



## Avian influenza: Global assessment of potential pandemic of the twenty first century

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### Abstract

The emergence of highly pathogenic avian influenza (HPAI) of Asian lineage and the subsequent spillover to other part of the globe and on going spread of Eurasian-Africa H5N1 epidemic into domestic, wild birds and human have generated unprecedented attention in recent times and threat of potential pandemic via the avian-human link. Historically, from 1878 through 1955, fowl plaque was described as a high mortality disease of poultry in many countries throughout Europe, Asia, North and South America and Africa and the etiology was proved to be a filterable virus. In the 1930s through the 1950s, fowl plaque disappeared as an endemic disease in most part of the world. In 1949, the first report of a low virulent disease in chickens caused by LPAI virus was reported. In 1955, the etiological of fowl plaque was determined to be influenza A virus, which subsequently was identified as the H7 subtype. In 1959, a “fowl plaque-like” outbreak was described in chickens, which was the first report of fowl plaque caused by a non-H7 AI virus, i.e. first fowl plaque outbreak from H5 subtype of AI virus. In 1961 the first wild birds infection and deaths were reported in common terns of South Africa. In 1966 and 1971, the first H5 and H7 LPAI viruses, respectively were identified; prior to this period, only HPAI viruses had H5 and H7 subtypes. In 1970, the AGID serological test was introduced, which allowed easy and rapid identification of AI virus-infected poultry flocks. In 1972, there was the first isolation of LPAI viruses in asymptomatic wild birds: ducks in the United State and shorebirds in Australia. In 1981, the term “highly pathogenic avian influenza” was accepted as standard nomenclature for fowl plaque and related synonyms. In 1983, LPAI virus was observed mutating to HPAI virus during LPAI field outbreak, and specific genomic changes were identified in the proteolytic cleavage site of the hemagglutinin responsible for the virulence change. In the late 1980s and early 1990s, molecular criteria were added to the definition for classifying an AI virus as HPAI. In 2002, there were the first reported infections and deaths in a wide variety of wild bird species from AI virus H5N1 HPAI virus. The primary goal of this review is to highlight the global situation of HPAI and provide baseline information to show the potential pandemic nature of the virus, so that control and prevention strategies can be improved.

**Key words:** Highly pathogenic avian influenza (HPAI), H5N1, fowl plaque, LPAI virus, Global trend.

### Introduction

Avian influenza (AI) virus is a global virus that knows no geographic boundaries nor does it have any political agenda. AI viruses or evidence of their infection has been detected in seventeen taxonomic orders of birds irrespective of their agricultural or other anthropocentric systems on all the seven continents. These include Anseriformes (ducks, geese, swans); Casuariiformes (emu), Charadriiformes (turnstones, sandpipers, gulls, terns, puffins, guillemots); Ciconiiformes (herons, ibis); Columbiformes (doves); Falconiformes (raptors); Galliformes (chickens, turkeys, quail, pheasant, guineafowl, partridges); Gaviiformes (loons); Gruiformes (coots, moorhen); Passeriformes (mynahs, finches, weaverbirds); Pelecaniformes (cormorant); Piciformes (woodpecker); Podicipediformes (grebe); Procellariiformes (shearwater); Psittaciformes (parrots, cockatoos, parakeets); Rheiformes (rhea); *Struthioniformes* (ostrich)<sup>37, 109, 128</sup>. However, report of AI infections or disease in domestic and other birds vary with individual countries, regions and continents. The reported frequency of AI is greatly skewed by the availability of diagnostics, quantity of surveillance conducted, the type of birds and production sector tested, the time of year, geographic location, climatic conditions, and other undefined factors. Because

influenza is an international efforts and cooperation<sup>122</sup>. Understanding the global nature of AI has to do with the recognition of the changing definition of AI infections and the diseases they cause, based on scientific development in diagnosis and the new knowledge in the ecology, epidemiological dynamics over the past 125 years. Three major events have changed the definition of avian influenza and thus impacted the reported frequency of AI in the world: (1) early diagnosis of fowl plaque in domestic poultry was based primarily on clinical features, lesions and animal studies; (2) recognition of LPAI viruses and their infections in domestic poultry based on serology and virus isolation; and (3) discovery of AI in asymptomatic wild birds reservoirs<sup>27, 128</sup>.

Historically, AI is of relatively recent description in the poultry health literature with historical records reporting the first case of AI as a highly lethal, systemic disease of chicken in Italy during 1878, that is HPAI<sup>90</sup>. This systemic disease of chickens has most frequently been termed fowl plaque, fowl pest, but other names have been used, including pest aviaire, Geflügelpest, typhus exudatious gallinarum, Brunswick bird plaque, Brunswick disease, fowl disease, fowl or birds grippe, and others<sup>111, 112, 124</sup>. The uniform

international terminology of “highly pathogenic avian influenza” (HPAI) became the official designation for the virulent form of AI at the first international symposium on avian influenza<sup>14,124</sup>. “High pathogenicity” is an equivalent grammatical variant of “highly pathogenic” and can be used interchangeably<sup>122, 124</sup>.

From the 1870’s into the early 1990s, fowl plaque spread from Northern Italy into Europe with report in Austria, Belgium, France, Germany, Great Britain, Hungary, The Netherlands, Romania, Russia and Switzerland<sup>39,57,67,111,112</sup>. By the mid twentieth century, fowl plaque had been diagnosed in North Africa (Egypt), the Middle East, Asia (Japan and China), South America (United States), and much of Europe. Fowl plaque was endemic in parts of Africa into plaque the 1930s<sup>3</sup>. Quite interestingly, in many situations fowl plaque disappeared at the same time Newcastle was recognized as a disease of poultry. For instance, fowl plaque was reported in Italy into the early 1930s but extinguished itself by 1937 when epidemic of Newcastle disease began<sup>91</sup>. With the discovery of Newcastle and its similarity to fowl plaque in lesions, clinical presentation and high morbidity and mortality rates, this resulted in confusion on diagnosis of field cases and their respective viral etiologies. In some cases, the HPAI term “fowl plaque” was used interchangeable with “Newcastle disease,” and later “pseudo-fowl plaque and pseudo-fowl pest.”

The viral etiology of fowl plaque was unknown until 1955 when fowl plaque was determined to be caused by influenza A virus<sup>95</sup>. Those early outbreaks of fowl plaque were caused by HPAI viruses that are classified today as H7N1 and H7N7 subtypes<sup>37</sup>. However, at the time it was generally considered that the fowl plaque viruses were all the same because of antigenic and genetic differences between “individual strains” were not known (D. Alexander, personal communication, February 27, 2007). As a result, viruses that were exchanged between laboratories may not have kept the original names or were renamed for shipping laboratory. Today, any conclusion concerning the source and date of many historical fowl plaque isolates must be interpreted with caution.

The early fowl plaque cases in chickens and other gallinaceous poultry were diagnosed primarily based on the sudden high mortality; presence of specific lesions such as cyanotic combs, hemorrhage in the ventriculus and proventriculus and petechia on the heart; and identification of infiltrable virus. Such viruses cross-reacted I haemagglutination inhibition test using antisera from recovered birds, which resulted in the conclusion that a positive “H7” HI test indicated a fowl plaque virus (HPAI) or infection by such an agent. However, in 1959, 1961 and 1966, a clinical disease, distinguishable from classical fowl plaque (i.e. H7) was identified in chickens, common terms, and turkeys respectively, but these viruses were not inhibited by antisera from-recovered birds (i.e. these viruses were not H7). This gave rise to the briefly used term “fowl plaque-like” and was the first indication that another haemagglutination subtype, H5, could be an HPAI virus. Thus, the original AI infections in poultry were detected by severe clinical disease and linked serologically to two subtypes: H5, H7 HPAI viruses.

#### **Low Pathogenic Avian Influenza in Poultry and Man Made System**

Milder form of AI was first recognized in various domestic poultry species beginning in 1949, with occasional reports through the mid-1960s<sup>39</sup>. These forms of AI have been called low pathogenic,

pathogenic, non-HP and LP AI. In 2002, at the Fifth International Symposium on Avian Influenza, the term “low pathogenicity” (LP) was adopted as the official designation for AI viruses of low virulence, therefore, these AI viruses did not meet biological or molecular criteria for HPAI viruses<sup>43</sup>. The earliest known LP AI virus was the “Dinter” or “N” strain, isolated in 1949 from chickens in Germany [A/chicken/Germany/49(H10N7)]. However, this virus was not an LP AI virus until 1960<sup>39</sup>. These early LP AI viruses were a variety of hemagglutinin and neuraminidase subtypes. Initially H5, H7 subtypes of influenza A virus were only associated with fowl plaque viruses, but in 1966 and 1968, LP AI viruses were isolated from turkeys with low mortality or ill-defined syndromes that were typed as the H5 subtype, that is, the first H5 LP AI viruses<sup>2,39,106</sup>.

#### **Low and high pathogenicity avian influenza viruses in wild**

**birds:** Although early reports of fowl plaque suspected wild birds in the transmission, the first proof of AI virus infection in wild birds was in common terns with high mortality in South Africa during 1961<sup>23</sup>. In the late 1960s, a survey of migratory water waterfowl showed serological evidence of infection by virus AI<sup>88</sup>. However, the first isolates of LP AI viruses were not made until 1972 from migratory duck in a Newcastle disease virus surveillance program in California<sup>105</sup> and from pelagic seabird (shearwater) in Australia<sup>33</sup>. Since then numerous surveys have been conducted and demonstrated asymptomatic infection by AI viruses in health aquatic birds, principally in the order Anseriformes and Charadriiformes<sup>50, 51, 56, 108-110</sup>. These surveys have yielded thousands of LP AI viruses of all the 16 hemagglutinin and 9 neuraminidase subtypes from a symptomatic wild birds. However, some HPAI viruses have been isolated from wild birds<sup>4,23,30,62,64</sup>. Gallinaceous species of birds, both domestic and wild, are not natural reservoirs of AI viruses<sup>86,114</sup>.

**Regulatory organization:** Various governmental and non-governmental organization are involved in implementing eradication practices as means to deal with HPAI and protect food supply<sup>136</sup>. Initially those practices focused on identifying HPAI viruses using *in vivo* chicken pathogenicity test (pathotype) and differentiation of these viruses from LP AI viruses. However, in the 1994, specific molecular and *in vitro* criteria were added as alternatives to *in vivo* testing to define HPAI viruses<sup>133</sup>. Today, the World Organization for Animal Health (Office International des Epizooties, OIE) set the international sanitary and health standards for animals, including AI, and such code are used to safeguard international trade in the poultry and poultry products. Using the OIE code and other international standards, AI can be divided into three categories: (1) HP notifiable AI (HPNAI), which include all H5 and H7 HPAI; (2) LP notifiable AI (LPNAI), which includes all H5, and H7 LP AI; and (3) all other LP AI that are not notifiable to OIE, which includes H1-H4, H6 and H8-H16<sup>5,80</sup> and non-H7 LP AI-is not reportable to OIE but may be reportable to national and state/provincial authorities.

#### **Low pathogenicity avian influenza in domestic poultry and**

**captive birds:** There is no international mandate or uniform standards used around the world for LP AI surveillance, and no requirements to report LPNAI to the OIE other LPNAI (H5/H7). Therefore, published reports of LP AI are sporadic and infrequent,

with most reports being in peer-reviewed scientific literature concerning single cases or clusters of cases. Some countries lack the veterinary diagnostic infrastructure or financial resources to conduct adequate diagnostics and surveillance for LPAI or place a low priority on LPAI compared with other animal diseases, while some countries chose a policy of "you do not look and you do not have AI."

Mankind has developed new avian anthropocentric systems through captivity, domestication, rearing of birds at the agriculture-wild bird interface, non-industrial and industrial agriculture, national and international commerce and non-traditional raising practices. Avian influenza can be perpetuated in five different categories of man made. Ecosystems<sup>117, 122</sup>: (1) bird collection, trading, maintenance and exhibition systems; (2) village, backyard, and hobby flocks, especially outdoor rearing and mixing of bird species; (3) LPM systems; (4) range- or outdoor reared commercial poultry; and (5) integrated indoor commercial poultry. The frequency of LPAI viruses in domestic poultry, captive birds, and wild birds is largely unknown, but in most developed countries, infections are sporadic in poultry, being most frequent in chickens, turkeys and ducks<sup>2, 4</sup>. However, in the integrated commercial poultry systems in developed countries, AI has been a rare occurrence considering the 25 to 30 billion chickens raised each year<sup>131</sup>. Cases have been reported in captive wild birds<sup>2, 4</sup>.

For poultry, the reported frequency is highest in birds raised on small mixed species farm with outdoor access (village and rural poultry) which veterinary services, have poor control bird movement and lack biosecurity. However, incidence and distribution vary greatly with geographic region, country, species and age of birds, time of the year, and the environmental or agricultural system occupied<sup>122</sup>.

### Highly Pathogenicity Avian Influenza (1959-2007)

Over the past 48 years, since the development of consistent diagnostic and control strategies, 26 epidemics or limited outbreaks of HPAI have been documented worldwide and compiled (Table 1)<sup>6, 121, 122, 127</sup>. All these HPAI viruses were of the H5 or H7 haemagglutinin subtype. There have been no HPAI outbreaks with AI viruses of the other 14 haemagglutinin subtypes (H1-H4, H6 and H8-H16). However, several non-H5/H7 AI viruses have expressed high lethality in chickens in the intravenous pathogenicity test (H10N5, H10N4, H4N8). These viruses were not highly lethal on intranasal inoculation and lacked the haemagglutinin cleavage site sequence compatible with HPAI virus<sup>25, 143</sup>. The number of epizootics, number of cases (i.e. farms) and the number of birds affected in HPAI has grown geometrically since 1959. From 1959 to 1998, the number of birds affected in HPAI outbreaks was calculated at 23 million, while from 1999 to early 2004 over 200 million were involved<sup>27</sup>. Through 2007, with completion of outbreaks in Canada and North Korea and the expanding H5N1 HPAI in Asia, Europe, and Africa, the latter number is now over 270 million. Since 1959, the primary control method has been stamping-out, which has been documented with eradication of the virus in 22 of the 26 epidemics (epidemic 1-13 and 17-26). In the three outbreaks<sup>14, 15, 25</sup>, vaccination programs with some depopulation have eliminated the clinical HPAI disease, but demonstration of eradication by surveillance programs was not completed. The H5N1 HPAI that appeared in 1996 (epidemic 16) has become the largest HPAI outbreak of the

past 50 years, exceeding 220 million birds affected by the disease or culled. This epidemic has spread from its initial cases in China during 1996 to affecting poultry and wild birds in over 60 countries in Africa, Europe and Asia (see Table 1). A few of the countries have conducted successful eradication campaigns, but the epidemicity of the virus in village poultry and LPM systems in many countries (especially in domestic ducks), the lack of movement controls on village poultry and LPM systems, and the infection of migratory waterfowl has created recurrent outbreaks of disease within countries and in some instances, reintroduction into countries that were declared free of HPAI in 2004 and 2005 (i.e. Japan, South Korea, and Thailand, late 2006 to early 2007)<sup>53, 55</sup>.

Wild aquatic birds are the primordial reservoirs for AI viruses, and these AI viruses or their genes have appeared in AI viruses that have infected domestic poultry and captive birds. However, the immediate source of LP and HP epidemic viruses is not always determined as feral wild birds, captive wild birds, village poultry, commercial poultry, etc. Some LP viruses, though, have been adapted to poultry and have been maintained in village/backyard/hobby poultry and LPM systems before introduction into commercial poultry. Each of the HPAI epidemics has involved different agricultural systems during the outbreaks. Some began as viruses in the LPM system such as the 1983-1984 H5N2 AI virus of the northern United States or the H5N1 in Hong Kong in 1997, or they began as LPAI viruses in range-reared layers, as in the 2003 H7N7 Dutch outbreak, before spreading into commercial poultry sectors<sup>59, 139, 142</sup>. Other were detected in the LPM system and were eliminated before spreading to commercial poultry, such as in the H5N2 HPAI virus in Italy during 1997 and the H5N2 HPAI virus in Texas during 2004. Other HPAI viruses appeared to have emerged after the introduction of LPAI virus in commercial poultry, such as with H7N3 viruses in Chile during 2002 and in Canada during 2004. In other outbreaks, the lack of good surveillance inhibits determination of initial source of infections, but the commercial sectors are more easily blamed because they have the majority of the surveillance while the village/rural sector has the least. However, when AI infections do occur in commercial industries, they sometimes spread rapidly throughout the integrated system from farm to farm, resulting in epidemics of HP or LPAI depending on how well the biosecurity measures contain the spread. Documented human infections with avian influenza viruses are given in Table 2.

### Control of HPAI

Control strategies for HPAI varied considerably, there is no single approach appropriate to all situations for control. Individual control must take into cognizant and match with the local disease situation, the likely risk of reinfection, and the available resource.

There are six basic "tools" used to prevent AI: enhancement of farm biosecurity, stamping-out, cleaning and disinfection, movement management, restructuring/modification of industry practices and vaccination<sup>104</sup>. None of these measures used alone is likely to lead to elimination of infection. Control and eradication of AI also depend on fully functional surveillance system that allows early detection of infection and disease. This requires a well resourced and trained veterinary service. Control programs should be backed by public education and behavioral change campaigns to provide accurate and timely information on the



nature of the disease to groups at risk. It is important that programs fully engage all stakeholders to ensure success.

### World Distribution of HPAI

HPAI was first reported in Italy 1878, South Africa 1961, USA 1971, Australia 1975, England 1979, Ireland 1983, Mexico 1994 and Pakistan 1994. In recent years, it has become topical in Asia including China 1996, Hong Kong 1997, 2001, 2002 and 2003, Cambodia, Indonesia, Japan, Malaysia, Korea, Laos, Taiwan, Thailand, Vietnam, Turkey and Romania 2005<sup>79</sup>. The most serious epidemic in recent times was in Hong Kong 1997-1998 and 2003.

### Conclusions

This review of AI from the global perspective and potential pandemic of the 21<sup>st</sup> century is entirely based on scientific publications and official governmental statistical documents. It is an attempt to place the spread of AI in historical perspective from global context.

Avian influenza viruses has been detected in both domestic and wild birds on all the seven continents. AI is a global virus that does not respect geographical boundaries or have any political agenda but can infect birds irrespective of their agricultural or other anthropocentric system. However, most of the reported cases of AI are tremendously affected by the availability and accessibility of diagnostics tools, quantity and quality of surveillance conducted, the species of birds, type of management system in place, the time of the year, geographical location, climatic conditions and several other undefined factors; so far the greatest quantity of surveillance of domestic and wild birds has been conducted in North America and Europe because of scientific interest, availability of molecular, virological and serological tests and financial resources<sup>128</sup>. Influenza being an international problem, solution will require international collaboration efforts and cooperation.

From the historical perspective, three major scientific advances have changed our definition of avian influenza and thus impacted the reported frequency of AI in the world: 1) early diagnosis of fowl plaque in domestic poultry limited to primary clinical features, lesions and animal studies; 2) recognition of LPAI viruses and their infections in domestic poultry based on serology and viral isolation; 3) discovery of AI in asymptomatic wild bird reservoirs. However, some very specific discoveries have impacted our understanding of the pathobiology of AI and how to better control the disease at its source.

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**Table 1.** Twenty-six documented epidemics / outbreaks of HPAI. As modified from (128, 127, 122, 121, 6).

No.	Date	Prototype AI virus	Subtype	HP	Number of cases affected with high mortality	References
1	1959	A/chicken/Scotland/59	H5N1	+	Chickens ( <i>Gallus gallus domesticus</i> ), No. of farms and birds not reported	60, 87
2	1961	A/tern/South Africa/61	H5N3	+	4 small areas, 1300 common terns ( <i>Sterna hirundo</i> )	23, 60
3	1963	A/turkey/England/63	H7N3	+	2 farms; 29,000 breeder turkeys ( <i>Meleagris gallopavo</i> )	14, 140
4	1966	A/turkey/Ontario/7732/66	H5N9	+	2 farms; 8100 breeder turkeys	58, 60
5	1975-76	A/chicken/Victoria/75, A/chicken/Victoria/76	H7N7	+	1 farm; 25,000 laying chicken, 17,000 broilers and 16,000 duck ( <i>Anas platyrhynchos</i> )	13, 19, 130
6	1979	A/chicken/Leipzig/(Germany)/79	H7N7	+	1 farm; 600,000 chickens, 80 geese (formerly East Germany)	6, 49, 92
7	1979	A/turkey/England/199/79	H7N7	+	3 commercial farms of turkeys; 9262 turkeys	1, 9, 12, 144
8	1983-84	A/chicken/Pennsylvania/1/83 A/chicken/Pennsylvania/	H5N2	+	452 flocks, 17 million birds; most were chicken or turkeys, a few partridges ( <i>Alectoris chukar</i> ) and guinea fowl ( <i>Nimida meleagris</i> )	37, 40, 60, 132
9	1983	A/turkey/Ireland/1378/83	H5N8	+	3 farms; 800 meat turkeys died on original farm; 8,640 turkeys, 28,020 chicken and 270,000 ducks were depopulated on original and 2 adjacent farms	4, 60, 68
10	1985	A/chicken/Victoria/1/85	H7N7	+	1 farm; 24,000 broiler breeders, 27,000 laying chickens, 69,000 broilers and 518 unspecified type of chickens	18, 31, 100
11	1991	A/turkey/England/50/92/91	H5N1	+	1 farm; 8000 turkeys	11, 110, 144
12	1992	A/chicken/Victoria/1/92	H7N3	+	2 farms, 1 backyard flock and 1 hatchery; 12,700 broiler breeders, 5,700 ducks, 105,000 day-old chicks	96, 104, 141
13	1994	A/chicken/Queensland/477/94	H7N3	+	1 farm; 22,000 laying chickens	86, 141
14	1994-95	A/chicken/Mexico/31381-7/1994 A/chicken/Puebla/8623 607/94(HPAIV)	H5N2	-	Chickens: stamping-out policy was not used for control Concurrent circulation of LP and HPAI virus strains, HPAI virus only from late 1994 to mid-1995.	37, 44, 85, 138
15	1994-95	A/chicken/Queretaro/ A/chicken/Pakistan/447/95 A/chicken/Pakistan/1369-CR/95 A/chicken/Pakistan/16/95	H7N3	+	Unknown number of birds infected with the HPAI virus, but 360 commercial chicken flocks were "depopulated" for AI in 1995 through controlled marketing Surveillance, quarantine, vaccination and controlled marketing used as control strategy. Two incursions: (1) 3.2 million broilers and broilers breeder chickens (northern part of the country 1994-95) and (2) 2.52 million layers (Karachi, 2004)	16, 37, 72-76
16	1996	A/goose/Guangdong/1/1996 A/chicken/Hong Kong	H5N1	+	Unknown commercial and non-commercial flocks (village poultry); over 220 million birds dead or culled, mostly chickens but also ducks, geese, Japanese quail, and some wild birds	42, 103, 113, 14
17	1997	A/chicken/New South Wales/165 1/97	H7N4	+	3 farms; 128,000 broilers 86,104 breeders, 33,000 broilers, 261 emu ( <i>Dromaius novaehollandiae</i> )	
18	1997	A/chicken/Italy/330/97	H5N2	+	8 rural flocks; 2116 chickens, 1501 turkeys, 731 g/fowl, 12,322 ducks, 204 quail (species unknown), 45 pigeons ( <i>Columba livia</i> ) and 1 pheasant (species unknown)	29, 59
19	1999-2000	A/turkey/Italy/977/99 A/turkey/Italy/4580/99	H7N1	-	413 farms; 8.1 million laying chickens, 2.7 million meat and breeders turkeys, 2.4 million broilers breeders and broiler; 247,000 guinea fowl; 260,000 quail, ducks and pheasants; 1,737 backyard poultry and 387 ostriches	17, 28
20	2002	A/chicken/Chile/176822/2002 A/chicken/Chile/4322/2002 A/chicken/Chile/4325/2002	H7N3	-	2 farms of 1 company, 557/200 multiple houses; 617,800 broiler breeders died (150,000) 18,500 turkey breeder destroyed	66, 93, 115

21	2003	A/chicken/Netherlands/621557/2003	H7N7	+	255 infected flocks, and 1381 commercial and 16,521 backyard/small-holder flocks depopulated. 30 million died: 175,035 backyard birds, commercial: 25 million infected or preemptive culled birds, 4.5 million birds for well fare reasons; Belgium, 8 farms 2.3 million chickens; Germany 1 farm, 419,000 chickens	9, 41, 49
22	2004	A/chicken/Canada/AVFV1/04A/c hicken/Canada AVFV2/04	H7N3	-	42 commercial and 11 backyard flocks infected (1.2 million poultry); approximately 16 million commercial poultry depopulated	52,74,84
23	2004	A/chicken/ Texas/298313/2004	H5N2	+	1 noncommercial farm (6608 chickens) and 2 live poultry markets infected and depopulated, 3 traditional LPM voluntarily depopulated	59, 78
24	2004, 2006	A/ostrich/South Africa/2004	H5N1	+	2004: 11 ostrich farms with depopulation of 23,625 ostriches and 3,550 other poultry (chickens, turkeys, geese, ducks) 2006: 2 farms, 7342 ostriches dead or culled	9,77,81,82
25	2005	A/chicken/North Korea/1/2005	H7N7	+	3 farms, 218,882 layer chickens culled; number of dead not reported	78,79
26	2007	NA	H7N3		1 farm, 48,560 broiler breeders culled; 540 roosters died	82a

**Table 2.** Documented human infections with avian influenza viruses\*.

Date	Country/area	Strain	Cases (deaths)	Symptoms	Source
1959	USA	H7N7 **	1	respiratory	overseas travel
1995	UK	H7N7	1	conjunctivitis	pet ducks (shared lake with migratory birds)
1997	Hong Kong	H5N1**	18(6)	respiratory/pneumonia	poultry
1998	China (Guangdong)	H9N2	5		unknown
1999	Hong Kong	H9N2	2	respiratory	poultry
2003 (Feb.)	Hong Kong	H5N1**	2(1)	respiratory	unknown
2003 (Mar.)	Netherlands	H7N7 **	89(1)	conjunctivitis (pneumonia, respiratory insufficiency in fatal case)	poultry
2003 (Dec.)	Hong Kong	H9N2	1	respiratory	unknown
2003	New York	H7N2	1	respiratory	unknown
2003	Vietnam	H5N1**	3(3)	respiratory	poultry
2004	Vietnam	H5N1**	29(20)	respiratory	poultry
2004	Thailand	H5N1**	17(12)	respiratory	poultry
2004	Canada	H7N3**	2	conjunctivitis	poultry
2005	Vietnam	H5N1**	61 (19)	respiratory	poultry
2005	Thailand	H5N1**	5 (2)	respiratory	poultry
2005	China	H5N1**	7(3)	respiratory	poultry
2005	Cambodia	H5N1**	4 (4)	respiratory	poultry
2005	Indonesia	H5N1**	16 (11)	respiratory	poultry
2006	Turkey	H5N1**	3 (3)	respiratory	poultry

\* Source: Avian influenza . assessing the pandemic threat. WHO,http://www.who.int/csr/disease/influenza/WHO\_CDS\_2005\_29/en/, accessed 06 January 2006.

\*\* Highly pathogenic for poultry.