

**EDITORIAL****Pandemic Influenza Virus: An expected rival encountered with empty arsenal**SU Munshi<sup>1</sup>

The epidemics of Influenza-A virus infection are of two distinct types – regional (seasonal) epidemics and global pandemic. The seasonal epidemic occurs annually or biannually among partially immune populations, and pandemic occurs at irregular and unpredictable intervals ranging from 11 to 30 years or more among the non-immune populations. The pandemics are related with new antigenic subtype of Influenza viruses. The seasonal Influenza costs around 13.9 thousand to 957.5 million of US dollar annually across US counties (Mao et al., 2012). A pandemic of Influenza is an epidemic that spreads on a worldwide scale and infects massive human population. These pandemics occur intermittently and remain unnoticed during which it infects many people. There have been about three Influenza pandemics in recorded history; naming Spanish flu (1918), Asian influenza (1957) and Hong Kong Influenza (1968). The Spanish flu is the most serious where approximately 50 million people or more died.

Haemagglutinins (HA) and Neuraminidase (NA) are the two important surface proteins of Influenza virus. Usually acquisition of cumulative point mutations in these proteins (antigenic drift) causes seasonal flu, whereas introduction of entirely a new antigen (antigenic shift) in relation to human immune experience through genetic re-assortment of human and animal viruses causes pandemic Influenza infection. There are a total of 16 HA (H1-H16) and 9 NA (N1- N9) subtypes in Influenza A virus which are maintained in aquatic birds, mammals and humans and can be readily re-assorted in some animals and humans and become virulent. The HAs are the initiators of the cellular entry which are usually cleaved only in a limited number of cell types in avirulent Influenza viruses but cleaved in a broad range of different host cells in virulent viruses and therefore are capable of causing lethal systemic infection. This has been thought to be one of the factors incriminated for the high pathogenicity of the pandemic viruses. Though the genome sequence analysis of the pandemic viruses of last century indicates that these were originated in birds or human reassortants, but the first pandemic strain of this 21st century is thought to be a mutation (re-assortment) of 4 known strains of Influenza A virus subtype H1N1; one each from humans and birds, and two from swine. This phenomenon has never happened before and it has created a twist and poses a new threat for generation pandemic Influenza.

It is speculated that three pandemics of Influenza can occur in a century. It was estimated that if a strain with similar virulence of 1918 Influenza virus emerged today, it could kill around 50-80 million people (Murray et al., 2006). The first pandemic of this century has already occurred in 2009. Though we are unaware about the type of HA and NA of next pandemic strain but we are expecting another pandemic in coming years. Now question comes whether we are ready to face such expected threat of pandemic? To combat against such virulent viruses, a comprehensive approach with modern armament is essential which includes appropriate diagnostics, vaccine, antivirals and surveillance. Unfortunately, these weapons against Influenza virus are woefully unsophisticated. Though early diagnosis is very crucial for the treatment of Influenza, still it remains out of reach. The current detection technologies - Polymerase Chain Reaction (PCR), virus culture, and immunoassays are having lack in the necessary sensitivity and specificity to distinguish avian from seasonal Influenza reliably (Lu 2006). Vaccination and antivirals are the two most important response measurers against

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Influenza virus that suffer from their own limitations. Usually within few years, flu strain changes and vaccine companies have to make a new batch of flu vaccine and people at risk have to be vaccinated annually. In case of pandemic it is not possible to prepare vaccine before the appearance and detection of actual virus strain. Production of Influenza vaccine is another drawback. It has to be grown in eggs; a process that takes up to several months and by this period of time, the virus could kill millions of people. Though the Neuraminidase inhibitors; Oseltamivir and Zanamavir are sensitive to Influenza viruses, the efficacy of them is discouraging. This is often due to the long interval between the recognition and treatment of human infections. Early treatment appears to be beneficial (WHO 2006). Inhaled Zanamivir is untried and may only be suitable as prophylaxis. In addition resistance of anti-Influenza drugs is also a growing concern.

Against all these cynical views there are some lights of optimism. Our understanding of the avian Influenza virus is growing rapidly and till November 2014 a total of 19,871 Influenza-A stains are sequenced from different global locations (IRD 2014). These data are invaluable for tracking viral evolution and transmission, and for developing new diagnostics, vaccines and drugs. Some of the viral proteins has been targeted to be exploited for the detection, vaccine production and making new antivirals. Especially abundantly expressed NS1 viral protein of avian Influenza exists in a specific form which could therefore be detected in a rapid diagnostic test by agents that are capable of binding to it but not to the NS1 proteins of typical non-avian human Influenza. Such target-based tests will not only permit detection of today's avian Influenza but may also be able to detect tomorrow's (Lu 2006). Currently different streamline vaccine manufactures can produced inactivated vaccine within few weeks by using 'reverse genetics technique' and clinical trial is currently under way to test the safety, immunogenicity and appropriate dosage of vaccine (Neumann et al., 2005). A DNA-based vaccination, which will be faster to manufacture is also in clinical trial, determining safety and efficacy (NIH 2011). In addition, a cell culture vaccine has already approved by FDA (Flucelvax 2012). To make all these research in reality, there is an urgent need for more international cooperation between clinicians, epidemiologists and researchers. Unlike previous flu pandemics, now we have the advanced knowledge and improved technology to develop countermeasures for this deadly disease. However, unless we improve our capacity to produce such countermeasures, we may experience again the devastation of past pandemics. [*Journal of Science Foundation, 2013;11(2): 35-36*]

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