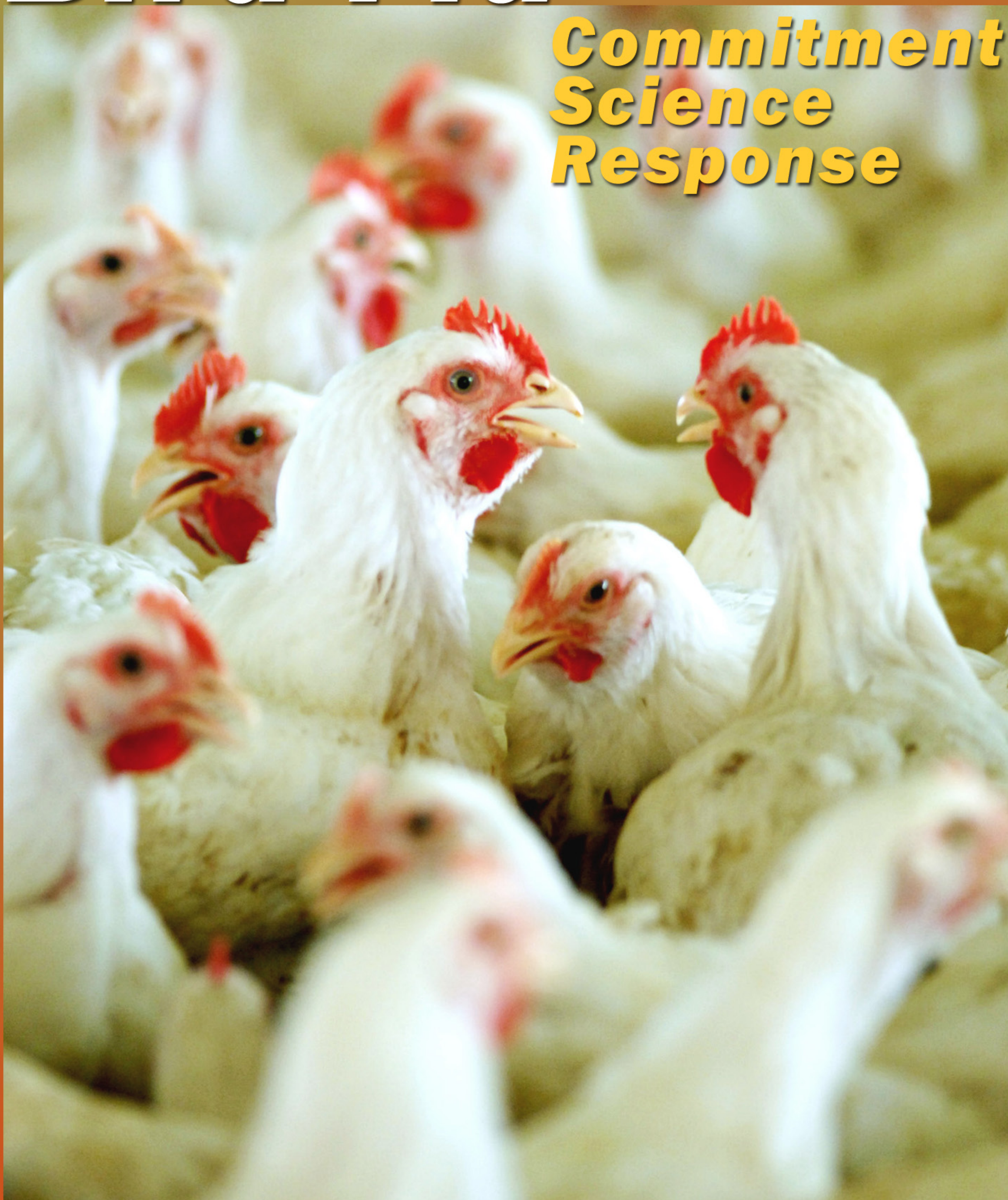
Meeting the Challenge of Bird Flu

Commitment
Science
Response



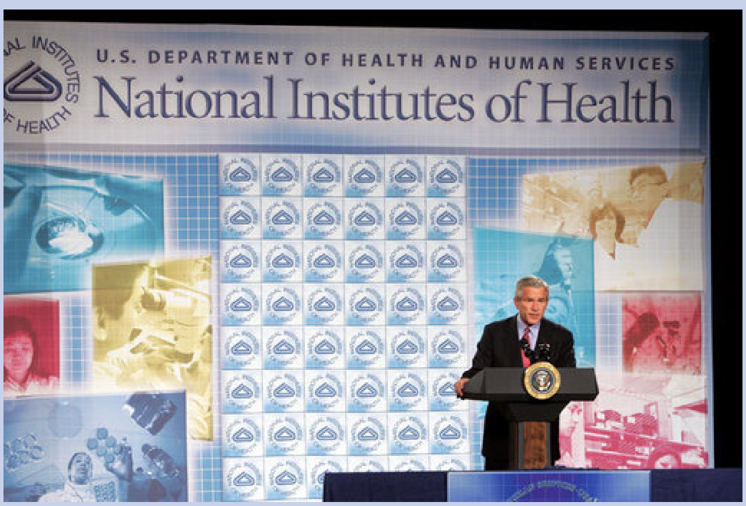
U.S. Department of State   Bureau of International Information Programs   April 2006

A Commitment

A deadly and contagious strain of avian influenza has stricken nations across East and Southeast Asia, and now spread to bird populations in Europe, the Near East and Africa. While the number of human cases of H5N1 avian flu are still small, over half of those infected have died. What happens if this strain mutates to easily spread from human to human?

A human influenza pandemic could emerge from this animal disease, health officials warn. In September 2005, President Bush announced the International Partnership on Avian and Pandemic Influenza during the United Nations General Assembly. This partnership has pledged to combat this potential world crisis, pursuing the following goals:

+ Elevate the avian influenza issue on national agendas.
+ Coordinate efforts among donor and affected nations.
+ Mobilize and leverage resources.
+ Increase transparency in disease reporting and the quality of surveillance.
+ Build local capacity to identify, contain and respond to an influenza pandemic.



President Bush announces the National Strategy for Pandemic Influenza, November 1, 2005. (White House Photo)

"At this moment, there is no pandemic influenza in the United States or the world. But if history is our guide, there is reason to be concerned. In the last century, our country and the world have been hit by three influenza pandemics — and viruses from birds contributed to all of them."

George W. Bush

Meeting the Challenge of
Bird Flu

Commitment: **Understanding the Challenge**

Scientists are working to understand how the bird flu virus works and how it can be combated. Bird flu viruses among poultry occur worldwide from time to time and are spread when birds infect other birds.

Science: **Combating Bird Flu**

As researchers discover more about bird flu and search for vaccines, early diagnosis remains key to containing the spread of the virus. Global cooperation and surveillance allows countries to share information critical to vaccine development.

Response: **Working Together**

America and the world are responding to the threat of pandemic influenza. Working at home and abroad, the U.S. government is joining with international partners to prevent the spread of bird flu and a global pandemic.

Internet Resources

Bird Flu FAQ

Questions and Answers About Avian Influenza (Bird Flu) and Avian Influenza A (H5N1) Virus

U.S. Centers for Disease Control, March 17, 2006

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What is avian influenza (bird flu)?

Avian influenza is an infection caused by avian (bird) influenza (flu) viruses. These flu viruses occur naturally among birds. Wild birds worldwide carry the viruses in their intestines, but usually do not get sick from them. However, avian influenza is very contagious among birds and can make some domesticated birds, including chickens, ducks, and turkeys, very sick and kill them.

Infection with avian influenza viruses in domestic poultry causes two main forms of disease that are distinguished by low and high extremes of virulence. The "low pathogenic" form may go undetected and usually causes only mild symptoms (such as ruffled feathers and a drop in egg production). However, the "highly pathogenic" form spreads more rapidly through flocks of poultry. This form may cause disease that affects multiple internal organs and has a mortality rate that can reach 90–100 percent, often within 48 hours.

How does avian influenza spread among birds?

Infected birds shed influenza virus in their saliva, nasal secretions, and feces. Susceptible birds become infected when they have contact with contaminated excretions or with surfaces that are contaminated with excretions or secretions. Domesticated birds may become infected with avian influenza virus through direct contact with infected waterfowl or other infected poultry or through contact with surfaces (such as dirt or cages) or materials (such as water or feed) that have been contaminated with the virus.

Do avian influenza viruses infect humans?

(© AP/WWP)

Bird flu viruses do not usually infect humans, but as of April 2006, close to 200 confirmed cases of human infection with bird flu viruses have occurred since 1997. The World Health Organization (WHO) maintains situation updates and cumulative reports of human cases of avian influenza A (H5N1).

How do people become infected with avian influenza viruses?

Most cases of avian influenza infection in humans have resulted from direct or close contact with infected poultry (living or dead, domesticated chicken, ducks, and turkeys) or surfaces contaminated with blood, secretions and excretions from infected birds. The spread of avian influenza viruses from an ill person to another person has been reported very rarely, and transmission has not been observed to continue beyond one person. During an outbreak of avian influenza among poultry, there is a possible risk to people who have direct or close contact with infected birds or with surfaces that have been contaminated with secretions and excretions from infected birds.

What are the symptoms of avian influenza in humans?

Symptoms of avian influenza in humans have ranged from typical human influenza-like symptoms (fever, cough, sore throat, and muscle aches) to eye infections, pneumonia, severe respiratory diseases (such as acute respiratory distress syndrome), and other severe and life-threatening complications. The symptoms of avian influenza may depend on which specific virus subtype and strain caused the infection.

How is avian influenza detected in humans?

The initial symptoms a patient presents are typical of seasonal flu. A laboratory test is needed to confirm avian influenza in humans.

What are the implications of avian influenza to human health?

Two main risks for human health from avian influenza are 1) the risk of direct infection when the virus passes from the infected bird to humans, sometimes resulting in severe disease; and 2) the risk that the virus – if given enough opportunities – will change into a form that is highly infectious for humans and spreads easily from person to person.

How is avian influenza in humans treated?

Studies done in laboratories suggest that the prescription medicines approved for human influenza viruses should work in treating avian influenza infection in humans. However, influenza viruses can become resistant to these drugs, so these medications may not always work. Additional studies are needed to determine the effectiveness of these medicines.

Does the current seasonal influenza vaccine protect me from avian influenza?

No. Influenza vaccine for the 2005-06 season does not provide protection against avian influenza.

Should I wear a surgical mask to prevent exposure to avian influenza?

Currently, wearing a mask is not recommended for routine use (in public) for preventing influenza exposure. In the United States, disposable surgical and procedure masks have been widely used in health-care settings to prevent exposure to respiratory infections, but the masks have not been used commonly in community settings, such as schools, businesses, and public gatherings.

Is there a risk for becoming infected with avian influenza by eating poultry?

There is no evidence that properly cooked poultry or eggs can be a source of infection for avian influenza.

What is the avian influenza A (H5N1) virus that has been reported in Africa, Asia, Europe and the Near East?

Influenza A (H5N1) virus – also called "H5N1 virus" – is an influenza A virus subtype that occurs mainly in birds, is highly contagious among birds, and can be deadly to them.

Outbreaks of avian influenza H5N1 occurred among poultry in eight countries in Asia (Cambodia, China, Indonesia, Japan, Laos, South Korea, Thailand, and Vietnam) during late 2003 and early 2004. At that time, more than 100 million birds in the affected countries either died from the disease or were killed in order to try to control the outbreaks. By March 2004, the outbreak was reported to be under control.

Since late June 2004, however, new outbreaks of influenza H5N1 among poultry and wild birds have been reported in countries in Africa, Asia, Europe and the Near East. Human cases of influenza A (H5N1) infection have been reported in Cambodia, China, Egypt, Indonesia, Iraq, Thailand, Turkey, and Vietnam. For the most current information about avian influenza and cumulative case numbers, see the World Health Organization website at http://www.who.intl/csr/disease/avian_influenza/en/

(© AP/WWP)

What are the risks to humans from the current H5N1 outbreak in Africa, Asia, Europe and the Near East?

H5N1 virus does not usually infect people, but as of April 2006, close to 200 human cases have been reported. Most of these cases have occurred from direct or close contact with infected poultry or contaminated surfaces; however, a few cases of human-to-human spread of H5N1 virus have occurred.

So far, spread of H5N1 virus from person to person has been rare and has not continued beyond one person. Nonetheless, because all influenza viruses have the ability to change, scientists are concerned that H5N1 virus one day could be able to infect humans and spread easily from one person to another. Because these viruses do not commonly infect humans, there is little or no immune protection against them in the human population.

If H5N1 virus were to gain the capacity to spread easily from person to person, an influenza pandemic (worldwide outbreak of disease) could begin. No one can predict when a pandemic might occur. However, experts from around the world are watching the H5N1 situation in Africa, Asia, Europe and the Near East very closely and are preparing for the possibility that the virus may begin to spread more easily from person to person.

How does H5N1 virus differ from seasonal influenza viruses that infect humans?

Of the few avian influenza viruses that have crossed the species barrier to infect humans, H5N1 virus has caused the largest number of reported cases of severe disease and death in humans. In the current situation, more than half of the people infected with the virus have died. Most cases have occurred in previously healthy children and young adults. However, it is possible that the only cases currently being reported are those in the most severely ill people and that the full range of illness caused by the H5N1 virus has not yet been defined.

Unlike seasonal influenza, in which infection usually causes only mild respiratory symptoms in most people, H5N1 infection may follow an unusually aggressive clinical course, with rapid deterioration and high fatality. Primary viral pneumonia and multi-organ failure have been common among people who have become ill with H5N1 influenza.

How is infection with H5N1 virus in humans treated?

Most H5N1 viruses that have caused human illness and death appear to be resistant to amantadine and rimantadine, two antiviral medications commonly used for treatment of patients with influenza. Two other antiviral medications, oseltamivir and zanamavir, would probably work to treat influenza caused by H5N1 virus, but additional studies are needed to demonstrate their current and ongoing effectiveness.

Is there a vaccine to protect humans from H5N1 virus?

There currently is no commercially available vaccine to protect humans against the H5N1 virus that is being detected in Africa, Asia, Europe, and the Near East. However, vaccine development efforts are taking place. Research studies to test a vaccine that will protect humans against H5N1 virus began in April 2005, and a series of clinical trials is under way.

(© AP/WWP)

The results of one trial reported in March 2006 indicate that a candidate vaccine had produced an immune response, but extremely high doses were required to do so. Work continues at the National Institute of Allergy and Infectious Diseases to develop a vaccine that will be effective in the event of pandemic emergence.

What does the U.S. government recommend regarding H5N1 virus?

In February 2004, the Centers for Disease Control (CDC) provided U.S. public health departments with recommendations for enhanced surveillance (detection) of H5N1 influenza in the country. Follow-up messages, distributed via the Health Alert Network, reminded U.S. public health departments about recommendations for detecting (domestic surveillance), diagnosing, and preventing the spread of H5N1 virus. The alerts also recommended measures for laboratory testing for H5N1 virus.

As part of the national strategy, the U.S. government is issuing a series of targeted and specialized preparedness plans to help businesses, churches, communities and other institutions consider the impact pandemic influenza might have on their activities, and urge the development of appropriate readiness strategies. Those plans are available at http://pandemicflu.gov.

What changes are needed for H5N1 or another avian influenza virus to cause a pandemic?

Three conditions must be met for a pandemic to start: 1) a new influenza virus subtype must emerge; 2) it must infect humans and causes serious illness; and 3) it must spread easily and sustainably (continue without interruption) among humans. The H5N1 virus in Africa, Asia, Europe and the Near East meets the first two conditions: it is a new virus for humans (H5N1 viruses have never circulated widely among people), and it has infected close to 200 humans, killing over half of them.

However, the third condition, the establishment of efficient and sustained human-to-human transmission of the virus, has not occurred. For this to take place, the H5N1 virus would need to improve its transmissibility among humans. This could occur either by "reassortment" or adaptive mutation.

Reassortment occurs when genetic material is exchanged between human and avian viruses during co-infection (infection with both viruses at the same time) of a human or pig. The result could be a fully transmissible pandemic virus—that is, a virus that can spread easily and directly to humans. A more gradual process is adaptive mutation, where the capability of a virus to bind to human cells increases during infections of humans.

Good health habits to help prevent the flu

Avoid close contact. Avoid close contact with people who are sick. When you are sick, keep your distance from others to protect them from getting sick too.
Stay home when you are sick. If possible, stay home from work, school, and errands when you are sick. You will help prevent others from catching your illness.
Cover your mouth and nose. Cover your mouth and nose with a tissue when coughing or sneezing. It may prevent those around you from getting sick.
Clean your hands. Washing your hands often will help protect you from germs.
Avoid touching your eyes, nose, or mouth. You can catch disease when you touch something that is contaminated with germs and then touch your eyes, nose, or mouth.

Unlocking Secrets of the Bird Flu Virus

Scientists around the world are working to understand how the bird flu virus works and which components of the flu may be the best targets for drugs. By April 2006, the World Health Organization confirmed close to 200 human cases of bird flu and 107 deaths since December 2003.

By 2006, the H5N1 virus had spread and human cases were reported in Africa, the Near East, Asia and Europe. The virus has resulted in the deaths of millions of birds in more than 30 nations.

Experts say that it is only a matter of time before the virus mutates into a form that can infect people and be easily transmitted from person to person. Such an outbreak could develop into a global pandemic, potentially taking millions of lives.

Diseases From Animals

Bird flu is just one disease that has arisen in animals and mutated to infect people. HIV/AIDS, severe acute respiratory syndrome (SARS), West Nile virus and the Spanish flu of 1918 are just a few examples.

The 1918 Spanish flu was a global disaster, killing up to 50 million people, nearly half of them otherwise healthy adults. Researchers have partially reconstructed the Spanish flu virus and discovered in part what made the virus so lethal. Such information is essential for influenza drug and vaccine research. Researchers say that the Spanish flu virus is related more closely to avian flu viruses than other human flu viruses.

Therapies against a new flu strain would need to disarm parts of the virus that are most damaging to the body.

Recreating the Spanish Flu

To learn which virus components would be the best targets for therapies, scientists at the U.S. Centers for Disease Control and Prevention (CDC) recreated the 1918 Spanish flu virus.

A scientist recreates the 1918 Spanish Flu virus, at CDC laboratories in Atlanta, in 2005. (CDC photo)

Using the virus's genome sequence, they created a live virus with all eight of the Spanish flu viral genes. The genome sequence information was recovered in fragments and lung tissues from three 1918 flu victims: two U.S. soldiers and a woman who was buried in the Alaskan permafrost.

The virus is contained at CDC, following stringent safety and security conditions designed for flu viruses mandated by the CDC's Select Agent program.

To make the virus, the researchers used an approach called reverse genetics, which involves transferring gene sequences of viral RNA into bacteria and then inserting combinations of the genes – often after manipulating them – into cell lines, where they combine to form a virus.

Like DNA, RNA is a nucleic acid. One of its main functions is to copy genetic information from DNA and translate the information into proteins. The researchers also produced variations of the virus for comparison, replacing certain

Spanish flu genes with corresponding genes from other flu viruses. They then studied the viruses' effects in mice, chicken embryos and human lung cells, and identified the genes responsible for the Spanish flu virus's extreme virulence.

More research is needed on antivirals and vaccines for a future flu pandemic, but there are encouraging signs. The U.S. Food and Drug Administration-approved flu antiviral drugs oseltamivir (Tamiflu®), zanamavir (Relenza®), and amantadine (Symmetrel®) have been shown to be effective against viruses carrying certain genes from the Spanish flu virus. And vaccines containing other Spanish flu genes were protective in mice.

Flu Virus Overview

Influenza A and B are the two kinds of flu viruses that cause epidemic human disease. Since 1977, according to the CDC, influenza A and influenza B viruses have been in global circulation. In 2001, H1N2 viruses began circulating widely. Bird flu subtype H5N1 is an influenza A virus. Influenza A is a constantly mutating virus; influenza B does not mutate as rapidly.

Two kinds of vaccines protect against the influenza A and B strains that sweep populations during the winter months. Each vaccine contains three flu viruses, representing one of the three groups of viruses that circulate among people in a given year. Each of the three vaccine strains in both vaccines – two A viruses , H3N2 and H1N1 – represent flu vaccine strains that flu experts think will be the dominant strains that year.

The yearly flu shot administered around the world is an inactivated vaccine (containing killed virus) that is given with a needle, usually in the arm. The flu experts formulate their recommendations for the composition of the vaccine each year after much research and some guesswork.

Confirmed instances of the H5N1 avian influenza virus infecting humans since 1997

Hong Kong, 1997: Avian influenza A (H5N1) infections occurred in both poultry and humans. This was the first time an avian influenza virus had ever been found to transmit directly from birds to humans. During this outbreak, 18 people were hospitalized and six of them died.

China and Hong Kong, 2003: Two cases of the A H5N1 virus infection occurred among members of a Hong Kong family that had traveled to China. One person recovered, the other died.

Thailand and Vietnam, 2004 and through November 2005: A poultry outbreak of the H5N1 virus began in January 2003; human infection appeared in these two countries in 2004. Thailand and Vietnam have reported the highest numbers of human cases as illness was detected sporadically through 2005 with 92 cases and 42 deaths in Viet Nam and 21 cases and 13 deaths in Thailand.

Cambodia, China, and Indonesia, 2005: As poultry outbreaks continue to emerge in the region, so have reports of human disease. While infection has been shared among some family groups, no evidence of a community cluster of disease has been reported, indicating a sustained human transmission. Cambodia has detected five cases, all ending in death. Indonesia has reported 29, with 22 deaths. China has confirmed 16 cases with 11 deaths.

Turkey, Iraq, Azerbaijan, and Egypt, 2006: The H5N1 virus spread among wild and domestic birds beyond Asia in 2005 Human cases of infection began appearing in 2006 in other regions. Turkey reported 12 human cases, with four deaths. Azerbaijan had seven cases with five deaths. Iraq detected two cases, both ending in death while Egypt confirmed five cases with two deaths.

In these nations overall, 191 cases of H5N1 have been confirmed by the World Health Organization, resulting in 107 deaths as of April 2006. *Sources: CDC, WHO*

Early Diagnosis: A Critical Step in Bird Flu Prevention

If avian influenza (bird flu) mutates sufficiently to jump from chickens and migratory birds to people, early diagnosis and identification of the viral strain that has developed the capability to infect humans will be a critical step in preventing a human pandemic.

According to researchers at Cornell University in New York, successful containment will depend on getting a start on creating a vaccine. To create a vaccine, researchers will have to learn more about how the flu virus enters human cells.

The influenza virus is one of the most extensively studied and best-understood viruses, but it is also one of the most adaptable. The way flu virus works has been studied in great detail – but parts of the puzzle remain missing.

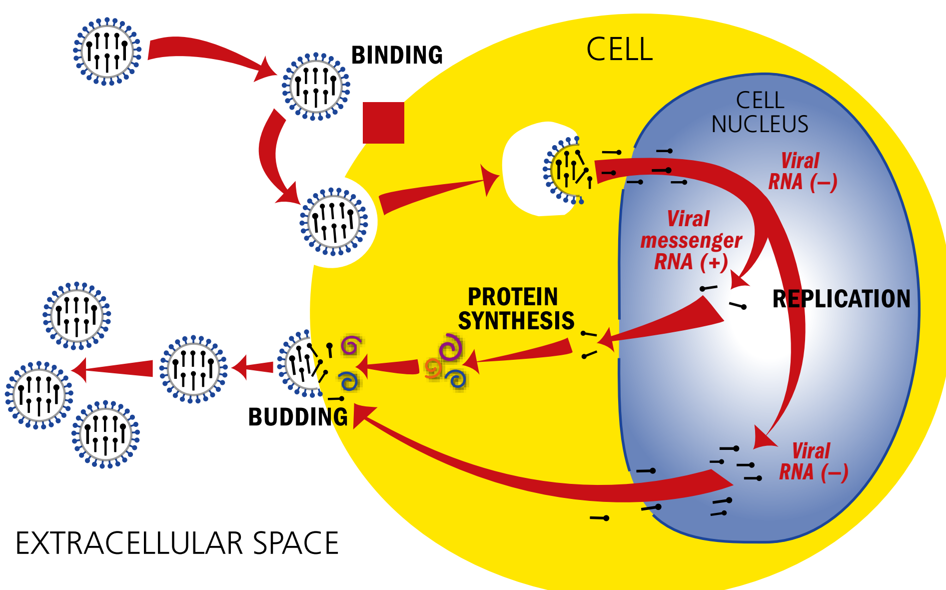
How the Flu Virus Works

A virus is a package of genetic material – DNA or RNA – surrounded by a shell of protein and fat (lipid).

The type A influenza virus – the family to which bird flu belongs – consists of 10 proteins and eight strands of RNA that carry the code for making the proteins.

To invade a host, the virus shell uses certain proteins that bind to receptors on the outside of cells in victims' airways and lungs.

This so-called binding draws the virus into the normally protective cell membrane. The virus shell fuses with membrane and moves through it, emerging into the cell's cytoplasm, where the shell opens and releases its RNA.



After binding to a receptor on the cell membrane, the influenza virus moves into the cytoplasm where the virus shell opens, releasing RNA. In the nucleus, viral RNA is copied to messenger RNA, which moves back to the cytoplasm as a template to make more viral proteins. Copies of the viral RNA join with the viral proteins to make more viruses, which bud on the outer surface of the cell and seek new cells to infect. (Kathryn Seely/Cornell University)

The cytoplasm is a gel-like substance that helps maintain the cell's shape and consistency, stores chemicals critical to life, and is home to the organelles, which produce proteins and energy for the cells.

The viral or infected RNA is called "negative sense" RNA – it is a mirror image of the messenger RNA the cell uses to make proteins.

The viral RNA then moves into the cell nucleus, where the cell's machinery makes "positive" copies that travel back out into the cytoplasm.

Bird Flu Hijacks the Cell's Protein Factory

The cell treats the viral RNAs like any other messenger RNAs and uses them to make copies of the viral proteins – essentially hijacking the cell's own protein-making machinery.

Meanwhile, inside the nucleus, other positive copies of the viral RNA act as templates to churn out more negative viral RNA. The new viral RNA then moves back into the cytoplasm where it joins with the newly made viral proteins to form new copies of the complete virus.

The assembly occurs inside the cell membrane and, as the process is completed, the new flu virus moves out through the cell wall and is released into the airway to find another cell to infect — or it is ejected from the body in a cough or sneeze and launched to find a new host.

Eventually, the virus replication takes over so much of the cell's machinery that the cell dies. Dead cells in the airways result in a runny nose and scratchy throat. Too many dead cells in the lungs result in death.

Moving From Species to Species

The shape of receptors in the cell wall is a little different from one species to another, so a virus that can latch onto a chicken cell usually cannot infect a human. But the process is not exact and there are minor variations from one organism to another, even within a species.

The 107 people who have died of avian flu infections from December 2003 to April 2006 may have had just enough variation in their cell structure to let the avian virus attach. Or a few copies of the avian virus may have mutated enough to infect a person. Some species have receptors whose shapes are about halfway between birds and humans.

Avian and human flu strains both can infect pigs, for example. Scientists fear that a pig somewhere could be infected with both viruses at the same time. With proteins and RNA strands from both viruses inside the cell, new viruses might assemble, perhaps with the proteins that attach to a human cell but with features that give it the virulence of the avian virus, including the ability to infect cells outside the respiratory tract.

Research continues, but development of a vaccine effective against all flu viruses is a long way off.
(© AP/WWP)

Another Step

The Cornell University researchers found that attaching to a single receptor is not sufficient to allow the flu virus to enter a cell. Another receptor or another process must be involved.

The primary receptor, already extensively studied, varies from one virus to another, but whatever the additional step is, it seems to be the same for many different flu viruses and perhaps for all.

The researchers believe that understanding the process could lead to the development of new anti-viral drugs or even a vaccine effective against all flu viruses, but they caution that such a result is a long way off.

Global Surveillance Yields Annual Vaccines

Scientists around the world are working to develop a human vaccine against the H5N1 strain of bird flu that has moved steadily westward since its 2003 appearance in Asia, but experts are not sure how well such a vaccine will work if a pandemic strikes. Meanwhile, the World Health Organization (WHO) conservatively estimates that such a pandemic could cause a "large number of deaths" – on the order of 2 million to 8 million deaths.

The problem is that flu viruses, including the avian influenza virus, mutate so rapidly that a vaccine created one year is not effective the next year.

As of April 2006, the WHO has confirmed 191 human cases of H5N1 infection in nine nations, resulting in at least 107 deaths. Because access to medical care is poor in some rural areas and cases may go undiagnosed, the human count could be higher.

Since the first confirmed appearance of the H5N1virus in European flocks October 13, 2005, and subsequently in the Near East and Africa concern and vigilance has been heightened in many more capitals. Human cases were reported in Azerbaijan, Egypt, Iraq, Turkey by early 2006.

Global Flu Surveillance

Surveillance is the close observation of someone or something – in this case, influenza. Because viruses do not respect national boundaries, such surveillance is international and is coordinated by the WHO Global Influenza Surveillance Network, established in 1952.

The WHO network is made up of four collaborating centers – in the United States, Australia, Japan and the United Kingdom – and 112 institutions in 83 countries that are called WHO National Influenza Centers. The national influenza

Annual flu shots are highly recommended for the elderly and other vulnerable age groups. (© AP/WWP)

centers collect specimens in their countries and isolate and scientifically characterize the viruses. The centers then ship the newly isolated strains to WHO collaborating centers for more scientific and genetic analysis. WHO flu experts use this analysis to recommend the formulation of each year's flu vaccines for the Northern and Southern Hemispheres, then prepare and distribute the candidate vaccine strain to manufacturers.

Viruses that go into flu vaccines have been grown the same way for more than 50 years – in fertilized (embryonated) chicken eggs. Eleven days after the eggs are fertilized, each of three flu virus strains is injected into an egg and accumulates in the fluid around the embryo. The virus infects the embryo and multiplies.

After several days of incubation, a machine opens the egg and harvests the virus. The virus is then purified, chemically killed and used to produce the vaccine. On average, it takes between one and two eggs to produce one dose of annual flu vaccine. The process takes six to nine months and uses 100 million eggs in the United States alone.

The egg-based method is problematic for a potential H5N1 vaccine because the virus kills chicken embryos before much of the virus can grow. Thus there is an urgent need for alternative methods of vaccine production which the U.S. National Strategy is trying to address.

The WHO Influenza Surveillance Network serves also as a global alert mechanism for the emergence of influenza viruses with pandemic potential, like the H5N1 bird flu strain.

U.S. Flu Surveillance

In the United States, the Centers for Disease Control (CDC) is one of the four WHO collaborating centers. As part of its local surveillance process, the Influenza Branch collects and reports information on flu activity in the United States each week from October through May.

The U.S. flu surveillance system has seven components that tell CDC when and where flu activity is occurring, which flu viruses are circulating, how the flu viruses are changing, where flu-related illness is occurring and the effect of flu in deaths.

The surveillance system includes reports from more than 120 laboratories, 2,000 "sentinel" health care providers, vital statistics offices in 122 cities, research and health care personnel at specific surveillance sites, and flu surveillance coordinators and state epidemiologists from all state health departments. All flu activity reporting by states and health care providers in the United States is voluntary.

Such surveillance is critical to keep up with mutating influenza A viruses and ensures each year's flu vaccine protects against the currently circulating strains.

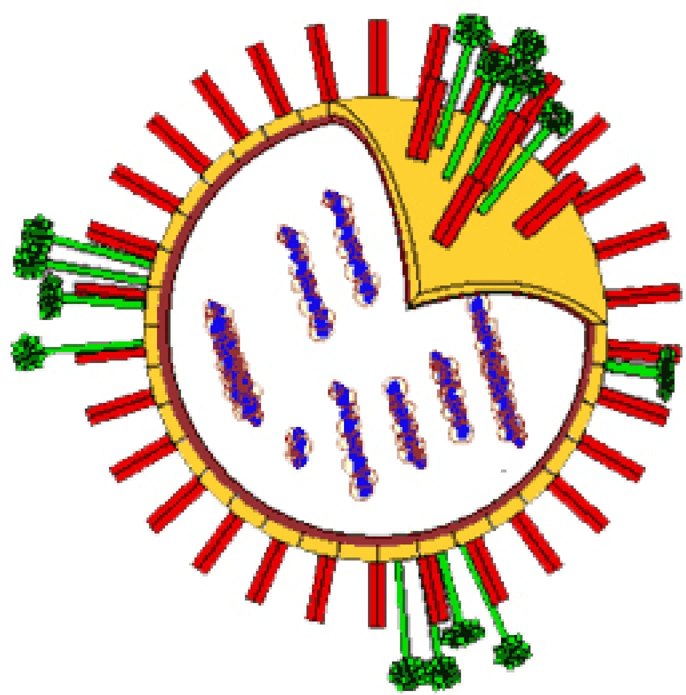
Influenza Viruses: Types, Subtypes, and Strains

There are three types of influenza viruses: A, B, and C.

Influenza Type A

Influenza type A viruses can infect people, birds, pigs, horses, seals, whales, and other animals, but wild birds are the natural hosts for these viruses. Influenza type A viruses are constantly mutating and are divided into subtypes based on two proteins on the surface of the virus. These proteins are called hemagglutinin (HA) and neuraminidase (NA). There are 15 different HA subtypes and nine different NA subtypes. Many different combinations of HA and NA proteins are possible. Only some influenza A subtypes (H1N1, H1N2, and H3N2) are currently in general circulation among people. Other subtypes are found most commonly in other animal species, for example, H7N7 and H3N8 viruses affect horses.

Subtypes of influenza A virus are named according to their HA and NA surface proteins. Thus an "H5N1" virus has an HA 5 protein and an NA 1 protein.



The influenza virus contains eight interior "genetic segments." The outside is lined with H and N receptors that vary from strain to strain. (Los Alamos National Laboratory)

Influenza Type B
Influenza B viruses are normally found only in humans. Unlike influenza A viruses, these viruses are not classified according to subtype as these do not mutate rapidly. Although influenza type B viruses can cause human epidemics, they have not caused pandemics.

Influenza Type C
Influenza type C viruses cause mild illness in humans and do not cause epidemics or pandemics. Influenza Type C viruses are not classified according to subtype.

Strains (subgroups)
Influenza B viruses and subtypes of influenza A virus are further characterized into strains. There are many different strains of influenza B viruses and of influenza A subtypes. New strains of influenza viruses appear and replace older strains. This process occurs through a type of change called "drift."

When a new strain of human influenza virus emerges, antibody protection that may have developed after infection or vaccination with an older strain may not provide protection against the new strain. Thus, the influenza vaccine is updated on a yearly basis to keep up with the changes in influenza viruses.

Human Influenza Viruses Versus Avian Influenza Viruses
Humans can be infected with influenza types A, B, and C. However, the only subtypes of influenza A virus that are circulating now among people are influenza A subtypes H1N1, H1N2, and H3N2.

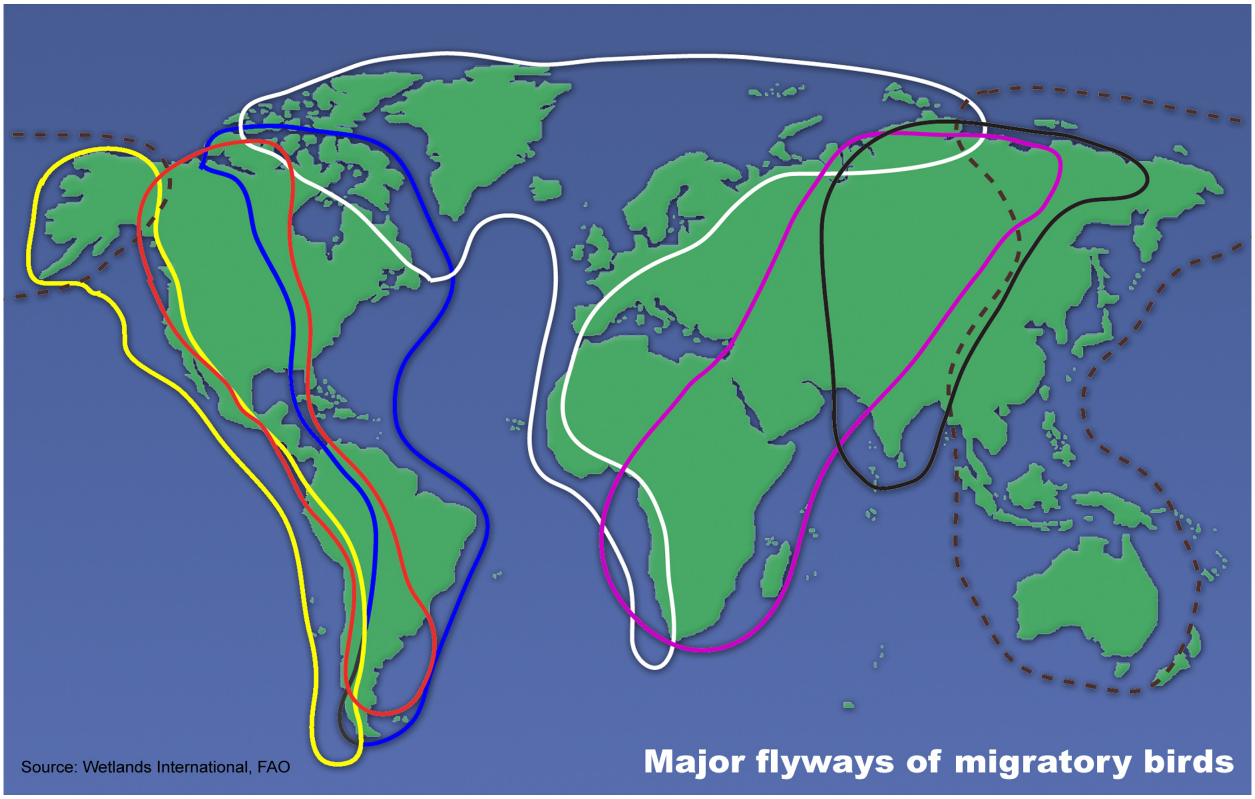
Only influenza A viruses infect birds. Wild birds are the natural host for all subtypes of influenza A virus. Typically, wild birds do not get sick when they are infected with influenza virus. However, domestic poultry, such as turkeys and chickens, can get very sick and die from avian influenza, and some avian viruses also can cause serious disease and death in wild birds.

These baby geese in Poland are kept indoors to prevent infection from wild birds. (© AP/WWP)

Low Pathogenic Versus Highly Pathogenic Avian Influenza Viruses
H5 and H7 subtypes of avian influenza A viruses can be further classified as either highly pathogenic avian influenza (HPAI) or low pathogenic avian influenza (LPAI). This distinction is made on the basis of genetic features of the virus. HPAI is usually associated with high mortality in poultry. It is not certain how the distinction between "low pathogenic" and "highly pathogenic" is related to the risk of disease in people. HPAI viruses can kill 90 to 100 percent of infected chickens, whereas LPAI viruses cause less severe or no illness if they infect chickens. Because LPAI viruses can evolve into HPAI viruses, outbreaks of H5 and H7 LPAI are closely monitored by animal health officials.

Avian Influenza Viruses in Birds
Bird flu outbreaks among poultry occur worldwide from time to time. Domesticated birds may become infected with the avian influenza virus through direct contact with infected birds, or through contact with surfaces (such as dirt or cages) or materials (such as water or feed) that have been contaminated with the virus. People, vehicles, and other inanimate objects, such as shoes or equipment, can help spread the virus. When this happens, bird flu outbreaks can occur among poultry.

Whether outbreaks cause much havoc depend on whether the avian influenza viruses are of low or high pathogenic forms. Low pathogenic forms of bird flu viruses are responsible for most out-



breaks in poultry but these outbreaks usually result either in no illness or mild illness (e.g. chickens producing fewer or no eggs), or low levels of mortality. However, when outbreaks involve highly pathogenic forms of H5 and H7 viruses, mortality is close to 100 percent among infected poultry, leading to massive culling in efforts to keep the virus from spreading.

Annual Bird Migration: Facilitating the Spread?

Scientists do not fully understand how the H5N1 virus has spread across Asia and into Europe since its first appearance in 2003 in China. They do know that wild migratory birds serve as nature's reservoir for the highly pathogenic virus, and can pass it to domestic birds through direct contact. Wild birds also shed the virus, so domestic birds may be exposed through contact with contaminated dirt, water, or feed.

Thus, the flyways of seasonally migrating flocks are under great scrutiny, particularly during the time of year when various bird populations fly from continent to continent. As shown above, certain wild flocks from Asia make a seasonal trip to North and South America while other migrating birds from Northern Asia and Northern Europe make a yearly journey to Africa. Because of that, attention on the possibility of a pandemic has heightened monitoring in all these areas.

No definitive proof confirms that migrating birds have carried the H5N1 virus as far as it has traveled in the two years since its reappearance. The virus does have other means of travel. The virus can survive outside a host at moderate temperatures for long periods and can survive indefinitely in frozen material. The H5N1 virus can travel from farm to farm in the mud of a farmer's truck or in the dust on his shoes. It can survive on the bars of cages that may be used in the commercial transport of live animals. For these reasons, animal health experts are calling for increased attention to biosecurity, and some nations are barring the import of live poultry.

The great distance encompassed by the nations so far affected demonstrates the capability of the H5N1 virus to survive and spread.

Safeguarding Against Pandemic Influenza

Most people are familiar with influenza or the "flu," a respiratory illness that makes hundreds of thousands of people sick every year. For most healthy people, the flu is not usually life-threatening. Pandemic influenza is another matter. It occurs when a new strain of influenza emerges that can be transmitted easily from person to person and against which people have no immunity. Unlike seasonal flu, it can kill the young and healthy as well as the frail and sick.

International Partnership on Avian and Pandemic Influenza

In September 2005, President Bush announced the International Partnership on Avian and Pandemic Influenza during the U.N. General Assembly to coordinate efforts and mobilize resources in the global movement to prevent a pandemic. The first meeting of the International Partnership took place October 6-7 in Washington, DC, hosted by the U.S. Department of State.

The meeting involved top foreign affairs, health and agriculture officials from 88 countries, as well as representatives from eight international organizations, including the World Health Organization, the Food and Agricultural Organization, and the World Organization for Animal Health.

Goals of the International Partnership:

+ Elevate the avian influenza issue on national agendas.
+ Coordinate efforts among donor and affected nations.
+ Mobilize and leverage resources.
+ Increase transparency in disease reporting and the quality of surveillance.
+ Build local capacity to identify, contain and respond to an influenza pandemic.

This global surveillance and preparedness network is helping detect and respond quickly to any outbreaks of disease. The Partnership requires countries that face an outbreak to immediately share information and provide samples to the World Health Organization. By requiring transparency, governments can rapidly respond to outbreaks.

President Bush addresses the United Nations General Assembly, September 14, 2005. (© AP/WWP)

U.S. National Strategy: Coordinating Efforts at All Levels

The U.S. government is concerned that the ongoing outbreaks of avian influenza in birds have the potential to turn into a human influenza pandemic that would have significant global health, economic, and social consequences.

In November 2005, President Bush outlined the National Strategy to Safeguard Against the Danger of Pandemic Influenza. The President discussed the avian and pandemic influenza threat and the U.S. strategy to detect outbreaks, expand domestic vaccine production capacity, stockpile treatments, prepare to respond to a pandemic, and ensure the health and safety of citizens.

Drawing on the combined efforts of government officials and the public health, medical, veterinary, and law enforcement communities, as well as the private sector, this strategy is designed to meet three critical goals:

+ detecting human or animal outbreaks that occur anywhere in the world;
+ protecting the American people by stockpiling vaccines and antiviral drugs while improving the capacity to produce new vaccines;
+ preparing to respond at the federal, state, and local levels in the event an avian or pandemic influenza reaches the United States.

The U.S. government has adopted $3.8 billion pandemic influenza preparedness plan, with $334 million devoted to a global pool of almost $2 billion to help hard-hit and vulnerable nations combat outbreaks of avian influenza, which might escalate into a human pandemic.

U.S. assistance funds will be used to help nations develop and exercise national preparedness plans, improve disease surveillance, train local rapid-response teams and medical personnel, and support communications and public awareness campaigns to limit practices that contribute to the spread of viruses.

As part of the National Strategy, the U.S. is launching a Bio-Surveillance Initiative to help rapidly detect, quantify, and respond to outbreaks of disease and deliver information quickly to local, state, national, and international public health officials. The U.S. government is working with state and local public health officials and the medical community to develop effective pandemic emergency plans, including creating rosters of medical personnel ready to respond.

U.S. Assistance to Stricken Nations

2005

U.S. high-level and technical health delegations visit countries affected by H5N1 outbreaks to assess how best to direct U.S. assistance.

U.S. gives about $38 million in technical assistance and grants to affected countries and to the World Health Organization to support pandemic preparedness.

2006

President Bush signs an emergency funding law that provides $3.8 billion for pandemic flu preparedness, including funding for vaccine and cell-culture technology development. Of that amount, $280 million is additional foreign assistance to help other nations detect and contain H5N1 avian influenza, in both animals and humans, improve planning and preparedness to respond to outbreaks, and reduce human exposure to infected animals.

The United States pledges more than $334 million in grants and technical assistance to countries threatened by H5N1 at the International Pledging Conference on Avian and Pandemic Influenza in Beijing. Overall, the U.S. and other donors pledge almost $2 billion to help contain the spread of H5N1 avian influenza and avert a global human influenza pandemic.

Working with other partners, U.S. funding will help countries to:

- develop and exercise national preparedness plans
- improve surveillance and rapid response systems
- train and equip national response teams, animal handlers, and medical staff
- monitor and evaluate the use and distribution of animal vaccine
- produce and test vaccines for humans
- support communications and public awareness campaigns to limit practices that spread the bird flu virus among animals and place humans at risk of exposure
- support the influenza-related research work of international technical agencies, private-sector partners, and non-governmental organizations

Ten Things You Need to Know About Pandemic Influenza

1. Pandemic influenza is different from avian influenza.

Avian influenza refers to a large group of different influenza viruses that primarily affect birds. On rare occasions, these bird viruses can infect other species, including pigs and humans. The vast majority of avian influenza viruses do not infect humans. An influenza pandemic happens when a new subtype emerges that has not previously circulated in humans.

For this reason, avian H5N1 is a strain with pandemic potential, since it might ultimately adapt into a strain that is contagious among humans. Once this adaptation occurs, it will no longer be a bird virus – it will be a human influenza virus. Influenza pandemics are caused by new influenza viruses that have adapted to humans.

2. Influenza pandemics are recurring events.

An influenza pandemic is a rare but recurrent event. Three pandemics occurred in the previous century: "Spanish influenza" in 1918, "Asian influenza" in 1957, and "Hong Kong influenza" in 1968. The 1918 pandemic killed up to 50 million people worldwide. That pandemic, which was exceptional, is considered one of the deadliest disease events in human history. Subsequent pandemics were much milder, with an estimated 2 million deaths in 1957 and 1 million deaths in 1968.

A pandemic occurs when a new influenza virus emerges and starts spreading as easily as normal influenza – by coughing and sneezing. Because the virus is new, the human immune system will have no pre-existing immunity. This makes it likely that people who contract pandemic influenza will experience more serious disease than that caused by normal influenza.

3. The world may be on the brink of another pandemic.

Health experts have been monitoring a new and extremely severe influenza virus – the H5N1 strain – for almost eight years. The H5N1 strain first infected humans in Hong Kong in 1997, causing 18 cases, including six deaths. Since mid-2003, this virus has caused the largest and most severe outbreaks in poultry on record. In December 2003, infections in people exposed to sick birds were identified.

4. All countries will be affected.

Once a fully contagious virus emerges, its global spread is considered inevitable. Countries might, through measures such as border closures and travel restrictions, delay arrival of the virus, but cannot stop it. The pandemics of the previous century encircled the globe in six to nine months, even when most international travel was by ship. Given the speed and volume of international air travel today, the virus could spread more rapidly, possibly reaching all continents in less than three months.

5. Widespread illness will occur.

Because most people will have no immunity to the pandemic virus, infection and illness rates are expected to be higher than during seasonal epidemics of normal influenza. Current projections for the next pandemic estimate that a substantial percentage of the world's population will require some form of medical care. Few countries have the staff, facilities, equipment, and hospital beds needed to cope with large numbers of people who suddenly fall ill.

6. Medical supplies will be inadequate.

Supplies of vaccines and antiviral drugs – the two most important medical interventions for reducing illness and deaths during a pandemic – will be inadequate in all countries at the start of a pandemic and for many months thereafter. Inadequate supplies of vaccines are of particular concern, as vaccines are considered the first line of defense for protecting populations. On present trends, many developing countries will have no access to vaccines throughout the duration of a pandemic.

7. Large numbers of deaths will occur.

Historically, the number of deaths during a pandemic has varied greatly. Death rates are largely determined by four factors: the number of people who become infected, the virulence of the virus, the underlying characteristics and vulnerability of affected populations, and the effectiveness of preventive measures. Accurate predictions of mortality cannot be made before the pandemic virus emerges and begins to spread. All estimates of the number of deaths are purely speculative.

8. Economic and social disruption will be great.

High rates of illness and worker absenteeism are expected, and these will contribute to social and economic disruption. Past pandemics have spread globally in two and sometimes three waves. Not all parts of the world or of a single country are expected to be severely affected at the same time. Social and economic disruptions could be temporary, but may be amplified in today's closely interrelated and interdependent systems of trade and commerce. Social disruption may be greatest when rates of absenteeism impair essential services, such as power, transportation, and communications.

9. Every country must be prepared.

WHO has issued a series of recommended strategic actions (see Internet resources) for responding to the influenza pandemic threat. The actions are designed to provide different layers of defense that reflect the complexity of the evolving situation. Recommended actions are different for the present phase of pandemic alert, the emergence of a pandemic virus, and the declaration of a pandemic and its subsequent international spread.

10. WHO will alert the world when the pandemic threat increases.

WHO works closely with ministries of health and various public health organizations to support countries' surveillance of circulating influenza strains. A sensitive surveillance system that can detect emerging influenza strains is essential for the rapid detection of a pandemic virus.

Internet Resources

U.S. Government Agencies

http://www.pandemicflu.gov/
U.S. Department of Health and Human Services (HHS)

http://www.hhs.gov/nvpo/
HHS – National Vaccine Program Office

http://www.usaid.gov/
U.S. Agency for International Development (USAID)

http://www.cdc.gov/flu/pandemic.htm
U.S. Centers for Disease Control (CDC)

http://www.usda.gov/birdflu
U.S. Department of Agriculture (USDA)

http://deploymentlink.osd.mil/medical/medical_issues/immun/avian_flu.shtml
U.S. Department of Defense

http://usinfo.state.gov/birdflu
http://www.state.gov/g/oes/avianflu
U.S. Department of State

http://www2.niaid.nih.gov/
National Institutes of Health (NIH)

International Organizations

http://www.who.int/en
World Health Organization (WHO)

http://www.who.int/csr/resources/publications/influenza/WHO_CDS_CSR_GIP_05_8-EN.pdf
WHO Recommended Strategic Actions

http://www.fao.org/ag/againfo/subjects/en/health/diseases-cards/special_avian.html
U.N. Food and Agriculture Organization

http://www.oie.int/eng/AVIAN_INFLUENZA
World Organization for Animal Health (OIE)

http://www.asean-disease-surveillance.net/ASNBFHome.asp
Association of Southeast Asian Nations (ASEAN)

Additional Reading and Video Links

http://www.whitehouse.gov/homeland/pandemic-influenza.html
U.S. Pandemic Influenza Response and Preparedness Plan
The White House, November 1, 2005

http://www.pbs.org/wnet/wideangle/shows/vietnam/video.html
Video Documentary: H5N1 – Killer Flu
U.S. Public Broadcasting Service program

http://www.hhs.gov/nvpo/pandemics/flu3.htm
Pandemics and Pandemic Scares in the 20th Century
HHS

http://www.aphis.usda.gov/vs/birdbiosecurity/campaign.html
Biosecurity for the Birds
USDA

http://www.osha.gov/dsg/guidance/avian-flu.html
Guidance For Protecting Workers Against Avian Flu
U.S. Department of Labor, Occupational Safety & Health Administration (OSHA)

The U.S. Department of State assumes no responsibility for the content and availability of the resources from other agencies and organizations listed above. All Internet links were active as of November 2005.

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