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## Foreword

Infectious viral diseases have always afflicted mankind and always will. New infectious diseases emerge as microbes adapt to new hosts and new environments. Asia has been a breeding ground for viruses where severe epidemics of dengue hemorrhagic fever (1954) and a variety of flu pandemics have originated such as the Asian flu (H2N2; 1957), the Hong-Kong flu (H3N2; 1968), and the Russian flu (H1N1; 1977). During the last 10 years, however, very dangerous viruses have repeatedly originated from Southeast Asia, e.g. the avian flu (H5N1) in Hong-Kong (1997), Nipah virus encephalitis in Malaysia (1998,) and, above all, the SARS outbreak from Southern China (2002).

An estimated 75% of emerging infectious diseases in humans are zoonotic in origin. Microbes usually evolved to reach an equilibrium with their natural hosts without causing any disease. This microbe-host equilibrium which is a delicate balance, gets disturbed by economic development and land use leading to perturbations in the natural microbial environment, human demographics and behavior, and international travel and commerce thus creating an imbalance and increased possibilities to trigger the emergence of new infectious diseases. Microbes possess the ability to adapt naturally to their hosts, their environment, and to new ecological niches offered to them as humans encroach upon their territory. They are also adept at circumventing efforts to suppress them, whether as a result of internal host pressures such as innate and adaptive immune responses or in reaction to external pressure applied by antibiotics, antivirals, or vaccines. In the face of our efforts to eliminate them, microbes almost always adapt successfully, thwarting our efforts to destroy them. A prototypic example of the constant struggle between microbes and man is the evolutionary success

of influenza viruses as they adapt to their many hosts, including humans. Similarly, the destruction of rainforests has led to exposure of humans to viruses and other microbes that otherwise would not have occurred, for example, an outbreak of Nipah virus in Malaysia occurred when pigs penned near fruit orchards contracted the virus from the droppings of bats, whose habitat had shifted as a result of deforestation. The infected pigs readily transmitted the virus to their handlers.

Also, the success viruses have gained in the emergence of new occurrences may be attributed to the development of large industry poultry flocks increasing the risks of epizootics, dietary habits, economic and demographic constraints, and negligence in the surveillance and reporting of the first cases. New viruses do not emerge against a background of established infectious diseases and host-microbe interactions that have existed for centuries. For example, the newly emerging infectious diseases like Severe Acute Respiratory Syndrome (SARS), Nipah virus encephalitis, Lassa fever, and most recently, human disease caused by the H5N1 strain of avian influenza virus were at some point emerging diseases that had never been observed previously in human populations but are now slowly becoming a part of the background infectious disease burden. Infectious diseases that have previously occurred in humans also can re-emerge or resurge in different forms or in different environments as has been exhibited by the West Nile; monkeypox, and dengue virus. The SARS virus although contained, poses a similar threat since it is still at large in its zoonotic hosts viz., bats, civet cats and pigs.

Today the world faces a threat of a much more unpredictable pandemic influenza, caused by the emergence of a new strain of influenza virus to which humans have never been exposed. Pandemics occur when a new influenza virus variant emerges to which the human population has no immunity. Influenza A viruses are most dangerous to humans because of their wide host range, their rapid mutation rate, and their capacity to cause serious disease. Over the past 2 years, the risk of an influenza pandemic has grown as an exceptionally virulent form of the H5N1 avian influenza virus and has circulated widely among domestic poultry and wild migratory birds in Asia, Europe, the Middle East, and Africa. As of February 9, 2006, the virus also has infected more than 166 people since late 2003, of whom half have died (WHO).

Whether the virus develops into a strain capable of spreading from human to human in an efficient and sustained manner, thereby triggering a human pandemic, will depend on how the virus evolves and adapts to new hosts. Since its re-emergence in Southeast Asia in 2003, the virus has appeared in poultry in at least 18 countries and in multiple species of migratory birds, pigs, tigers, and leopards. As the virus has infected chickens and other domestic poultry, it has become increasingly virulent and has achieved the capability of jumping

species to humans and to other animals with lethal consequences. Most alarmingly, the virus now seems to be transmitted from poultry back to migratory birds and, for the first time, is causing disease in the migrating bird population. This unprecedented pattern of transmission is an important reason why public health officials are watching the H5N1 virus carefully because it is a strain with the potential to cause the next influenza pandemic.

Compared to 1918, we are much better equipped scientifically. We have the tools to monitor genetic sequences of influenza viruses as they evolve in both humans and birds. We also have the capacity to develop and manufacture countermeasures against new strains of influenza. As we prepare for the possibility of the next pandemic influenza, it will be important to optimize the use of available public health measures and scientific tools and technologies.

Ongoing efforts in basic biomedical research are also critical to the comprehensive pandemic preparedness effort, including studies to understand viral pathogenesis, the ongoing search for new antivirals, new platforms and targets for vaccines, such as recombinant DNA and vector approaches, as well as improved vaccine manufacturing methods.

It is essential to have a multipronged approach including surveillance, public health measures, and biomedical research – with the ability to isolate infectious agents, decipher pathogenic mechanisms, and develop appropriate diagnostics, therapies, and vaccines – are all critical components of a multipronged response to emerging and re-emerging infectious diseases, including both seasonal and pandemic influenza to develop effective antiviral drug stockpiling and vaccine development and distribution.

*Sunil K. Lal, New Delhi*