Avian Influenza: Public Health and Food Safety Concerns*

Revis Chmielewski and David E. Swayne

Southeast Poultry Research Laboratory, Agricultural Research Service, U.S. Department of Agriculture, Athens, Georgia 30605; email: David.Swayne@ars.usda.gov

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Abstract

Avian influenza (AI) is a disease or asymptomatic infection caused by *Influenzavirus* A. AI viruses are species specific and rarely cross the species barrier. However, subtypes H5, H7, and H9 have caused sporadic infections in humans, mostly as a result of direct contact with infected birds. H5N1 high pathogenicity avian influenza (HPAI) virus causes a rapid onset of severe viral pneumonia and is highly fatal (60% mortality). Outbreaks of AI could have a severe economic and social impact on the poultry industry, trade, and public health. Surveillance data revealed that H5N1 HPAI has been detected in imported frozen duck meat from Asia, and on the surface and in contaminated eggs. However, there is no direct evidence that AI viruses can be transmitted to humans via the consumption of contaminated poultry products. Implementing management practices that incorporate biosecurity principles, personal hygiene, and cleaning and disinfection protocols, as well as cooking and processing standards, are effective means of controlling the spread of the AI viruses.

INTRODUCTION

What is the Bird Flu?

Avian influenza (AI) is a disease or asymptomatic infection caused by viruses in the family *Orthomyxoviridae*, genus *Influenzavirus* A, which contains a genome composed of eight segments of single-stranded negative-sense RNA (Swayne & Halvorson 2008). The virus surface contains spikes of hemagglutinin and neuraminidase glycoproteins. The segmented RNA allows for the easy reassortment of the viral genome. The viral genome encodes for ten proteins: one nucleocapsid (NP), three transcriptase proteins (PB-1, PB-2, and PA), the hemagglutinin and neuraminidase surface glycoproteins (HA and NA), two matrix proteins (M1 and M2), and two nonstructural proteins (NS1 and NS2) (Alexander 2000, Lee & Saif 2009). Nucleocapsid and the three transcriptases (PB-1, PB-2, and PA) form the ribonucleoprotein complex that is responsible for mRNA transcription. AI viruses are characterized by their subtypes, pathotypes, genetic lineages, and clades. AI viruses are subtyped by their surface HA and NA glycoproteins, which are major determinants of the pathogenicity, transmission, and adaptation of the AI virus to other species, but these three traits plus infectivity are multigenic. However, the major determinant of pathogenicity is the HA. The HA is important for attachment and entrance into cells to replicate, whereas the function of neuraminidase is to release newly formed viruses (Swayne & Halvorson 2008). There are 16 different hemagglutinin (H1–16) and nine different neuraminidase (N1–9) subtypes. Such viruses have been detected in more than 100 species of wild birds, mostly from the orders *Anseriformes* (ducks, geese, and swans) and *Charadriiormes* (gulls, terns, and shorebirds), but usually without causing clinical signs and are thus of low pathogenicity (LP) (Stallknecht & Brown 2007). Mammals such as humans, pigs, horses, seals, whales, and cats have been sporadically infected with AI viruses (Swayne & Halvorson 2008). In the cases involving carnivores, infection occurred mainly through the consumption of H5N1 HPAI virus–infected birds or their products. Only H5 and H7 have been seen in nature in the high pathogenicity (HP) form, but most H5 and H7 AI viruses are of LP. Most commercially reared poultry in developed countries are free of AI viruses and such infections are rare (Swayne 2008b). When AI is present, it is usually as low pathogenicity avian influenza (LPAI) virus, but if infected by high pathogenicity avian influenza (HPAI) virus, the outcome can be devastating with near 100% mortality in chickens and turkeys. Commonly used vernacular for Eurasian H5N1 HPAI is bird flu, but technically, any AI virus could be termed bird flu.

Human Infection

AI viruses are considered species specific and rarely cross the species barrier (Cox & Uyeki 2008). However, since 1959, some AI virus isolates of subtypes H5, H7, and H9 have caused sporadic infections in humans (INFOSAN IFSAN- 2004). H5N1 HPAI virus was isolated from a domestic goose in Guangdong, China in 1996, and the following year was isolated from an outbreak in the live bird markets in Hong Kong. During the live bird market outbreaks of 1997, the first human case of H5N1 occurred in May, and by the end of 1997, there were 18 hospitalized cases with six fatalities. Other incidences of human infections associated with H5N1 HPAI outbreaks in poultry were reported in China in 2003 and throughout Southeast Asia from 2004 to the present. Human infections were mostly due to direct contact with infected birds (CDC 2006, WHO 2006). Unlike the human H1N1 and H3N2 seasonal flu as upper respiratory infection and low mortality, the H5N1 HPAI virus causes a rapid onset of severe viral pneumonia and has a high fatality rate (60% mortality). There are many cultural practices that increase the risk of exposure of human to HPAI virus. In many Southeast Asian and Middle Eastern countries, poultry flocks are reared in the backyard, rooftops, or in close proximity to human dwellings with close interaction with humans.

The close proximity of birds to humans increases the risk of transmission to humans via aerosol or large airborne droplets, fecal contamination with dispersion via fomites, and direct contact with infected birds. Also, sick birds may be slaughtered for consumption in the developing world, leading to increased risk of exposure (WHO 2005a). H5N1 HPAI virus has expanded its host range, as it has infected dogs and other mammals through the consumption of uncooked infected poultry, wild birds, or their products (Thanawongnuwech et al. 2005, CDC 2007, WHO 2007). This has raised concern that dogs and other pets have the potential to be intermediate carriers that can transfer the H5N1 influenza virus to humans. Although rare, evidence of direct human-to-human transmission of H5N1 associated with a poultry outbreak occurred in Southeast Asia. Sustained human-to-human transmissibility of H5N1 HPAI would require genetic adaption of AI PB2 internal protein (Hatta et al. 2001, WHO 2008, Gao et al. 2009). In addition, because the human population lacks immunity to H5, H7, and H9 viruses, emergence of a pandemic virus that is adapted to humans could be devastating. To date, there have been 493 human infections with 293 fatalities due to H5N1, 114 infections due to H7N7 HPAI with one death, and four infections of young children from H9N2 LPAI viruses (Cox & Uyeki 2008, WHO 2010). Currently, these AI viruses are not adapted to humans and a pandemic has not developed.

Economic Consequence to Poultry Producers

The Food and Agriculture Organization (FAO) estimated the global poultry production in 2007 at 83.7 million metric tons with 8.1 million metric tons in global trade (FAO 2007). The United States, China, the European Union (EU), and Brazil were the largest producers of poultry, with Brazil, the United States, and the EU being the largest exporters. The United States exported 2.3 million metric tons of poultry meat in 2005. Outbreaks of AI since the 1990s have had severe economic and social effects on the poultry industry, international agricultural trade, and public health (Burns et al. 2008). Reductions in consumer sales both domestically and internationally owing to fear and loss of confidence, additional costs for implementing control and prevention measures such as culling, block eradication, and compensation to producers, and other costs (restocking costs, biosecurity, surveillance, vaccinations) are some of the economic consequences of an outbreak (Yalcin 2006). There is also the loss in the export market due to international embargoes and the loss of market share due to competition from other poultry-producing nations. Importing nations also bear the economic impact of increased cost for importing product because of a lack of international competition (Lokuge 2005, McLeod et al. 2005). In regions of the world where there have been HPAI outbreaks, changes in the consumption pattern have been evident, with temporary decreases in poultry consumption. For example, the domestic impact in Turkey in 2006, where 2.5 million birds were culled due to an outbreak of H5N1 HPAI, had a cost of $226 million. In the capital city, Ankara, there was a 54% decrease in sales of poultry products, with a 32% decrease in poultry meat prices, and prices of eggs and other poultry products also decreased (WHO 2005a, Oner et al. 2006, Yalcin 2006).

At least 62 countries reported outbreaks of H5N1 HPAI in either domesticated or wild birds between 1996 and 2010 (OIE 2009). The HPAI virus has caused devastating economic losses to poultry growers and rural households in Asia, Europe, and Africa (McLeod et al. 2005, Otte et al. 2008, FAO 2010). In developing countries, most poultry production occurs in small backyard flocks in rural and periurban areas, so outbreaks economically impacted these small farmers more than commercial industries. Between 1996 and 2003, there were 1,645 H5N1 HPAI outbreaks worldwide that resulted in 43 million birds dead or destroyed, and between 2004 and 2007 more than 250 million birds died or were destroyed (McLeod et al. 2005). The economic consequence of HPAI outbreaks in Southeast Asia for 2003–2005 was between 0.5% and 2% of the area's GDP,

or about $10 billion. More than 50% of the Southeast Asian population derived its income from poultry. For example, in Indonesia 20% of the commercial farm workers lost their jobs as a result of the outbreak. In Vietnam, 44 million birds, or 17% of the bird population, were culled at a cost of $120 million (World Bank 2010). HPAI outbreaks have had a major impact on the livelihood of small and large farmers and have negatively impacted the nutritional stature of millions of people in the developing world.

Effect on International Trade

AI is a notifiable disease and is defined by the World Organization for Animal Health [Office Internationale des Epizooties (OIE)] Terrestrial Animal Health Codes as a poultry disease caused by influenza A viruses of subtypes H5 and H7 or AI virus with an intravenous pathogenicity index of 1.2 or higher. The worldwide monitoring of notifiable diseases is the responsibility of the OIE. Although H5N1 HPAI is primarily an animal health issue, the increasing frequency of human infection has raised concerns about its pandemic potential. The world human and animal health organizations [FAO, OIE, and World Health Organization (WHO)] are collaborating with and aiding countries in the development of risk management strategies to reduce the circulation of AI viruses in the poultry population, to assess the risk of human exposure from production-to-consumption, and to implement mitigation measures. The OIE is responsible for the phytosanitary safety standards (SPS) for the international trade of terrestrial animals and animal products, including poultry. These standards are implemented by national veterinary agencies of the importing and exporting countries. The World Trade Organization enforces the standards in an effort to prevent disease transmission and to ascertain fair trade (OIE 2009). The individual countries may implement trade embargoes on countries that have reported notifiable diseases, such as AI and virulent Newcastle disease, as nontariff trade barriers, but such embargoes must be science based and not political in scope.

International trade implications following an outbreak with HPAI could be economically severe. Gaining the confidence of importing nations require improvements in biosecurity systems, surveillance, vaccination, and other preventative measures (Lokuge 2005, McLeod et al. 2005) At least ten Southeast Asian countries have been impacted by H5N1 HPAI since 2003, although the countries most severely impacted have been China, Cambodia, Indonesia, Laos, and Thailand. Southeast Asian countries account for a quarter of the world's poultry production, and one third to one half of the population derives income from poultry, hence the consequence of HPAI outbreaks with the limitation of trade within and between countries has been devastating to their economies and worsened food security for rural communities. In 2004, Thailand was the fourth largest exporter of poultry and poultry products in the world. The country exported 40% of its poultry production, primarily to Europe and Japan, but following the HPAI outbreak and the ban on international trade of poultry, its poultry industry was economically devastated by losing 50% of its export market (Lokuge 2005). The Netherlands experienced a similar reduction in exports (30%) following its H7N7 HPAI outbreak in 2003. Exporting countries that did not have concurrent outbreaks of HPAI had the advantage of gaining export market share when such outbreaks occurred in Asia. Trade embargoes or bans imposed on a country due to animal disease outbreaks affect all poultry producers as well as importing countries.

Concerns Related to Food-Borne Transmission

Surveillance data revealed that H5N1 HPAI virus was detected in imported frozen duck meat and on the surface and in internal contents of contaminated eggs (Tumpey et al. 2002, Beato et al.

2009, Harder et al. 2009). Experimentally, HPAI virus was detected in breast and thigh meat, and blood and bones, as well as in eggs of HPAI virus–infected chickens (Swayne 2006). Although there is no direct evidence that AI has been transmitted to humans via the consumption of contaminated poultry products, there is anecdotal and experimental evidence that the consumption of uncooked poultry blood or meat has transmitted the H5N1 HPAI virus to carnivorous animals, including tigers, leopards, domestic cats, domestic dogs, and a stone martin (WHO 2005a, CDC 2007, Writ. Comm. Second WHO Consult. Clin. Aspects Hum. Infect. Avian Influenza A Virus 2008).

VIRUS ECOLOGY AND EPIDEMIOLOGY

Natural Reservoirs

Wild waterfowl and shorebirds are natural reservoirs for LPAI viruses, whose replication is primarily limited to the epithelial cells of the intestinal tract (Ito et al. 2000, Webster et al. 2007), and infected birds remain asymptomatic but shed the virus into the environment via feces, and less frequently saliva and nasal secretions (Hinshaw 1985). One of the primary routes of transmission is via the fecal-oral route. LPAI viruses can survive up to 20 days in chicken manure (−4°C) (CDC 2006), in water for at least 10 days (Guan et al. 2002a, Domanska-Blicharz et al. 2010), and on fomites for up to three weeks (Lu et al. 2003), and can replicate in feather follicles and survive on feathers for at least six days (Tiwari et al. 2006, Yamamoto et al. 2008). However, survival is highly temperature and moisture content dependent, i.e., survival is shortened by high environmental temperatures and dry conditions. LPAI viruses with antigenic subtypes H3 and H6, as well as N2, N6, and N8, were the most frequently isolated viruses from wild ducks, whereas H9, H11, and H13 were predominant HA subtypes in shorebirds and gulls (Suarez 2008, Swayne & Halvorson 2008). By contrast, HPAI viruses have not been maintained in wild bird reservoirs but have been derived from H5 and H7 LPAI viruses after circulation in poultry populations (Horimoto et al. 1995). The insertion of multiple basic amino acids, insertion of large amounts of extraneous RNA coding for additional amino acids, substitution of nonbasic with basic amino acids, or loss of shielding glycosylation sites in the cleavage site of HA motif can enable a H5 or H7 LP virus to become HP (Perdue et al. 1996, Suarez 2008).

H5 in Poultry

Many neuraminidase subtypes have been linked with H5 subtypes associated with poultry in both HP (N1–3 and N8–9) and LP (N1–9) forms. The largest outbreak of HPAI in the past 50 years has been the H5N1 HPAI epizootic in Asia, Africa, and Europe (1996–present). This epizootic has affected at least 62 countries and has been isolated from infected poultry flocks in Asia, the Middle East, Africa, and Europe, as well as, but less frequently, from waterfowl, shorebirds, passerine birds, pigeons, and falcons (Stallknecht & Brown 2007). H5N1 HPAI virus was first reported in 1996 in China (HPAI virus type strain A/goose/Guangdong/1/1996) followed by reports of outbreaks in live poultry markets (LPM) of Hong Kong and in humans in 1997, and spread in 2003–2004 through eastern and southeastern Asia, affecting poultry, captive birds, and the human population. Genetic characterization of the Hong Kong viruses revealed that these H5 viruses had the H5 HA gene from A/goose/Guangdong/1/96, NA gene from H6N1 LPAI virus related to A/teal/HK/W312/97, and the internal genes of H9N2 LPAI virus associated with Japanese quail or H6N1 viruses (Xu et al. 1999, Guan et al. 2002a, Kim et al. 2009). Surveillance and phylogenetic analysis revealed that in Hong Kong between 1999 and 2002 there was transmission of H5N1 HPAI virus from domestic poultry to domestic ducks. In general, the ducks were less susceptible

to AI virus infection than chickens and remain asymptomatic when infected. However, in 2002 a H5N1 HPAI virus appeared in Hong Kong that infected and killed captive-reared ducks in a wildlife park.

LPAI viruses usually replicate in the intestines of the ducks. However, the H5N1 HPAI virus in ducks produces primary infection with higher titers in the respiratory tract than in the intestinal tract. Recent studies revealed that some species of ducks have high susceptibility to the H5N1 virus. Experimental evidence with wild-type mallard and Muscovy ducks indicates that mallards may be more resistant to the H5N1 virus than Muscovy ducks (Hulse-Post et al. 2005; Kim et al. 2009; C Cagle, J Wasilenko, E Spackman E, TL To, T Nguyen, M Pantin-Jackwood, unpublished results). However, when mallards become immunocompromised due to another infection, the birds have increased susceptibility to H5N1 infection (Ramirez-Nieto et al. 2010). Since appearing in 1996, the H5N1 HPAI virus has changed genetically, by drifting, to have 10 distinguishable clades (clade 0–9) with at least six subclades. A few of these subclades (2.1, 2.2, 2.3, 2.5) have been responsible for the human H5N1 infections and deaths, with clade 2.2 being the most frequently reported in humans in Asia, Europe, the Middle East, and Africa (CDC 2007, Webster et al. 2007). Other aspects of concern are the transmission of H5N1 from domestic birds to migratory aquatic birds, as occurred in Qinghai Lake, China in 2005 (Chen et al. 2006). Today, the H5N1 HPAI viruses have predominantly replicated in the respiratory tract and less so in the intestinal tract. Some wild waterfowls are more susceptible to H5N1 virus infection than others (Webster et al. 2007, WHO 2007).

The persistence of H5N2 LPAI virus in the poultry population of Mexico for over a year eventually led to critical mutations that resulted in the 1994 outbreak of H5N2 HPAI. Phylogenetic analysis indicated the H5N2 LPAI virus that circulated in the poultry population in Mexico in 1993 was derived from a North American lineage circulating in migratory aquatic birds, which was mutated by adding an insert of two basic amino acids and substitution of a nonbasic with basic amino acid in the HA cleavage site, and consequently caused an outbreak of HPAI in 1994–1995 (Horimoto et al. 1995, Perdue et al. 1996). Mexico initiated a vaccination program in January 1995, and the last HPAI virus was isolated in June 1995. However, H5N2 LPAI virus has continued to circulate.

H7 in Poultry

Several NA combinations with H7 HA subtypes have been reported for LPAI (N1–4, N7, and N9) and HPAI (N1, N3, N4, and N7) viruses in birds and/or humans. Since 1995, infection of poultry with H7 AI viruses has greatly increased, as well as its geographic spread. Outbreaks of H7N1 LPAI occurred in Italy (1999–2001) and in Canada (2000). H7N2 LPAI outbreaks occurred in the Unites States (1996–98, 2002, 2003, 2004) and the United Kingdom (2007). H7N3 LPAI outbreaks occurred in Italy (2002–2003), Chile (2002), Canada (2004), the United Kingdom (2006), and Pakistan (2001–2004), whereas H7N7 LPAI outbreaks occurred in Australia (1976, 1979), the United Kingdom (1996), Ireland (1995, 1998), and Germany (2001, 2003). Outbreaks of H7N1 HPAI have occurred in Italy (1999–2000), whereas outbreaks of H7N3 HPAI occurred in the United Kingdom (1963), Australia (1992 and 94), Pakistan (1995–2004), Chile (2002), and Canada (2004). In Australia, there were outbreaks of H7N4 HPAI (1997) and H7N7 HPAI (1976, 1985, and 1996), but the most severe outbreak of H7N7 HPAI occurred in The Netherlands (2003) (Capua & Alexander 2004, Belser et al. 2009). The H7N7 HPAI virus in the Netherlands resulted in the culling of 30 million birds. Since 1995, at least 75 million poultry (chicken/turkey) worldwide have been culled or depopulated because of H7 HPAI epizootics (Capua & Alexander 2004, Swayne 2008c, Belser et al. 2009). For LPAI viruses in the United States, the LPM system has various frequencies of poultry infected with various LPAI viruses. H7N2 LPAI viruses have

been circulating in LPM from 1994 to 2006, whereas H5N2 LPAI viruses have been sporadically isolated from LPM in the northeast United States since 1983 (Senne et al. 2003, Suarez et al. 2002, Senne 2010). Phylogenetic analysis of H7N2 LPAI isolates from commercial poultry outbreaks in Pennsylvania (1997–98, and 2001–2002); Virginia, West Virginia, and North Carolina (2002); and in Connecticut (2003) were linked to H7N2 LPAI viruses circulating in the LPM in the northeastern United States (Spackman et al. 2003, Akey 2009). The fact that H5 and H7 LPAI viruses can mutate to HPAI viruses after circulating in the poultry population (Horimoto et al. 1995, Dusek et al. 2009) has prompted surveillance studies to track the genetic changes of the H5 and H7 subtypes circulating in LPM in the United States over a seven-year period (Horimoto et al. 1995, Spackman et al. 2003). These researchers noted specific substitution changes at the hemagglutinin cleavage site of H7 with the addition of basic amino acids.

Public Health Concerns

Outbreaks of HPAI viruses in wild and domestic birds are rare, but once infection occurs it can be serious from veterinary, medical, and public health perspectives. Since the outbreaks of H5N1 HPAI in poultry and humans in Hong Kong in 1997 and H7N7 HPAI in the Netherlands in 2003, there have been concerns that AI viruses could persist in some poultry populations and emerge as a pandemic virus for humans through multiple mutations or reassortment. For an AI virus to cause a pandemic requires the virus to develop the ability to be transmitted from human-to-human and cause high morbidity or mortality rates. During the twentieth century, the emerged viruses had been new hemagglutinin subtypes for which the human population has no exposure and thus no immunity (CDC 2007). The 2009 pandemic H1N1 was the result of a reintroduction of H1N1, which over time had mutated and reassorted influenza A genes from various avian, human, and swine influenza viruses (Dunham et al. 2009, Liu et al. 2009, Sinha et al. 2009). Today, AI viruses of concern as potential pandemic strains are some H5, H7, and H9 subtypes that have crossed the human species barrier multiple times to produce sporadic infections. This will be discussed in following sections (Li et al. 2003, WHO 2005, CDC 2007, Webster et al. 2007, Pappas et al. 2007).

H5 in Humans

Although very rare, subtype H5 AI viruses have crossed the species barrier to produce sporadic infections of humans (Gilsdorf et al. 2006, Cox & Uyeki 2008, Writ. Comm. Second WHO Consult. Clin. Aspects Hum. Infect. Avian Influenza A Virus 2008). The first case of transmission of H5 HPAI virus from birds to humans occurred in association with the LPM of Hong Kong in 1997, which caused 18 hospitalized cases and six fatalities. To date, 493 human cases of H5N1 illness have been reported, of which 292 died, for a case fatality rate of 60% (WHO 2005a, 2010; Kim et al. 2009). The vast majority of human infections occurred as a result of direct exposure to live or dead infected poultry, with one instance through the consumption of raw duck blood, and another in which individuals in Azerbaijan (2006) became infected while defeathering dead wild swans (Gilsdorf et al. 2006, WHO 2007, Writ. Comm. Second WHO Consult. Clin. Aspects Hum. Infect. Avian Influenza A Virus 2008). Although human-to-human transmission of AI virus is limited, reports of this type of transmission have occurred in Thailand (2004), Vietnam (2004), Azerbaijan (2006), Indonesia (2006), Pakistan (2007), and Egypt (2007), usually as a result of one of the family members having direct contact with infected poultry prior to infecting members of the household or one family member or health care worker becoming infected from an infected patient (CDC 2006, WHO 2008). These transmissions were mainly among family members and

not communal. H5N1 HPAI viruses continued to evolve, although transmission from the avian to human host is relatively low. However, with increased exposure to a human host, the chance of the virus adapting for efficient human infectivity increases or reassorting with a human-adapted influenza virus may occur.

The symptoms of H5N1 HPAI virus infection in humans include fever, severe respiratory disease, dyspnea, multi-organ failure, and death, with an incubation period between five and ten days (Tam 2002, Ungchusak et al. 2005, Gilsdorf et al. 2006). The case fatality rate has been approximately 60%. In 2004, patients in Thailand infected with HPAI virus exhibited drastically different clinical symptoms than seasonal flu. Within two to eight days following exposure, patients symptoms progressed from flu-like to vomiting, diarrhea, and abdominal pain (Yuen et al. 1998, Ungchusak et al. 2005, WHO 2005a).

H7 in Humans

Humans have rarely been infected with H7 AI viruses, but when infected they usually had symptoms of mild respiratory disease and conjunctivitis. The North American H7 LPAI and HPAI viruses caused milder, self-limiting infection with no human-to-human transmission, as compared with the Eurasian 2003 H7N7 HPAI virus in which limited human-to-human transmission occurred. There have been sporadic reports of individual cases of mild respiratory disease due to H7N2, H7N3, and H7N7 virus infections. In the United Kingdom in 1996, a patient was infected with H7N7 LPAI virus after an eye abrasion, leading to conjunctivitis. In the United States (Virginia, 2002; New York, 2003) and the United Kingdom (2007), patients infected with H7N2 LPAI viruses developed mild respiratory symptoms. These infections were phylogenetically linked with the H7N2 circulating in the live bird market (Spackman et al. 2003, Suarez et al. 2009). Similarly, other sporadic cases of H7N3 LPAI and HPAI virus infections occurred in Canada (2004), resulting in two cases of conjunctivitis and mild respiratory symptoms. In Wales in 2007, an infection with H7N2 LPAI virus was associated with poultry obtained from a live bird market (Nguyen-Van-Tam et al. 2006, Editorial team 2007). The patients had symptoms of conjunctivitis, flu-like symptoms, and neurological and gastrointestinal symptoms (Capua & Alexander 2004, Editorial team 2007). However, the greatest numbers of H7 human cases were associated with the H7N7 HPAI epizootic in the Netherlands in 2003, which also spread to neighboring commercial farms in Belgium and Germany. Eighty-nine farm workers became infected; 78 with conjunctivitis, five with conjunctivitis and flu-like symptoms, two with flu-like symptoms, four with other symptoms, and one death from severe respiratory disease. Three of the cases were as a result of human-to-human transmission from a farm worker to his family (Fouchier et al. 2004, Koopmans et al. 2004). Phylogenetic analysis revealed the H7N7 virus from a patient and viruses from infected chickens were identical, indicating that the HA had nearest homology with A/mallard/Netherland/12/00 (H7N3) and the NA had nearest homology with A/mallard/NL/2/00 (H10N7) viruses isolated from mallards. All the internal genes (NP, PA, PB1 and 2, NS, MA) of the outbreak isolate were of the Eurasian lineage. The genomic analysis from the fatal case (A/NL/219/03) had a 26-nucleotide substitution, of which four were in the HA gene and eight in the PB2 gene (Fouchier et al. 2004). The Eurasian lineage of H7N7 HPAI virus maintained tropism toward α2-3 sialic acid cell membrane receptor, which preferentially binds to cells in avian species. HA of the North American H7N2 LPAI virus (A/turkey/Virginia/4529/02 and A/chicken /Connecticut/260413-2/03), and the H7N3 HPAI virus (A/chicken/Canada/504/04) had adapted to recognize and have increased affinity for α2-6 sialic acid cell receptors, which preferentially bind to some human cells, but neither virus changed sufficiently to be pandemic viruses. Nevertheless, the Eurasian lineage of the H7N7 HPAI virus (2003) caused one fatality, indicating greater

virulence for humans and that other factors such as mutation in the PB2 (E627K) internal protein may have contributed to the human pathogenicity of the Eurasian lineage (Belser et al. 2009).

Other AI Subtypes: H9

There have been sporadic cases of humans infected with H9N2 LPAI viruses. Outbreaks of H9N2 have occurred throughout the world beginning in the 1990s in poultry flocks in China, Pakistan, and the Middle East. There were reported outbreaks in Europe, such as in domestic ducks, chickens, and turkeys in Germany (1995–1998), in ostriches in South Africa, and in turkeys in the United States, the Middle East, and Korea (Capua & Alexander 2004). However, these H9N2 viruses were not associated with human infections. By comparison, rare H9N2 human infections occurred in China in 1999 and again in 2003, producing self-limiting mild respiratory disease. These infections occurred in young children (Capua & Alexander 2004).

EVOLUTION AND PATHOGENICITY

Genetic Changes in the Virus: Antigenic Drift and Antigenic Shift

AI viruses are genetically unstable and are constantly evolving. The antigenic variation for some HA subtypes is large, with conserved regions being as little as 30% of the genome (Lee & Saif 2009). Genetic changes occur either by antigenic drift or by antigenic shift.

Antigenic Drift

AI viruses lack a proofreading and error correction mechanism during replication, therefore small, constant genetic changes occur due to point mutation, deletion, or substitution, which can result in new mutants (CDC 2005, Escorcia et al. 2008). The insertion of multiple basic amino acids in the cleavage site of the HA motif can enable an H5 or H7 LPAI virus to become an HPAI virus. An example of such a mutational event occurred with the H5N2 LPAI virus that appeared in Mexico in 1993, circulated in poultry for more than one year, and mutated into an HPAI virus in November 1994. By 1995, phylogenetic analysis revealed that the virus had acquired an insertion of two additional basic amino acids and a basic for nonbasic substitution at the hemagglutinin proteolytic cleavage site, which was responsible for the acquired HP phenotype. Genetic analysis also revealed the poultry LPAI virus originated from the LPAI virus of migrating waterfowls prior to introduction into the poultry population (Horimoto et al. 1995, Perdue et al. 1996). Since 1995, the H5N2 LPAI virus has continued to circulate among poultry in Mexico with continued antigenic drift in the protective epitopes of the HA protein as compared to the 1994 vaccine seed strain. Outbreaks as a result of the mutation of H5 and H7 LPAI to the HPAI viruses have also occurred in Pennsylvania (1983) and Italy (2000), respectively (Kawaoka et al. 1984, Donatelli et al. 2001, Spackman et al. 2003, Suarez et al. 2009)

Antigenic Shift

Reassortment of gene segments has occurred due to coinfection of a host with more than one subtype of influenza A virus. Such a mechanism was responsible for development of the human pandemic H1N1 (1918), H2N2 (1957), and H3N2 (1968) viruses that arose in the human population. This shift in gene segments has also occurred in birds, with H5N1 HPAI virus appearing in Hong Kong in 1997, following the reassortment of the H5 gene from H5N1 of Guangdong

lineage virus, NA from an H6N1 virus, and internal genes (NS, PB2, M, and PA) from the H9N2 virus (Xu et al. 1999, Guan et al. 2002a). This suggests that poultry were infected with a reassortant virus of wild waterfowl origin that circulated in the poultry and adapted by optimizing AI virus gene segments through mutations and reassortment.

Host Restriction

The ability of the virus to infect a host depends on its affinity to bind with the host cell receptor and initiate the replication process. In general, receptor binding contributes to the infectivity of AI viruses. The virus HA binds to the host α-sialic acid cell receptors, so the receptor cell motif restricts the ability of viruses to bind and invade the host cell. The HA of most AI viruses has the affinity for α2-3 sialic acid receptors that are predominant on avian cells, whereas human influenza A viruses have the affinity for α2-6 sialic acid receptors that are predominant on human cells. Although α2-3 sialic acid is predominant in avian species, including chickens, turkeys, and ducks, some investigators have found that reduced numbers of α2-6 sialic acid receptors may be expressed in the epithelial tissue of many organs in various poultry species (Ito et al. 2000, Gambaryan et al. 2002, Matrosovich et al. 2004, Kuchipudi et al. 2009). Influenza viruses have found other means of circumventing host restrictions. For example, virus adaptation to its host after passage in that species can result in changes in viral molecular structure. Adaptation of virus from wild duck-to-chicken produces common adaptive changes such as the shortening of the NA stalk by deletion of 19 amino acids. Pathogenicity studies revealed that a deletion in the stalk of the NA of AI viruses resulted in increased viral replication and an increase in pathogenicity in chickens (Webster et al. 1992, Matrosovich et al. 2004, Munier et al. 2010, Ramirez-Nieto et al. 2010). Genetic adaptations are evident in H9N2 LPAI viruses in Asia that have acquired human virus-like specificity for binding to α2-6 sialic acid receptors and in H5N1 HPAI viruses that have selective tropism for α2-3 sialic acid receptors that are present in the alveoli of the lower human lungs (Matrosovich et al. 2004, Wan et al. 2008).

Adaptive Mutation to Infect Humans

Viral adaptation is an important factor in enabling human cell receptor binding and virus transmission. Influenza viruses alter the receptor-binding properties of HA to increase infectivity and transmission. The HA proteins in H5N1 HPAI viruses have low affinity for α2-6 sialic acid receptors (human), therefore adaptations are needed to efficiently infect and transmit between humans. Studies of the HA binding of AI viruses to sialic acid receptors of host cells revealed that mutation of amino acid residues 226leu and 228ser at the HA binding site increased the binding affinity for the human α2-6 sialic acid receptors. Mutation of the PB2 internal protein at amino acid residues 627K and 701N was also correlated with increased virus replication efficiency and host range, but did not increase virus transmission. These studies indicated that multiple genes may regulate virus replication and transmission. Genetic studies of the H5N1 HPAI virus clade 2.2 revealed changes both in the HA receptor site and PB2 genes. These changes imply that H5N1 (clade 2.2) is evolving its efficiency for transmission to humans, but additional undefined changes are necessary for the virus to become a pandemic virus (Gao et al. 2009).

Pathogenicity in Birds

AI viruses are also classified by pathotypes, i.e., LPAI and HPAI viruses. Birds infected with LPAI virus can exhibit mild signs such as ruffled feathers, a decrease in egg production, and mild

respiratory disease that lasts for approximately 10 days. Birds infected with HPAI viruses exhibit severe respiratory and neurological signs, multiple organ failure, and death within 48–96 h. The peak mortality rate is between 90% and 100%. The H5 and H7 AI viruses have been introduced into the poultry population as LPAI viruses (WHO 2005a) and, with adaptation and sustained replication, this has led to the emergence of HPAI viruses. In addition to tissue tropism and adaptive mutation, protease activity of the host on the HA cleavage site of the virus is one of the major determinants for pathogenicity. The ability of the host proteases to cleave the HA is important for infectivity and viral spread (Hatta et al. 2001, Lee & Saif 2009), hence the conversion of LPAI to HPAI viruses is dependent on changing the cleavability of HA from trypsin-like enzymes to the host's furin-like proteases (Hatta et al. 2001, Lee & Saif 2009). LPAI viruses can replicate in localized tissues (respiratory and digestive) in which trypsin-like proteases are present, whereas HPAI viruses replicate systemically in most organs and cell types by using ubiquitous furin-like proteases or trypsin-like proteases. In LPAI viruses, there are two basic amino acids at the HA cleavage site motif (Walker & Kawaoka 1993). This restricts the cleavage of this site to extracellular trypsin-like enzymes present primarily in the respiratory and digestive tracts. In HPAI viruses, the multiple basic amino acids at the HA cleavage sites can be cleaved by a larger range of intracellular enzymes (furin and subtilisin) commonly found in many organs and tissues allowing the virus to infect and grow systemically, i.e., pantropic (Hulse-Post et al. 2005).

TRANSMISSION/DISTRIBUTION

The transmissibility of AI viruses to poultry or humans is dependent on the virus strain, environmental factors, and host species susceptibility.

Bird Transmission and Exposure

As the natural reservoir for AI, infected waterfowl are believed to pass the AI virus to domestic poultry by the fecal-oral route through contaminated water sources, feed, and housing facilities/shared environment, where infectious virus can be excreted by birds for up to 10 days. The virus can survive at 4°C in feces for at least 35 days (Brown et al. 2007, Stallknecht & Brown 2007). Transmission is possible via aerosols or airborne droplets, as well as by wind dispersion of fomites including contaminated dust. Indirect exposures occur through surface contamination of equipment, clothing, and shoes from dust, feces, secretions, and contaminated feathers (CDC 2006, Gilsdorf et al. 2006, Yamamoto et al. 2009).

In developing countries such as Vietnam, Indonesia, and Egypt, it is estimated that 80%–85% of poultry are reared in small flocks outdoors or on rooftops as village poultry (Branckaert & Guye 1997, Biswas et al. 2009). These flocks are a vital source for the LPM and are valuable commodities to these subsistence growers, whose cultural preference is to consume freshly slaughtered meat. The close living proximity of these small backyard or rooftop flocks to humans increases the chance for AI virus transmission through contact with contaminated feces or airborne virus. There are also exposures due to bird respiratory secretions, contaminated dust, and contaminated bodies of water such as ponds. Surveillance studies in the United States have traced H7N2 LPAI virus from the LPM system to poultry on commercial farms (turkeys; layer, breeder, and meat chickens) in the northeastern United States, resulting in millions of infected birds. Historically, the LPM system in Hong Kong also contributed to the interaction of domestic quail and domestic chickens, giving rise to the reassortant H5N1 HPAI viruses (Spackman et al. 2003, Duan et al. 2007, Suarez et al. 2009, WHO 2005a). However, interspecies transmissions of AI viruses have occurred in other species as well. H1N1 and H3N2 commonly circulate in swine in Europe and the United States, and have

crossed species to infect turkeys, particularly breeder hens, which require a lower exposure dose of virus to produce a productive infection in turkeys than is needed to infect chickens (Pillai et al. 2010). H1N2 swine influenza virus has also infected turkeys. Recently, several flocks of breeder turkey hens in Canada, Chile, and the United States were infected with 2009 pandemic H1N1 virus, and the field syndrome was experimentally reproduced by reproductive tract insemination (Suarez et al. 2009, Pantin-Jackwood et al. 2010). Epidemiologic evidence in the Canadian case suggested that a poultry worker with respiratory illness may have transmitted the virus to the turkey flock (OIE 2009).

Human Transmission

Most reports indicate that human infection with H5N1 HPAI virus was the result of direct contact with live or dead infected birds. An exposure survey in Hong Kong in 1997 determined that 3%–10% of the poultry workers involved in the culling of birds in the live bird market were seropositive for H5N1 when surveyed after working in the depopulation program (Bridges et al. 2000, Katz et al. 2008). People at greatest risk for AI virus exposure and infection include farm workers, live bird market workers, butchers and home processors of poultry, hunters that slaughter, eviscerate, and defeather infected wild birds, and those preparing to cook contaminated meat getting viruses on their hands and transferring them by touching mucus membranes (WHO 2005b, 2007). Veterinarians are also at high risk when working with infected flocks. Other sources of exposure are due to cultural practices of slaughtering sick birds and close living conditions between human and infected birds (INFOSAN IFSAN- 2004). Direct human-to-human transmission mostly occurs in clusters as a result of family or health-care worker exposure (WHO 2004, 2008). There appears to be an undefined human genetic factor that is responsible for the familial association.

Food Transmission: Meat

In some countries, the cultural preference for the consumption of freshly slaughtered poultry meat supports village production systems and LPM, which increases the risk of transmission of AI virus (Katz et al. 2008). AI virus has survived in imported raw infected meat, such as frozen infected duck carcasses, in Korea (2001), Japan (2003), and Germany (2007), and was isolated from chicken thigh and breast meat from experimental studies with HPAI viruses (Tumpey et al. 2002, Swayne & Beck 2004, Mase et al. 2005, Beato et al. 2009, Harder et al. 2009). The titers of H5N1 HPAI virus recovered from experimentally infected chicken thigh meat were as high as 10^7 EID_{50} (median egg infectious dose) g^{-1} (Swayne & Beck 2004, Swayne 2006, Thomas & Swayne 2007). In Southeast Asia, one of the cultural practices is to slaughter sick poultry instead of accepting an economic loss. Butchering or home slaughtering of sick birds increases the risk of AI virus exposure through cross contamination from live and dead birds to human handlers or airborne virus generation during slaughter. Improper cooking, handling, and preparation may allow AI virus survival and increases the potential for productive exposure, therefore the consumption of raw or undercooked food is not advisable. Although there is no evidence of human infection due to food consumption, there is one anecdotal incident of infection through the consumption of raw duck blood, and natural and experimental infection in mammals occurred when infected meat was consumed by tigers, leopards, house cats, dogs, ferrets, and other mammals (Beato et al. 2009). Experimental studies in simulated LPM slaughter of H5N1 HPAI virus–infected chickens produced airborne viruses that were transmitted to chickens and ferrets, resulting in fatal infections (Swayne 2005, 2008a; D.E. Swayne, unpublished data). In commercially produced poultry, HPAI virus–infected poultry are destroyed and not used for human food consumption.

Eggs

HPAI virus has been found on egg shells and internally in albumen and yolk from eggs produced by experimentally infected chicken, but with LPAI viruses, only egg shells have been determined to be contaminated and not the internal contents (Cappucci et al. 1985, Promkuntod et al. 2006). When experimentally added to products, H5N2 LPAI virus survived in egg yolk and albumen for at least 17 days when held at 4°C–20°C (de Wit et al. 2004), but LPAI viruses have not been shown to contaminate eggs from the field (de Wit et al. 2004). Most birds infected with HPAI virus stop laying eggs, but the last few eggs produced may be infected. No human cases from consumption of infected eggs have been reported, but pigs were infected from consuming raw eggs with shell from H7N7 HPAI virus–infected flocks in the Netherlands (WHO 2007). In many developed countries, markets have developed for deshelled, liquid eggs because of a drop in demand for shelled eggs (Lokuge 2005). Early HPAI virus infection of a flock before clinical signs provides the possibility of AI virus–contaminated eggs being included in the liquid egg product. However, the egg pasteurization process inactivates HPAI and LPAI viruses (Swayne & Beck 2004).

Water

Fecal-contaminated water can be a source of infectious AI virus. AI virus can survive in water for at least 10 days and for up to a year (Brown et al. 2007, Domanska-Blicharz et al. 2010). The survival and infectivity of AI is influenced by temperature, pH, and salinity of the water. Survival increases as temperature decreases (Guan et al. 2002b, Brown et al. 2007, Domanska-Blicharz et al. 2010). Open bodies of water such as ponds and lakes may be a haven for AI virus–infected migratory ducks and birds, which may become AI virus contaminated and used as a water source for domesticated birds. When ducks were experimentally infected with AI virus, they shed as much as $10^{7.8}$EID g^{-1} in their feces, which in turn can contaminate the water source (Brown et al. 2007, Stallknecht & Brown 2007, Stallknecht et al. 2010). This reinforces the need for growers to implement proper biosecurity measures to ensure that potable water does not become contaminated with AI virus from wild bird sources.

Fomites

Equipment, surfaces, shoes, and clothes can be sources of contamination, as AI viruses can survive up to three weeks on some fomites (Lu et al. 2003, Tiwari et al. 2006).

PREVENTION/CONTROL

Farm to Table Risk Management

The control of AI in poultry, from village to commercial sectors, requires farm-to-table risk management. Some of the basic needs include implementation of good agricultural practices such as training of workers in good management and biosecurity practices, in particular poultry cullers, establishing a biosecure environment to isolate poultry from potential AI virus carriers, supplying a source of potable water, providing a feed supply that is secure and free of contaminants, disinfection and decontamination of the premises and equipment prior to the introduction of a new flock or after culling of poultry flocks, establishing routine composting of litter and carcasses for all flocks, and safe disposal of carcasses from known infected farms (Brglez & Hahn 2008, Swayne 2008b, Guan et al. 2009). Good risk communication with workers, veterinarians, and suppliers is

essential to manage risk. Following an outbreak, disease surveillance and inspection, controlled depopulation, rapid culling, and potentially a vaccination program must be implemented. Although the vaccination program may be country specific, a delay in this control measure when rapid depopulation is not a viable option could result in enormous economic cost, whereas rapid intervention could dramatically reduce costs and the spread of infection. From a national level, effective risk communication with growers and producers is essential as affected countries must address improvements in biosecurity as a cost-effective investment (Koopmans & Duizer 2004, Lokuge 2005). In developed countries, commercially produced HPAI virus infected poultry and their products are prohibited from going into the food chain. In addition, LPAI and HPAI viruses are rare in commercial and noncommercial poultry in developed countries.

In developing countries with H5N1 HPAI virus infections, on a local level safe food handling such as keeping raw meat separate from cooked foods, cleaning of all work surfaces, cooking meat to the proper temperature (70°C), and maintaining proper storage temperatures must be practiced. It is essential to inform food preparers that AI can survive refrigeration and freezing. Low temperature increases its stability (INFOSAN IFSAN- 2004), so refrigeration is not a means of control. Therefore practicing good hygiene is essential to prevent cross contamination (INFOSAN IFSAN- 2004). Effective vaccination prevents systemic infection of poultry and mitigates the risk of H5N1 HPAI virus from being in meat and other poultry products (Swayne & Suarez 2007).

In 2004, WHO began contemplating whether H5N1 HPAI virus–infected poultry products (refrigerated or frozen carcass) or eggs may pose some risk to human health in developing countries. Deshelled liquid eggs are typically pasteurized to inactivate bacteria such as *Salmonella*. The pasteurization processes have been validated with established critical limits in the HACCP

Table 1 Thermal death times (D_T) for low pathogenicity avian influenza A/Ck/NY/13142-5/1994 and high pathogenicity avian influenza A/Ck/PA/1370/1983 in egg products (imitation egg, whole homogenized egg, liquid egg white, 10% salted egg, dried egg white) heated at 55°C to 63°C

Temp °C	Imitation egg product (IEP)		Whole homogenized eggs (WHE)		Liquid egg white (LEW)		10% salted egg (SEW)	
	D_T							
	[1]LPAI-NY	[2]HPAI-PA	[1]LPAI-NY	[2]HPAI-PA	[1]LPAI-NY	[2]HPAI-PA	[1]LPAI-NY	[2]HPAI-PA
55	2.9 min	18.6 min	6.7 min	11 min	6.6 min	4.3 min	41 s	20.3 s
56.7	1.4 min	8.5 min	20 min	4.5 min	52 s	33 s	36 s	<20 s
57	0.8 min	3.8 min	1.6 min	3.2 min	21 s	23 s	22 s	<20 s
58	0.7 min	2.6 min	22 s	22 s	<19 s	<19 s	<20 s	<20 s
59	0.7 min	2 min	<20 s	<19 s	<19 s	<19 s	<20 s	<20 s
61	0.5 min	0.8 min	<20 s	<19 s	<19 s	<19 s	<20 s	<20 s
63	<0.1	<0.5	<20 s	<19 s	<19 s	<19 s	<20 s	<20 s

[1]low pathogenicity avian influenza A/Ck/NY/13142-5/1994.
[2] high pathogenicity avian influenza A/Ck/PA/1370/1983.
LPAI-IEP: Log $_{10}$D-value = $0.0239(\text{Temp})^2 - 2.8927(\text{Temp})x + 87.30$.
HPAI-IEP: Log $_{10}$D-value = $-0.3565(\text{Temp}) + 1.6407$.
LPAI-HWE: Log $_{10}$D -value = $0.0305(\text{Temp})^2 - 3.7702(\text{Temp}) + 116$.
HPAI-HWE: Log $_{10}$D -value = $0.0324(\text{Temp})^2 - 4.0265(\text{Temp}) + 124.75$.
LPAI-LEW: Log $_{10}$D value = $0.0467(\text{Temp})^2 - 5.6432(\text{Temp}) + 169.77$.
HPAI-LEW: Log $_{10}$D -value = $0.057(\text{Temp})^2 - 6.8432(\text{Temp}) + 204.5$.
LPAI-SEW: Log $_{10}$D -value = $0.0115(\text{Temp})^2 - 1.3848(\text{Temp}) + 41.32$.
HPAI-SEW: Log $_{10}$D-value = Undetectable after 20 s of heat exposure regardless to temperature.

Table 2 FSIS pasteurization standards for egg products with thermal death times (D_T) based on the thermal inactivation of *Salmonella*

FSIS Standards		
	Temp °C	**Inactivation time for 7 log10 of *Salmonella***
Whole egg	60	3.5 min
Whole blend	60	6.2 min
Whole blend	61.1	3.5 min
Liquid egg white	55.6	6.2 min
Liquid egg white	56.7	3.5 min
10% salted yolk	62.2	6.2 min
10% salted yolk	63.3	3.5 min
Imitation egg product	56.7	4.6 min
Dried egg white (pan dried)	51.7	5 d
Dried egg white (spray dried)	54.4	7 d

(Hazard Analysis Critical Control Point) process control and risk management scheme (Whiting & Buchanan 1997). Thermal inactivation data have been obtained to validate the United States pasteurization standards for egg products. AI viruses, HP and LP, were artificially inoculated in whole homogenized eggs, liquid egg whites, 10% salted egg, dried egg whites, and imitation egg products. The inoculated egg products were heat treated at various time and temperature combinations to obtain pasteurization inactivation curves. Heat inactivation data were generated for poultry eggs products (**Table 1**) showing the time required to inactivate AI viruses by one log at a specific temperature (D_T-value). The heat inactivation data for AI virus inoculated in the egg products (whole homogenized eggs, liquid egg whites, 10% salted egg, and dried egg whites) revealed that the USDA pasteurization standards were adequate to inactivate HPAI (A/Ck/PA/1370/1983) virus (**Tables 1** and **2**) and that a standard cooking temperature of 70°C for poultry meat would adequately inactivate HPAI viruses in chicken meat at levels produced in experimental studies (**Table 3**) (Swayne & Beck 2004, Thomas & Swayne 2007, Thomas et al. 2008, Chmielewski & Swayne 2010).

Table 3 Thermal death times (D_T) for highly pathogenic avian influenza A/Ck/PA/1370/1983 in chicken meat heated at 57.8°C to 73.9°C and the FSIS pasteurization standard for cooking meat

	[1]HPAI-PA/83	[1]HPAI- PA/83	FSIS standards based on 1% fat level
Temp °C	[2]**D-value**	**log10 (EID50) reduction of HPAI virus titer using FSIS time to inactivate 7log10 *Salmonella***	**Time to inactivate 7log10 *Salmonella***
57.8	4 min	15.8	63.3 min
58.9	2.2 min	18	39.7 min
60	1.2 min	21	25.2 min
61.1	37.6 s	25.6	16.1 min
70	0.24 s	91.3	21.9 s
73.9	0.03 s	33/s	<10 s

[1]high pathogenicity avian influenza A/Ck/PA/1370/1983.
[2]Log $_{10}$D-value = [(-0.2157)(temperature) + 14.677].

CONCLUSIONS

AI outbreaks have caused severe economic losses and agricultural trade restrictions. Migratory aquatic birds cannot be controlled, but biosecurity measures can be established to prevent interaction of wild birds and domestic poultry, thereby reducing the risk of AI virus introduction into domestic poultry. The LPM system may be a reservoir for some AI viruses, so risk management strategies have to be implemented, including AI testing and restriction of infected birds from sale, implementing appropriate cleaning, disinfection, and hygiene practices, and enforcing movement restrictions and one-directional movement of poultry from farm to market. H5N1 HPAI viruses have caused sporadic infection of humans, primarily from direct contact with infected birds, producing a high case fatality rate (60%) for human infections, but with limited human-to-human spread and rare transmission through raw food products. AI viruses are a minor food safety issue, as cooking and pasteurization are effective in inactivating the virus, and poultry meat is seldom consumed without undergoing heat treatment or cooking sufficient to inactivate the virus.

SUMMARY POINTS

1. AI is caused by type A influenza viruses, and infections in humans can range from asymptomatic to mild respiratory disease, and in chickens symptoms range from decreased egg production to fatal systemic disease. On the rare occasions when humans were infected with H5N1 HPAI virus, the disease was serious and had a high case fatality rate of 60%. Most other human infections with AI viruses have been mild and self limiting.
2. Wild ducks and other aquatic birds are the natural host of LPAI viruses and exhibit no signs of illness when infected.
3. Transmission of AI viruses among wild birds and poultry usually results from exposure to contaminated feces, respiratory secretions, and feathers, and occasionally from cannibalization of carcasses. Between farms, spread is through airborne viruses, viruses adherent to dust, and contaminated equipment, shoes, and clothing. Poultry in LPM systems and village flocks are a high risk for being infected and spreading AI viruses.
4. The economic consequence of HPAI outbreaks is severe due to the cost of culling and bird replacement, loss of customer confidence, local and international trade losses, the cost of biosecurity, and the cost for veterinary and infrastructure improvement. All segments of the poultry industry within a country lose as a result of international trade embargoes.
5. There is concern for public health from the H5N1 HPAI viruses because of human infections and fatalities.
    a. Most infections have resulted from direct exposure to live or dead infected poultry.
    b. There is limited evidence of human-to-human transmission.
    c. There are rare cases of human AI virus infections obtained through consumption of raw or undercooked contaminated poultry products.
6. Various components are needed for successful control and mitigation strategies.
    a. Most countries prohibit HPAI virus–infected poultry from entering the food chain, but in developing countries, asymptomatic or sick HPAI virus–infected village poultry may enter the food chain.

b. Management practices that incorporate biosecurity principles are the key to preventing infection of poultry flocks by AI viruses.

c. Essential components for control include quarantine of infected flocks with depopulation and environmentally sound disposal, cleaning and disinfection of facilities, and composting of manure.

d. Education and risk communication are essential for all persons involved in poultry production to know how they can prevent the spread of the virus.

e. Standard cooking and pasteurization processes are effective at inactivating both LPAI and HPAI viruses in food products.

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Errata

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