Avian Influenza infection in Human

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Avian Influenza ("Flu")

Avian influenza is an infectious disease of birds caused by type A strains of the influenza virus. The devastating form of influenza in chickens was recognized as a distinct disease entity as early as 1878 in Italy. The isolation of an avian influenza virus in 1901 preceded the discovery of mammalian and human influenza viruses, but it was not until 1955 that it was recognized that avian and mammalian influenza viruses are closely related.

Avian influenza A viruses - subtypes

Avian species can be infected by each of the 15 HA (Haemagglutinin) and nine NA (Neuraminidase) subtypes of influenza A viruses recognized up to now, in apparently any possible combinations. To date all outbreaks of the highly pathogenic form have been caused by influenza A viruses of subtypes H5 and H7. Highly pathogenic viruses possess a telltale genetic "trade mark" or signature - a distinctive set of basic amino acids in the cleavage site of the HA - that distinguishes them from all other avian influenza viruses and is associated with their exceptional virulence.

Natural Host and Reservoir

The reservoir of influenza A virus is in aquatic birds, especially ducks, shorebirds and gulls. Influenza A viruses appear well adapted to wild aquatic birds that are considered to be their natural hosts, and in which disease signs rarely appear. Considerable circumstantial evidence has long suggested that wild waterfowl introduce avian influenza viruses, in their low pathogenic form, to poultry flocks, but do not carry or directly spread highly pathogenic viruses. This role may, however, have changed very recently. The die-off of more than 6000 migratory birds, infected with the highly pathogenic H5N1 virus that began at the Qinghai Lake nature reserve in central China in late April 2005, was highly unusual and probably unprecedented. Prior to that event, wild bird deaths from highly pathogenic avian influenza viruses were rare, usually occurring as isolated cases found within the flight distance of a poultry outbreak.

Susceptible Host

The host range of influenza virus is generally unpredictable. Domestic poultry including chickens and turkeys are particularly susceptible to epidemics of rapidly fatal influenza. Influenza A viruses have been isolated from humans and from several other mammalian species. Domestic swine and Humans are now considered as mixing vessel since they are susceptible to infection with both avian and mammalian viruses, thus resulting in emergence of novel subtype.

Transmission among birds

Large amounts of virus are secreted in bird droppings, contaminating dust and soil. Airborne virus can spread the disease from bird to bird causing infection when the virus is inhaled. Contaminated equipments, vehicles, feed, cages or clothing-especially shoes can carry the virus from farm to farm. The virus can also be carried on the feets and bodies of animals, such as rodents, which act as "mechanical vectors" for spreading the disease. Direct or indirect contact of domestic flocks with wild migratory waterfowl has been implicated as a frequent cause of epidemics. Live bird markets have also played an important role in the spread of epidemics.

Disease in Birds

Infection causes a wide spectrum of symptoms in birds, ranging from mild illness to a highly contagious and rapidly fatal disease resulting in severe epidemics. The later is known as "highly pathogenic avian influenza" (HPAI). This form is characterized by sudden onset, severe illness and rapid death, with a mortality that can approach 100 percent. If the birds survive for more than 48 hrs,

there is cessation of egg laying, respiratory distress, lacrimation, sinusitis, diarrhea, edema of the head, face and neck and cyanosis of unfeathered skin, particularly the comb and wattles. To date, all outbreaks of the highly pathogenic form of avian influenza have been caused by viruses of the H5 and H7 subtypes. Recent research has shown that H5 and H7 viruses of low pathogenicity can, after circulation for sometimes short periods in a poultry population, mutate into highly pathogenic viruses. Low pathogenic avian influenza (LPAI) viruses cause only mild disease or asymptomatic infection.

Flu and its significance to Humans

Influenza viruses are normally highly species-specific, meaning that viruses that infect an individual species (humans, certain species of birds, pigs, horses, and seals) stay "true" to that species, and only rarely spill over to cause infection in other species. Of the hundreds of strains of Avian influenza A viruses, only four are known to have caused human infections: H5N1, H7N3, H7N7, and H9N2. 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.

Scenario Before 1997

Despite the warnings to the poultry industry about these viruses, only influenza A H1N1, H2N2, H3N2 viruses have caused widespread respiratory illness in humans in the 20th century including pandemics in 1918, 1957 and 1968 heralding the emergence of each human subtype respectively.

The pandemics had its first recognizable wave in the spring of 1918, with descriptions of outbreaks in the United States, Europe and Asia by the end of April. Sequence and phylogenetic analysis of the completed 1918 gene segments suggest that the haemagglutinin and neuraminidase gene segments were derived from an avian influenza source but not directly. The HA and NA gene segments of the 1918 virus have acquired a number of changes from the avian consensus that suggests to us that the precursor to the pandemic strain spent some period of time, perhaps 5 to 10 year, adapting and evolving in a mammalian host.

In 1957, the Asian pandemic virus (H2N2) had acquired the HA, NA and PB1 gene from an avian virus, while in 1968, the Hong Kong pandemic strain (H3N2) had acquired the HA and PB1 gene from an avian source, retaining the NA from the preceding H2N2 subtype. The mechanism of emergence of subtypes in 1957 and 1968 (Reassortment of genes with avian influenza virus) is different from its first pandemic 1918.

Thus pandemic strains possessing novel HA derived from avian or animal influenza viruses, with or without other accompanying avian virus genes, sporadically emerge in humans and have the potential to cause a pandemic of influenza if the virus is capable of transmitting among a human population that lacks immunity to the novel HA. Indeed, reassortment viruses, harbouring a combination of avian and human viral genomes have been responsible for major pandemics of human influenza.

Mixing vessel

Swine have long been considered a likely mixing vessel in which avian and human viruses may reassort, since these animals possess respiratory epithelium that bear cell surface sialyloligosacharides that are preferentially recognized by avian (sialic acid (SA) a 2,3 galactose) and human influenza viruses (SA a 2, 6 galactose). Largely because of these differences in receptor specificity, avian influenza viruses were not considered to be able to directly infect humans and cause influenza like respiratory illness.

Scenario after 1997

However in the late 1990's two subtypes of avian influenza emerged that caused respiratory infections in humans. In 1997, a high pathogenicity avian H5N1 influenza virus circulated among poultry on farms and in retail markets in Hong Kong. The H5N1 viruses were transmitted to humans, causing 18 documented cases of respiratory disease, including six deaths. In 1998-99, a second influenza A virus subtype, H9N2, was isolated from humans with respiratory disease.

This event established for the first time that these avian influenza viruses were to be considered a risk to public health. The relatively high rates of H5 and H9 antibody seroprevalence among Hong Kong poultry workers highlight the potential for avian viruses to transmit to humans, particularly those with occupational exposure. Such transmission increases the likelihood of reassortment between a currently circulating human virus and an avian virus and thus the creation of a strain with pandemic potential. All human cases have coincided with outbreaks of highly pathogenic H5N1 avian influenza in poultry.

All evidence to date indicates that close contact with dead or sick birds is the principal source of human infection with the H5N1 virus. Especially risky behaviours identified include the slaughtering, defeathering, butchering and preparation for consumption of infected birds. In a few cases, exposure to chicken faeces when children played in an area frequented by free-ranging poultry is thought to have been the source of infection. Swimming in water bodies where the carcasses of dead infected birds have been discarded or which may have been contaminated by faeces from infected ducks or other birds might be another source of exposure. In some cases, investigations have been unable to identify a plausible exposure source, suggesting that some as yet unknown environmental factor, involving contamination with the virus, may be implicated in a small number of cases.

Situation in India

The first outbreak of Avian Influenza occurred in domestic poultry on 18th February 2006 in Navalpur village in Maharashtra. Over 1.5 lakh birds were killed in Maharashtra and the loss was estimated at Rs.20 crore. The strain reported was H5N1.The reported outbreaks continued through April 2006.On 25th July 2007; an outbreak occurred in backyard poultry, the first report since April 2006 in Chingmeirong village, East Imphal District of Manipur. Samples tested at the High Security Animal Disease Laboratory in Bhopal and the National Institute of Virology in Pune confirm that the samples are positive for H5N1 strain of Avian Influenza.

The Ministry of Health and Family Welfare has informed WHO that no human cases of H5N1 infection have been detected to date. Tests conducted on samples taken from persons under investigation and their close contacts have yielded no positive results as of today.

In India, as in all countries experiencing their first outbreaks of highly pathogenic H5N1 avian influenza, WHO strongly recommends that patient samples be sent to WHO collaborating laboratory for diagnostic confirmation. Certainty about the status of human cases in a newly affected country is important for accurate risk assessment.

In addition, analyses conducted by WHO approved laboratories can yield information about the possible evolution of the virus and clues about how the virus may have arrived in the country. Genetic and antigenic studies of circulating viruses also help ensure that work on the development of a pandemic vaccine strays on track.

Conclusion

Outbreaks caused by the H5N1 strain are presently of the greatest concern for human health. In assessing risks to human health, it is important to know exactly which avian virus strains are causing the outbreaks in birds.All available evidence points to an increased risk of transmission to humans when outbreaks of highly pathogenic avian H5N1 influenza are widespread in poultry. There is mounting evidence that this strain has a unique capacity to jump the species barrier and cause severe disease, with high mortality, in humans. There is no evidence, to date that efficient human to human transmission of H5N1 strain has occurred and very often. Efficient transmission among humans is a key property of pandemic strains and a property that the avian H5N1 and H9N2 viruses apparently lacked. The biological and molecular basis for effective aerosol transmission among humans is not known. The virus can improve its transmissibility among humans via two principal mechanisms. The first is a “reassortment” event, in which genetic material is exchanged between human and avian viruses during co-infection of a human or pig.Reassortment could result in a fully transmissible pandemic virus, announced by a sudden surge of cases with explosive spread.

The second mechanism is a more gradual process of adaptive mutation, whereby the capability of the virus to bind to human cells increases during subsequent infections of humans. Adaptive mutation, expressed initially as small clusters of human cases with some evidence of human-to-human transmission, would probably give the world some time to take defensive action, if detected sufficiently early.

As the number of human infections grows, the risk increases that a new virus subtype could emerge, triggering an influenza pandemic. Humans as well as swine must now be considered a potential mixing vessel for the generation of such a virus. This link between widespread infection in poultry and increased risk of human infection is being demonstrated right now in Asia.

However, urgent control of all outbreaks of avian influenza in birds - even when caused by a strain of low pathogenicity- is of utmost importance. Research has shown that certain, avian influenza virus strains, usually of low pathogenicity can rapidly

mutate (within 6 to 9 months) into a highly pathogenic strain if allowed to circulate in poultry populations. Altogether, more than half of the laboratory-confirmed cases have been fatal. H5N1 avian influenza in humans is still a rare disease, but a severe one that must be closely watched and studied, particularly because of the potential of this virus to evolve in ways that could start a pandemic. The challenge for all of us is to gain an under-standing of how just 10 or 11 proteins of these viruses to replicate and be transmitted not only bet-
ween hosts of one species but also between species.

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PETA is protesting against what it claims is cruel teaching procedures being conducted on animals at the Ross University School of Veterinary Medicine

BASSETERRE, St Kitts, March 14, 2008 - The world's largest animal rights organisation is protesting against what it claims is cruel teaching procedures being conducted on animals at the Ross University School of Veterinary Medicine in St. Kitts.

People for the Ethical Treatment of Animals (PETA) has called on the American Veterinary Medical Association's (AVMA) to withhold accreditation from the school until it abandons "teaching exercises that harm and kill animals and switches to humane, modern teaching methods, including computer models and clinical training."

AVMA is currently conducting an accreditation process for Ross University which is owned by the Chicago-based education company, DeVry Inc.

PETA made the appeal in letter which it said it sent on Wednesday to Assistant Director for Education and Research Division at AVMA's Center for Veterinary Education Accreditation, Dr Elizabeth Sabin. The call came after the organisation received complaints and photographs from students documenting the mutilation of animals who they claimed were subjected to multiple surgeries before being killed and dissected. Students who objected to the procedures were reportedly threatened with a failing grade if they did not participate.

"Ross veterinary students are given dogs and donkeys to care for and are forced to perform painful surgeries on them, over and over. Then they are forced to kill the animals," said PETA Research Director Kathy Guillermo.

"Ross must be penalised for forcing students to harm animals in their quest to learn how to help them." In its correspondence to Dr Sabin, PETA contended that the activity was in violation of St Kitts' Protection of Animals Act.

"Other veterinary schools train their students without resorting to multiple surgeries on animals and euthanizing healthy animals. As the law in St. Kitts forbids causing "unnecessary suffering" to animals, we urge you to investigate this matter and suspend the accreditation process for Ross University if it refuses to discontinue its reportedly abusive and apparently illegal practices," the group wrote to Dr Sabin.

PETA said it has also contacted the director of the Caribbean Accreditation Authority for Education in Medicine and other Health Professions, as well as Deputy Prime Minister Sam Condor, asking for the accreditation to be suspended.