Influenza: The Most Devastating Disease Known to Man

Donna K. Carver, DVM, PhD, ACPV

"Ring around the rosie,
A pocket full of posies,
Ashes, Ashes,
We all fall down."

Mention the words bubonic plague and people think of the worst epidemic in history. This disease became so much a part of the culture that children composed a nursery rhyme to describe the natural history of the disease. The first line of the rhyme refers to a ring around the red skin lesions. Posies were thought by some to ward off disease and by others to mask the odors of decaying bodies. Ashes refer to eminent death (ashes to ashes, dust to dust), and the last line also refers to death. Major epidemics of plague occurred in the 6^{th}, 14^{th}, and 17^{th} centuries. The death toll from plague was approximately 137 million victims. As a result, the plague is considered by the average person to be the worst epidemic of all time. At its worst, the bubonic plague killed 2 million victims a year. Though a formidable disease, it is not the worst.

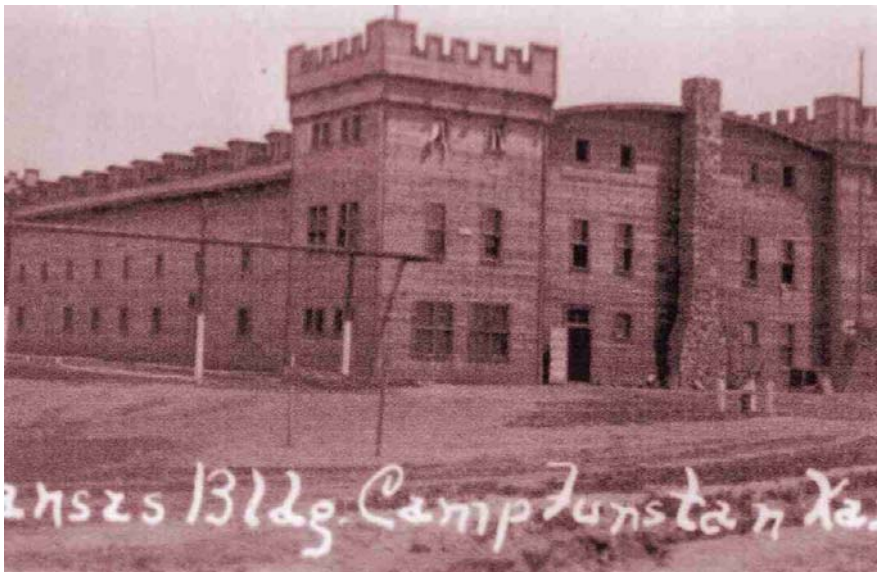
Epidemic - an occurrence of disease in excess of its anticipated frequency

Pandemic – a geographically widespread (sometimes globally) epidemic

Written records trace human outbreaks of influenza-like disease back to 412 BC. More precise descriptions of the disease date from an epidemic in 1173. Since then there have been numerous outbreaks exhibiting variations in severity. The deadliest disease outbreak in history was the influenza pandemic of 1918. This pandemic killed more people than the Great War (World War I). More people died from influenza in a single year than in four years of the bubonic plague from 1347-1351. The influenza pandemic of 1918 was a global disaster that is credited by some for ending World War I.

The influenza virus that spread world–wide in 1918 was commonly called the "Spanish Flu" or "La Grippe". Epidemiologic evidence suggests that the pandemic did not arise in Spain. In fact it was present in many other countries prior to the outbreak in Spain. Because Spain was not involved in the war there were no efforts made to censor information in the press. Other affected countries

that were involved in the war did not release information about the outbreak. This resulted in Spain “reporting” the disease first, thus, the “Spanish Flu”.



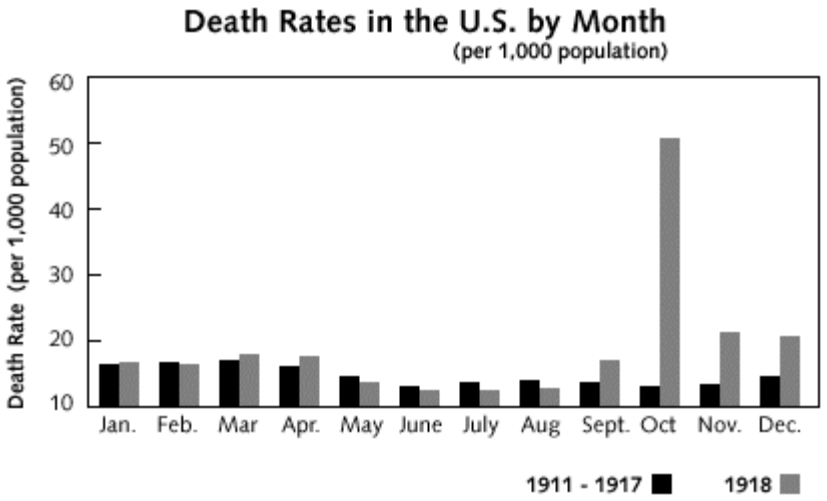
The first case of influenza is believed to have occurred on March 9, 1918, in Fort Riley, Kansas. An army private reported to the camp hospital before breakfast complaining of fever, sore throat, and headache. He was quickly followed by another soldier and by noon the camp’s hospital had seen over 100 ill soldiers. By week’s end that number jumped to 500. All cases reported in the spring of 1918 were from military hospitals and prisons. Over 500 prisoners at San Quentin came down with the condition. Influenza spreading among men living in close quarters did not particularly alarm public health officials.

The war was foremost on the minds of Americans and in March 84,000 “dough boys” set out for Europe, followed by another 118,000 the next month. Little did they know they were carrying a virus that would prove more deadly than their rifles. The trans-Atlantic voyage incurred 36 cases of influenza resulting in six deaths. By May, influenza was established on two continents.

Deep within the trenches, soldiers lived through brutal conditions. The virus spread quickly in this environment and men from all sides were killed by influenza. Great Britain reported 31,000 influenza cases in June alone. By early summer, the flu extended its reach beyond the U.S. and western Europe. Cases of flu were reported in Russia, North Africa, and India. Geographic barriers such as mountains and water did not deter this virus, influenza spread to China, Japan, and the Philippines, Brazil, and to New Zealand. Globally, tens of thousands had fallen ill and died. This first wave was a mere sample of what was to come in the fall.

As troops returned from Europe they brought influenza back with them. First hundreds, then thousands, of soldiers lined up outside infirmaries and hospitals at military bases across the country. In September the disease spread to the civilian population and that month 12,000 Americans died of influenza.

Unlike any other flu, this influenza struck quickly with people that were healthy in the morning being dead by nightfall. Young, robust people were more likely than not to become infected and die. The medical profession was helpless to stop the influenza of 1918.



October 1918 revealed the epidemic's full horror. More than 195,000 people died in America alone. A nationwide shortage of caskets coupled with fear of interaction with other people resulted in the dead being left in gutters and stacked on porches. Public heath officials restricted people to their homes and gauze masks were required in public.

As suddenly as it struck, influenza vanished. The virus ran out of susceptible people to infect. It had killed an estimated 20-50 million people worldwide. There have been other pandemics of influenza since 1918 but none as deadly.

Influenza Pandemics During the 20th Century

During the 20th century, the emergence of new influenza A virus subtypes caused three pandemics, all of which spread around the world within 1 year of being detected.

- **1918-19, "Spanish flu,"** [A (H1N1)], caused the highest number of known influenza deaths: more than 500,000 people died in the United States, and up to 50 million people may have died worldwide. Many people died within the first few days after infection, and others died of complications later. Nearly half of those who died were young, healthy adults. Influenza A (H1N1) viruses still circulate today after being introduced again into the human population in the 1970s.

- **1957-58, "Asian flu,"** [A (H2N2)], caused about 70,000 deaths in the United States. First identified in China in late February 1957, the Asian flu spread to the United States by June 1957.

- **1968-69, " Hong Kong flu,"** [A (H3N2)], caused about 34,000 deaths in the United States. This virus was first detected in Hong Kong in early 1968 and spread to the United States later that year. Influenza A (H3N2) viruses still circulate today.

Both the 1957-58 and 1968-69 pandemics were caused by viruses containing a combination of genes from a human influenza virus and an avian influenza virus. The origin of the 1918-19 pandemic virus is not clear but is believed to be of swine origin.

Fast forward to 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. To control the outbreak, authorities killed about 1.5 million chickens to remove the source of the virus. Scientists determined that the virus spread primarily from birds to humans, though rare person-to-person infection was noted.

- China and Hong Kong, 1999: Avian influenza A H9N2 illness was confirmed in two children. Both patients recovered, and no additional cases were confirmed. The evidence suggested that poultry was the source of infection and the main mode of transmission was from bird to human. However, the possibility of person-to-person transmission could not be ruled out. Several additional human H9N2 infections were reported from mainland China in 1998-99.

- Virginia, 2002: Following an outbreak of H7N2 among poultry in the Shenandoah Valley poultry production area, one person was found to have serologic evidence of infection with H7N2.

- China and Hong Kong, 2003 : Two cases of avian influenza A (H5N1) infection occurred among members of a Hong Kong family that had traveled to China. One person recovered, the other died. How or where these two family members were infected was not determined. Another family member died of a respiratory illness in China, but no testing was done.

- Netherlands, 2003 : The Netherlands reported outbreaks of influenza A (H7N7) in poultry on several farms. Later, infections were reported among pigs and humans. In total, 89 people were confirmed to have H7N7 influenza virus infection associated with this poultry outbreak. These cases occurred mostly among poultry workers. H7N7-associated illness included 78 cases of conjunctivitis (eye infections) only; 5 cases of conjunctivitis and influenza-like illnesses with cough, fever, and muscle aches; 2 cases of influenza-like illness only; and 4 cases that were classified as “other.” There was one death among the 89 total cases The death occurred in a veterinarian who visited one of the affected farms and developed acute respiratory distress syndrome and complications related to H7N7 infection. The majority of these cases occurred as a result of direct contact with infected poultry; however, Dutch authorities reported three possible instances of transmission from poultry workers to family members. Since that time, no other instances of H7N7 infection among humans have been reported.

- Hong Kong, 2003 : H9N2 infection was confirmed in a child in Hong Kong. The child was hospitalized but recovered.

- New York, 2003: In November 2003, a patient with serious underlying medical conditions was admitted to a hospital in New York with respiratory symptoms. One of the initial laboratory tests identified an influenza A virus that was thought to be H1N1. The patient recovered and went home after a few weeks. Subsequent confirmatory tests conducted in March 2004 showed that the patient had been infected with an H7N2 avian influenza virus. An investigation to determine the source of infection is ongoing.

- Thailand and Vietnam, 2004: In January 2003, outbreaks of highly pathogenic influenza A (H5N1) in Asia were first reported by the World Health Organization. From December 30, 2003, to March 17, 2004, 12 confirmed human cases of avian influenza A (H5N1) were reported in Thailand and 23 in Vietnam, resulting in a total of 23 deaths.

- Canada, 2004: In February 2004, human infections of H7N3 among poultry workers were associated with an H7N3 outbreak among poultry. The H7N3-associated illnesses consisted of eye infections.

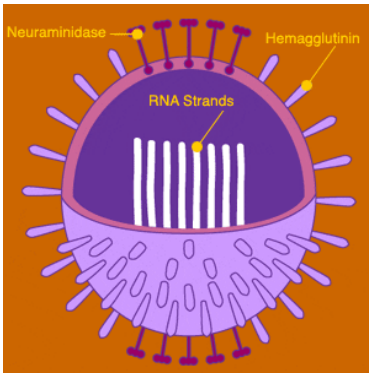
- Thailand and Vietnam, 2004 and 2005: Beginning in late June 2004, new lethal outbreaks of H5N1 among poultry were reported by several countries in Asia. The new outbreaks of H5N1 in poultry in Asia were followed by renewed sporadic reporting of human cases of H5N1 infection in Vietnam and Thailand beginning in August and continuing into 2005. Of particular note is one isolated instance of probable limited human-to-human transmission occurring in Thailand in September.

- Beginning in late July 2005, official reports that the H5N1 virus has expanded its geographical range. Both Russia and Kazakhstan reported outbreaks of avian influenza in poultry in late July, and confirmed H5N1 as the causative agent in early August. Deaths in migratory birds, infected with the virus, have also been reported. Outbreaks in both countries have been attributed to contact between domestic birds and wild waterfowl via shared water sources.

- In early August, 2005, Mongolia issued an emergency report following the death of 89 migratory birds at two lakes in the northern part of the country. Avian influenza virus type A has been identified as the cause, but the virus strain has not yet been determined. Samples have been shared with WHO reference laboratories and are currently being investigated. Also in early August, an outbreak of H5N1 in poultry was detected in Tibet, China.

What do the cases in Asia have to do with the pandemic of 1918?

In a perfect world, avian influenza (AI) viruses infect birds and human influenza viruses infect humans. These viruses are easy to identify because they have surface proteins that are unique to their virus “type”, “subtype”, and “strain”. Type A influenza viruses infect birds and mammals. The subtypes are generally more specific in their infectivity. Subtypes are determined based on their Hemagglutinin (HA) and Neurominidase (NA) surface proteins.



There are three subtypes of influenza that are associated with birds:

Influenza A H5

- Potentially nine different subtypes
- Can be highly pathogenic or low pathogenic
- H5 infections have been documented among humans, sometimes causing severe illness and death

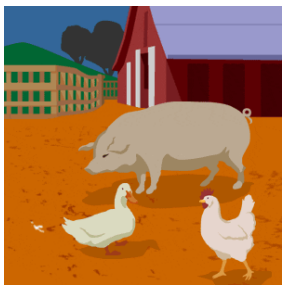
Influenza A H7

- Potentially nine different subtypes
- Can be highly pathogenic or low pathogenic
- H7 infection in humans is rare, but can occur among persons who have close contact with infected birds; symptoms may include conjunctivitis and/or upper respiratory symptoms

Influenza A H9

- Potentially nine different subtypes
- Documented only in low pathogenic form
- Three H9 infections in humans have been confirmed

Recent evidence suggests that in some cases avian influenza viruses have changed or undergone a shift in their genetic material that renders them capable of infecting humans. This has occurred in Asia over the past 5-7 years. Living conditions in that area enhance the chances for this shift to occur. People live in very close proximity to their livestock. Chickens, ducks and pigs are routinely reared together in confined spaces. Because ducks carry influenza viruses without becoming sick or exhibiting any signs of disease, they are a source of infection for pigs and chickens. Pigs are considered mixing vessels for human and avian influenza viruses, meaning that pigs can be infected by viruses from both humans and chickens at the same time and the viruses can swap genetic material. This process can render the avian viruses capable of infecting humans.


Human cases, most of which have been linked to direct contact with diseased or dead poultry in rural areas, have been confirmed in four countries: Viet Nam, Thailand, Cambodia, and Indonesia. Avian influenza viruses that infect humans can cause severe disease and death because humans have no immunity to avian viruses. This was the case in 1918, when humans were often dead within 12 hours of exhibiting clinical signs. The mortality rate in the human cases, caused by the H5N1 circulating in birds in Asia, approaches 75%. If this virus develops the ability to readily spread from human to human, we could be faced with the next great pandemic. This is the major concern of public health officials and why avian influenza viruses have become the focus of their surveillance efforts.

Implications for human health

The poultry outbreaks in Russia and Kazakhstan are caused by a virus that has repeatedly demonstrated its ability, in outbreaks in Hong Kong in 1997, in Hong Kong in 2003, and in south-east Asia since early 2004, to cross the species barrier to infect humans, causing severe disease with high fatality. A similar risk of human cases exists in areas newly affected with H5N1 disease in poultry.

Experience in south-east Asia indicates that human cases of infection are rare, and that the virus does not transmit easily from poultry to humans. To date, the majority of human cases have occurred in rural areas. Most, but not all, human cases have been linked to direct exposure to dead or diseased poultry, notably during slaughtering, defeathering, and food preparation. No cases have been confirmed in poultry workers or cullers. No cases have been linked to the consumption of properly cooked poultry meat or eggs.

Factors relating to poultry densities and farming systems seen in different countries may also influence the risk that human cases will occur. During a 2003 outbreak of highly pathogenic avian influenza, caused by the H7N7 strain, in the Netherlands, more than 80 cases of conjunctivitis were detected in poultry workers, cullers, and their close contacts, and one veterinarian died. That event, which was contained following the destruction of around 30 million poultry, underscores the need for newly affected countries to follow recommended precautions when undertaking control measures in affected farms.

Pandemic risk assessment

The possible spread of H5N1 avian influenza to poultry in additional countries cannot be ruled out. Heightened surveillance for outbreaks in poultry and die-offs in migratory birds, and rapid introduction of containment procedures are needed. Heightened vigilance for cases of respiratory disease in persons with a history of exposure to infected poultry is also recommended in countries with known poultry outbreaks.

The expanding geographical presence of the virus is of concern as it creates further opportunities for human exposure. Each additional human case increases

opportunities for the virus to improve its transmissibility. The emergence of an H5N1 strain that is readily transmitted among humans would mark the start of a pandemic.

What does this mean for the average poultry grower in the United States?

- Avian Influenza is considered a Foreign Animal Disease (FAD) in the United States (US), which means that the government (both State and Federal) work to prevent the introduction of AI into commercial and backyard poultry flocks. Flocks that are confirmed positive for AI are depopulated and buried onsite. Sometimes growers are paid for depopulated birds, but it may be only a portion of the true value of the birds, and can result in severe economic loss for owners and producers of the diseased poultry flocks.
- Avian influenza is considered by public health officials to be a good candidate for causing the next great pandemic. There will be increased surveillance and overall scrutiny of poultry flocks testing positive for AI. This will probably involve submission of samples from birds, growers, and plant workers for detection of AI virus.
- Growers and flock supervisors should be aware of the clinical signs associated with AI and be actively looking for signs in birds. Flocks exhibiting signs of AI should be reported as rapidly as possible. A false positive is preferable to a missed infection.
- Introduction of H5N1 into our state would most likely occur from backyard flocks or wild waterfowl. Because we import no poultry from Asia, AI virus would likely enter the U.S. illegally, probably as fighting birds. On average, there are two backyard flocks within a one mile radius of every commercial operation.
- Growers should take measures to prevent the introduction of AI into their flocks.

What you should know to protect yourself.

Avian influenza (AI) is a highly contagious disease of birds which can be devastating for poultry growers. Because of the structure of the commercial poultry industry and the events which many non-commercial or hobbyist poultry people attend, there is consider-able movement of poultry and individuals associated with poultry across state lines and around the countryside. Whether your poultry interests are large or small, everyone needs to exercise caution when coming in contact with another poultry person or their birds. The AI virus is most often transmitted from one infected flock to another flock by infected birds, people or equipment. AI infected birds secrete virus via nasal secretions and feces. Moving infected birds would naturally result in transferring the virus to the new location. People most often spread viruses via contaminated clothing and/or boots. AI can live in manure for up to 105 days, so it could easily be spread from

one farm to another on soiled boots or clothing. Equipment, used on multiple farms, that is contaminated with infective feces or nasal secretions can spread viruses to multiple new locations. A major problem with stopping the spread of AI is that apparently healthy birds can be infected and transmitting the virus to other birds before exhibiting any clinical signs or symptoms. This is why one of the best ways to prevent this disease is to avoid contact with other poultry.

Symptoms and Diagnosis

There are two forms of AI in poultry, one is highly pathogenic or severe, and the other is low pathogenic or milder. The symptoms of AI are varied depending on the form of AI present, the species of bird infected, and other diseases present in the infected birds. All cases of AI infection require laboratory confirmation. The most common symptoms seen in infected chickens and turkeys include: depression and decreased activity, decreased feed consumption, decreased egg production, coughing, sneezing, wet eyes, huddling, and ruffled feathers. Birds infected with the severe or hot form of AI may have edema or accumulation of fluid in the comb and wattles, blueness of the head area, and severe production drops. Severe cases will show bleeding under the skin in the shanks and high mortality. The less severe form may not be as dramatic as the severe form, but it is still important to eradicate low pathogenic AI. Countries that have chosen to "live with" the milder form of AI have seen the virus become more pathogenic, or hot, after circulating through millions of birds. Any form of AI should be considered very serious. That is why laboratory diagnosis is important. The N.C. Department of Agriculture and Consumer Services' (NCDA&CS) Animal Diagnostic Labs can test your birds for AI infection. There is no charge to you for this service. Additional information on AI may be obtained from the N.C. Poultry Federation, any County Extension Service office or the NCDA&CS Diagnostic Laboratories.

Prevention is the Key

Preventing the introduction of AI and other viruses onto your farm should be the goal of all producers. Preventing the introduction of AI into your flock is not difficult to do if you follow some "common sense" guidelines.

1. Restrict access to wild birds of all types, especially waterfowl.
2. Do not visit other poultry farms or premises that have backyard poultry.
3. When entering poultry houses, wear clothes and boots that stay on your farm.

Additionally, Dr. Bob Hillman, Executive Director of the Texas Animal Health Commission recommends simple biosecurity measures that can be taken to help protect flocks:

1. “Keep a spare pair.” Buy a pair of inexpensive rubber boots, and wear them only on your own premises, to avoid ‘tracking in’ disease.

2. “Give germs the brush off!” Use a long-handled brush to scrape off manure, mud or debris from tires, equipment or boots, then disinfect.

3. “Disinfection prevents infection!” Mix a solution of three parts bleach to two parts water, and use it liberally to clean rubber boots and equipment brought onto your farm. If visitors don’t want their vehicle tires sprayed with disinfectant, ask them to park outside your gate. Other disinfectants that work against AI virus and should be mixed according to package labels include, detergents, hypochlorites, alkalis, phenols, Virkon S and gluteraldehyde.

4. “Make visitors take cover.” Don’t be shy about asking visitors or customers to disinfect their footwear -- or better yet, provide guests with disposable shoe covers, or footwear worn only on your place.

The measures that you take to protect your birds from AI will also protect them from other viral and bacterial diseases. Commercial poultry operations have found that the additional precautions and sanitation measures which they are using have helped them reduce or prevent other disease problems. You may find the same benefits.

The Devastating Disease

While no one can predict if avian influenza will, in fact, cause the next great pandemic, we know that the disease is devastating in poultry flocks. Keeping your flock disease-free is in your best interest irrespective of what happens with H5N1. Efforts to prevent introduction of AI to your flocks will also go a long way in providing a positive image of our industry on the world stage. As these viruses smolder in Asia, we should pay close attention to what is happening there, but we should pay closer attention to what is happening in our own backyards. The next AI outbreak in the U.S. will be scrutinized by regulatory agencies, both animal and human. Early detection and swift and thorough containment efforts will be essential for disease eradication and for maintaining our excellent reputation as an industry.

I had a little bird,
Its name was Enza.
I opened the window,
And in-flu-enza.

-Rhyme created for skipping rope in 1918

For More Information

Centers for Disease Control and Prevention- www.cdc.gov

The Influenza Pandemic of 1918- www.stanford.edu

The American Experience: Influenza 1918- www.pbs.org

The Devil's Flu: The World's Deadliest Influenza Epidemic and the Scientific Hunt for the Virus that Caused It – by Pete Davies, 2000