Bird Flu: A Pandemic Waiting to Happen

by Colin Lowry

Faced with the looming threat of a new flu epidemic, the World Health Organization (WHO) called an unprecedented influenza summit meeting of health officials and vaccine companies in November 2004, to start work on preparing a vaccine and antiviral medicine production. Since then, the avian influenza virus has shown no signs of going away, as outbreaks in domestic chicken farms have recurred in Asia, and more cases of human infections continue. At present, the avian influenza, type H5N1, has infected 69 people in Thailand, Vietnam, and Cambodia, causing 46 deaths.

This very lethal influenza virus has only to acquire the ability to spread easily from person to person to become the most deadly flu pandemic ever recorded. However, most of the world remains sorely unprepared to deal with the public health crisis that the new flu pandemic will bring. The U.S. government has done nothing to address the lack of hospital and clinic capacity that would be required to deal with a pandemic, although a typical flu season already overwhelms the hospitals in many areas of the country.

Flu vaccine production in the United States depends on only two companies, neither of which could produce enough vaccine to protect the U.S. population. Antiviral medicines, which may be the only effective treatment in the absence of a vaccine, are in short supply, and WHO recommendations to increase the production of these medicines and to stockpile supplies have been mostly ignored here.

What Makes Avian H5N1 So Dangerous?

H5N1 influenza is a type A influenza virus, which is the most highly unstable, and prone to genetic mutation. In addition to mutation, the virus can reassort genetically, by combining with another influenza virus. In this way, the virus can pick up new genes from other viruses in a sort of swap of genetic material. The virus is further defined by the variety of surface antigens for Hemagglutinin (H) and Neuraminidase (N) it contains. Although avian influenza viruses usually cause disease only in birds, H5N1 jumped the species barrier in 1997, and caused the first documented human infections, with severe disease and deaths. This outbreak in Hong Kong in 1997, started with a highly pathogenic H5N1 on poultry farms and in live bird markets, which was then transmitted directly from birds to human beings, resulting in 18 cases and 6 deaths. A wider epidemic was averted by the decision to destroy the province's entire poultry population.

An unusual feature of the H5N1 human cases was the presence of primary viral pneumonia, which is usually not seen, or only as a secondary bacterial infection in an influenza patient. The quick action of the Hong Kong authorities to cull the poultry flock probably saved the world from an immediate pandemic then, but the virus itself simply retreated into the wild waterfowl population, and slowly began to mutate.

The Hong Kong outbreak put the world on notice that H5N1 avian flu had pandemic potential, and scientists began to track and study this virus. In southern China, samples of the virus were taken from wild ducks and geese over the years 1999-2002. The wild ducks themselves showed no signs of disease, but were found to excrete large amounts of virus. These viral isolates from the ducks were then experimentally introduced into chickens, which caused severe disease and often death. The H5N1 viral isolates were also tested on mice, to see if the virus was somehow acquiring the ability to infect mammals. Over the three-year period, the virus did indeed gain greater infectivity in the mice, and caused progressively severe disease with increasing mortality. This startling finding shows that the virus may be reassorting with other mammalian influenza viruses, picking up genes needed to infect mammals more easily.

Pigs are sometimes susceptible to avian influenza, and it may be that in areas where pigs and ducks are kept in close proximity, this type of viral mixing may have occurred. Because wild ducks are resistant to H5N1, they act as a large mobile reservoir for the virus, which is almost impossible to control or eliminate. Compounding the difficulties of control efforts, is H5N1's ability to survive in water for up to four days, and in contaminated manure for three months.

Pandemic Waiting in the Wings.

In 1997, H5N1 initially caused only mild disease in chickens, but after months of mutation, it became a highly deadly virus that could kill a chicken in 48 hours by causing internal bleeding and organ damage. As quickly as it hit bird flocks in 1997, it disappeared from view for almost six years. Then, in December 2003, a large poultry farm near Seoul, Korea, reported large numbers of chicken deaths, and avian influenza was the suspected cause. Days later, two more farms were hit by the same influenza. Laboratory tests of the samples revealed that it was H5N1 subtype, just like the Hong Kong outbreak in 1997.

In January 2004, Vietnamese health officials reported a cluster of cases of severe respiratory disease in 11 children, of whom 7 eventually died. A little later, large numbers of poultry died from H5N1 in southern provinces, but there was no evidence at that time that suggested a link between H5N1 and the respiratory disease in the children. Several samples from the fatal cases were sent to the WHO reference laboratory for testing and identification, and in a week it was confirmed that the children had been infected by avian H5N1.

In early February 2004, H5N1 swept through poultry

farms in Japan, and Vietnam's epidemic had already infected 3 million poultry. Thailand soon followed with announcements of large outbreaks, and its first human cases of H5N1 infection in two young boys. At this point, H5N1 epidemics in birds had spread to Cambodia, Laos, Indonesia, and China. By March 2004, 120 million birds died or were destroyed in Asia as a result of the H5N1 virus. Never before had avian influenza caused outbreaks in so many countries at once. Massive control efforts had an effect by April, and outbreaks declined sharply. But as can be expected from the history of influenza epidemics, a second wave of outbreaks can produce an even more tenacious flu virus.

This started to be seen in July and August, with fresh outbreaks in Cambodia, China, Indonesia, Thailand, Vietnam, and Malaysia, which had been untouched in the first wave. The second outbreaks infected about 1 million poultry, but they were also followed by new human infections, including some fatalities. In September 2004, Thailand reported its first probable case of person-to-person transmission in a family cluster. This was the event that prompted the WHO to sound the alarm that the world was on the brink of the next flu pandemic that could kill millions.

Other events in Thailand showed that H5N1 was expanding its mammalian host range, when 147 captive tigers became ill from eating infected chicken. Tigers and other cats were not considered susceptible to infection with other influenza A viruses, so this marked a disturbing trend. By October, migratory birds were discovered that were dying from H5N1 in Asia, signalling another change in the composition of the virus.

A poultry market in Asia. Right now, the United States is not ready with a vaccine or the public-health infrastructure to combat what could potentially become the most lethal human flu epidemic ever recorded, as the H5N1 avian flu spreads to human beings.

Pandemics of the Past

To get a picture of what a new influenza pandemic would look like, it is useful to look back at the three pandemics that have occurred in the last century. The most severe pandemic took place in 1918, and estimates are that 40-50 million people died from the flu worldwide in less than one year. The flu started out in the spring in Europe and the United States, and travelled back and forth among the troops. It was not particularly deadly in this first wave. But by August, something had changed drastically, and young, previously healthy people were now dying in a matter of days in the United States, France, and Africa.

The second wave left no country untouched, and it caused symptoms so severe, including bleeding of the lungs, that influenza was not even considered as a cause when it first appeared. Unlike typical influenza epidemics that cause deaths in the very old and very young, this influenza caused the most deaths in the 15-35 age bracket. Primary viral pneumonia was common, and secondary bacterial pneumonia was very difficult to treat, as antibiotics were not available in 1918. It is estimated that 25-30% of the world's population fell ill from this influenza during 1918-19. Analysis of samples of the virus from 1918 recently showed that it was of type H1N1, and that it may have adapted over time from an avian flu virus. It is still not known what made the virus so deadly.

In 1957, the world was hit by what was called the Asian Flu, which started in Hong Kong and China in February and spread all over the world within six months. This was a much milder flu virus than 1918, and the pattern of deaths was mostly in the elderly and very young. Vaccines were being made against this flu virus in the United States, Britain, and Japan by the Fall of 1957, but limited production capacities made their introduction too late to do much to thwart the epidemic. As a result, about 70,000 people died of the flu in the United States in the 1957 pandemic.

Again, in 1968, the pandemic started in China, and rapidly spread to the rest of the world. However, this was an even milder flu virus than 1957, and it was of a similar subtype, so most of the population had some resistance to it. In the United States, about 34,000 deaths occurred from the flu that year, mostly in the elderly.

Unprepared for a New Pandemic

Most health experts believe it is only a question of time before H5N1 becomes able to spread from person to person, kicking off the next deadly flu pandemic. The present form

of the virus has shown near 70% lethality in people, but it is likely that the virus would lose some of this lethality as it acquires improved transmissibility. Still, it will be very dangerous, and the fact that no H5 subtype virus has ever circulated in the population, means that potentially, the entire human race will be vulnerable to it. This provides even more incentive for the development of a vaccine to protect the population.

Technically, there are some problems to be overcome, as the current H5N1 virus is so deadly to chickens, that the standard method of growing the virus in chicken eggs may have to be changed. Cell culture methods could certainly work, but the majority of vaccine manufacturers lack cell culture facilities of the scale needed to mass produce an influenza vaccine.

So far, the U.S. government has done nothing to address the lack of any plans to produce a vaccine against H5N1 influenza. Sen. Charles Schumer (D-N.Y.) proposed on March 6 that the Federal Government issue a guarantee of $200 million to ensure that vaccine manufacturers here produce the vaccine without the fear of losing money. He also called on the Centers for Disease Control to begin stockpiling antiviral medications that could be used to treat the flu in the event of a pandemic.

The total vaccine production capacity globally today is only 300 million doses per year, but WHO experts say that more than 1 billion vaccine doses would be needed to control a new pandemic. In the United States, only two companies, Aventis Pasteur and Chiron, produce flu vaccine, and their production capacity is sufficient only to produce enough vaccine in six months to cover about 10% of the U.S. population.

Obviously, the United States needs to increase its vaccine production capacity to deal with the threat posed by avian influenza, and Senator Schumer's proposal is a step in the right direction. However, the nation is also vulnerable in its lack of surge capacity in hospitals and clinics, to be able to handle the tremendous increase in hospitalizations required in a pandemic. To solve this, requires a long-term perspective of rebuilding our public health infrastructure, including new hospitals and public clinics, and well-trained public health personnel who can contribute to an increased disease surveillance network.

OECD Conference Backs Nuclear Energy

by Emmanuel Grenier

Seventy-four countries and ten international organizations came together in Paris on March 21-22, for an "International Conference on Nuclear Energy for the 21st Century," organized by the International Atomic Energy Agency (IAEA), in collaboration with the Organization for Economic Cooperation and Development (OECD) and its Nuclear Energy Agency.

The vast majority of the participants affirmed the desire to have nuclear energy, and also hydroelectric energy, make a major contribution to meeting energy needs and supporting world development. Because nuclear and hydroelectric energy sources would figure prominently in the international effort to reduce greenhouse gases, they were no longer the object of ideological exclusion, as has been the case up until now.

Such a meeting, and such conclusions, were unimaginable merely five years ago. In fact, it is the first time, since the launching of the Atoms for Peace program in 1954, that an international conference of this magnitude has been convened.

Patrick Devedjian, the French Minister of Industry who keynoted the conference, wanted the conference message to "reach out in particular to developing countries." In an interview in the French daily *Figaro,* Devedjian stated that nuclear power was "unavoidable" both in the context of the intransigently high price of oil and gas, and the challenge of limiting greenhouse gases.

Questioned at an OECD press conference on the lack of ministerial representation from those European countries that had announced their intention to abandon the nuclear power option, (Germany, Belgium, Austria, Italy, and Holland), Devedjian noted "a certain contradiction in these countries: They shun nuclear power at home, but wish to associate themselves with the relaunching of nuclear industry in France, especially via the development of a prototype of the EPR [the jointly sponsored European Power Reactor], and to develop the electrical grid to benefit clients of France."

Without a commitment to make nuclear energy the primary response to the energy challenges of the century, the conference, to a large degree, revolved around tactical considerations. Nuclear power, in effect, delivers electricity at a competitive and stable price, without emitting CO_2. Otherwise, in the majority of countries, it bolsters the security of their energy supplies.