Avian Influenza (Bird Flu)
Background Information

Introduction

Avian influenza (also known as bird flu or avian flu) is caused by viruses that usually infect birds, but, less commonly, has been known to infect pigs and some cats. All known avian influenza viruses belong to a species of virus called Influenza A virus and are non-infectious for most species.

Avian influenza is now commonly used to refer to infection from a particular subtype of Influenza A virus, H5N1, which has not only infected birds, but has caused cases of severe illness in humans who were infected with this strain of flu virus. Currently, H5N1 is transmitted through close contact with infected birds and may have been transmitted from one person to another in only a very few cases in Indonesia and Thailand.[1,2]

However, health authorities around the globe have identified this highly pathogenic form of avian influenza as a potential pandemic disease for the future and have taken action in order to prepare for large human outbreaks.

The spread of avian influenza amongst birds

Avian influenza was first identified in Italy in 1878, and is characterised by sudden onset of severe disease, rapid contagion and a death rate that can approach 100% within 48 hours.[3] A strain of the H5N1-type of avian influenza that emerged in 1997 has been identified currently as the most likely source of a future influenza pandemic.[4]

The H5N1 virus is present in the secretions and droppings of infected birds, which can contaminate food, soil and drinking water. The virus is capable of surviving in the environment for some time, and can be spread by contact with surfaces contaminated with faeces, secretions and blood etc.

The current outbreak of avian influenza started in South-East Asia in mid-2003.[5] It is the largest and most severe outbreak of avian influenza on record. Never before had so many countries

been simultaneously affected and the virus had the capacity to spread even further with the annual migration of birds and also through poultry trade. As a preventative measure millions of domestic birds were culled.

How can humans catch avian influenza?

Influenza viruses are normally highly species-specific, so that viruses that infect an individual species stay within that species, and only rarely cause infection in other species.

Over one hundred strains of avian influenza A viruses are known but only four are known to have caused human infections: H5N1, H7N3, H7N7 and H9N2.[4] In general, human infection with these viruses has resulted in mild symptoms and very little severe illness, with one notable exception: the highly pathogenic H5N1 virus that is the current threat.

Direct contact with dead or sick birds is the principal source of H5N1 infection in humans. Contact with surfaces contaminated by their faeces (eg, surfaces used to slaughter poultry or prepare them for cooking) is also a main route for infection.

The virus does not currently spread very easily from birds to humans and there have been 272 human cases in total and 166 deaths (61%) since 2003.[6]

According to a recent WHO analysis, 90% of human H5N1 influenza cases have been found in people under the age of 40.[7]

Cumulative number of confirmed human cases of avian influenza A/(H5N1) reported to WHO (6 February 2007)

Country	2003		2004		2005		2006		2007		total	
	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths	cases	deaths
Azerbaijan	0	0	0	0	0	0	8	5	0	0	8	5
Cambodia	0	0	0	0	4	4	2	2	0	0	6	6
China	1	1	0	0	8	5	13	8	0	0	22	14
Djibouti	0	0	0	0	0	0	1	0	0	0	1	0
Egypt	0	0	0	0	0	0	18	10	2	2	20	12
Indonesia	0	0	0	0	19	12	56	46	6	5	81	63
Iraq	0	0	0	0	0	0	3	2	0	0	3	2

Thailand	0	0	17	12	5	2	3	3	0	0	25	17
Turkey	0	0	0	0	0	0	12	4	0	0	12	4
Viet Nam	3	3	29	20	61	19	0	0	0	0	93	42
Total	4	4	46	32	97	42	116	80	9	8	**272**	**166**

Symptoms of human avian influenza

The incubation period for H5N1 avian influenza may be longer than that for normal seasonal influenza, which is around two to three days.[3] In humans, the H5N1 strain of avian influenza has caused symptoms that include high fever (usually higher than 38^{o}C) and influenza-like symptoms.[3] Diarrhoea, vomiting, abdominal pain, chest pain, and bleeding from the nose and gums have also been reported as early symptoms in some patients.[3] Clinical deterioration is rapid - in severe cases clinicians have observed respiratory failure three to five days after symptom onset. [3]

The pandemic threat

Fears of a pandemic have been heightened by the alarming spread of avian influenza (viruses of the H5N1 subtype) in bird populations around the globe. The concern is that the virus could ultimately mutate into a strain that is spread easily from human to human leading to a pandemic and potentially millions of deaths worldwide. [8]

The H5N1 virus has three of the four properties necessary to cause a serious pandemic: it can infect people, nearly all people are immunologically naive, and it is highly lethal. Therefore, the virus meets all prerequisites for the start of a pandemic apart from one: the ability to spread efficiently and sustainably among humans. [4]

Since mid-2003, 48 countries have reported the virus in domestic or wild birds, and of the 29 countries with outbreaks in poultry, only two have successfully eradicated the virus from their territories and maintained a disease-free status.[9] The pandemic threat will continue as long as the virus continues to circulate in birds, which could endure for many years. In addition, each new human case of H5N1 gives the virus an opportunity to evolve towards a fully transmissible pandemic strain.

Accurate predictions of mortality from such a pandemic cannot be made before the pandemic virus emerges and begins to spread, and all estimates of the number of deaths are purely speculative. The World Health Organization (WHO) has used a relatively conservative estimate

– from 2 million to 7.4 million deaths – purely as a useful and plausible planning target. This estimate is based on the comparatively mild 1957 influenza pandemic. Estimates based on a more virulent virus, closer to the one seen in 1918, are much higher but this particular pandemic was considered exceptional.

The warning signs

The warning signs of an impending pandemic include[10]:

- Clusters of patients with clinical symptoms of influenza, closely related in time and place that suggests human-to-human transmission
- The detection of cases in healthcare workers caring for infected patients.

Studying the viruses can complement field investigations by identifying genetic and other changes in the virus that could indicate their ability to infect humans. The sharing of new viral strains from affected countries and information with the international research community is therefore essential.

Preparing for a pandemic

According to the World Bank, a severe avian influenza pandemic among humans could cost the global economy up to $2 trillion with estimates suggesting that more than 3% of the global economy's gross national product would be lost.[11] Earlier estimates of $800 billion no longer meet the recent financial modelling should the virus mutate and pass to humans.

The WHO has issued a series of strategies[12] for responding to the influenza pandemic threat and has defined six distinct phases in order to facilitate pandemic preparedness planning, with roles defined for governments, industry and the WHO.

The present situation is categorised as phase three: *a novel influenza virus subtype is causing human infections, but does not spread efficiently or sustainably from one person to another.*[13]

Tracking a potential pandemic		***Phase***
Interpandemic phase New virus in animals, no human cases	Low risk of human cases	***1***
	Higher risk of human cases	***2***
Pandemic alert New virus causes human cases	No or very limited human–to–human transmission	***3***
	Evidence of increased human–to–human transmission	***4***
	Evidence of significant human–to–human transmission	***5***
Pandemic	Efficient and sustained human–to–human transmission	***6***

Source: WHO

According to the WHO, vaccination and the use of antiviral drugs are two of the most important response measures for reducing morbidity and mortality in the event of a pandemic.[14] Conventional influenza vaccines may not be the most appropriate course of treatment for a pandemic that is caused by a new strain of influenza and therefore it is imperative that new vaccines are developed that specifically target the H5N1 virus.

Candidate pandemic vaccines are in development at GSK and at other companies. These are urgently needed in order to meet the anticipated demand should a pandemic of avian flu emerge in the human population. Also, a pre-pandemic vaccination strategy is currently being evaluated. This entails developing a vaccine with a flu strain that is considered to be of pandemic potential eg H5N1 and then vaccinating a population in advance of a pandemic. To be of any benefit such a vaccine needs to show a cross-protective immune response against 'drifted' variants of the vaccine strain. The current stockpile of antiviral drugs for a rapid response, though it is a substantial part of an overall prevention strategy, is unlikely to be adequate in a pandemic setting, due to the high number of people infected and the rapid spread of the disease.[15]

REFERENCES:

1 http://www.cdc.gov/flu/avian/gen-info/avian-flu-humans.htm (Accessed 12.10.06)
2 http://www.who.int/csr/don/2006_05_23/en/index.html (Accessed 12.10.06)
3 http://www.who.int/mediacentre/factsheets/avian_influenza/en/ (Accessed 12.10.06)
4 WHO. Avian influenza (" bird flu") - Fact sheet at http://www.who.int/mediacentre/factsheets/avian_influenza/en/#humans (Accessed 12.10.06)
5 WHO, Avian Influenza A (H5N1) in Humans and Poultry in Viet Nam, Jan. 13, 2004, at http://www.who.int/csr/don/2004_01_13/en/ (Accessed 12.10.06)
6 http://www.who.int/csr/avian_influenza/en/ (Accessed 13.02.06)
7 WHO Weekly Epidemiological Record. No. 6, 2007, 82, 41–48
8 Ungchusak K *et al*. Probable person-to-person transmission of avian influenza A (H5N1). N Eng J Med 2005; 352: 333-40.
9 http://www.who.int/gb/ebwha/pdf_files/WHA59/A59_4-en.pdf (Accessed 12.10.06)
10 WHO Avian Influenza Frequently Asked Questions at: http://www.who.int/csr/disease/avian_influenza/avian_faqs/en/index.html#drugs (accessed 10.06.06)
11 Annual IMF World Bank Meeting, Singapore, September 2006.
12 WHO global influenza preparedness plan: the role of WHO and recommendations for national measures before and during pandemics. Annex 1. 2005 [cited 2005 Apr]. Available from www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_2005_5/en. (Accessed 12.10.06)
13 http://www.who.int/csr/disease/avian_influenza/phase/en/index.html (Accessed 12.010.06)
14 WHO, Responding to the avian influenza pandemic threat. Communicable Disease Surveillance and Response Global Influenza Programme. At: http://www.who.int/csr/resources/publications/influenza (Accessed 12.10.06)
15 http://www.who.int/csr/disease/avian_influenza/avian_faqs/en/index.html#pandemic (Accessed 12.010.06)