Influenza, birds and the pandemic threat.

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Influenza remains a significant annual cause of human illness and death. The capacity for ongoing antigenic change by influenza viruses (referred to as antigenic drift) results in repeated infections throughout life and frequent, often severe, epidemics. Older members of the community, and those with underlying diseases such as heart or lung disease and diabetes, are more likely to become seriously ill, or to die, if they contract influenza and the full impact of outbreaks is often underestimated because illnesses or deaths are frequently attributed to the worsening of an underlying disease and not recognized as due to influenza; this is referred to as excess mortality

From time to time the human population experiences a global influenza epidemic or pandemic. This is the result of the evolution of a new influenza virus that is both markedly different from those that have been circulating previously in the human population and has the ability to transmit readily from person to person. In a population devoid of immunity the new virus spreads rapidly and usually causes more severe disease than normal. Three pandemics were experienced during the 20th century, the devastating Spanish Influenza of 1918-19, which is estimated to have claimed up to 50 million lives, and the less severe, but nevertheless serious, Asian and Hong Kong pandemics of 1957 and 1968-69.

Two types of influenza viruses, influenza A and influenza B, cause epidemic disease in humans but, of these, only influenza A has been associated with pandemics. It is now recognised that the influenza viruses evolved in aquatic birds such as ducks, geese and wading bird species in which they are normally carried as harmless gut infections and spread by the faecal-oral route in water habitats. Sixteen distinct antigenic subtypes of influenza A, designated H1 to H16, have been distinguished based on the viral haemagglutinin, the major protein on the virus surface. All of these subtypes have been found in birds whereas only three of them, H1-H3, are known to have established themselves as ongoing transmissible infections in the human population. The transfer into humans may involve genetic mixing between avian and human viruses as occurred for the Asian and Hong Kong pandemics, whereas there is now evidence that the Spanish influenza made the transition by direct adaptation without genetic mixing. It is the unique genetic structure of influenza viruses, a segmented single-stranded genome, which facilitates both their adaptive mutational changes and genetic reassortment.

Influenza A viruses have become successfully established in a number of animal species and a some of the avian influenza subtypes have been found to infect domestic poultry, usually causing mild disease symptoms. However, two of them the H5 and H7 subtypes, once introduced into a flock, can rapidly progress from a mild infection to a dramatic severe infection, referred to as highly pathogenic avian influenza. This spreads quickly killing most of the infected birds within a day or so. Until 1997 such outbreaks had been recognized in Europe, the Americas and Australia but had not been recorded in Asia. In addition, there was essentially no evidence that the infection could be passed from domestic poultry to humans. Then during 1997, in

Hong Kong 18 human cases of H5 infection were recorded, with 6 deaths. The source of infection was traced to exposure to infected poultry which had occurred largely in the wet markets where live poultry was sold. Since then H5 infection in domestic poultry has become widespread in Asia with an increasing number of human cases that have occurred as a result of contact with infected poultry or poultry products with a mortality rate around 50%. However, to date there is little evidence that the virus has gained the ability to transmit from person to person. Attempts to control the international poultry outbreak, by culling and vaccination, have had limited success. While there have been no recent human cases in Vietnam or Thailand which were most seriously affected in the initial outbreak, human cases have occurred in 8 other countries and the number continues to grow. It now appears that the virus, in its highly pathogenic state, being harboured in domestic ducks and, in addition, there is evidence that it is also being spread by migratory species and this has contributed to its presence in the Russian Federation, Europe, the Middle East and most recently in Africa.

The ongoing spread of the virus, continuing human infections and severity of the disease in man is causing growing concern that the virus may acquire the ability to readily transmit from person to person and give rise to the first influenza pandemic of this century. Recent research suggests that the current H5 avian viruses share some characteristics with the virus responsible for the Spanish 'flu pandemic, heightening fears that any pandemic that does eventuate may be particularly serious.

Nationally and internationally there has been an accelerating pandemic preparedness planning ever since the 1997 bird 'flu in Hong Kong. International surveillance for evidence of changes in the viruses infecting humans or of human to human transmission has increased in the hope that an outbreak may be contained at its source or at least of slowing its spread. The World Health Organization has a stockpile of an antiviral which can be used for this purpose. However, the very nature of the areas where infections have occurred mean that this is difficult, there may be delays in detecting such occurrences and distributing the drugs, and their effectiveness in a pandemic situation has yet to be confirmed. Several countries, including Australia, have also acquired stockpiles of antiviral drugs that it is hoped may prove life-saving in a pandemic or may be used to afford temporary protection of exposed people such as medical staff. But these stockpiles are adequate for no more that a percentage of the population, they are expensive, have a limited expiry dating and production capacity is limited. Authorities are, therefore, also considering other actions such as border closure to slow the spread of the virus.

There is little doubt, though, that should a pandemic start it will rapidly become a global problem with global consequences. The only truly effective means of protecting individuals and populations will be by vaccination with an appropriate and effective vaccine. Currently, experimental work and clinical trails are in progress to overcome problems that have been experienced with making an effective vaccine against H5 influenza and Australia is contributing to these trials. Nevertheless, even if successful the world's manufacturing capacity for influenza vaccine is limited and could cater for a relatively small percentage of the global population. There is a definite risk that spread of the virus would outstrip the time to produce, distribute and administer significant quantities of vaccine and that other interventions to limit spread and maintain essential services will be necessary.