

## Avian Influenza: Human Pandemic Concerns

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### Introduction

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The likelihood that the next human influenza pandemic virus will emerge from the bird influenza virus circulating in Eurasia remains unknown.

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The likelihood that the next human influenza *pandemic* virus will emerge from the Asian strain of the H5N1 high pathogenic bird influenza virus that is causing widespread outbreaks in Eurasia remains unknown. (See **Glossary** for italicized terms.) Because these bird influenza outbreaks remain primarily an animal disease, there is hope that a human pandemic can be prevented. Eradication of the H5N1 high pathogenic bird influenza virus needs to occur at the farm level in the countries where it is currently circulating. Funding of prevention, surveillance, and eradication efforts in the countries where outbreaks are occurring or in at-risk countries will provide tools needed to facilitate the eradication process of this virus where it is detected and will prevent further spread and subsequent economic loss. Most importantly, stopping the spread of this virus will decrease the opportunity for the virus to emerge as the next human pandemic influenza virus. Every new poultry infection, and subsequent human exposure, gives the virus an opportunity to adapt directly to humans or to exchange genetic material with other influenza viruses, including human influenza subtypes; either event increases the chances that the bird influenza will become a significant human disease.

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Pandemics occur when human populations are exposed to highly transmissible disease organisms to which they have little or no immunity.

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### Pandemics

A pandemic is an occurrence of a disease in excess of its anticipated frequency that is geographically widespread (perhaps globally). Essentially, a pandemic is an *epidemic* with a much broader geographic distribution. Pandemics occur when human populations are exposed to highly transmissible disease organisms to which they have little or no immunity. This exposure can result in infections, which result in disease. The organism then escapes the infected human and is transmitted to the next susceptible human. Because the human population is immunologically naïve, every person exposed

to the organism is potentially susceptible and may become infected. This process can result in rapid spread of the disease within a population and subsequent spread to distant populations. Pandemics generally spread worldwide within 1 to 3 years. As long as susceptible humans continue to come into contact with the infectious organism, the disease continues to spread. This cycle stops only when large portions of the population become immune to the infection and are no longer shedding the organism in large numbers. Immunity occurs when people become infected, recover from the disease, and have circulating antibodies to protect them from future disease.

### Influenza A Viruses

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Influenza A viruses have caused several pandemics in humans throughout history.

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Influenza viruses are identified by proteins that are unique to their virus “type” and “subtype.” The type designation comes from two internal proteins, known as the nucleoprotein and matrix proteins and includes the type A, B, and C influenza viruses. Type A influenza viruses are the most common, and infections have been reported in mammals such as swine, horses, cats, dogs, marine mammals, mink, and humans, as well as in birds. Influenza A viruses have caused several pandemics in humans throughout history; type B and C influenza viruses also commonly cause human disease, but disease outbreaks generally are limited in size. Influenza A viruses are characterized further according to the *antigenic* characteristics of two surface proteins known as hemagglutinin (H) and neuraminidase (N), resulting in a subtype designation. There are 16 H subtypes and 9 N subtypes currently identified, resulting in 144 different possible combinations of H and N subtypes among the influenza A viruses. The unique segmented structure of the genetic material in influenza A viruses makes them inherently unstable and subject to genetic change (Swayne and Halvorson 2003).

Humans are commonly infected with H1, H2, and H3 subtypes of influenza A viruses. Viruses of the H5 and H7 subtype are of the most concern to agriculture because some strains have historically caused severe disease in poultry. Because most influenza A viruses are relatively host specific, human influenza viruses generally do not infect birds and bird viruses generally do not infect humans. Certain influenza A viruses, however, have exhibited an unusual ability to infect more than one host species. When influenza A viruses from two host species co-infect the same animal, the viruses have the opportunity to exchange genetic material that codes for the internal and surface proteins, a process known as *antigenic shift*. This exchange could result in an emerging virus with a new or expanded host range. As a result, the new virus could infect host species that have never been susceptible before and also could cause a change in the ability of the virus to cause severe illness (Perdue and Swayne 2005). This type of change in a virus capable of spreading among humans could produce a pandemic.

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Influenza A viruses change, or drift, frequently.

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Although some *pathogenic* organisms remain unchanged for many years and can be controlled with vaccines that protect the recipient for a lifetime, influenza A vaccines do not fit into this category. The influenza A viruses accumulate point mutations resulting in sequential minor changes in the dominant circulating strains. This process is known as *antigenic drift*. Therefore, the influenza vaccine is evaluated yearly and changed frequently to protect against new and emerging strains of influenza A viruses. This is why people in high-risk groups are encouraged to be vaccinated with updated influenza A vaccines every year.

The subtle changes seen from year to year in influenza viruses generally do not lead to widespread severe disease, but they do make it unfeasible to stockpile large quantities of vaccine for periods longer than 1 to 2 years. Subtle changes in influenza viruses can render vaccines less effective with time. Sudden major changes can render vaccines totally ineffective.

### Historical Pandemics

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1918–19 Spanish flu  
[A (H1N1)]  
1957–58 Asian flu  
[A (H2N2)]  
1968–69 Hong Kong flu  
[A (H3N2)]

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There were three influenza A pandemics in the twentieth century. The influenza pandemic of 1918 was the deadliest. This pandemic may have begun in the United States as an epidemic that was confined largely to military bases and prisons. Public health officials were not overly concerned with the disease because infections tend to spread rapidly among people living in crowded conditions. When American troops took the virus to Europe during World War I, it quickly became established in Europe and spread to Russia, North Africa, India, China, Japan, the Philippines, Brazil, and New Zealand. American troops returning home brought the virus back to the United States and it spread into the civilian population. Almost 700,000 people died from influenza in the United States alone, and 20 to 50 million people died worldwide. Two additional influenza A pandemics have occurred since 1918: the “Asian flu” that resulted in one to two million deaths in 1957–58, and the “Hong Kong flu” that resulted in approximately one million deaths in 1968–69 (Carver 2005). Each pandemic introduced a new subtype of influenza A virus into the human population. Because people had no immunity to the new subtypes, infection rates were very high, resulting in the spread of the viruses around the world within 1 year of detection. All three pandemics were traced to viruses that originated in birds and could be considered to be *zoonotic* diseases, that is, diseases that originate as an animal disease, but also are capable of causing disease in humans.

### Avian Influenza

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Avian influenza viruses are carried by healthy ducks, geese, and shorebirds.

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All known subtypes of influenza A viruses have been recovered from birds living in an aquatic environment, and these birds are considered to be the natural reservoir. Avian influenza (AI) viruses are carried *asymptotically* by ducks, geese, and shorebirds; they typically do not exhibit any signs of disease. These bird species are the perfect disseminators of influenza A viruses worldwide because they migrate for long distances, spreading viruses through contaminated feces.

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Highly pathogenic avian influenza viruses are considered to be foreign animal diseases in the United States.

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Pathogenicity is a measure of the degree of illness that AI viruses cause in chickens. By the current definition from the Office International des Epizooties (OIE) in France, highly pathogenic avian influenza (HPAI) viruses cause death in at least six of eight experimentally infected chickens. In addition, if the genetic sequence of the AI virus in question is similar to that observed for other HPAI strains, then the virus must be considered to be highly pathogenic, whether or not it causes overt disease. All other AI viruses are considered to be of low pathogenicity (LPAI) (Swayne and Halvorson 2003). This definition of the ability of these viruses to make chickens sick does not apply to humans or human infections with AI viruses. The HPAI viruses are considered to be foreign animal diseases (FADs) in the United States, meaning that they do not normally occur here and they are required to be reported to the state veterinarian’s office and to the U.S. Department of Agriculture–Animal and Plant Health Inspection Service (USDA–

APHIS) immediately after detection. To date, all recorded HPAI viruses have been of the H5 or H7 subtypes. The LPAI viruses are *endemic* to the United States, exist in wild waterfowl and live-bird market reservoirs, and occasionally infect commercial poultry flocks. The LPAI viruses of the H5 and H7 subtypes also are reportable to state authorities because of their historical ability to mutate to the highly pathogenic form. High pathogenic AI infections cause severe economic losses to affected poultry producers and are, therefore, considered an emergency disease requiring immediate eradication efforts.

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Surveillance systems currently are in place in the United States that focus on detecting AI viruses in poultry.

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Surveillance systems currently are in place in the United States that focus on detecting AI viruses in poultry. Detection and rapid response are key elements of the U.S. AI control program. The National Poultry Improvement Plan (NPIP), a program of USDA–APHIS in cooperation with the poultry industry, monitors breeder birds (parents) of commercial egg-type chickens, meat-type chickens, and meat-type turkeys for the presence of antibody to AI viruses. The NPIP currently is establishing a monitoring program for table egg chickens, meat-type chickens, and meat-type turkeys. The NPIP program tested 390,000 AI samples from commercial poultry in 2003 to assure the U.S. poultry industry and their trading partners that poultry products in the United States are free of AI. In addition, many state diagnostic laboratories routinely test backyard and commercial birds presented with respiratory disease signs for the presence of AI. For example, the state of North Carolina tested almost 200,000 birds in 2004 and Georgia tested 100,000 birds in 2003. The USDA–APHIS is developing an AI monitoring program for the live-bird market system in the northeastern United States.

This early detection must be complemented with rapid and complete containment plans. Avian influenza outbreaks involving low pathogenic strains of the H5 and H7 subtype generally are handled at the state level. Plans to eradicate H5 and H7 strains in poultry flocks have been developed in most poultry-producing states. These plans are widely disseminated and are activated immediately upon detection of one of these strains. These procedures allow poultry producers to protect their investments by quickly eradicating an influenza virus before it becomes highly pathogenic.

### **Human Cases of Avian Influenza**

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The farming practices and culinary customs unique to Asia are believed to be associated with the transmission of AI viruses from birds to humans.

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In recent years, there were fewer than 100 reported human deaths worldwide associated with AI. Most of these deaths were attributed to the Asian HPAI (H5N1) virus that is circulating in parts of (Eurasian) Asia. Most human deaths attributed to Asian HPAI (H5N1) have occurred in Asian countries (Sims et al. 2005). It seems that the virus has spread beyond Asia as migratory waterfowl move to winter nesting grounds or through the movement of infected domestic fowl, but only a small number of human cases have been reported outside of Asia. The farming practices and culinary customs unique to Asia are believed to be associated with the transmission of AI viruses from birds to humans. In most of the human cases of Asian HPAI (H5N1), there was close contact with infected live or recently dead birds. There have been no human cases of Asian HPAI (H5N1) associated with eating properly cooked poultry meat or eggs. The Asian HPAI (H5N1) virus strain infecting humans can cause severe disease and death partly because humans have little to no immunity to the H5 subtype viruses. There have been fewer than 200 documented human cases of Asian HPAI (H5N1) resulting in fewer than 100 deaths during an 8-year period despite the probable exposure of millions of

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Human-to-human transmission of Asian HPAI (H5N1) has been limited.

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people in these countries, making the transmission of the virus from birds to humans rare. Human-to-human transmission of Asian HPAI (H5N1) has been limited and sustained human-to-human transmission has not been documented; however, each additional human case increases the chance that the virus eventually will improve its transmissibility in humans. The emergence of an Asian HPAI (H5N1) virus strain that is transmitted readily among humans could result in the start of a new pandemic.

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Asian HPAI (H5N1) remains primarily an animal disease. It is not easily transmitted from birds to humans.

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### **Pandemic Risk Assessment**

Asian HPAI (H5N1) remains primarily an animal disease. It is not easily transmitted from birds to humans and human-to-human transmission has not been shown to be sustained. The relatively few confirmed human deaths that have occurred worldwide reflect how rare this virus infection is in humans. During the 8-year period cited previously, approximately 288,000 Americans died from human influenza. Currently, the risk of humans contracting Asian HPAI (H5N1) is extremely low.

The spread of Asian HPAI (H5N1) to poultry in additional countries is likely during waterfowl migration, through trade in the live-bird markets, and through the movement of infected domestic fowl, especially ducks. Heightened surveillance for waterfowl die-offs and outbreaks in poultry flocks is needed to quickly identify virus spread and to initiate response programs. Because the Asian HPAI (H5N1) virus is highly pathogenic in most poultry species and some wild birds, disease detection should not be difficult in most cases, provided adequate diagnostic capability is available. Domestic ducks, however, have been shown to be asymptomatic carriers of the virus and may serve as a silent reservoir for the disease. Heightened efforts to detect influenza viruses in asymptomatic birds are important to ensure early detection and eradication. Rapid depopulation and destruction of infected flocks followed by thorough cleaning and disinfection are essential in ensuring that Asian HPAI (H5N1) remains an animal disease and is eventually eradicated altogether. Intensified testing of flocks in close proximity to known positive flocks could prevent asymptomatic flocks from moving to processing or to other markets. Unfortunately, many at-risk countries in Eurasia, the Middle East, and Africa lack the necessary diagnostic and animal health infrastructure to adequately carry out surveillance for the presence of Asian HPAI (H5N1) and will require significant financial help from the more developed countries.

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Introduction of Asian HPAI (H5N1) to the United States could occur via infected birds or infected humans.

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Introduction of Asian HPAI (H5N1) to the United States could occur via infected birds or infected humans. Because the United States does not import live birds or poultry products from countries where the Asian HPAI (H5N1) has been reported, the most likely bird source for Asian HPAI (H5N1) would be migratory waterfowl or illegally smuggled birds. Birds migrating into and out of the Asian HPAI (H5N1) endemic areas are not likely to be an issue in the United States until spring migration and the return of birds to summer nesting grounds. The eastern-most flyways for migratory birds in Asia do include the Arctic and Alaska, although no positive birds have been detected there to date. Increased surveillance along these flyways could facilitate early detection if Asian HPAI (H5N1) were to be introduced. No major poultry-producing regions exist in the Arctic or in Alaska, but the west coast of Canada and of the United States (Washington, Oregon, and California) are potentially at risk.

Heightened human surveillance for signs of severe respiratory disease should be implemented, especially for those people traveling to or from endemic areas or those living there. Reporting of human cases of respiratory diseases and more intensive testing for influenza A viruses could provide early detection in the unlikely event that human infections occur.

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Birds grown in modern confinement housing are at a much lower risk of contracting AI from wild birds than are birds raised outside.

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The spread of Asian HPAI (H5N1) in Asia occurs mostly in small villages where poultry are raised in open fields with exposure to wild migratory birds and then sold live in village markets.

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Different farming systems are associated with the differing risks of both bird infection and human infection. Birds grown in modern enclosed housing are at a much lower risk of contracting AI from wild birds than are birds raised outside. Modern U.S. farm production practices provide for more control over the movement of poultry and allow for the implementation of strict biosecurity procedures designed to prevent the introduction of disease agents to domestic flocks. In addition, commercial poultry raised in integrated agricultural systems typically are grown on farms dedicated to a specific processing plant and are not sold or commingled in livestock markets. Effective surveillance systems and veterinary oversight help decrease the risk of spreading AI viruses in commercial poultry in this country. This modern type of poultry production is more protective of birds and their health than traditional agricultural systems in which birds are raised in small flocks outside, a system that is commonly found in countries in the developing world. The spread of Asian HPAI (H5N1) in Southeast Asia is mostly occurring in small villages where poultry, especially domestic ducks, are raised in open air fields with exposure to wild migratory birds and then sold live in village markets (Sims et al. 2005). This practice promotes the maintenance of the virus reservoir in domestic ducks and leads to recurring infections.

## Conclusions

The Asian HPAI (H5N1) remains primarily an animal agriculture disease today. Eradication of this disease needs to occur at the farm level in the countries where it is currently circulating. Adequate federal funding of prevention, surveillance, and eradication efforts in Asia and in the at-risk countries outside of Asia not only will facilitate the eradication process if this virus is detected but also will prevent further spread and subsequent economic loss to the affected country and decrease the opportunity for the virus to adapt to humans. Every new poultry infection, and subsequent human exposure, gives this virus an opportunity to exchange genetic material with other influenza viruses, including human influenza subtypes, and increases the chances that Asian HPAI (H5N1) will become a significant human disease. Education of U.S. citizens about the relatively low risk of becoming infected with Asian HPAI (H5N1) virus is needed to calm the fears of a pandemic created by the almost constant media publicity on this issue.

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Education of U.S. citizens about the relatively low risk of becoming infected with Asian HPAI (H5N1) virus is needed.

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## GLOSSARY

**Antigenic.** Having the properties of a substance that induces a specific immune response; usually resulting in the production of antibodies that prevent future disease from specific organisms.

**Antigenic drift.** Small, gradual changes in the genetic make-up of the virus resulting from errors in copying the genetic material.

**Antigenic shift.** Wholesale changes in the genetic make-up of the virus resulting from the exchange of gene segments between different viruses.

**Asymptomatic.** Without clinical signs or symptoms.

**Endemic.** The usual presence of a disease or infection.

**Epidemic.** An occurrence of disease in excess of its anticipated frequency.

**Pandemic.** A geographically widespread epidemic usually spreading worldwide in 1 to 3 years.

**Pathogenic.** Having the ability to produce disease.

**Zoonotic.** Having the ability to infect both animals and humans.

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#### WEBSITES OF INTEREST

[http://www.who.int/csr/disease/avian\\_influenza/en/](http://www.who.int/csr/disease/avian_influenza/en/)

<http://www.usda.gov/>

<http://www.cdc.gov/flu/avian/professional/protect-guid.htm>

<http://www.fao.org>



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