AVIAN INFLUENZA - WHAT DOES IT HOLD FOR SOUTH AFRICA?

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How serious is the threat?

Most authorities are of the opinion that the world faces an imminent threat of a major global influenza pandemic. The threat comes from two lines of evidence. At its simplest another pandemic is due because major pandemics have occurred in 10 to 50 year cycles for centuries and the last major pandemic occurred in 1968. However, there is far more substantive evidence that the cause of the next pandemic will be the highly pathogenic avian influenza (HPAI) H5N1 virus which is responsible for the unprecedented outbreak in wild and domesticated bird populations in South-East Asia.

The virus has met two of the three conditions for establishing the next pandemic:- Firstly, the virus has crossed the species barrier and infected humans in 5 South-East Asian countries and secondly the virus has caused severe disease in humans – 65 of 126 known human infected cases have died (as at 16 November 2005). The 3rd condition, which would need to be satisfied, is efficient human-to-human spread.

This, thankfully, has not yet occurred, although there is mounting evidence that the virus could adapt to the human influenza virus receptor.[7]

What determines human-to-human spread?

Influenza viruses attach to epithelial cells via glycoprotein (sialic/neuraminic acid) receptors. In the case of avian influenza, the receptor site is characterised by an a2,3 galactosyl linkage whereas human influenza virus uses an a2,6 galactosyl linkage.

The a2,3 receptor is plentiful in the avian gastrointestinal tract and is therefore where the virus is mainly found and excreted in faeces, polluting surface waters from where it can infect domestic poultry.

In humans the á2,3 receptor is very sparse in the upper respiratory tract and therefore to cross the species barrier requires an extremely high dose of the virus, such as would occur in the "wet markets" of South-East Asia. Infections in humans, once established, tend to affect the lower respiratory tract, where á2,3 receptors may be more profuse, but relatively little is excreted from respiratory droplets. In contrast, the á2,6 receptor is profusely expressed in the upper respiratory tract. This accounts for the predominance of upper respiratory symptoms and high viral load in respiratory excretions resulting in highly effective person-to-person spread of human influenza.

Recently published molecular studies of the virus responsible for the devastating 1918/19 pandemic indicate that it was essentially an avian virus, probably transmitted directly from birds to humans, but with a human á2,6 receptor preference. The present threat hinges on the possibility of genetic changes due to mutation or reassortment (gene swapping between humans and avian viruses) which could give the HPAI H5N1 a human á2,6 receptor preference.

Evidence that h5n1 could adapt to humanto-human transmission:-

Clinical and epidemiological observations have suggested that human-to-human transmission could certainly evolve in H5N1. A case report of transmission to a mother and aunt who nursed a sick child in the absence of any known contact with sick poultry or birds, suggests possible human-to-human transmission.

Observations of clusters of infection in families or close-knit populations in countries such as Vietnam are also suggestive of human-to-human transmission. Between 1997 when the first human cases were reported in Hong Kong, until 2004, there have been a number of changes in the properties of the virus indicating genetic evolution. Vaccines made with 1997 isolates have been shown to be antigenically distinct from those made with 2004 isolates and diagnostic tests have similarly demonstrated these antigenic differences. The virus has progressively acquired resistance to the antiviral drugs amantadine and rimantadine.

Greater virulence between 1997 and 2004 has been demonstrated in experimental mice. Similar changes in the virus were seen in the 1918/19 pandemic. The first wave in the spring of 1918 was relatively mild; it was the second wave, which occurred six months later, where the full effect of the pandemic was felt as the virus became fully virulent.

Host adaptation from avian to various mammalian species, including domesticated and wild felines, has also reflected genetic evolution.

Greater opportunities for spread to humans are developing as a result of infected migratory birds expanding the reservoir of infection to other countries in Asia and Europe. Also, asymptomatic infection of domestic ducks may pose an increasing danger of spreading infection to unsuspecting humans.

Risks for south africa

South Africa is on the route of at least two flyways of migratory birds which could theoretically introduce H5N1 infection into this country from Europe.

However, the risk of migratory birds introducing H5N1 into humans in South Africa is relatively small. The majority of commercial poultry in this country is not exposed to potentially polluted surface water. It should also be emphasised that adequately cooked poultry poses no risk of infection as the virus is rapidly inactivated by cooking temperature.

A far more likely route of importation of infection is via infected humans once human-to-human transmission has been established, probably in South-East Asia. Screening precautions would probably be similar to what was in place for the SARS outbreak of 2003.

Unfortunately, screening for H5N1 would be far more difficult as the incubation period for avian influenza is longer than human influenza (from 2 to 5 days) and individuals are infectious during the incubation period unlike SARS where infectivity generally only commences once recognisable symptoms are manifest.

Conclusion

There is deep concern that the H5N1 virus, which shares much of the molecular structure of the H1N1 virus responsible for the 1918/19 pandemic, may produce a similar devastating global disease. Most scientists feel that human adaptation of H5N1 is inevitable. How it will express itself clinically and epidemiologically is difficult to predict. It may be as devastating as 1918/19 or the virus may lose virulence once it has become human adapted. The 1918/19 H1N1 virus rapidly became less virulent for humans after the pandemic and is today one of the lesser virulent subtypes of circulating human influenza virus. In addition, surveillance methodologies have vastly improved since 1918/19 and the availability of antiviral drugs could curtail or even abort a threatening pandemic. Given the present uncertainty, it is undoubtedly wise to energetically prepare for the less favourable scenario. The established infection in birds will remain as a long-term potential threat to human health.