Community & Hospital Letter

Monthly Publication of the
Kansas City Health Department
2400 Troost
Kansas City, MO 64108

Influenza H5N1 — the Next Pandemic?

Influenza experts from around the world are anxiously watching the evolving epizootic in Asia of highly pathogenic avian influenza caused by A/H5N1. The rapidly expanding epizootic has killed or caused to be slaughtered approximately 19 million chickens and other birds, as well as a growing list of human victims in several countries. Of the 15 avian influenza subtypes which normally cause infection in birds and pigs, only the H5N1 strain has exhibited a unique capacity to cause severe disease, with high mortality, in humans. Infections in people with other avian influenza subtypes, such as H7N7 and H9N2 viruses generally cause only mild illness and rarely death.

The simultaneous occurrence in various countries (Cambodia, China, Indonesia, Japan, Laos, South Korea, Thailand, and Vietnam) of large epizootics of highly pathogenic H5N1 influenza in domestic poultry is historically unprecedented and the present situation may grow worse. Based on two stored samples given to the World Health Organization (WHO), it would appear that the current pandemic has been developing since last April. Furthermore, there have accusations in several Asian countries of government cover-ups about the avian influenza problem.

In bird populations, the disease is highly contagious and rapidly fatal, and spreads easily from farm to farm. Wild migratory waterfowl can spread infection to domestic flocks. Infected birds can shed large amounts of virus in their feces. It can survive for long periods of time in the tissues and feces of diseased birds and in water, especially when temperatures are low. In water, the virus can survive up to 4 days at 22 ^{o}C. and >30 days at 0 ^{o}C The virus survives in frozen material indefinitely. As typical with most diseases, a few birds survive H5N1 infection and these birds will continue to shed the virus in their feces for a minimum of 10 days.

This particular strain of H5N1 may be especially virulent for poultry. China has reported widespread die-offs of ducks due to this virus and ducks are generally considered fairly resistant to avian influenza viruses. This observation suggests greater virulence than would be normally expected.

The extent of the Asian epizootic increases the likelihood that more humans will become infected. Human morbidity has been confirmed or suspected in at least Vietnam, Thailand, and Indonesia with a case fatality rate among confirmed H5N1 human cases of approximately 70-80%.

When H5N1 influenza emerged in Hong Kong in 1997, 18 persons were infected and 6 died. An additional 2 cases, with 1 fatality, again occurred in Hong Kong in February 2003. The current widespread epizootic increases the opportunity for human influenza viruses and H5N1 to exchange genes in persons who are simultaneously infected. The frequency of such co-infections would raise the likelihood that a completely new influenza virus subtype might emerge, carrying sufficient human genes to allow efficient and sustainable person-to-person spread. Thus far, the H5N1 strain is still comprised of only avian genes. And, all human infections have been the result of direct contact with infected poultry. WHO is recommending quarantine for persons suspected of having avian influenza infection so that they will not come into contact with sufferers of regular influenza.

The potential for human contact with infected birds in Asia is enormous. In Thailand, with the world's 4th largest chicken industry, hundreds of thousands of persons are employed on 30,000 poultry farms and related industries. And, Hong Kong imports 70,000 live chickens a day from China. In January, a dead peregrine falcon in Hong Kong was found to be infected with H5N1, indicating its presence in that city.

Rapid elimination of the H5N1 virus in bird populations is an essential measure to prevent the emergence of a new influenza subtype with pandemic potential. This measure not only helps prevent further spread in bird populations, but also reduces opportunities for human infection. In 1997, 1.4 million birds were killed in Hong Kong. During the current epizootic, while most of the affected countries have instituted massive kill programs (culling) for infected flocks, the control effort is compounded by the large number of "backyard" farms where chickens are kept in rural areas. Further, culling operations can place large numbers of workers at risk of brief but intensive exposure to the H5N1 virus, thus prevention of infection in cull workers is a high priority. Consequently, WHO is rushing protective gowns and masks to affected countries in order to protect workers involved in the culling.

Genetic sequencing of the 2004 H5N1 strains from people and poultry have shown significant differences between these viruses and strains obtained during the 1997 and 2003 outbreaks in Hong Kong, indicating that the virus has mutated. In addition, the 2004 strain exhibits resistance to both amantadine and rimantadine, one of the two main classes of drugs used to treat influenza A infections. Preliminary data suggests, however, that the strains are susceptible to the neuraminidase inhibitors, such as Tamiflu. Consequently, the Centers for Disease Control and Prevention (CDC) has begun to create a stockpile of neuraminidase inhibitors.

As a precaution, WHO already is working to develop a human vaccine based on the H5N1 strain. Using reverse engineering, WHO announced it will have a prototype virus strain for a human vaccine by mid-February and hopes to begin phase 1 clinical trials by the end of February or early March. However, there are many patent, legal, and other issues that need to be addressed before a candidate vaccine could become a reality (New Scientist, 1/24/04). These issues could prevent or significantly delay the vaccine from reaching the countries most at risk.

Even if such a strain can be rapidly produced, mass production of a flu vaccine would still be dependent upon growing the virus in eggs, a process that could take 5 months or so. In addition, there is uncertainty whether regulatory agencies would approve a human influenza vaccine made using reverse genetics. As an aside, since growing any influenza virus vaccine strain in chicken eggs has been criticized as too slow to allow rapid production of vaccine in a global pandemic, Aventis Pasteur has contracted with a small Dutch biotech company, Crucell, to develop a cell-based technology that could shave off several months of production time.

Meanwhile, WHO wants to use current human flu vaccines to immunize the populace in affected Asian countries to diminish the risk of someone becoming co-infected with both human and avian influenza viruses. The problem is that the vaccine used in the northern hemisphere this flu season has poor to little efficacy against the A/Fujian strain, the dominant circulating virus. Vaccine being produced for the Southern Hemisphere, however, is protective against this strain, therefore, WHO is attempting to convince countries to release portions of their vaccine orders to WHO for use in the avian flu affected areas.

Both the US and United Kingdom have issued guidance to persons traveling to countries where H5N1 virus is active. Basically, this advice is stay away from poultry farms, live animal markets or any surfaces contaminated with bird droppings. In addition, CDC is urging physicians to ask

patients with flu-like symptoms if they have traveled to places in Asia were the disease is active.

Avian influenza was first identified in Italy more than 100 years ago and occurs worldwide. All birds are thought to susceptible to infection, although some species are more resistant than others. 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 latter is known as highly pathogenic avian influenza and is characterized by sudden onset, severe illness, and rapid death, with a mortality rate approaching 100%. To date, only two subtypes, H5 and H7, have caused outbreaks of highly pathogenic avian influenza. Domestic poultry are particularly susceptible to highly pathogenic avian influenza due to the conditions under which the birds are raised. In 2003, an outbreak of highly pathogenic H7N7 avian influenza in poultry caused infection, with mild illness, in 83 persons, with 1 fatality.

In a somewhat related incident, the US government has charged two former executives of Maine Biological Laboratories with conspiracy and mail fraud linked to smuggling a H5 bird flu virus into the country. The company allegedly agreed to secretly produce a flu vaccine for a Saudi Arabian poultry producer that did not want to buy it openly, as this would have revealed the presence of the disease and obligated it to destroy its flocks. The virus allegedly was smuggled into the US in 1998 was not a “highly pathogenic” strain and posed little threat to US flocks.

The Kansas City Health Department will hold a **Principles of Epidemiology** course on May 3rd-6th, 2004. This is an introductory course to epidemiology and is open to employees of local health departments, community based organizations, medical care providers, infection control practitioners, and other interested parties. The course is free.

To enroll, please contact Gerald L Hoff, PhD, at 816-513-6149 or e-mail at gerald_hoff@kcmo.org. Registration is limited to 15 individuals and closes on April 1, 2004.

Mad Cow Disease – Update

On the 23rd of December 2003, the US cattle industry was rocked by the news that bovine spongiform encephalopathy (BSE), otherwise known as mad cow disease, was diagnosed in a 6.5 y old dairy cow in the state of Washington. The cow had been non-ambulatory (termed a downer cow) prior to slaughter, a condition attributed to calving. Meat and rending products from this animal and all other cattle slaughtered the same day at the abattoir were located and recalled. Subsequent investigation revealed that this animal had been born in Canada and was one of some 300,000 cattle imported into the US from Canada each year. Testing of other cattle in the herd has not revealed any other infections. The US Department of Agriculture (USDA) has completed its tracing of other cattle raised in the same herd as the index case as well as other imported animals born into the herd where the index case was calved.

BSE cases have been identified in 20 European countries, Japan, Israel, and Canada. Since BSE surveillance was initiated in 1990, the USDA has tested brain tissue from approximately 57,000 cattle, targeting those at high risk for BSE (e.g., downer cattle and cattle with neurologic signs); the cow from Washington state represents the 1st identification of BSE. This diagnosis resulted in imposition of importation bans by other countries of US cattle and cattle products.

The feeding of cattle the rendered products of other animals, particularly from downer cattle, is thought to play a major role in transmission of BSE. In the US, the feeding of rendered cattle products to other cattle has been prohibited since 1997, and the importation of cattle and cattle products from countries with BSE or considered to be at high risk for BSE has been prohibited since 1989. These measures have

minimized the potential exposure of animals and humans to the BSE agent Since the recognition of the Washington cow, new restrictions have been imposed on the use of downer cattle meat for human consumption. Of the 36 million cattle slaughtered in the US each year, approximately 195,000 are downers. Also, the feeding of cow blood and chicken wastes to cattle has been banned. Consumer confidence in beef products fell following the recognition of BSE, with 20% of US adults saying that fear of mad cow disease will change their eating habits (Harris Interactive Health Care Poll 1/13/04).

The public health risk from cattle with BSE is the development of the neurodegenerative disease known as variant Creutztfeldt-Jacob disease (vCJD). In the United Kingdom (UK) there have been 103 definite and 42 probable cases of vCJD since 1995, with no indication that the incidence of new cases is declining. Six of the probable cases were alive as of the 5th of January 2004. Human cases have also occurred in France, Ireland, Italy, Canada, and the US, although those in the latter four countries are considered imported cases from the UK.

Mystery Solved?

In the summer of 1485 a mysterious illness surfaced in England and struck 4 more times over the next century before disappearing. This frequently fatal disease caused profuse sweating, headaches, and extreme shortness of breath. Death usually came quickly, often killing within 2-3 hours of onset. Young males in rural parts of England were the primary victims of the disease. Known as the English sweating sickness, the cause of this aliment has never been identified although a variety of agents have been proposed including hantavirus pulmonary disease (N Engl J Med 336:580, 1997). The most recent suggestion for the etiology is inhalational anthrax as the described symptoms were similar to those observed among persons infected during the 2001 anthrax attack in the US (Med Hypotheses 62:155, 2004). This could be tested by opening the tombs of two known victims of the English sweating illness and examining the corpses for anthrax spores.

Office of Epidemiology & Community Health Monitoring - 233-050-1025
Kansas City Health Department
2400 Troost Ave, Suite 4000
Kansas City MO 64108