza capable of infecting ferrets raises some interesting and relevant issues. One of the central issues is does the publication of such scientific data offer the potential for the production of a bioterrorism agent.

Influenza A virus is a serious human pathogen. The pandemic influenza outbreak in 1918 (“Spanish flu”) may have killed at least 50 million people worldwide.1 The WHO estimates that up to 50% of the world’s population became infected approximating to a mortality rate of 2–2.5%. In fact, this is almost definitely an underestimation and progressive studies tend to result in an upwards revision of mortality estimates. Post record keeping, loss of data and probability, in some parts of the world, little documentation of cases account for the difficulty in establishing the total number of cases. Just how lethal the 1918 virus was can be put in context when compared to a death rate of approximately 100,000 cases for the combined 1957 and 1968 influenza pandemics. The 1918 flu pandemic came in three waves, the first wave occurred in the spring of 1918, the second wave in the autumn (September to November) and the third wave in the spring of 1919. The second wave was by far the most virulent and lethal and probably resulted from the virus acquiring mutations that dramatically improved its human to human transmission and pathogenic characteristics.

It has not been definitively established that the 1918 influenza pandemic virus was an avian virus that adapted to successfully infect humans or whether it may have originated from gene reassortment (antigenic shift) as was observed in the subsequent fully infecting human to human transmission and pathogenic characteristics of the 1957 and 1968 pandemic viruses. The 1918 flu pandemic came in three waves, the first wave occurred in the spring of 1918, the second wave in the autumn (September to November) and the third wave in the spring of 1919. The second wave was by far the most virulent and lethal and probably resulted from the virus acquiring mutations that dramatically improved its human to human transmission and pathogenic characteristics. The recent controversy about the potential dangers of publishing scientific methodologies on the generation of variants of avian H5N1 influenza capable of infecting ferrets raises some interesting and relevant issues. One of the central issues is does the publication of such scientific data offer the potential for the production of a bioterrorism agent.

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preferring to choose to look at the potential negative impact of the discovery. Should we as scientists be concerned about the public perception of scientists and scientific experimentation? Public opinion can influence legislators who can in turn influence funding, particularly government funding, of research. A not insignificant number of people still believe that the HIV virus was generated by some sinister forces as a blight on mankind. They fail to be convinced that the virus is the progeny of a simian immunodeficiency virus likely to have evolved to infect humans sometime in the last 100 years. Indeed there are HIV seropositive blood samples identified as far back in 1957, only 4 years after the discovery of the structure of DNA and many years before the development of molecular biology techniques capable of genetically manipulating viral genomes.

The development of molecular biology methodologies during the 1960s and 1970s lead to the “Berg letter” and the subsequent Asilomar Conference in 1975 to examine the biohazard potential and draw up procedures for the safe handling of recombinant DNA molecules. This was an appropriate response by scientists to the emergence of a new technology with far reaching consequences.

Should we be performing science that is of a questionable nature? What are the pros and cons of genetically manipulating an avian influenza virus to more effectively infect mammalian species. When do the risks outweigh the benefits? The dangers associated with the inappropriate use of such information has been highlighted. Can the generation of H5N1 mutants and subsequent infectivity studies in ferrets greatly advance our knowledge and help predict likely H5N1 viruses capable of infecting humans? If so, this knowledge should guide us and emphasise the importance of epidemiological surveillance of emerging H5N1 strains that are naturally accumulating these mutations.

True, there are vaccines that protect against H5N1 and H1N1. The questions with influenza A vaccines are always, “Is there enough virus vaccine stockpiled to deal with a pandemic? How good is its shelf life over an extended period of time and, ultimately, the great unknown? Will it protect (totally or partially) against an avian strain that may naturally emerge to successfully infect humans?” Similar considerations can be applied to antivirals like oseltamivir. The incubation period for influenza A infection is short, the order of days, pandemics can be established in weeks.

In light of a number of existing publications on H1N1 and H5N1, it’s difficult to fully understand the hesitancy to publish the ferret H5N1 infection papers, but caution is never a bad thing. Let’s hope the issue can be resolved in a timely manner. The more likely event is that nature will dictate, by mutation and natural selection, whether some variant in the present pool of circulating avian H5N1 viruses acquires the ability to successfully infect humans, and will perform umpteen natural genetic engineering experiments. Let’s be steadfast in our monitoring and hope nature doesn’t get it right.

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