衞生防護中心
Centre for Health Protection

Scientific Committee on Emerging and Zoonotic Diseases

Latest Development in Avian Influenza

Purpose

This paper provides an updated situation of avian influenza H5N1 pertaining to human infections, bird and poultry infections, virology, and vaccine aspects.

Background

2. The World Health Organization (WHO) has designated 6 different phases in relation to global situation of influenza and influenza pandemic. On 5 November 2005, the WHO announced that the world is presently in phase 3 of the WHO global influenza preparedness plan – that means a new influenza virus subtype is causing disease in humans, but not yet spreading efficiently and sustainably among humans.[1]

Human infections

3. As of 30 November 2005, there were altogether 133 WHO confirmed human cases of H5N1 infection with 68 deaths since December 2003. The majority of these cases occurred in countries of South-East Asia.[2]

4. On 17 November 2005, the Ministry of Health in China announced two laboratory-confirmed human cases of H5N1 infection. The first case involved a 9-year-old boy from Hunan Province and the other case was a 24-year-old poultry farmer from Anhui Province. In addition, the 12-year old sister of the 9-year-old boy had died with

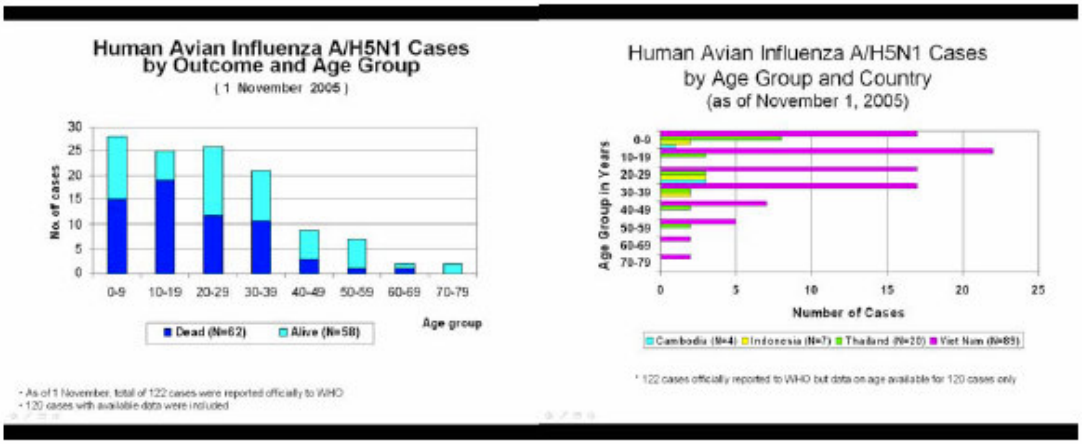
clinical features compatible with H5N1 infection, but laboratory confirmation was not available in her case. On 24 November 2005, the Ministry of Health in China confirmed the 3rd case of human infection. She was a 35-year-old poultry farmer living in Anhui Province. She developed symptoms on 11 November and passed away on 22 November 2005. Poultry outbreaks of H5N1avian influenza have occurred in both Hunan and Anhui in October and November.[3]

5. The first phase of human infections (Dec03 – Mar04) caused 35 cases with 24 deaths in Vietnam and Thailand. The second phase (Jul04 – Oct04) in Vietnam and Thailand resulted in 9 cases with 8 deaths. The third phase (Dec04 – Jun05) was the largest, causing 64 cases including 22 deaths in Cambodia and Vietnam. The fourth phase (Jul05 – Nov05) is ongoing and as of 30 November 2005, caused 25 infections including 14 deaths in China, Indonesia, Thailand and Vietnam.[2]

Date of WHO Report	Cambodia		China		Indonesia		Thailand		Vietnam		Total		CFR (Wave)
	Case	Death	Case	Death	Case	Death	Case	Death	Case	Death	Case	Death	
Dec03-Mar04	0	0	0	0	0	0	12	8	23	16	35	24	68.6%
Jul03-Oct04	0	0	0	0	0	0	5	4	4	4	9	8	88.9%
Dec04-Jun05	4	4	0	0	0	0	0	0	60	18	64	22	34.4%
Jul05-Nov05	0	0	3	2	12	7	4	1	6	4	25	14	56.0%
Total	4	4	3	2	12	7	21	13	93	42	133	68	51.1%
CFR (Country)	100%		66.7%		58.3%		61.9%		45.2%		51.1%		--

6. The overall case fatality rate (CFR) was 51%, compared with 33% in the Hong Kong outbreak in 1997.[4] Phase 3 appeared to have a lower CFR compared with other phases. Two of the four fatal cases in Cambodia were hospitalized in Vietnam.[5] The majority of cases had history of contact with diseased / dying poultry before onset of illness.

7. There are 120 cases with details of age and outcome available (WHO's information as of 1 November 2005). More than 80% of cases (100 cases) were below 40 years old. The case fatality rate was the highest among 10-19 years old group (76%), follow by 0-9 years old group (54%) and then 30-39 years old group (52%).



Birds and poultry

8. As of 30 November 2005, 15 countries were confirmed to be affected by H5 / H5N1 avian influenza, namely Cambodia, China, Croatia, Indonesia, Japan, Kazahkstan, Korea, Laos, Malaysia, Mongolia, Romania, Russia, Thailand, Turkey and Vietnam. The poultry outbreaks have caused huge economical loss and at least 150 million of birds has been culled / slaughtered to limit the spread of the condition in recent 2 years.[6]

9. Countries in South-East Asia were affected most. The increased concentration of birds in large scale, intensive, farming as well as greater numbers in backyard farms is likely to be an important factor for evolution of highly pathogenic avian influenza in recent years.[7] High intensity systems result in the production of genetically similar animals in close quarters, which predisposes to rapid spread and uniform mortality levels once a pathogen enters the stock. In addition, many of the production systems that supply feedstock and day old chicks to these large producers, as well as those that process and market poultry products within countries are centralized, allowing rapid transmission of disease from one area to another.

10. In April 2005, large numbers of wild birds in Qinghai Lake were found to die of H5N1 infection. Previously wild birds were believed to be an asymptomatic reservoir for the virus. Since then, the same strain of H5N1 was found to spread in a north-western direction and cause outbreaks of wild migratory birds and poultry deaths in Mongolia, Kazahkstan, southern part of Russia, Turkey, Romania and Croatia.[8,9] In October and November 2005, H5N1 poultry outbreaks were reported in some provinces in China, including Anhui, Hubei, Hunan, Liaoning, Shanxi, Xinjiang, Inner Mongolia, Ningxia, and Yunnan. Meanwhile, Japan, Korea and Malaysia were considered H5N1-free by OIE.[10] Control measures targeted at poultry are considered the most cost-effective way to substantially reduce the risk of a human pandemic evolved from H5N1.[11]

Virology

11. Phylogenetic analyses indicate that the Z genotype has become dominant and that the virus has evolved into two distinct clades, one encompassing isolates from Cambodia, Laos, Malaysia, Thailand, and Vietnam and the other isolates from China, Indonesia, Japan, and South Korea.[12] More recently, a separate cluster of isolates has appeared in northern Vietnam and Thailand. The importance of these genetic and biological changes with respect to human epidemiology or virulence is uncertain.[12]

12. Studies of hospitalized patients indicate that viral replication is prolonged. Nasopharyngeal replication is less than in human influenza.[13] There is a significant proportion of diarrhea among affected patients, coupled with detection of viral RNA in fecal samples, including infectious virus in one case, suggesting that the virus replicates in the gastrointestinal tract.[13]

13. In terms of antiviral resistance, in contrast to isolates from the 1997 outbreak, recent human influenza H5N1 isolates are highly resistant to adamantanes.[12] A recent joint FAO/OIE/WHO statement mentioned the prophylactic use of amantadine in poultry production in Asia and current H5N1 strains in poultry seem to be sensitive to amantadine.[14] There was a report of reduced susceptibility to oseltamivir following treatment but the isolate remained sensitive to zanamivir.[15] No circulating strain of H5N1 was found to have spontaneous resistance to neuramindase inhibitors.[16]

Vaccines

14. At least seven vaccine manufacturers are currently using the WHO prototype H5N1 strain as the "seed" to develop H5N1 vaccines (e.g., Sanofi-Pasteur, Chiron, Glaxo-Smith-Kline). Data regarding the optimal antigen dose, dose regimen, and effects of adjuvant are not currently available, but some early results from clinical trials are expected in December 2005.

15. Production of influenza vaccines based on fertilized eggs is a major limiting step to mass production. Cell culture-based H5N1 vaccines are being developed by a number of vaccine manufacturers (e.g., Baxter, Chiron, GSK, Solvay). Cell culture-based vaccines have the advantages of being grown in a serum and protein free medium, and contain a high yield of virus antigens. At present, Baxter's and Chiron's cell culture influenza vaccine has reached their phase two and three trial respectively.

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